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POSTER PLUS VIDEO I – Poster Area

P001 THE FEASIBILITY STUDY OF CHEMICALLY ASSISTED ENDOSCOPIC SUBMUCOSAL DISSECTION USING MESNA FOR SUPERFICIAL OESOPHAGEAL SQUAMOUS NEOPLASMS

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INTRODUCTION: In Western countries, ESD was not commonly performed because the submocosal dissection is technically challenging. We reported that the injection of mesna solution (sodium-2-mercaptoethanesulfonate) made submucosal connective tissues chemically softened and facilitated mechanical dissection of the submucosal layer in the stomach [1]. Our previous study suggested that mechanical dissection with mesna might make an ESD for gastric cancer safer and easier. There has been no study to evaluate the feasibility of mechanical dissection with mesna for superficial oesophageal squamous neoplasms (SOSNs).
AIMS&METHODS: The aim of this study was to evaluate the feasibility and safety of chemically assisted ESD using mesna in 20 consecutive patients with SOSNs. Submucosal fluid cushion was made by 0.4% sodium hyaluronate and then the lesion was circumferentially isolated from surrounding normal mucosa as a conventional ESD method with needle knife (Dual knife, Olympus medical systems). After that, 4 to 8 mL of 10% mesna solution was injected into the submucosal layer and mechanical submucosal dissection was performed by cleaving the submucosal layer with the tip of a cap-fitted endoscope. The number of electrosurgical incision as well as coagulation for hemostasis by stepping the foot switch of high-frequency wave apparatus (VIO 300, ERBE) and the procedural time were recorded by dedicated software (VIO Doku, ERBE) in real time. We also performed conventional ESD without mesna for each consecutive10 SOSNs as control during before and after mesna ESD. Operators and lesion size matched paired t test was analyzed by comparing each result of mesna and conventional ESD groups.
RESULTS: The mean size of resected sample was 31.1 ± 8.6 mm, with an en bloc resection rate of 100%. The number of electrosurgical incision during submucosal dissection procedure in mesna group was significantly smaller than that in conventional group (mean; 89.8 ± 82.3 vs. 232.4 ± 150.9 times, $p < 0.01$). The procedural time of submucosal dissection in mesna group tended to be shorter than that in conventional group (mean; 10.5 vs. 17.3 minutes, p=0.056) while there was no significant difference. There was also no significant difference between mesna and conventional groups in the number of coagulation for hemostasis (mean; 7.1 vs. 3.8 times, p=0.19). There was no perforation and no uncontrollable hemorrhage. Ulcerations healed normally within 2 months.
CONCLUSION: The mechanical submucosal dissection with mesna for SOSNs deem safe and may facilitate procedure of conventional ESD.
REFERENCES:
1. *Sumiyama K et al*. Endoscopy 2010; 42: 627–632
Disclosure of Interest: None Declared
Keywords: ESD (endoscopic submucosal dossection), mesna, Oesophageal carcinoma

P002 ENDOSCOPIC SUBMUCOSAL DISSECTION OF SPORADIC NON-AMPULLARY DUODENAL SUPERFICIAL NEOPLASMS - EVOLUTION OF THE TECHNIQUE TOWARDS THE DECREASE OF THE COMPLICATION RATE

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INTRODUCTION: Endoscopic submucosal dissection (ESD) technique enables treatment of lesions untreatable by conventional mucosal resection (such as incomplete lifting and residual lesions) and makes en-block resection more feasible. ESD in the duodenum is more challenging and has higher risk of complications than in the other parts of the digestive tract.
AIMS&METHODS: Endoscopic database in a single tertiary university centre was cross-examined to identify sporadic non-ampullary duodenal neoplasms treated by ESD between 1/2006 and 3/2013, ESD being only used in case of poor lifting during mucosal resection. Procedure was qualified as ESD when any type of an endoscopic knife was used: either as pure ESD (when the en-block resection was achieved) or as hybrid endoscopic procedure (when polypectomy snare was also used in a piecemeal manner). Procedures were divided into two halves according to the order of the procedure. Results were expressed as medians, first and third quartiles and were compared using Student's t-test and Fisher's exact test.
RESULTS: 26 ESD procedures in 25 patients were identified (out of a total of 110 duodenal non-ampullary mucosectomies): the first 13 in the group A, the rest in the group B. There were no significant differences between two groups in terms of age (66 [63-67] vs. 63 [58-69], p=0.2); sex (8 vs. 9 females; p very close to 1); lesion size (20 [15-30] vs. 25 [20-30], p=0.9) and presence of high grade dysplasia (2 vs. 5; p=0.4). 3 procedures in both groups were pure ESDs, prophylactic closure of the mucosal defect was used significantly more often in the group B (2 vs. 10 cases, p=0.005). The length of the procedure did not differ between groups (111 [80-149] vs. 96 [67-143] min, p=0.6). There were 4 (31%) vs. 2 (15%) intra-procedural perforations, 2 (15%) vs. 1 (8%) post-procedural bleedings and 2 (15%) vs. 0 post-procedural perforations. Sum of the complications was significantly reduced in the group B (8 [62 %] vs. 3 [23 %], p=0.05). No difference in the length of hospital stay was observed (3 [3-4] vs. 4 [3-5] days, p=0.6). Post-procedural complications were significantly reduced in prophylactic closure cohort (regardles of the order of procedures): 0 vs. 5 (36 %), p=0.04.
CONCLUSION: ESD in the duodenum is a laboured procedure with a significant risk of complications. During 7 years experience prophylactic closure of the mucosal defects was introduced without prolongation of the operation time and with a significant reduction of bleedings and perforations.
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Disclosure of Interest: None Declared
Keywords: duodenal superficial neoplasm, endoscopic submucosal dissection (ESD)

P003 USEFULNESS OF THE OROPHARYNGEAL INVERSION METHOD BY MEANS OF NASAL ENDOSCOPY

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INTRODUCTION: Accompanying the progress in endoscopy, the number of discoveries of superficial carcinoma in the head and neck region has increased, but with oral-route endoscopy, there are areas that have proven to be difficult to view.
AIMS&METHODS: As a technique for observing in detail the root of tongue, which is an area that is difficult to observe, an oropharyngeal inversion method by means of nasal endoscopy is proposed. We intend to clarify the usefulness of such a method. The scopes used were EG-580NW and EG-530NW (Fujifilm, Tokyo). The image quality was good, and the angular field of view was wide-angle, at 140 degrees, with FICE used as standard equipment. An upward angle of 210° and significant flexing of the scope tip were possible.The subjects consisted of 172 cases in which the oropharyngeal inversion method by means of nasal endoscopy was performed, from April to October, 2012. After observation of the buccal cavity, the endoscope was inserted through the nose, and around where the endoscope passed the uvula, the patient was asked to open the mouth wide, stick the tongue forward as much as possible, and make a sound like "ayyy", whereupon the endoscope was set to its full upward angle, inverted, and observation was carried out. Recording was performed on a video recording device, and it was studied whether it was possible to obtain observations from the lingual root to the lingual apex.
RESULTS: Observation up to the lingual apex was possible in 160 cases (93%). It is now easier to obtain a frontal view of the vallate papillae, which until now could only be observed tangentially, using the oral route. We have found two superficial carcinomas of the root of tongue in half a year.
CONCLUSION: The oropharyngeal inversion method by means of nasal endoscopy is thus considered to be useful for observing the oropharynx.
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Disclosure of Interest: None Declared
Keywords: FICE, head and neck cancer, oropharyngeal cancer, transnsal endoscopy

P004 MAGNIFICATION ENDOSCOPY IN COMBINATION WITH ACETATE INSTILLATION AND A NARROW-BAND IMAGING SYSTEM FOR PREDICTING HISTOLOGIC CHARACTERISTICS OF GASTRIC MUCOSAL NEOPLASMS

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INTRODUCTION: Magnification endoscopy with narrow-band imaging (NBIME) that enables a detailed visualization of the capillary patterns (CP) of superficial gastric neoplasms is useful for predicting their histologic types, although CP is often difficult to interpret. NBIME with acetate enhancement (acetate-NBIME) is effective for the observation of mucosal microstructure patterns (SP) of gastric mucosa.
AIMS&METHODS: The aim of this prospective study is to compare the predictability of acetate-NBIME and NBIME for the histologic types of gastric mucosal neoplasms. We photographed 147 gastric lesions (35 adenomas, 96 differentiated and 16 undifferentiated adenocarcinomas) with NBIME and acetate-NBIME. CP by NBIME was classified into the following four groups: Type C1: capillaries with homogenous diameters and distributions form round or oval networks, or grow within the regular microstructures, Type C2: capillaries with heterogeneous diameters and irregular distributions form a polygonal or incomplete network, or grow within the irregular microstructures, Type C3: capillaries with heterogeneous diameters and distributions grow in disorder with unclear mucosal microstructure, and Type C4: capillaries are invisible or obviously decreased. SP by acetate-NBIME was classified into the following three

groups: Type S1: glandular crypts are homogeneously sized, shaped and arranged, Type S2: glandular crypts are heterogeneous, and Type S3: glandular crypts are absent or severely decreased. Three experts independently reviewed the endoscopic images, and judged CP and SP. The correlations of CP and SP agreed by two or all of three reviewers with each histologic type were statistically analyzed, and the predictability of the histologic types was compared between both modalities.

RESULTS: The kappa values of interobserver agreement for CP and SP diagnosis were 0.61(0.57-0.64) and 0.63(0.55-0.71), showing good diagnostic concordances. Adenomas, differentiated, and undifferentiated mucosal adenocarcinomas were statistically related to type C1, C2, and C3 ($P<0.01$) in NBIME and to type S1, S2, and S3 ($P<0.01$) in acetate-NBIME, respectively. Type C4 was difficult to use as an indicator of specific histologic types. The kappa values of diagnostic concordance between each CP and SP and their related histologic types were 0.45(0.30-0.59) and 0.77(0.68-0.87), showing a statistical difference.

CONCLUSION: Acetate-NBIME shows a good clinical feasibility and the superiority to NBIME in predicting the histologic types of gastric mucosal neoplasms.

Disclosure of Interest: None Declared

Keywords: NBI, acetate, gastric neoplasm, histological diagnosis, magnification endoscopy

P005 ENDOSCOPIC SUB-MUCOSAL DISSECTION WITH A WATER JET SYSTEM ALLOWING INJECTION OF DIFFERENT VISCOUS SOLUTIONS: COMPARISON VERSUS SALINE ON EX-VIVO PIG STOMACHS

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INTRODUCTION: Long lasting lifting is a key factor during ESD and can be obtained by water-jet injection of saline or by injection of viscous macromolecular solutions. These 2 techniques have never been used simultaneously. A new water-jet system with a high-pressure generator allowing injection of viscous solutions, even with retroflexed endoscope, has been developed.

AIMS&METHODS: We assessed the ability of this new system to inject viscous solutions in direct viewing and in retroflexion and we then compared injection of saline or hyaluronate 0.5% to perform ESD on ex-vivo pig stomachs. Using the jet-injector, four viscous solutions were tested. 10 ESD larger than 25 mm (5 in direct viewing and 5 in retroflexion) and one of more than 10 cm were performed with each solution. ESD with hyaluronate jet-injection was then compared to ESD with saline jet-injection performing 50 ESD in each group. A single low experienced operator conducted all the procedures.

RESULTS: All 145 resections were complete including all marking points with two perforations. We performed 11 jet ESD with hydroxyethyl starch, glycerol mix, hyaluronate sodic (0.5%) or poloxamer mix without injection issue. In the second part of the study, when compared to saline, significant benefit of hyaluronate was observed on dissection speed (0.80 cm2/min versus 1.08 cm2/min).

Solution	**Saline Serum**	Hyaluronate 0.5%	Statistics
Mean Maximal diameter	4.0 cm	4.2 cm	p=0.242
Mean duration	12.9 min	10.7 min	p=0.002
Surface (ellipse area)	9.9 cm^2	10.8 cm^2	p=0.483
Speed (surface/time)	0.80 cm^2/min	1.08 cm^2/min	$p<0.001$
Perforations	**1**	**0**	NS
Injection issue	**0**	**0**	NS

CONCLUSION: This is the first report on a water jet system allowing injection of macromolecular viscous solutions even with retroflexed scope. Dissection speed using jet injection of hyaluronate was significantly higher than using jet injection of saline. This jet injection of macromolecular solutions should be now tested on humans to evaluate the effect on morbidity.

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Keywords: endoscopic submucosal dissection (ESD), viscous solutions, water jet system

P006 "TORNADO ESD": A NOVEL ESD TECHNIQUE WITH ROBUST AND ADJUSTABLE TISSUE TRACTION USING OVER-TUBE WITH A WORKING CHANNEL

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INTRODUCTION: Adequate tissue traction is a key to success in any kinds of advanced endoscopic intervention as well as surgical intervention. A simple over-tube, compatible with currently available flexible gastrointestinal endoscopes and instruments, has been newly developed to improve tissue traction.

AIMS&METHODS: The aim of this study was to evaluate this new over-tube in performing esophageal ESD using porcine models.

The prototype is a polyvinyl chloride tube (19mm OD and 22cm length) with a built-in side-channel (3mm OD), where a standard grasping forceps is passed for tissue traction. The strength and direction of traction is controlled by rotating the over-tube around the endoscope (i.e. "tornado technique"), while keeping the forceps grasping the tissue, and also by adjusting the depth of the grasping forceps inside the side-channel. After confirming its feasibility on bench tests, the prototype device was evaluated in acute porcine models (n=5). Two 20-mm virtual lesions were created in each animal (n=10). The "tornado ESD" was attempted on each lesion using a grasping forceps (FG-6L-1, Olympus) via side-channel, and a scissors-type electrosurgical knife (SB knife, Sumitomo Bakelite) via biopsy channel. Measured outcomes were completion rate of procedure, incident rate of any complication, rate of en bloc resection, and procedure time.

RESULTS: Esophageal ESD was successfully performed without any complications. En bloc resection was accomplished in all 10 lesions. Median procedure time for submucosal dissection was 22 minutes (ranged 10-50 minutes). The "tornado technique" was robust, adjustable, reproducible and effective in obtaining adequate tissue counter-traction during mucosal cutting and submucosal dissection.

CONCLUSION: The study revealed that "tornado technique" might contribute to safer and more efficient ESD by providing robust and adjustable tissue traction. This inexpensive technique may become an attractive option in standardizing technically demanding endoscopic interventions.

Disclosure of Interest: None Declared

Keywords: ESD(endoscopic submucosal dossection), experimental endoscopy, Standardization

P007 DIRECT OBSERVATION OF ESOPHAGEAL VASCULATURE IN VIVO USING INTRALUMINAL AND THROUGH THE WALL GASTROINTESTINAL ENDOSCOPY. ANATOMICAL LESSON FROM ADVANCED ENDOSCOPY

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INTRODUCTION: The esophageal vascular system has been studied for long time as an *ex vivo* evaluation but with the advent of the endoscopy a clear direct view of the esophageal wall has been achieved, moreover with the NBI-magnifying endoscopy.

AIMS&METHODS: A comprehensive evaluation of all the esophageal vasculature from the endoscopists' point of view using advanced endoscopic techniques is here proposed.Images from 39459 upper GI endoscopies and 519 endoscopic treatment, performed at a single institution from may 2008 to august 2012, were collected and analyzed. To confirm the results achieved, an immunostained histological analysis was performed in 8 esophageal non-pathological specimens with the evaluation of the expression of CD34 and D2-40.

RESULTS: The entire esophageal wall is organized, from the lumen to outside, into five layers (epithelium, lamina propria with lamina nuscularis mucosa, submucosa, muscle layer, adventitia) with different vascular system belonging to each of them and connecting each other: Mucosa with the IPCL (Intra Papillary Capillary Loop) in the epithelium and the SECN (Sub-Epithelial capillary network) in the lamina propria and at the LES (Lower esophageal Sphincter) level also with the palisade vessels; Submucosa with the drainage vessels and the spindle veins just under the LES; Muscle layer with the perforating vessels; periesophageal veins in Adventitia. Advanced endoscopy allows the direct visualization of all these structures (Fig 1). Histopathologically, all (8/8) the specimens analyzed showed a high expression of CD34 in the areas corresponding with the IPCL, SECN and branching vessels.

Fig. 1 Schematic illustration of vascularization in the esophageal wall and at the esophago-gastric junction with the endoscopic corresponding images. Vessels are indicated with black arrows.

A: perforating vessel from the outer esophagus to the submucosa; image captured during POEM B: submucosal drainage vessel C: submucosal vessels connecting the drainage veins with the mucosal (lamina propria) branching vessels; D: Spindle veins immediately below the gastro-esophageal junction; E and F: white light and NBI of the Branching vessels. G: Palisade vessels, in the same level of branching vessels (lamina propria).

CONCLUSION: Magnifying endoscopy and operative endoscopy enable direct observation of esophageal wall vasculature in vivo from epithelium to adventitia.

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Disclosure of Interest: None Declared

Keywords: Branching veins, IPCL, POEM, Spindle veins

P008 FABRICATED ALLOGENEIC EPIDERMAL CELL SHEET IN PORCINE MODEL: CELL TISSUE ENGINEERING APPROACH FOR THE PREVENTION OF ESOPHAGEAL STRICTURE AFTER CIRCUMFERENTIAL ESD

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INTRODUCTION: Sever stricture is one of the major problems of endoscopic submocosal dissection (ESD) for widespread superficial esophageal carcinoma. There are no effective preventive measures or treatment for this complication. We recently developed the fabricated epidermal cell sheet. The fabricated autologous epidermal cell sheet could inhibit esophageal constriction after circumferential ESD in swine model[1)]. For the standardization of this approach, it is important to evaluate not only autologous but also allogeneic transplantation.

AIMS&METHODS: We evaluated whether fabricated allogeneic epidermal cell sheets are safety and effectiveness for the prevention of severe esophageal constriction after circumferential ESD in swine model.

Firstly, fabricated epidermal cell sheet was optimized, and the function of epidermal cell sheet was histologically evaluated.

Secondly, fabricated epidermal cell sheets were transplanted after circumferential esophageal ESD and evaluated the effectiveness for the prevention of esophageal constriction after circumferential ESD. In more detail, after circumferential ESD of esophagus, allogeneic epidermal cell sheets were endoscopically transplanted to 3 pigs without immunosuppression referred as transplanted group. Other 3 pigs were only performed circumferential ESD and they referred as control group. Endoscopic and histological analyses were performed at 2 weeks after ESD.

RESULTS: Epidermal cells were cultured in temperature-responsive cell culture insert for 2 weeks at 37°C. After epidermal cell sheets were incubated at 20°C for 20 minutes, they were noninvasively harvested. Fabricated epidermal cell sheet was consisted of 3-5 layers and has a basement membrane-like extracellular matrix. Cytokeratin patterns of epidermal cell sheet were similar to the cytokeratin pattern of native epidermis. Labeled epidermal cell sheet was transplanted on the ulceration surface of esophageal ESD. Labeled epidermal cell sheet was histologically detected at 1 postoperative day.

In transplantation experiments, all pigs of transplanted group kept their clinical conditions in contrast to control group. Endoscopic and histological analysis demonstrated that allogeneic epidermal cell sheets promoted the healing of the artificial ulcer after ESD and prevented the esophageal stricture after ESD.

CONCLUSION: Fabricated allogeneic epidermal cell sheets have the potential for the prevention of esophageal constriction after extensive ESD.

REFERENCES:

1. Kanai N et al. Fabricated autologous epidermal cell sheets for the prevention of esophageal stricture after circumferential ESD in a porcine model. Gastrointest Endosc 2012.

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Disclosure of Interest: None Declared

Keywords: ESD complications, tisse repair

P009 NARROW BAND IMAGING-BASED MAGNIFYING ENDOSCOPY POTENTIALLY PREDICTIVE OF EARLY GASTRIC CANCER IN BORDERLINE LESIONS BEFORE ESD

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INTRODUCTION: Endoscopic resection (ER) includes endoscopic submucosal dissection (ESD) is widely accepted as standard treatment for early gastric cancer (EGC) without lymph node metastasis. The procedure has some advantage that minimally invasive, safe, and convenient. Especially, large lesions can be resected en bloc by ESD technique. However, some incomplete resection will happen because we still do not have any appropriate diagnostic tool for decide benign-malignant borderline lesion. Recently, we have seen that narrowband imaging-based magnifying endoscopy (M-NBI) is more accurate than conventional white-light imaging (C-WLI) in diagnosis of gastric cancer. Our goal is to clarify potentially useful findings to predict the existence of gastric cancer in borderline lesions diagnosed by M-NBI, we retrospectively analyzed certain endoscopic features.

AIMS&METHODS: We diagnosed 168 consecutive gastric benign-malignant borderline lesions (152 cases) by C-WLI and M-NBI before ESD treatment. After we resected EGC lesions by ESD, we compared M-NBI diagnosis of borderline with pathological findings. M-NBI diagnosis was classified according to VS (vessel plus surface) classification system.

RESULTS: The final diagnosis for 149 lesions (88.7%) was adenocarcinoma, and for 19 lesions (11.3%) was adenoma. 168 lesions include 115 of mucosal and 34 of submucosal cancer. 156 of 168 (92.8%) lesions could successfully diagnose of the tumor by M-NBI. There was no significant difference of diagnostic accuracy in tumor size (>20mm, 54/62: < 20mm, 102/106). However, we found 12 mismatch (M-NBI and pathological findings) lesions that were mostly slightly depressed type (9 lesions of slightly depressed type, 3 lesions of flat type). Moreover, we pathologically found intraluminal bridge form in one mismatch case.

CONCLUSION: We were able to distinguish all protruded types of cancer. Endoscopic findings using VS classification system were potentially predictive of EGC in borderline lesions diagnosed by M-NBI before ESD.

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Disclosure of Interest: None Declared

Keywords: Early gastric cancer, ESD(endoscopic submucosal dossection), NBI

P010 PENTAX I-SCAN™ WITH ELECTRONIC MAGNIFICATION FOR THE REAL-TIME HISTOLOGICAL PREDICTION OF COLONIC POLYPS: A PROSPECTIVE STUDY USING A NEW DIGITAL CHROMOENDOSCOPY SETTING

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INTRODUCTION: *i*-Scan is a digital chromoendoscopy (DCE) tool that has the potential for in vivo optical diagnosis of colonic polyps. EPK-I processors permits the combination of DCE with electronic magnification (EM). EPK-I combine 6 DCE post-processing settings (d, e, c, g, r and b) called tone enhancement (TE) with different levels of Contrast (CE) and Surface enhancement (SE) resulting in 216 possible combinations. However, 3 established modes (*i*-Scan 1, 2, 3) are available, leading to an under use of other setting combinations

AIMS&METHODS: AIM: to evaluate the DCE-settings available in EPK-I processors establishing ''New ISCAN Setting'' (NIS) modes and measuring its effectiveness with EM for the real-time histological prediction of colonic polyps. After approval by the ethics committee a single-center, prospective study was performed in 255 consecutive patients undergoing screening colonoscopy from Oct-2011/Sept-2012. Exclusion criteria were: <18 years; pregnancy, history of IBD, coagulopathy, absence of polyps and bad bowel preparation. To determine the NIS modes, initially 10 lesions were recorded as HD quality images with EM for each DEC setting combination, including the original settings and HD white light image. Analysis of all images was done using a visual analogue scale VAS (bad: 1 - excellent: 10) assessing the quality of image regarding the pit and vascular mucosal pattern rated by 3 endoscopists to determine the parameters of the *i*-Scan settings based on the highest VAS scores. Finally, an histological prediction of neoplastic (N) and non-neoplastic (NN) polyps using the unified NICE classification for pit and vascular pattern was done using the three highest score NIS modes and the established *i*-Scan modes. Results were compared with histology as the gold standard

RESULTS: 2170 HD images were analyzed and 3 settings were identified: NIS 1, 2, 3 showing a statistical significance ($p > 0.05$) for pit and vascular mucosal pattern compared to original setting (mean VAS: 9.2 vs. 4.16). 183 patients were excluded. Finally 72 patients with 122 polyps were analyzed, 34 males, mean age 59.3 (ranges: 18-91). NIS diagnosed 19/20 N and 102/102 NN lesions and *i*-Scan 16/20 N and 95/102 NN. The NIS was more precise to predict N and NN lesions when compared with *i*-Scan showing a sensitivity of 95% vs. 80%, specificity 100% vs. 93%, PPV 100% vs. 70% ($p < 0.05$), NPV 99% vs. 96% (p 0.2)

CONCLUSION: Identification of under-utilized *i*-Scan modes was possible regarding analyses of mucosal pattern. NIS is effective for real-time histological prediction of colonic polyps and warrants further study

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Keywords: COLONIC POLYPS, endoscopic diagnosis, magnifying colonoscopy, sessile serrated adenoma, ISCAN

P011 ENDOCYTOSCOPY IS AN EFFICIENT TOOL FOR DIFFERENTIATING AMONG TYPES OF SERRATED POLYPS

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INTRODUCTION: Accurate endoscopic criteria are needed to differentiate among serrated polyps, including hyperplastic polyp (HP), sessile serrated adenoma/polyp (SSA/P), and traditional serrated adenoma (TSA), because some are precursors of colorectal cancers.

AIMS&METHODS: The aim of this study was to determine the endocytoscopic features of each type of serrated polyps, especially the shapes of lumens and nuclei. The endoscopic and pathological database of Showa University Northern Yokohama Hospital was searched for serrated polyps removed from May 2005 to December 2012. Lumen shapes were assessed as straight, star-like, oval, serrated and villous, and nucleus shapes were assessed as small round and fusiform.

RESULTS: Of the 58 eligible lesions, 27 were classified as HP, 12 as SSA/P, and 19 as TSA. Most HPs (77.8%) had star-like lumens, and most SSA/Ps (83.3%) had oval lumens. The lumens of TSA were serrated (31.6%) or villous (68.4%), with both shapes seen only in TSA. Most HPs (92.6%) and SSA/Ps (75.0%) had small round nuclei, and all TSAs had fusiform nuclei. Features significantly differentiating TSAs from HPs and SSA/Ps were the presence of fusiform nuclei ($P < .001$) and villous ($P < .001$) and serrated ($P = .002$) lumens. The presence of oval lumens was significantly characteristic of SSA/Ps ($P < .001$), and the presence of star-like lumens was significantly characteristic of HPs ($P < .001$).

CONCLUSION: The shape of lumens and nuclei on endocytoscopy can efficiently differentiate among the different types of serrated polyps.

Disclosure of Interest: None Declared

Keywords: endocytoscopy, hyperplastic polyp, sessile serrated adenoma/polyp, traditional serrated adenoma

P012 EFFICACY OF COLOR INTENSITY ANALYSIS USING A NOVEL AUTO-FLUORESCENCE IMAGING SYSTEM FOR PREDICTING DEPTH OF INVASION IN COLORECTAL NEOPLASIA

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INTRODUCTION: The effectiveness of auto-fluorescence imaging (AFI) systems in distinguishing colorectal non-neoplastic lesions from neoplastic lesions has been reported. Recently, a novel high-resolution AFI system with a noise reduction algorithm was developed.
AIMS&METHODS: The purpose of this study was to evaluate the efficacy of color intensity analysis of AFI images using the novel AFI system to predict depth of invasion of colorectal neoplasia. A total of 96 consecutive patients with colorectal neoplasia were examined using the novel AFI system from May 2011 to December 2012, and the results were retrospectively reviewed. The neoplasias were resected endoscopically or surgically at the Jikei University Hospital and pathological assessments were conducted. First, the regions of interest (ROI) were determined based on findings from chromoendoscopy under white light imaging, then color tone sampling from the ROI in the AFI images was conducted using software which enables the analysis of each color intensity. Finally, the green/red (G/R) ratio for the ROI was calculated. The G/R ratio was compared between the intra-mucosal neoplasia or submucosal (SM) superficial (less than 1,000 μm from the muscularis mucosae) cancer and SM deep (1000 μm or more from the muscularis mucosae) cancer. The endoscopic diagnosis for predicted depth of invasion of colorectal neoplasia (regardless of whether the cancer was SM deep) based on the findings of magnifying chromoendoscopy was also retrospectively reviewed using electronic medical records.
RESULTS: The mean G/R ratios $\pm$ standard deviations were 0.796 $\pm$ 0.062 in intra-mucosal neoplasia or SM superficial cancer and 0.671 $\pm$ 0.069 in SM deep cancer. The G/R ratio of intra-mucosal neoplasia or SM superficial cancer were significantly higher than those of SM deep cancers ($P < 0.001$), and the area under the receiver operating characteristic (ROC) curve was 0.9164. If a cut-off value for the G/R ratio of < 0.70 was applied to this result to determine SM deep cancers, the sensitivity, specificity, positive predicting value (PPV), and negative predicting value (NPV) were 75.0%, 92.5%, 66.7%, and 94.8%, respectively. Regarding the endoscopic diagnosis for SM deep cancers, the sensitivity, specificity, PPV, and NPV were 56.3%, 88.3%, 69.2%, and 91.6%, respectively.
CONCLUSION: Color intensity analysis using the novel AFI system was considered an effective modality to determine the depth of invasion of colorectal neoplasia.
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Disclosure of Interest: None Declared
Keywords: AFI, colon cancer

P013 ADDITIONAL DIAGNOSTIC VALUE OF ENDOCYTOSCOPY TO MAGNIFYING CHROMOENDOSCOPY FOR COLORECTAL NEOPLASMS: A LARGE RETROSPECTIVE ANALYSIS

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INTRODUCTION: Pit pattern (PIT) diagnosis with magnifying chromoendoscopy is effective diagnostic method for predicting a massively invasive submucosal colorectal cancer (SMm) which has possibility of metastasis, whereas endocytoscopy (EC) is recently reported to provide excellent diagnostic ability by enabling *in vivo* visualization of cells and nuclei.
AIMS&METHODS: The aim was to assess the additional diagnostic value of EC to PIT for diagnosing colorectal lesions. We conducted a retrospective comparative study using a prospectively recorded database in a referral hospital. The subjects were 538 patients who were detected of a colorectal lesion with use of a magnifying colonoscope with EC capability. Each detected lesion was initially diagnosed by PIT findings followed by EC diagnosis by the on-site endoscopist. The main outcome measures were the diagnostic abilities of PIT and EC in predicting neoplastic change and SMm.
RESULTS: Overall, 514 lesions from 455 patients were available for analysis. Of them, there were 58 non-neoplastic lesions, 352 adenomas, 15 slightly invasive submucosal cancers, and 89 SMm. The diagnostic abilities of predicting neoplastic change were comparable between PIT and EC diagnosis: sensitivity was 97.8% versus 97.4%, specificity was 91.4% versus 89.7%, and accuracy was 97.1% versus 96.5%. Regarding those of predicting SMm, EC diagnosis showed additional specificity and accuracy to PIT diagnosis: specificity was 99.1% versus 97.6% (P=0.041), and accuracy was 96.3% versus 93.8% (P=0.004).
CONCLUSION: Though PIT has feasible diagnostic ability for predicting both neoplastic change and SMm, EC provides additional diagnostic value to PIT diagnosis for predicting SMm.
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Disclosure of Interest: None Declared
Keywords: endocytoscopy, pit pattern

P014 NEXT-GENERATION NARROW BAND IMAGING SYSTEM (ELITE) FOR COLON POLYP DETECTION: A PROSPECTIVE, MULTICENTER RANDOMIZED TRIAL

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INTRODUCTION:
Previous studies have yielded conflicting results on the polyp detection rate with narrow band imaging (NBI) compared with white light imaging (WLI).
AIMS&METHODS:
To overcome the confounding factors of these studies, we aimed to evaluate the colon polyp detection rate with NBI versus that with WLI by using a next-generation NBI system (EVIS LUCERA ELITE, OLYMPUS) with/ without wide angle (WA) colonoscopy.
Design: A 2 $\times$ 2 factorial designed prospective, multicenter randomized controlled trial.
Setting: This study was conducted at five academic centers in Japan.
Interventions: Patients were allocated to 1 of 4 groups: (1) WLI without WA – colonoscopy using WLI with standard colonoscopy (H260AZI); (2) NBI without WA–colonoscopy using NBI with standard colonoscopy (H260AZI); (3) WLI with WA–colonoscopy using WLI with WA colonoscopy (CF-HQ290); and (4) NBI with WA–colonoscopy using NBI with WA colonoscopy (CF-HQ290). All polyps were removed except polyps less than 5mm in size diagnosed hyperplastic lesion endoscopically in the recto-sigmoid colon.
Main outcome: The difference in polyp detection rate (number of detected polyps per patient) between the WLI with/without WA and NBI with/without WA.
RESULTS:
After recruiting for 454 patients, a total 449 patients who consent to join the study, were included. A total 18 patients were excluded due to exclusion criteria. Finally 431 patients, mean aged 65 (26-86), including 287 (67%) male patients were enrolled (WLI without WA: 119 Pts, NBI without WA: 100 Pts, WLI with WA: 99 Pts, and NBI with WA: 113 Pts). A total number of polyps (hyperplastic/ SSAP/ adenoma/ invasive carcinoma) detected in the WLI without WA, NBI without WA, WLI with WA, and NBI with WA were 164 (10/ 1/ 150/ 3), 176 (22/ 1/ 150/ 4), 188 (22/ 5/ 159/ 2), and 241 (22/ 6/ 209/ 4), respectively. The polyp detection rate in the NBI group was significantly higher than in the WLI group (2.01 vs. 1.56; P =. 032). The polyp detection rate in the colonoscopy with the WA group did not show higher rates than in that with standard group (1.97 vs. 1.61 P =. 089).
CONCLUSION:
REFERENCES:
1. UMIN000007150
Although a wide angle colonoscopy did not eliminate polyp detection rate, next-generation brighter narrow band imaging colonoscopy represented a significant improvement in the detection of colonic polyps.
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Disclosure of Interest: None Declared
Keywords: colon polyp, colonoscopy, narrow band imaging, randomized controlled trial

P015 LAPAROSCOPY-ASSISTED TRANSGASTRIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY FOR THE MANAGEMENT OF BILIOPANCREATIC DISORDERS IN BARIATRIC ROUX-EN-Y GASTRIC BYPASS PATIENTS

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INTRODUCTION: Endoscopic retrograde cholangiopancreatography (ERCP) in Roux-en-Y gastric bypass (RYGB) patients is technically challenging. The success rate of the balloon enteroscopy-assisted ERCP technique is about 60% in most of the literature whereas ERCP by laparoscopic transgastric access (ERCP-LTA) provides a direct access to the biliary tract which may lead to higher technical success rates[§]. In addition, many post-RYGB patients with biliary complications will still have a gallbladder in place. Hence, in these cases, combining ERCP-LTA and cholecystectomy (CCE) is a valuable strategy.
AIMS&METHODS: The goal of the present study is to assess the feasibility of ERCP-LTA after RYGB. We retrospectively analysed the data of post-RYGB patients who underwent an ERCP-LTA in the study centres from May 2008 to April 2013. The ERCP-LTA technique was similar in all cases, except for some subtle differences. A purse-string suture was fashioned around a gastrotomy on the anterior wall of the gastric remnant 5 cm proximal to the pylorus. A side-viewing endoscope was introduced through a 15 or 18 mm trocar placed into the gastrotomy and ERCP was completed under fluoroscopic guidance.
RESULTS: A total of 20 patients were identified (mean age 53 years, range 26-80). 3 patients had a history of open surgery, 17 patients were operated laparoscopically. 6 patients had a history of prior CCE. Indications included ascending cholangitis (n=1), cholecystitis and cholangitis (n=1), radiologically proven choledocholithiasis (n=14), recurrent biliary pancreatitis (n=3) and combination of a typical pain syndrome, cholelithiasis, elevated liver enzymes and a dilated common bile duct on ultrasound (n=1). 14 patients underwent concomitant

CCE, 9 prior to and 5 after ERCP completion. Laparoscopic access was converted to a minilaparotomy in 1 patient due to severe adhesions. ERCP findings included papillary stenosis (n=1), normal cholangiogram (n=1), choledocholithiasis (n=17) and biliary sludge (n=1). All patients successfully underwent biliary cannulation and sphincterotomy. The mean endoscopic procedure time was 53 minutes (range 15-120). No ERCP-related complications occurred. Mean hospital stay was 3.3 days (range 2-5).

CONCLUSION: ERCP-LTA is a feasible approach in the treatment of biliopancreatic disorders in post-RYGB patients and allows for ERCP and CCE to be performed consecutively in a single procedure, without major complications in our series.

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Disclosure of Interest: None Declared

Keywords: ERCP, Roux-en-Y gastric bypass

P016 THE SAFETY AND EFFICACY OF PANCREATIC DUCT STENT PLACEMENT IN THE EMERGENCY ERCP OF ACUTE BILIARY PANCREATITIS BUT DIFFICULT SPHINCTEROTOMY

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INTRODUCTION: Several prospective, randomized trials have demonstrated that early ERCP and biliary endoscopic sphincterotomy (ES) with/without stone extraction was superior in reducing the mortality and morbidity rates in acute biliary pancreatitis (ABP) compared with conservative treatment. Prophylactic pancreatic duct (PD) stent placement has been shown to reduce the risk of post-ERCP pancreatitis in high risk patients. However, there are few reports about the safety and efficacy of PD stent placement in the emergency ERCP of ABP.

AIMS&METHODS: The aim of current study was to evaluate the effectiveness of emergency ERCP and PD stent placement in patients with ABP. Between January 2002 and March 2013, 90 patients with ABP referred to our institution. Total 60 consecutive patients were enrolled in the study. The inclusion criteria were as follows: 1) symptoms consistent with ABP, 2) serum amylase or lipase levels at three times over the upper limits, 3) elevated aspartate aminotransferase and alanine aminotransferase or alkaline phosphatase level, 4) radiological and/or EUS evidence of gallstones, 5) the possibility to accomplish ERCP within 48h following the onset of symptoms. Patients were randomly assigned to either the stent group (n=26) or the no-stent group (n=34). In the stent group, 5F, 3cm-long, straight, double-flanged polyethylene stent insertion was applied at initial ERCP. PD stent was safely removed within 3 weeks in majority of cases.

RESULTS: Mean age, gender, initial symptom-to-ERCP times, admission-to-ERCP times, Glasgow scores, Balthazar scores (CT severity index), BISAP scores, serum amylase and CRP levels at admission were not significantly different in the stent group vs. the no-stent group. The initial selective biliary cannulation was achieved in 88.5% (23/26) of the stent group and in 94.1% (32/34) of the no-stent group (P=0.645). Endoscopic sphincterotomy or needle knife sphincterotomy were performed in 73.1% (19/26) of the stent group and in 100% of the no-stent group (P=0.017). There was no statistical difference in pancreatic complication rates (need for endoscopic necrosectomy) between the two groups (3.8% vs. 5.9%). Mortality rates related to ABP were less frequent in the stent group without any significant differences (0% vs. 11.8%, P=0.126).

CONCLUSION: PD stent placement is a safe and effective procedure for ABP, and is recommended for ABP in patients with failed or difficult ES. Prospective controlled studies are required to support this innovating approach.

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Disclosure of Interest: None Declared

Keywords: Acute Pancreatitis, biliary pancreatitis, gallstone pancreatitis, pancreatic stent

P017 COMPARISON OF EUS-CD, EUS-HG AND EUS-AG AS TECHNIQUES OF EUS GUIDED BILIARY DRAINAGE (EUS-BD)

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INTRODUCTION: ERCP fails in 5-10% patients due to various causes. EUS guided biliary drainage (EUS-BD) is an alternative. EUS-BD may be as EUS-ERCP rendezvous (EUS-RV); or as purely EUS guided procedure by transmural choledocho-duodenostomy (EUS-CD) or hepatico-gastrostomy (EUS-HG), or antegrade trans-papillary stenting (EUS-AG). EUS-RV is an access technique similar to PTBD rendezvous & is not designed for therapy. Other EUS-BD procedures have differences in technical aspects, success rates & complications.

AIMS&METHODS: To compare technical aspects, success rates, clinical outcomes & complications of EUS-CD, EUS-HG & EUS-AG. Retrospective study. Patients undergoing EUS-CD, EUS-HG or EUS-AG included. Those undergoing EUS-RV excluded. All 3 groups comparable for clinical profile, etiology of biliary obstruction & cause of failed ERCP. All EUS-BD procedures performed by a single endoscopist using a 3.8mm channel therapeutic echoendoscope. Parameters compared - technical & clinical success (defined as 50% reduction in bilirubin level @ 1 week), mean procedure time, need for aggressive track dilatation & complications. Statistical analysis using simple 't' test & Chi square test. P-value < 0.05 considered significant.

RESULTS: 31 EUS-BD procedures in 7 years (2005-12); EUS-CD – 13 (42%), EUS-HG – 9 (29%), EUS-AG – 9 (29%). (Table) Complications – 5/14 in EUS-CD (4 minor leaks), 2/9 in EUS-HG (1 – major – biliary peritonitis & death) & 1/10 in EUS-AG (late stent occlusion).

Parameter		EUS-CD, N = 13 (%)	EUS-HG, N = 9 (%)	EUS-AG, N = 10 (%)	P value
Technical success#		13 / 14 (92.9)	7 / 9 (77.7)	9 / 10 (90)	P > 0.05
Clinical success		11 / 13 (84)	6 / 7 (85.7)	7 / 9 (77.7)	P > 0.05
Failure / conversion		1 Conversion (EUS-AG)	2 1 – conversion (PTBD) 1 Failure	1 Conversion (EUS-HG)	
Median procedure time – min (range)		26 (20 – 40)	38 (30 – 90)	35 (25 – 60)	P > 0.05
Stent (SEMS / PS)		10 / 3	9 / 0	9 / 0	P > 0.05
Track dilatation	**Bougie**		6 / 14 (43)	1 / 9 (11)	9 / 9 (100)
	Balloon (4mm)		2 / 14 (14)	2 / 9 (22)	0 / 9 (0)
	Diathermy (6Fr. cystotome)		6 / 14 (43)	6 / 9 (67)	0 / 9 (0)

CONCLUSION: All 3 EUS-BD techniques– EUS-CD, EUS-HG & EUS-AG are comparable for technical success & clinical efficacy to achieve biliary drainage. EUS-CD had shortest procedure time. Aggressive track dilatation was not required in EUS-AG – possibly preventing immediate complications. EUS-HG was technically more difficult and resulted in one severe complication. Further randomized prospective studies comparing these 3 techniques are needed to confirm these findings.

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Disclosure of Interest: A. Bapaye : No conflict of interest, N. Dubale : No conflicts of interest, A. Aher : No conflicts of interest

Keywords: ESCP, EUS guided biliary drainage, EUS-AG, EUS-BD, EUS-CD, EUS-HG

P018 A COMPARATIVE STUDY IN THE CAPABILITY OF DELINEATION BETWEEN RADIAL AND CURVED LINEAR ARRAYED EUS FOR PANCREAS AND BILIARY TRACT: RESULTS OF A PROSPECTIVE STUDY

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INTRODUCTION: Endoscopic ultrasonography (EUS) is categorized into radial and curved linear array EUS based on the difference in scanning methods. Few studies have reported the difference in the capability of delineation between the two techniques.

AIMS&METHODS: The aim of this study is to prospectively compare the capability of delineating the pancreas and biliary tract between radial EUS(R) and curved linear array EUS(C). A total of 201 consecutive cases that required EUS examination from May 2011 to December 2012 were studied in our center. Exclusion criteria were as follows: (1) history of treatment for pancreaticobiliary or upper intestinal disease; (2) suspected intestinal obstruction or stenosis; (3) if patient consent was not obtained. The endpoint of the study was the capability of the system to delineate 11 regions in the pancreas and biliary tract (the head, neck, body and tail of pancreas, bile ducts, cystic duct, gallbladder, papilla, upper bile duct, porta hepatis, branch of celiac artery and superior mesenteric artery). The observation standards for each region were developed and the capability was rated on a three-graded scale: 2, clearly observable; 1, partly observable; 0, unobservable.

RESULTS: Of 201 consecutive patients, one was found to have undergone gastrectomy during examination and was thus excluded from the evaluation. The remaining 200 patients were divided randomly into two groups, with 99 in the R group and 101 in the C group. No differences were found in the age and sex distribution between the R and C groups. The overall average score was 18.59 points in the R group and 19.62 points in the C group, indicating the superiority of the C group ($P < 0.001$). When the arterial branch was excluded from the assessment, the average was 15.34 points in the R group and 15.62 points in the C group, showing no significant difference between the two groups ($p = 0.13$). For the capability of delineation by regions, the C group was non-inferior to the R group for delineating the head, body and tail of pancreas ($p = 0.63$, N/A, 0.505), while it was superior for the neck of pancreas ($p = 0.008$). In the biliary tract system, the C group was inferior for delineating the ampulla of Vater and gallbladder ($p < 0.001$ for both).

CONCLUSION: There is no significant difference between radial EUS and curved linear array EUS for observations in routine screening. However, the selection of the scope should be taken into consideration for detailed examinations in specific regions.

Disclosure of Interest: None Declared

Keywords: Curved linear array EUS, endoscopic ultrasound, Imaging, radial EUS

P019 USE OF ANCILLARY TECHNIQUES IN IMPROVING THE YIELD OF SAMPLES OBTAINED AT EUS-FNA OF THORACIC AND ABDOMINAL LYMPH NODES

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INTRODUCTION: Imaging techniques such as computed tomography (CT) and positron-emission tomography–CT or PET-CT, can detect enlarged thoraco-abdominal lymph nodes, but cannot predict pathological diagnoses. Endoscopic ultrasound-guided fine needle aspirate (EUS-FNA) is a well-established technique for obtaining tissue, but samples obtained are small, and may be insufficient to result in a definitive diagnosis.
Ancillary techniques, such as special histochemistry (SHC), immunohistochemistry (IHC) and flow cytometry may increase the diagnostic yield of EUS-FNA.
AIMS&METHODS: Between November 2005 and December 2012, 278 patients (age 8-87y, mean 45y) underwent EUS-FNA of enlarged thoracic and abdominal nodes at our institution. All specimens were subjected to rapid on-site evaluation (ROSE) by an experienced cytopathologist. We reviewed data on all patients in whom ancillary techniques were employed.
RESULTS: Ancillary techniques were performed in 111/278 cases. 27/111 were neoplastic while 84/111 were non-neoplastic. Nodes sampled were subcarinal (73; 11 neoplastic), other mediastinal (10; 2 neoplastic), coeliac (11; 7 neoplastic) and other abdominal (17; 7 neoplastic).
IHC was performed in 24 cases - one of these also needed SHC stain. 3 cases required flow cytometry. SHC staining was performed in 84 non-neoplastic cases. IHC aided in reaching a definitive diagnosis in 19/24 (79%) cases. Diagnoses made after IHC were metastatic carcinoma in 7 (29.1%), requiring CK (AE1/AE3), CK7, CK20, CK19, CAM5.2, ER, Hep-Par1, EMA and p63, classic Hodgkin's lymphoma in 6 (25%), which required CD30 and CD15, diffuse large B cell lymphoma (DLBCL) (CD20 and CD3), metastatic gastrointestinal stromal tumour (CD117) and metastatic neuroendocrine tumor (CD56).
Flow cytometry led to a definitive diagnosis in 3 neoplastic cases. These were DLBCL in two cases and chronic lymphocytic leukaemia in one.
SHC stains (Ziehl Neelson (ZN), PAS, GMS and mucicarmine)) were performed in 85 cases, of which 84 were non-neoplastic. These were granulomas in 72 (85.7%), (2 staining positive for acid fast bacilli (AFB) on ZN stain and 1 for Aspergillus on PAS/GMS stain), necrosis/calcified material in 7 (8.3%) and reactive lymphoid hyperplasia in 5 (5.9%). ZN staining for AFB was performed on all cases. Additional PAS stain was performed in two and mucicarmine and GMS stains in one case each.
CONCLUSION: IHC and flow cytometry improved the yield of EUS FNA in 22/111 (20%) of cases. SHC studies provided additional information in a further 3 (2.7%) cases. Ancillary studies in EUS-guided FNA of thoracic and abdominal lymph nodes can significantly improve the yield of this very effective diagnostic tool.
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Disclosure of Interest: None Declared
Keywords: Ancillary techniques, EUS-FNA, Thoracic and abdominal nodes

P020 MR ENTEROGRAPHY IN CROHN'S DISEASE – A HOSPITAL EXPERIENCE

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INTRODUCTION: Magnetic resonance enterography (MR enterography) is important in evaluating Crohn's disease (CD), particularly in assessing the activity and extension of the disease, as well as in revealing extraluminal complications, like abscesses and fistulas.
AIMS&METHODS: The present study proposes to evaluate the impact of MR enterography in the management of these patients. The retrospective study of MR enterography and subsequent management of suspected or diagnosed Crohn's disease patients between January and December of 2011 in our hospital.
RESULTS: MR enterography was performed in 69 patients (48 females and 21 males, with median age of 33.1±12.6 years). For 17 patients with suspected DC, MR enterography confirmed the diagnosis in only 2. To the remaining 52 patients a MR enterography was performed to establish the extent or detect complications of CD. In this group, MR enterography did not change the location of the disease previously diagnosed by endoscopy. In 26 (50%) patients, the exam has shown imagiologic signs of active disease, in 19 (13%) patients the exam has detected 23 complications (18 stenosis, 3 fistulas and 2 abscesses) and in 7 patients the exam was normal. MR enterography was associated with a change in the clinical management of 29 (56%) patients: 24 had therapeutic progression (13 patients started azathioprine and 11 patients anti-TNF therapy); 3 patients required surgery and 2 patients required endoscopic dilatation. Multivariate analysis has shown that positive findings (active disease and/or complications) on MR enterography ($p = 0.0001$) and previously surgery for CD ($p = 0.02$) were associated with management modification. Age, gender, location of CD and medical therapeutic were not significant for management alteration. Twenty-nine imagiologic findings not related with CD were documented.
CONCLUSION: The main role of MR enterography in Crohn's disease is to evaluate disease activity and its complications. As has been shown in this study, MR enterography has a significant impact in the management of these patients.
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Disclosure of Interest: None Declared
Keywords: crohn's disease, MR enterography

P021 ENDOSCOPIC RETROGRADE APPENDICITIS THERAPY (ERAT): A MULTICENTER RETROSPECTIVE STUDY IN CHINA

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INTRODUCTION: Endoscopic retrograde appendicitis therapy (ERAT) proved to be one feasible and effective therapeutic method for the treatment of acute uncomplicated appendicitis.
AIMS&METHODS: This study tried to evaluate the long-term outcomes following ERAT and examined the use of ERAT as an alternative treatment to acute uncomplicated appendicitis. From December 2009 to February 2013, 39 consecutive patients with suspected acute uncomplicated appendicitis who come from three different hospitals recieved ERAT and were reviewed retrospectively. False-positive rate of clinical diagnosis (the rate of patients with incorrectly diagnosed as acute appendicitis proved by appendiceal radiography during ERAT) and outcomes of ERAT were examined.
RESULTS: Endoscopic appendiceal intubation and radiography were successful in 38/39 (97.4%) patients during the procedures. The false-positive rate was 8/38 (21.1%). Immediate appendiceal decompression were performed in all 30 patients, including simple endoscopic cleaning of appendiceal lumen in 19/30 (63.3%) patients, and plastic stent drainage in 11/30 patients (36.7%, including one patient underwent appendiceal fecalith extraction by Dormia basket). Abdominal pain disappeared immediately and abdominal tenderness alleviated within 12 hours in 28/30 patients. Liquid diet was resumed after the procedure. Nine patients recieved ERAT in outpatient clinic without hospitalization. There is not severe complication occurred in any patients, however, 2 patients (5.3%) recurred appendicitis during 36 months follow-up, and then accepted operations.
CONCLUSION: ERAT appears to be a safe, effective and minimally invasive diagnosis and treatment modality for patients suspected with acute appendicitis.
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Disclosure of Interest: None Declared
Keywords: acute appendicitis, Endoscopic therapy, ERAT, minimally invasive

P022 CLINICAL EVALUATION OF A NEW CRYOBALLOON FOCAL ABLATION SYSTEM FOR THE ELIMINATION OF BARRETT'S ESOPHAGUS

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INTRODUCTION: RFA has become the preferable method for elimination of BE, when indicated. Although highly effective, RFA suffers from drawbacks such as the need for precise sizing, multiple deployment steps, and large controller units.
AIMS&METHODS: The aim was to assess the feasibility, safety, and dose-response of a newly developed Cryoballoon Focal Ablation System (CbFAS) in patients with flat BE with or without dysplasia. The system was designed to address many of the limitations of current ablation techniques.
In this multi-center, prospective non-randomized trial, up to 40 patients will be enrolled with each subject receiving up to 2 ablations using the CbFAS using two doses. The CbFAS consists of a TTS catheter with a balloon probe made of a conformable material obviating the need for sizing. The balloon is simultaneously inflated and cooled with cryogenic fluid delivered from a small disposable canister, resulting in ablations of approximately 2 cm^2. Symptoms were assessed directly after and 2 days after CbFA. FU endoscopy with photo documentation and biopsy of the treated areas was scheduled at 6-8 weeks. Primary outcomes were incidence of adverse events, pain, esophageal stricture formation, and ablation response by cryogen dose.
RESULTS: By May 2013, 21 ablations (6s in 10, 8s in 11) were performed in 15 patients. Median (range) procedure time was 12 (3-38) min. Device malfunction was encountered in 1 additional patient. No major adverse events occurred – 2 patients had minor mucosal lacerations that required no additional intervention. Mild pain was reported immediately after the procedure in 2 of 15 patients and in one patient at 2 days. Thirteen (ten 6s, three 8s) ablation areas (10 patients) had reached FU endoscopy. No strictures developed. Squamous regeneration was seen in 7 treated areas (5/10 areas treated with 6s, 2/3 areas treated with 8s).
CONCLUSION: Preliminary results of this multicenter prospective trial suggest that focal cryobablation of BE with the newly developed CbFAS is feasible, safe, and results in squamous regeneration in the majority of patients.
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Keywords: Barrett's esophagus, Cryoablation

P023 ENDOSCOPIC TREATMENT FOR SUPERFICIAL CARCINOMA OF THE PHARYNX AND BORDERLINE LESIONS BETWEEN THE CERVICAL ESOPHAGUS AND HYPOPHARYNX

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INTRODUCTION: Early diagnosis and early treatment are the best ways to improve cancer patient prognoses and keep QOL of patients after treatment. We developed ELPS (endoscopic laryngo-pharyngeal surgery) as an endoscopic treatment and a minimal invasive surgery for superficial pharyngeal carcinoma. Also we developed a hybrid endoscopic surgery (ESD+ELPS) for borderline lesions between the cervical esophagus and hypopharynx. ELPS is transoral endoscopic surgery for pharyngeal cancer. We lift the larynx by the curved type laryngoscope. After lifting the larynx, the scopist inserts endoscope and the operator inserts forceps and electric device transorally. After the iodine staining, we mark the normal mucosa just 1-2mm out of the cancer margin and inject Epinephrine-added physiological saline solution to the sub-epithelial layer. After the circumferential cutting, we resect the lesion with the forceps and electric device. ELPS was applied for all lesions of the pharynx. However, ELPS has not been applied for cervical esophagus carcinoma because of the narrow working space and interference of endoscopy, forceps and electric device. We applied a hybrid endoscopic surgery (ESD+ELPS) for borderline lesions between the cervical esophagus and hypopharynx.
AIMS&METHODS: The purpose of this study was to examine the usefulness and effectiveness of endoscopic treatment for superficial carcinoma of the pharynx and cervical esophagus. We defined the superficial carcinoma of the pharynx as the carcinoma which depth of tumor invasion is within the sub-epithelial layer. ELPS was performed on 278 patients of superficial carcinoma of the pharynx and hybrid endoscopic surgery (ESD and ELPS) was performed on 10 patients for superficial carcinoma of borderline lesions between the hypopharynx and cervical esophagus during the period from January 2000 to April 2012.
RESULTS: All lesions were completely resected. The complications of ELPS were laryngeal edema for 18 patients, which required overnight intubation or tracheotomy, postoperative bleeding for 3 patients, temporary vocal cord palsy for 11 patients. The complications of hybrid endoscopic surgery (ESD and ELPS) were laryngeal edema for 3 patients, which required overnight intubation, and stricture for 3 patients, which required endoscopic dilation more than 10 times. There were no long-term complications in all patients.
CONCLUSION: The results indicated the usefulness and effectiveness of ELPS for superficial carcinoma of the pharynx and hybrid endoscopic treatment (ELPS+ESD) for superficial carcinoma of borderline lesion between the cervical esophagus and hypopharynx.
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Disclosure of Interest: None Declared
Keywords: cervical esophagus, ELPS, endoscopic treatment, ESD, pharynx

P024 LAPAROSCOPY AND ENDOSCOPY COOPERATIVE SURGERY FOR GASTRIC SUBMUCOSAL TUMOR LOCATED NEAR THE ESOPHAGOGASTRIC JUNCTION

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INTRODUCTION: Laparoscopic wedge resections are increasingly applied for gastric submucosal tumors (SMT) such as gastrointestinal stromal tumor (GIST). For tumors located near the esophagogastric junction (EGJ), especially intragastric-type SMT, wedge resection of the stomach is quite difficult. Thus intragastric-type SMT located near the EGJ usually undergo total gastrectomy or proximal gastrectomy.
AIMS&METHODS: This study aimed to introduce a laparoscopy and endoscopy cooperative surgery (LECS) for gastric wedge resection that is applicable for resections of intragastric-type SMT located near the EGJ.
Methods: We retrospectively analyzed 15 patients [7 men and 8 women, mean age 58 years (range, 26-79 years)] who underwent LECS for the resection of intragastric-type SMT located within 2cm from the EGJ at the Cancer Institute Hospital, Tokyo, between June 2006 and April 2013. To decide the precise resection line, both mucosal and submucosal layers around the tumor were circumferentially dissected using endoscopic submucosal dissection (ESD) via intraluminal endoscopy. Subsequently, the seromusclar layer was laparoscopically dissected along the incision line by ESD. After three-fourths of the circumference around the tumor had been resected, the SMT was exteriorized to the abdominal cavity and dissected with a standard endoscopic stapling device.
RESULTS: The mean tumor size was 3.5 cm (range, 2.0–5.0 cm). The mean distance from the lesions to EGJ was 0.5 cm (range, 0-2 cm). All surgical margins were clear. Histopathologic examination of the tumors showed GIST (n = 8), leiomyoma (n = 6), schwannoma (n = 1). The mean operation time was 219 min, and the estimated blood loss was 31 ml. In 11 of 15 cases, the LECS procedure was successful for dissecting out the gastric SMT and the postoperative course was uneventful. The remaining four were converted to open surgery because of extensive resection more than half of circumference of the EGJ. Among the cases converted to open surgery, anastomotic leakage occurred in two cases and anastomotic stenosis occurred in one. No recurrence or death was noted during follow-up (average 26 months).
CONCLUSION: LECS for dissection of intragastric-type SMT located near the EGJ may be performed safely with minimal resection lines, therefore is helpful for preserving cardia. But extensive resection around the EGJ is not feasible.
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Disclosure of Interest: None Declared
Keywords: cardia, Endoscopic submucosal dissection (ESD), esophagogastric junction, gastric submucosal tumor, Gastrointestinal stromal tumors, LAPAROSCOPY AND ENDOSCOPY COOPERATIVE SURGERY

P026 TRANSNASAL SMALL-CALIBER ESOPHAGOGASTRODUODENOSCOPY IMPROVES SAFETY IN PATIENTS WITH CONGESTIVE HEART FAILURE

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INTRODUCTION: Unsedated transnasal small-caliber esophagogastroduodenoscopy (TN-EGD) is often used to examine the upper gastrointestinal tract.TN-EGD has improved the safety of the endoscopic examination, showing fewer adverse effects on cardiopulmonary function and autonomic nerve function. Although we perform endoscopy on elderly and critically ill patients with increasing frequency, we have little information concerning the relative safety of transnasal small-caliber and transoral conventional EGD (TO-EGD) in these groups. The aim of this prospective, randomized study was to compare the effects of TN-EGD and TO-EGD on cardiac function in patients with risk of congestive heart failure.
AIMS&METHODS: We enrolled 200 patients (mean 71.1 years old) for unsedated diagnostic EGD and randomly allocated them to undergo either TN-EGD or TO-EGD (n=100 per group).All the EGDs were performed without administration of scopolamine butylbromide. We *evaluated cardiac functions by measuring* systolic and diastolic blood pressure (BP), and pulse rate (PR) at the following 3 time points during the endoscopic examination: baseline, 2 minutes after endoscopic intubation, and just after extubation. The rate-pressure product (RPP: PR x systolic BP /100) was also calculated. And in patients with a high risk of heart failure, the autonomic nervous responses were determined employing power spectral analysis (PSA) of heart-rate variations on electrocardiogram using amplitude of the high-frequency component (HF) and low-frequency-to-high-frequency power ratio (LF/HF) as indices of cardiac vagal activity and sympathetic activity. We used BNP levels according to heart failure risk, and divided all patients into 2 groups; high-risk (BNP level $\geq$100 pg/ml) and low-risk (BNP level $<$99 pg/ml).
RESULTS: In the TO-EGD group, RPP levels in patients with a high risk of heart failure were increased at 2 minutes after endoscopic intubation and significantly higher than those in patients without heart failure risk. On the other hand, endoscopic intubation did not influence the RPP levels in any patients in the TN-EGD group. in Further in patients with a high risk of heart failure, PSA revealed a lower increase in LH /HF in TN-EGD than in TO-EGD.
CONCLUSION: In patients with a high risk of congestive heart failure, TO-EGD induced hemodynamic effects, while TN-EGD did not. TN-EGD is considered to be safe, as it is associated with few adverse effects on cardiac function.
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Disclosure of Interest: None Declared
Keywords: autonomic nervous responses, patients with risk of congestive heart failure, transnasal small-caliber esophagogastroduodenoscopy

P027 CARD15 MUTATIONS AND GASTRIC CANCER IN A PORTUGUESE POPULATION

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INTRODUCTION: *CARD15* is involved in the innate immune response and mutations of this gene have been linked with increased risk of Crohn's disease and colorectal cancer. The relation between *CARD15* mutations and Gastric Cancer (GC) remains controversial.
AIMS&METHODS: The aim of this study was to assess whether *CARD15* mutations are risk factors for GC in Portugal and whether there are genotype-phenotype correlations in these patients.
The 3 main *CARD15* mutations (3020insC, R702W and G908R) were searched in 150 patients with GC and in 202 healthy controls.
RESULTS: Overall, *CARD15* mutations were found in 28 patients (18.7%) and in 27 controls (13.4%) ($p = 0.176$).
Individually, the incidence of 3020insC was significantly higher in patients than in controls (6.0% *vs.* 1.0%, $p = 0.021$). This polymorphism was linked with an increased risk for the intestinal-type of GC ($p = 0.002$), whilst no association was found with the diffuse and/or mixed types. Genotype frequencies for R702W (10.0% *vs.* 7.9%) and G908R (4.0% *vs.* 4.0%) were not statistically different between the two groups. Similarly, no significant associations were detected between these two polymorphisms and the different histological GC types. No correlations were observed between *CARD15* mutations and family history, mean age at diagnosis or GC stage.
CONCLUSION: The *CARD15* 3020insC variant is a risk factor for intestinal GC in Portugal. *CARD15* variants are not correlated with age of diagnosis or family aggregation of the disease neither with the GC stage.
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Disclosure of Interest: None Declared
Keywords: Cancer risk, CARD15 mutations, Gastric cancer, Genetic susceptibility

P028 DOWN-REGULATION OF HSA-MICRORNA135B IN GASTRIC CORPUS

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INTRODUCTION: Micro RNAs(miRs) are small molecular, non-cording RNAs which consist of 8-25 bases. MiRs regulate the expression of target genes through translational repression or messenger RNA(mRNA) degradation. Considering miRs participate organ development and differentiation, and cellular growth, they greatly affect various diseases.
AIMS&METHODS: The present study was conducted to determine expression patterns of miR in gastric mucosa, with special reference to differences in expression patterns between the antrum and body. Using endoscopic biopsy specimens, miR expression patterns of gastric antrum and body were determined by microarray. The differentially expressed miRs were quantitated by real-time reverse-transcriptase polymerase chain reaction (RT-PCR) in the test samples. Biopsy specimens were obtained from gastric mucosa of the antrum and body in chronic gastritis patients with or without *H.pylori* infection, and total RNA was isolated.
RESULTS: Upon micro array analysis, certain miRs, such as miR-135b, miR-1, miR-193b, miR-34a, miR-34b and miR-455-5p were differentially expressed (more than 2-fold) between the antrum and body. Among these miRs, miR-135b was one of the most down-regulated miRs in the body irrespective of *H.pylori* status. So, we quantitated miR-135b expression levels via quantitative RT-PCR. RNU48 was employed as the internal control. As a result, in 17 of 20 patients, the miR-135b expression levels were higher in the antrum than in the body. The average of expression ratio with the internal control (miR135/RNU48) was 0.015 in the antrum, while it was 0.006 in the body. Thus, there was a significant difference in miR-135b expression between the antrum and body ($p<0.0001$). Based on in silico analysis representative of TargetScan, miR-135b could repress ADCYAP1 (adenylate cyclase activating polypeptide 1) which stimulates gastric acid secretion by inducing histamine release, implying down-regulation of miR-135b in the acid secretion from gastric body.
CONCLUSION: MiR-135b was differentially expressed within gastric mucosa. Further studies are warrant to explore clinical significance of the down-regulation of miR-135b in gastric body.
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Disclosure of Interest: None Declared
Keywords: gastric corpus, microRNA

P029 GENETIC POLYMORPHISMS OF MAFK ARE ASSOCIATED WITH THE ABERRANT DNA METHYLATION OF CDKN2A IN JAPANESE SUBJECTS

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INTRODUCTION: CpG island aberrant methylation is shown to be an important mechanism in gene silencing. We have already reported that genetic polymorphisms of NRF2 are associated with the aberrant DNA methylation of CDKN2A in gastric mucosa. An activation of transcription factor Nrf2 is regulated by dimerized with small Maf proteins. MafK, encoded by MAFK gene, is one of the small Maf proteins. Within 20kbp around MAFK gene, there are two linkage disequilibrium blocks, with above 0.05 of HWE p value and above 0.05 of minor allele frequency. In this study, we investigated an association between aberrant DNA methylation of CDKN2A in gastric mucosa and each tag polymorphism, rs4268033G>A and rs3735656 (*910T>C), and the other one rs10226620 (*1506T>C).
AIMS&METHODS: Gastric mucosal samples were obtained from 381 subjects without malignancies. Methylation status of genes ($p14^{ARF}$ and $p16^{INK4a}$) was determined by methylation-specific polymerase chain reaction. Both $p14^{ARF}$ and $p16^{INK4a}$ methylations were defined as CDKN2A methylation. The genotypings of *MAFK* were performed by PCR-SSCP.
RESULTS: Mean age of the subjects was 60.2 years old, male/female ratio was 221/160 and *H. pylori* (HP) positive ratio was 230/381. Methylation of $p14^{ARF}$ and $p16^{INK4a}$ was seen in 126 and 106 of 381 subjects, respectively. The ration of CDKN2A methylation was 45/381. The distribution of rs4268033, rs3735656 and rs10226620 genotypes were 173GG, 175GA and 33AA (HWE p=0.29), 151TT, 184TC and 46CC (HWE p=0.44) and 157TT, 176TC and 48CC (HWE p=1.00). By a logistic regression analysis after adjustment for age, gender and HP infection status, rs4268033 AA, rs3735656 CC and rs10226620 CC homozygous were significantly associated with the susceptibility to CDKN2A methylation (OR, 3.10; 95%CI, 1.14-8.41; p=0.027, OR, 4.55; 95%CI, 1.86-11.1; p=0.0009 and OR, 3.49; 95%CI, 1.47-8.27; p=0.0045, respectively). Regarding as $p14^{ARF}$ methylation, rs3735656 CC homozygous had a significantly increased risk (OR, 2.28; 95%CI, 1.11-4.70; p=0.025). In addition, rs3735656 CC and rs10226620 CC homozygous had also a significantly increased risk for $p16^{INK4a}$ methylation (OR, 2.99; 95%CI, 1.42-6.29; p=0.0039 and OR, 2.37; 95%CI, 1.16-4.82; p=0.018).
CONCLUSION: MAFK polymorphisms are significantly associated with the increased risk for the development of CDKN2A mathylation in non-cancerous gastric mucosa. In particular, rs3735656 *910T>C is closely associated with CDKN2A methylation.
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Disclosure of Interest: None Declared
Keywords: CDKN2A-gene, gene methylation, genetic polymorphism, MAFK

P030 THE EFFECTS OF MDR-1 GENE POLYMORPHISMS ON THE CLINICAL COURSE OF CHRONIC HEPATITIS B INFECTION

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INTRODUCTION: The treatment modilities of chronic HBV infectionand resistance is currently investigated (1). P-glycoprotein(P-gp), the product of multidrug resistance gene(MDR-1), is well-known mechanism of MDR phenotype. MDR gene C1236T polymorphism is associated with decreased P-gp function (2). The mutation of MDR gene can affect the clinical course of disease and response rate to treatment (2,3). It was aimed to investigate the relationship between MDR gene polymorphism and clinical course and treatment responses in chronic HBV infection in our study.
AIMS&METHODS: A total of 90 (male/female:69/21) patients with chronic HBV infection under Lamivudine treatment was enrolled in this study. The patients were categorized as: Treatment responded (group 1: HBV-DNA is negative at 24th week) and treatment refractory (group 2: HBV-DNA is still positive after 24th week). Group 1 was consisted of 51 (M/F: 38/13) and group 2 was consisted of 39 (M/F: 31/9) patients. YMDD mutation was investigated in 19 patients of group 2. Polymerase chain reaction-restriction fragment length polymorphism was used for the detection of C1236T single nucleotide polymorphism. MDR-1 gene C1236T alleles' frequencies and CC, CT, TT genotype distributions were investigated in two groups.
RESULTS: Genotype distributions were as follows: CC, CT, TT genotypes were detected as 8(15.7%), 37(72.5%), and 6(11.8%) in patients at group 1, respectively. CC, CT and TT genotypes were found 13(33.3%), 21(53.8%), and 5(12.8%) in patients at group 2, respectively. CC genotype was more common in group 2 than group 1 (p=0.044). C and T alleles' frequencies in the group 1 and 2 were 51.96% and 60.26%, 48.04% and 39.74%, respectively ($p>0.05$). The patients with YMDD mutation positive at group 2 (n:11), 5(45%) had have CC genotype, 5(45%) had have CT, 1(9%) had have TT genotype. The patients with YMDD mutation negative at group 2(n:8), 3(37%) patients had have CC and 5 (63%) patients had have CT genotype. CC genotype was more common in the patients with YMDD mutation positive than group 1 (p=0.043). Moreover, CC genotype was more common in the patients with HBV-DNA positive at 12nd month of Lamivudine treatment than group 1 (p=0.042).
CONCLUSION: Consequently; MDR-1 and p-gp polymorphisms are important factors in the clinical course of chronic HBV infection and may influence the treatment responses. In the current study, it was found that the CC genotype of MDR-1 gene C1236T was more common in the patients with lamivudine resistant HBV infection.
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Disclosure of Interest: None Declared
Keywords: Hepatitis B, Lamivudine resistance, MDR-1 gene polymorphism

P031 IMPACT OF INTERFERON LAMBDA GENE POLYMORPHISM ON TREATMENT OF HCV-4 INFECTION IN DIABETIC PATIENTS

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INTRODUCTION: IL28B polymorphisms are strongly associated with response to treatment for HCV infection. IL28B acts on interferon-stimulated genes via the JAK-STAT pathway, which has been implicated in development of insulin resistance[1].
AIMS&METHODS: This study aimed to evaluate the Impact of interferon lambda gene polymorphism on treatment of HCV-4 infection in diabetic patients. Occurrence of variants at three IL28B-Related Single Nucleotide Polymorphisms (rs12979860, rs12980275, and rs8099917) was correlated with virologic response to combined treatment with pegylated interferon and ribavirin among 104 HCV - 4 infected Egyptian patients (41 diabetic Vs. 63 non diabetic patients).

RESULTS: IL28B-Related Single Nucleotide Polymorphisms had significant impact on virologic responses to combined treatment among non diabetic patients; CC subtype of rs12979860 and AA subtype of rs12980275 had the highest rapid virologic response rates (p=0.02 and 0.04 respectively).Early virologic response rates were significantly higher among non diabetic patients with CC subtype of rs12979860 (p=0.005), AA subtype of rs12980275 (p=0.04) and TT subtype of rs8099917 (p=0.01).Significant higher percentage of sustained virologic response rates was found among non diabetic patients with CC subtype of rs12979860 (p = 0.003) and AA subtype of rs12980275 (p = 0.004). Strikingly, all the subtypes of the three IL28B-Related Single Nucleotide Polymorphisms (rs12979860, rs12980275, and rs8099917) had no impact on virologic responses to combined treatment among diabetic patients.
CONCLUSION: Non diabetic patients with chronic hepatitis C-4 infection are more likely to benefit from the assessment of IL28B-related SNPs (rs12979860, rs12980275, rs8099917) in the prediction of virologic response to combined treatment than diabetic patients.
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Disclosure of Interest: None Declared
Keywords: HCV-4, DM, IL28B, rs12979860, rs12980275, SVR

P032 DISCOVERY OF POTENTIAL PLASMA BIOMARKERS OF CHOLANGIOCARCINOMA UTILISING SURFACE-ENHANCED LASER DESORPTION/IONIZATION TIME-OF-FLIGHT MASS SPECTROMETRY (SELDI-TOF MS)

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INTRODUCTION: Cholangiocarcinoma (CC) is a malignant neoplasm of the bile duct. Diagnosis of CC is hampered by the inadequate performance of current plasma markers of disease, particularly in patients with preexisting primary sclerosing cholangitis (PSC). We aimed to identify potential new protein biomarkers of CC
AIMS&METHODS: In an initial discovery study, blood plasma samples from 18 subjects with CC, 17 with PSC and 10 healthy controls were subjected to SELDI-TOF MS. Comparisons of m/z peak intensity were made between groups using the Mann-Whitney U test. Differentiating m/z peaks were then confirmed in a further validation study of 81 subjects with CC, 54 with PSC and 90 healthy controls. Pearson's correlation was used to investigate the relationship of each m/z peak's intensity to routine laboratory indices. Diagnostic performance was investigated using receiver operator characteristic area-under-the curve (ROC-AUC) analyses. Multiple linear regression was used to investigate the performance of combinations of differentiating m/z peaks, as well as the combination of m/z peaks with routine laboratory markers (including CA19-9).
RESULTS: Seven differentially expressed m/z peaks were identified in the CC group and these were subsequently confirmed in the validation study (p=2.6x10-4 to 9.4x10-13). The intensity of the seven m/z peaks of interest did not correlate with creatinine, ALP, bilirubin, CRP, white cell count or CA19-9. A panel of three peaks discriminated CC from PSC subjects with ROC-AUC of 0.76 (sensitivity 75%, specificity 64%). A panel of five peaks discriminated CC subjects from healthy controls with ROC-AUC of 0.90 (sensitivity 95%, specificity 74%). Addition of routine laboratory indices did not change the diagnostic performance of these models significantly.
CONCLUSION: SELDI-TOF has been used to successfully identify seven m/z peaks that are differentially intense in CC subjects (total n=99), when compared to PSC subjects (n=64) and healthy controls (n=107). These peaks appear to be independent of standard markers of renal impairment, cholestasis, sepsis and inflammation, as well as CA19-9. Individually, and more so in combination, these peaks exceed the expected diagnostic performance of CA19-9, particularly in discriminating CC from PSC. Work to identify the proteins represented by these m/z peaks is ongoing.
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Disclosure of Interest: None Declared
Keywords: biomarkers, cholangiocarcinoma

P033 GENETIC FACTORS AND THEIR INVOLVEMENT IN NONALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Family and interethnic studies suggested that the genetic variability is implied to be one of the most important factors of NAFLD progression in individual patients.
AIMS&METHODS: The aim of our study was to identify the role of PNPLA3rs738409 in progression of the disease. We included 138 subjects with NAFLD and 125 age and sex matched healthy controls. In both groups we determined anthropometric mesurements, aminotransferases levels, presence or not of diabetes mellitus, insulin resistence, abdominal ultrasound and the PNPLA3 gene polymorphism. The genotyping assays were performed at Molecular and Cellular Biology Department, University of Medicine and Pharmacy from Craiova, using predesigned *TaqMan SNP Genotyping Assays*.
RESULTS: 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 (p=0.046). The PNPLA3 polymorphism was associated with an increased risk of hepatic steatosis in patients with BMI <30 kg/m2, 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 ≥30 kg/m2, 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). [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).
CONCLUSION: The risk [G] allele carriers have a 3 times higher risk of developing hepatic steatosis in the absence of obesity, of insulin- resistance and of the metabolic syndrome.
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Disclosure of Interest: None Declared
Keywords: nafld, PNPLA3 gene polymorphism

P034 CARD15 MUTATIONS AND ALCOHOLIC LIVER CIRRHOSIS IN THE PORTUGUESE POPULATION

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INTRODUCTION: *CARD15* gene is involved in the immune response regulation. *CARD15* mutations were initially linked with increased risk of Crohn's disease and, more recently, have been associated with a higher risk of some infections and neoplasms. In liver cirrhosis, *CARD15* mutations have been related with an increase in the risk of Spontaneous Bacterial Peritonitis (SBP).
AIMS&METHODS: Aims: The aim of this study was to assess whether *CARD15* mutations are risk factors for Alcoholic Liver Cirrhosis (ALC) in Portugal and whether there are genotype-phenotype correlations in these patients. **Methods:** Case-control study involving the research of the 3 main *CARD15* mutations (3020insC, R702W e G908R) in 128 patients with ALC and in 202 healthy controls.
RESULTS: Overall, *CARD15* mutations were found in 25 patients (19.5%) and in 27 controls (13.4%) (p=0.134). The mean age of patients was 61.1 ± 11.9 years old, and 77.3% were males. The average age at diagnosis of ALC was significantly lower in patients with mutation (49.0±12,6 *vs.* 56.7±11.7 years old; p=0.014). The incidence of *CARD15* mutations, especially of the R702W variant, was significantly higher in patients with hepatorenal syndrome (HRS) (overall – 36.3% *vs.* 16.0%; p=0.029; R702W variant – 27.3% *vs.* 10.4%, p=0.034). No significant associations were detected between *CARD15* mutations and SBP (27.3% *vs.* 16.8%, p=0.193), hepatocellular carcinoma (17.6% *vs.* 19.8%, p=0.833), hepatic encephalopathy (22.7% *vs.* 16.1%, p=0.347), gastroesophageal variceal bleeding (18.6% *vs.* 20.0%, p=0,851), acute alcoholic hepatitis (30.0% *vs.* 18.0%, p=0,384), or other infectious intercurrences (18.0% *vs.* 20.5%, p=0.726).
CONCLUSION: Within the portuguese population, *CARD15* mutations are not linked with increase risk of ALC, but are associated with earlier onset of the disease and represent a risk factor for HRS. *CARD15* variants are not correlated with other ALC complications.
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Disclosure of Interest: None Declared
Keywords: ALCOHOLIC LIVER DISEASE, CARD15 mutations

P035 FREQUENCY OF ADRENAL FAILURE IN AMBULATORY PATIENTS WITH CIRRHOSIS

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INTRODUCTION: Previous studies have shown that adrenal failure is frequent among patients with advanced cirrhosis with septic shock (65%), or in acute liver failure (33%). Although adrenal failure is well documented in critically ill patients with cirrhosis, it's unclear if it's a pre-existing condition or if it's triggered by a critical illness.
AIMS&METHODS: Establish the frequency of adrenal failure in stable cirrhotic patients by insulin tolerance test. In a period between September 2011 and August 2012 patients attending a gastroenterology clinic of a tertiary medical center were evaluated. The study was approved by the local ethics committee and all patients signed informed consent. Patients with sepsis, cancer, adrenal failure, treatment with steroids, ischemic heart disease, arrhythmias, seizures, gastrointestinal bleeding, hepatic encephalopathy grade III-IV or serum creatinine >3mg/dL were excluded. Adrenal failure was identified by the insulin tolerance test. Patients remained sited and medically supervised during the test, hypoglycemia was induced by the administration of a 0.15 U/kg insulin IV bolus. Capillary glucose levels were measured every 15 minutes, until adequate levels of hypoglycemia (50% decrease from basal glucose or <45mg/dL) were reached. Blood samples were obtained at time of 0, 30, 60 and 90 minutes

after the insulin bolus. Serum levels of cortisol were analyzed by *electrochemiluminescence* (Roche diagnostic) with ELECSYS 2010 system. Adrenal failure was defined with a total serum cortisol level <18μg/dl at 30 minutes after the hypoglycemia induced by insulin, patients were classified as responders or non-responders according to levels of cortisol.
RESULTS: A total of 40 insulin tolerance tests were performed, 16 patients (40%) were classified as responders with a serum cortisol level >18μg/dl at 30 minutes of hypoglycemia and 24 patients (60%) were considered non-responders. The values of MELD score were different between groups, responders 9.81+1.25 (IC95%8.56-11.06) vs. non-responders 15.1+2.6 (IC95%12.5-17.7) (p=0.001), also Child-Pugh scores were statistically different 7.18 +0.88 (IC95% 6.3-8.06) vs. 8.87+1.04 (IC95% 7.83-9.91) (p=0.02). In this study patients with a MELD score >12 had an increased risk of adrenal failure (OR 7.22) (IC95% 1.60 a 32.46). Patients with Child class C had an 80% prevalence of adrenal failure.
CONCLUSION: We found that adrenal failure is highly frequent among ambulatory cirrhotic patients in absence of a critical illness, and its frequency is related to hepatic reserve and severity of the disease measured by MELD and Child-Pugh scores.
Disclosure of Interest: None Declared
Keywords: adrenal failure, CIRRHOSIS, Insulin Tolerance Test

P036 HEPATITIS VIRUS B INACTIVE CARRIERS: PREDICTIVE FACTORS OF SPONTANEOUS SEROCONVERSION TO ANTI-HBS

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INTRODUCTION: Patients infected with hepatitis B Virus (HBV) may evolve to an inactive carrier status (IC): low or undetectable DNA (<2000 UI/mL) and normal liver enzyme levels, which predict a good prognosis. The described spontaneous seroconversion is 1-3% per year.
AIMS&METHODS: Evaluation of patients who seroconverted and their predictors. Retrospective cohort study of 157 IC patients followed as Hepatology outpatient for 15 years (1998-2013). Of those, we exclude 33 previously treated with interferon (n=20 reached seroconversion, n=7 with reactivation). In the sample analyzed (n=124), seroconversion to anti-HBs occurred in 15 patients (12.1%, HBVs), 107 patients (86.3%, HBVns) did not have seroconversion and reactivation occurred in 2 patients (1.6%). We used the Chi-square and Mann-Whitney test and logistic regression to compare groups and to evaluate the predictive factors.
RESULTS: Most of the HBVs were male (n=10) and older (60vs52 years,p=0.002) with genotype A and D. In HBVs no patient presented enough viremias to perform genotype and comparing with HBVns was lower (33vs5350UI/mL,p<0.001) and more uniform (p=0.035). The fibrosis documented in liver biopsy was lower in HBVs (p=0.003) but similar when estimated by fibroscan (5.2vs5.5 KPa,p=0.350). No HBVs patient presented complications, evolution to chronic hepatitis, liver cancer or died. The incidence of seroconversion was 1% patients per year. The follow-up time was longer in HBVs (14vs6 years,p=0.003). The predictive factors of seroconversion were older age (OR 1.07,p=0.004), lower viremias (OR 0.99,p=0.049) and longer follow-up (OR 1.23, p=0.002).
CONCLUSION: Patients with lower viremias and those who performed previous treatment with interferon had higher probability of seroconversion. Those who presented reactivation were only detected because the follow-up was keptand they were treated thereafter.
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Disclosure of Interest: None Declared
Keywords: Hepatitis B virus, Inactive carrier, Seroconversion

P037 SIMVASTATIN INHIBITS THE LIPOPOLYSACCHARIDE INDUCED EPITHELIAL-TO-MESENCHYMAL TRANSITION OF HUMAN BILIARY EPITHELIAL CELLS VIA DOWNREGULATION OF TLR4

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INTRODUCTION: The epithelial-to-mesenchymal transition (EMT) of biliary epithelial cells (BECs) plays a role in biliary fibrosis and is promoted by lipopolysaccharide (LPS).
AIMS&METHODS: We studied the effects of simvastatin (1mM) on the EMT of BECs induced by LPS or transforming growth factor-β1 (TGF-β1) and investigated the underlying molecular mechanism. Immortalized normal human cholangiocyte line (H69) were exposed to LPS (2μg/mL) or TGF-β1 (5 ng/ml) for 24 h. The expressions of E-cadherin, vimentin, and toll-like receptor 4 (TLR4) were determined by real-time PCR, Western blotting, and confocal microscopy. The effect of simvastatin on the EMT induced by LPS or TGF-b was determined by changes in the expression of E-cadherin, vimentin, and TLR4 and in cell morphology.
RESULTS: BECs stimulated with TGF-β1 or LPS showed EMT changes that occurred by TLR4 upregulation, including increased vimentin and decreased E-cadherin expression at the mRNA and protein levels. Simvastatin inhibited the EMT induced by TGF-β1 or LPS via TLR4 downregulation, manifested as increased E-cadherin and decreased vimentin and a change from a spindle-like to a round morphology. Therefore, LPS or TGF-β1 promoted EMT, and the treatment of the BECs with simvastatin blocked these changes by inhibition of TLR4.
CONCLUSION: Simvastatin inhibits the LPS induced EMT of cultured human BECs and therefore can be considered as a new agent for the prevention of biliary fibrosis associated with the EMT of BECs.
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Disclosure of Interest: S. M. Park : No Conflict of Interest to declare, N. Kim : No Conflict of Interest to declare, E. J. Lee : No Conflict of Interest to declare, M. Ji : No Conflict of Interest to declare, J.-W. Choi : No Conflict of Interest to declare, Y. Kim : No Conflict of Interest to declare
Keywords: Biliary epithelial cell, Epithelial-to- mesenchymal transition, Lipopolysaccharide, Simvastatin, Transforming growth factor-β1

P038 HEREDITARY TRANSTHYRETIN AMYLOIDOSIS AND COMMON MUTATIONS IN GERMANY

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INTRODUCTION: Hereditary amyloidosis (familial amyloid polyneuropathy) is composed of a heterogenous group of diseases transmitted as an autosomal dominant trait. The most common form is associated with a mutation of the transthyretin gene (TTR) with so far more than 100 TTR-variants known to form amyloid. The varying mutations are correlated with differing clinical manifestations, which is a significant factor for the outcome of liver transplantation – currently the only curative treatment option. This highlights the importance for identifying the specific mutation involved in order to optimize patient selection. Certain high frequency mutations have been reported in countries such as Portugal, Sweden and Japan. Common TTR-variants in Germany have yet to be identified.
AIMS&METHODS: The mutational pattern of TTR-amyloidosis in Germany was studied. 86 patients with TTR-amyloidosis from 46 unrelated families were included. Diagnosis was confirmed histologically. Mutations were identified by genomic DNA extraction from patient's blood and direct sequencing. Patients were examined for clinical signs and symptoms.
RESULTS: Val30Met, identified in 42 patients from 25 families, was found to be the most prevalent mutation. The Gly47Ala variant was found in 19 patients. However 18 of those patients belonged to one family. Patients with a Val30Met mutation were mainly affected by polyneuropathy, with involvment of other organ systems developing later in the clincial course. A primarily cardiac presentation and a later onset of polyneuropathy was associated with the Gly47Ala variant. Furthermore we identified following mutations: Gly47Glu, Leu58His, Ile107Val, Gly53Ala, Asp39Val, Arg34Thr, Val20Ile, Thr60Ala, Thr59Lys and Glu89Gln. 16/86 patients received a liver transplant and 21/86 patients are currently on treatment with Tafamidis. Outcomes are still being followed.
CONCLUSION: This is the first report on mutational analyisis of amyloidogenic TTR-variants in Germany. Similar to Portugal, Sweden and Japan, areas with the largest FAP foci, Val30Met was found to be the most prevalent mutation. Our ongoing analysis with a growing number of FAP-patients may help to categorize the mutational pattern in Germany and may facilitate to identify prognostic factors for patients treated with Tafamidis or liver transplantation.
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Disclosure of Interest: None Declared
Keywords: familial amyloidotic polyneuropathy, hereditary amyloidosis, transthyretin

P039 NUCLEOTIDE-BINDING OLIGOMERIZATION DOMAIN PROTEIN 2 (NOD2/CARD15) MUTATION P.R702W PREDISPOSES TO A FATAL OUTCOME OF SEVERE ACUTE PANCREATITIS

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INTRODUCTION: Acute Pancreatitis is a common non-malignant gastrointestinal disorder and, when severe, burdened with a mortality of up to 20%. Nucleotide-binding oligomerization domain protein 2 (NOD2/CARD15) acts as an intracellular sensor of pathogen-associated molecular patterns (PAMP), namely the peptidoglycan derivate muramyl-dipeptide. Loss-of-function mutations in the NOD2-gene have been identified as a susceptibility factor for several

inflammatory disorders including Crohn's disease, Blau-Syndrome, and early-onset sarcoidosis. We have investigated whether loss-of-function mutations in the NOD2/CARD15-gene affect the risk of developing acute pancreatitis or the patient's survival

AIMS&METHODS: A total of 941 patients with acute pancreatitis were prospectively recruited (761 Europe, 180 US) as well as 926 blood donor controls (662 Europe, 264 US). 59 patients did not survive pancreatitis (overall mortality 6.3%). Genotyping of three established loss-of-function mutations in the NOD2/CARD15 gene. Stratification of patients according to disease severity, complications and survival. A total of 941 patients with acute pancreatitis were recruited (761 Europe, 180 US) as well as 926 blood donor controls (662 Europe, 264 US). 59 patients did not survive pancreatitis (overall mortality 6.3%).

RESULTS: Carrier status for the p.R702W mutation, but not for the p.G908R or the p.L1007fs mutations conferred an increased risk for severe pancreatitis with fatal outcome (11% vs. 4.5%; $p<0.01$ on meta-analysis, odds ratio 2.64; CI 1.35-5.05). Among patients who died from severe pancreatitis 40% carried the p.R702W allele and 16.4% the wild type allele with an odds ratio for death of 2.5 (CI 1.25-5.02) for heterozygous carriers and 9 (CI 0.8-100.93) for homozygous p.R702W carriers. Stratification for different complications found a positive association with multiple organ failure (odds ratio 4.25; CI 1.28-14.3; $p<0.02$) but not for infected necrosis, sepsis of single organ failure.

CONCLUSION: This study identifies the p.R702W mutation in NOD2/CARD15 as a genetic risk factor for developing organ complications and for mortality related to acute pancreatitis. Patients known to carry this allele may require specific measures to prevent multiple organ failure early in their disease process.

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Disclosure of Interest: None Declared

Keywords: Acute Pancreatitis, bacterial infection, disease outcome, Genetic susceptibility

MONDAY, OCTOBER 14, 2013 9:00–17:00

LIVER & BILIARY I – Poster Area

P040 THE HIV ENVELOPE PROTEIN GP120 DIRECT ACTIVATES THE INFLAMMASOME COMPLEX THROUGH THE ENGAGEMENT OF CCR5 IN BOTH HUMAN HEPATIC STELLATE CELLS AND FRESH ISOLATED MONONUCLEAR CELLS

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INTRODUCTION: Patients with HCV/HIV co-infection show a faster progression of hepatic fibrosis and more severe inflammation. The HIV envelope protein gp120 has been previously shown to modulate different aspects of hepatic stellate cells (HSCs) biology, including directional migration and expression of profibrogenic cytokines, at least in part via activation of the chemokine receptor CCR5. Recent work has identified the NALP3 inflammasome as a critical pathway in the generation of proinflammatory signals during liver injury, but no information is available on a possible direct link between the inflammasome and HIV proteins.

AIMS&METHODS: Aim of this study is to elucitated the role of HIV envelope protein gp120 to activates inflammsome components in HSCs and PBMCs. Myofibroblastic HSCs were isolated from normal human liver tissue and cultured on plastic until fully activated. freshly isolated mononuclear cells (PBMCs) were separated from human whole blood. Gene expression was measured by qPCR. Protein IL-1β protein levels were assayed by ELISA. Where reported TAK-779 or α-CCR5 were pre-incubated 1h before treatment.

RESULTS: HSCs or PBMCs were exposed to 500 ng/ml recombinant M-tropic gp120 (CN54) for 2, 8 and 24 hours. A time-dependent, significant up-regulation of ASC and NALP3, components critical for the assembly of NALP3-dependent inflammasome was observed in both cell types. This effect was associated with increased expression of caspase-1, which caused conversion of pro-IL-1β into mature IL-1β, in both HSCs and freshly isolated PBMCs. Remarkably, a significant increase in gene expression of IL-1β was observed in both cell types, together with increased protein levels in the supernatant. Notably, preincubation with TAK779, a CCR5 receptor antagonist, or with neutralizing CCR5 antibody significant abolished gp120-mediated IL-1β expression and production by both HSCs and PBMCs. Furthermore, gp120 induced significant up-regulation of pro-inflammatory chemokine IL-8 expression on HSCs and PBMCs, a potent chemokine. Pre-incubation with TAK-779 prevented, at least in part, the mRNA expression of IL-8 in both cellular model, suggesting that also in this case CCR5 is the mainly receptor involved.

CONCLUSION: HIV-gp120 significantly increased the expression of components of the NALP3 inflammasome in human HSCs and PBMCs, mainly through activation of CCR5. These data identify a novel mechanism by which HIV-gp120 may directly influence hepatic necroinflammation and fibrosis during HCV/HIV coinfection, through increased production of the pro-inflammatory cytokine IL-1β.

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Disclosure of Interest: None Declared

Keywords: HIV gp120, Human hepatic stellate cells, inflammasome

P041 AGING INCREASES THE PROGRESSION OF DIET-INDUCED STEATOHEPATITIS BY PROMOTING LCFA UPTAKE

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INTRODUCTION: Obesity and aging are associated with a state of chronic low-grade inflammation, however little is known regarding the mechanisms that trigger the development of non-alcoholic-fatty-liver-disease(NAFLD) in aging.

AIMS&METHODS: To link lipid availability at the cell membrane to inflammation, we hypothesized that a diet-induced increase in fatty acid uptake may underlie the development of hepatic inflammation in obesity and aging.

Mice:To investigate this, we subjected young and aged C57Bl6 mice on a chow diet. Also young and aged mice were fed a high-fat diet (HFD, 60% kcal fat (Research Diets) for 12 weeks.

Human liver biopsies:

- Young ($\leq$ 38 years; n=16) and old ($\geq$ 50 years; n=14) patients with histologically normal liver (NL)
- Young ($\leq$ 42 years; n=11) and old ($\geq$ 52 years; n=15) patients diagnosed with non-alcoholic steatosis (NAS)
- Subjects matched in terms of sex distribution, BMI, insulin resistance, and histological grade of steatosis
- Patients with alcohol intake $>$ 20 g/d, those with NASH, hepatitis B, C and HIV infection, and taking chronic medications were excluded

Analyses: Livers were dissected for gene expression (RT-PCR), immunoblot analyses and histological assessment of steatosis and CD36 expression

RESULTS: As a result, CD36, a long-chain-fatty-acid (LCFA) uptake protein, was increased in livers of aged normal-diet mice compared to young mice. This result correlated with normal-liver (NL) of patients above 50 years age compared to patients below 38 years age. Conversely, CD36 expression was increased at the plasma membrane of hepatocytes of non-alcoholic steatosis (NAS) above 50 years age in opposition to both NAS young and normal liver, confirming an important role for CD36 in the development of NAFLD. Moreover, high-fat feeding in aged mice severely augmented hepatic CD36 expression, TG accumulation and inflammatory signaling.

CONCLUSION: Our data suggest that a diet-induced increase in hepatic CD36 expression may underlie the development of hepatic inflammation in obesity and aging by promoting LCFA uptake.

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Disclosure of Interest: None Declared

Keywords: Aging, CD36, Inflammation, nafld, Obesity, steatosis

P042 PIOGLITAZONE-ALOGLIPTIN COMBINATION THERAPY IMPROVES LIVER STEATOSIS IN MURINE NONALCOHOLIC FATTY LIVER DISEASE MODEL COMPLICATED WITH TYPE 2 DIABETES MELLITUS

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INTRODUCTION: Accumulation of visceral fat and insulin resistance are major pathophysiologic abnormalities that occur in patients with nonalcoholic liver disease (NAFLD) and type 2 diabetes mellitus (T2DM), with thiazolidinedione and DPP-4 inhibitor known to be effective for several T2DM pathophysiologic processes. However, since the effectiveness of each drug individually for NAFLD is not adequate, their combination is speculated to provide effective therapy.

AIMS&METHODS: We investigated the effectiveness of combination therapy with thiazolidinedione and DPP-4 inhibitor in NAFLD model mice complicated with T2DM. Twelve-week-old male KK-A^y/TaJcl (KK-A^y) mice were given a choline-deficient (CD) diet supplemented with 0.02% pioglitazone (PIO) and/or 0.03% alogliptin (ALO) for 8 weeks. We assessed biochemical parameters, pathological changes, and hepatic mRNA levels in association with fatty acid metabolism.

RESULTS: Severe hepatic steatosis developed in KK-A^y mice given the CD diet. Although hepatic inflammation and fibrosis were not obvious in these mice, hepatic mRNA levels of monocyte chemoattractant protein-1 (MCP-1) and α-smooth muscle actin (α-SMA) were increased as compared to KK-A^y mice fed a normal diet. Hepatic steatosis was improved in mice that received the CD diet supplemented with PIO and/or ALO, as the level of adiponectin in serum increased and that of triglyceride decreased with that supplementation. Insulin resistance and serum HDL-C level were also improved by supplementing the CD diet with PIO and ALO. Furthermore, the hepatic mRNA levels of carnitine palmitoyltransferase-1a (CPT-1a) and superoxide dismutase-1 (SOD-1) were increased with ALO supplementation of the CD diet, as was Thr172 phosphorylation of AMP-activated protein kinase alpha in the liver. In contrast, the hepatic mRNA levels of sterol regulatory element-binding protein-1c (SREBP-1c) and fatty acid synthase (FAS) were decreased by supplementing with PIO.

CONCLUSION: PIO plus ALO combination therapy improved liver steatosis in NAFLD model mice complicated with T2DM. Also, PIO decreased hepatic mRNA levels for fatty acid synthesis, while ALO increased hepatic CPT-1a mRNA levels for fatty acid β oxidation. Our results suggest that ALO, similar to adiponectin, promotes CPT-1a expression through Thr172 phosphorylation of AMPKα.

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Disclosure of Interest: None Declared

Keywords: alogliptin, nonalcoholic fatty liver disease, pioglitazone, type 2 diabetes mellitus

P043 NECROPTOSIS IN PRIMARY RAT HEPATOCYTES AND IN PATIENTS WITH CHRONIC LIVER DISEASE

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INTRODUCTION: Regulated necrosis or necroptosis is arising as a prominent pathological feature of inflammation-driven liver diseases. Bile acids are well-established modulators of inflammatory and cell death processes in the liver, which may play a role in disease pathogenesis and progression.
AIMS&METHODS: The aim of this study was to investigate the role of necroptosis in liver cell injury in vitro and in patients. HepG2 cells and primary rat hepatocytes were incubated with hydrophobic toxic bile acids, free fatty acids, or tumour necrosis factor(TNF)-alpha/cycloheximide, in the presence or absence of pan-caspase inhibitor, zVAD-fmk, and/or with therapeutic ursodeoxycholic acid (UDCA) or necroptosis inhibitor necrostatin-1. Cytotoxicity and caspase-3/7 activity were assessed at 24 h. High-mobility group box 1 protein (HMGB1), extracellular marker of necrosis, was analysed by immunoblotting. Expression of receptor interacting protein 3 (RIP3) was evaluated by immunofluorescence in cultured cells and patient liver tissue.
RESULTS: In HepG2, cell death induced by toxic bile acids was completely abolished by inhibition of caspases. Conversely, toxic bile acids, free fatty acids or TNF-alpha plus zVAD-fmk induced caspase-3-independent cell death in primary rat hepatocytes, which was inhibited by both necrostatin-1 and UDCA; cellular leakage of HMGB1 and RIP3 expression followed the same trend, confirming the occurrence of necroptosis. Finally, RIP3 was strongly expressed in the liver of patients with chronic liver disease, irrespective of etiology.
CONCLUSION: Overall, our results suggest that cell death induced by toxic bile acids, free fatty acids or TNF-alpha shifts from apoptosis to regulated necrosis when caspase activation is blocked in primary rat hepatocytes. In contrast, UDCA effectively prevented caspase-dependent and -independent cell death. Necroptosis may play a role in the pathogenesis and progression of inflammation-driven liver disease and should be regarded as a potential therapeutic target.
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Keywords: Chronic liver disease, Inflammation, Necroptosis, Necrostatin-1, RIP3, Ursodeoxycholic acid

P044 DEOXYCHOLIC ACID INHIBITS NF-KB-MEDIATED ACTIVATION OF MIR-21 IN PRIMARY RAT HEPATOCYTES, PROMOTING APOPTOSIS IN A DOSE-DEPENDENT MANNER

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INTRODUCTION: Cytotoxic bile acids, such as deoxycholic acid (DCA), are usually associated with several liver and gastrointestinal disorders. We have recently shown that bile acids modulate microRNA (miRNA/miR) expression in the liver and that DCA inhibits miR-21 expression in hepatocytes.
AIMS&METHODS: We aimed to clarify the mechanisms by which DCA modulates the miR-21 pathway and contributes to apoptosis in primary rat hepatocytes. Primary rat hepatocytes were incubated with 25-100 μM DCA for 4 to 48 h. Cell death, viability and caspase-3 activity were determined by the ApoTox-Glo™ Triplex Assay. miR-21 expression was evaluated by qRT-PCR. Programmed cell death 4 (PDCD4) and phosphatase and tensin homolog (PTEN), two miR-21 targets, as well as NF-κB, IκB and caspases were analysed by immunobloting. NF-κB activation was evaluated using a specific luciferase assay, and by analysing NF-κB subcellular localization. For functional studies, miR-21 and NF-κB were modulated using specific genetic and pharmacologic inhibitors/activators.
RESULTS: Our results show that the miR-21 pathway is modulated by DCA in a dose-dependent manner. 100 μM DCA significantly induced caspase-2/-3 activities and apoptosis, while reducing cellular viability ($p<0.05$). Moreover, miR-21 expression was inhibited ($p<0.01$) with a concomitant increase in PDCD4 and PTEN proteins ($p<0.05$). In addition, DCA inhibited NF-κB expression and activity ($p<0.05$), NF-κB/IκB ratio ($p<0.05$) and NF-κB nuclear localization ($p<0.05$), in a similar pattern to miR-21 inhibition. Importantly, miR-21 overexpression impaired the ability of DCA to induce PDCD4 and PTEN expression, as well as apoptosis ($p<0.05$), but had little effect on NF-κB activation. Finally, after ectopic activation of NF-κB, DCA was less capable of repressing miR-21, and its cytotoxicity was decreased ($p<0.05$). NF-κB inhibition by BAY 11-7085 had opposite effects ($p<0.05$).
CONCLUSION: Dose-dependent modulation of the miR-21 pathway by DCA correlates with its effects on apoptosis. DCA significantly inhibits miR-21 expression, resulting in increased PDCD4 and PTEN protein levels, as well as caspase activation and apoptosis. Importantly, DCA appears to modulate the miR-21-dependent pro-apoptotic pathway *via* inhibition of NF-κB activation. A better understanding of the mechanisms by which DCA impacts on cell death may allow for the development of new therapeutic tools to treat apoptosis-related pathologies.
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Disclosure of Interest: None Declared
Keywords: Apoptosis, Deoxycholic acid (DCA), miR-21, NF-kB

P045 EFFECTS OF S-ADENOSYLMETHIONINE ON THE BIOLOGICAL BEHAVIOR OF ACTIVATED HUMAN HEPATIC STELLATE CELLS

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INTRODUCTION: Liver fibrosis is a common wound-healing event in response to a variety of chronic liver diseases, which characterizes the deposition of extracellular matrix (ECM) mainly originating from hepatic stellate cells (HSCs) that have transdifferentiated into myofibroblastlike cells (MFB). Previous studies have demonstrated that SAM could inhibit HSCs activation and reduce liver fibrosis.
AIMS&METHODS: To investigate the effects of S-Adenosylmethionine (SAM) on the proliferation, adhesion, migration, invasion and apoptosis of activated human hepatic stellate cells (HSCs) and to explore the relevant potential mechanisms.
Human HSCs LX-2 were cultured with SAM. The proliferation and adhesion were detected by CCK-8. Cell cycle distribution and apoptotic rate were analyzed by flow cytometry, and cell migration and invasion were tested by transwell assay. The expression of Rac1, MMP-2 and Cyclin D1 was identified by real-time PCR or western blotting, and activated Rac1 was detected by GST pull-down assay. The activity of MMP-2 and MMP-9 were analyzed by Substrate Zymography.
RESULTS: The proliferation of LX-2 cells was inhibited by SAM, exhibiting a dose-dependent manner. SAM retarded the LX-2 cells at the S stage and cell apoptotic rate induced by SAM was remarkably increased. SAM decreased the adhesion, migration and invasion of LX-2 cells. The mRNA of Cyclin D1 was up regulated and expression of α-SMA was inhibited by SAM. The expression and activation of Rac1 in LX-2 cells were significantly suppressed by SAM. In contrast, the activity of MMP-2 and MMP-9 was enhanced by SAM. SAM attenuated the up-regulated expression of Smad3/4 and Rac1 induced by TGF-β1.
CONCLUSION: SAM inhibits the proliferation, adhesion, migration and invasion of LX-2 cells in vitro probably via attenuating the expression and activation of Rac1 and up regulating MMP-2, MMP-9 and Cyclin D1 expression, which possibly provide a molecular basis for potential application of SAM in the therapy of liver fibrosis.
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Disclosure of Interest: None Declared
Keywords: biological behavior, hepatic stellate cells, liver fibrosis, S-Adenosylmethionine

P046 PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA INHIBITS MOUSE LIVER REGENERATION AFTER PARTIAL HEPATECTOMY VIA THE HGF/C-MET ERK1/2 PATHWAYS

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INTRODUCTION: Peroxisome Proliferator-Activated Receptor gamma (PPARγ) is a nuclear receptor demonstrated to play an important role in various biological processes. However, the role of PPARγ on liver regeneration remains unclear and controversial. Aim of this study was to determine the effect of PPARγ on liver regeneration upon partial hepatectomy in mice and to elucidate the underlying molecular mechanisms.
AIMS&METHODS: Eight- to ten-week-old female C57BL/6J mice were subjected to 2/3 partial hepatectomy by removal of the left and median lobe of the liver. Before surgery, mice were either treated with the PPARγ agonist rosiglitazone, the PPARγ antagonist GW9662 alone or in combination with the c-met inhibitor SGX523. Serum and tissue specimens were harvested and parameters, such as liver-to-body-weight ratio, serum transaminases, alkaline phosphatase, glucose, cholesterol, triglyceride levels, were assessed. To elucidate liver regeneration and hepatocyte proliferation, immunohistochemical analysis of PPARγ, Ki67 and PH3 was performed. Components of the PPARγ-specific signaling pathway during liver regeneration were identified by western blot (PPARγ, STAT3, CyclinD1, HGF, c-met, and ERK1/2) or RT-PCR (Tnfα and Il-6).
RESULTS: Our results indicate that liver regeneration after 2/3 partial hepatectomy is being inhibited by rosiglitazone and accelerated by PPARγ antagonist GW9662. Inhibition of c-met abrogates GW9662-induced liver regeneration and hepatocyte proliferation. In addition, STAT3 was found to be phosphorylated shortly after partial hepatectomy while hepatic cyclin D1 expression was delayed in rosiglitazone-treated mice. Similarly, HGF, phosphorylated c-met and phosphorylated ERK1/2 protein levels were significantly down-regulated after rosiglitazone treatment with oppositional tendency after GW9662 treatment.
CONCLUSION: These data support the concept that PPARγ does inhibit liver growth and hepatocellular proliferation by inhibition of the HGF/c-met ERK1/2 pathways. These pathways may represent potential targets during liver regeneration in response to liver disease and these findings could thus impact on the future development of molecular therapies in patients with liver disease.
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Disclosure of Interest: None Declared
Keywords: liver regeneration, partial hepatectomy, PPAR-γ

P047 DO GLP-1 ANALOGUES AFFECT EARLY PHASE OF LIVER REGENERATION AFTER PARTIAL HEPATECTOMY IN RATS?

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INTRODUCTION: GLP-1 is an incretin hormone known for its proliferative and antiapoptotic effects on pancreatic β-cells. These effects are currently routinely used in the therapy of diabetes mellitus. From literature data, it is evident that GLP-1 affects liver functions and liver metabolism. But very little is known about its ability to modulate liver regeneration and proliferation of hepatocytes.
AIMS&METHODS: To determine the effect of GLP-1 analogues, exenatide (Ex4) and liraglutide, on liver regeneration and selected metabolic parameters in a model of 2/3 partial hepatectomy in male Wistar rats. Animals (264 ± 17 g) were divided into 6 groups ($n = 6$). On the first day, two doses of either GLP-1 analogues (Ex4 10 nmol/kg, liraglutide 0.75 mg/kg), or equivalent amount of saline (S) were injected intraperitoneally. On the second day, the animals were submitted to the 2/3 partial hepatectomy (PHx) (1) or sham laparotomy (LAP). The third dose of analogues or saline was injected immediately after the surgery. The animals were sacrificed 24 h after the surgery and the intensity of liver regeneration and selected metabolic parameters were evaluated.
RESULTS: In the rats with PHx, both analogues compared to saline controls decreased bromodeoxyuridine (BrdU) labeling ($p < 0.001$) - marker of S-phase activity. Liraglutide compared to Ex4 caused even lower BrdU labeling ($p < 0.001$). This effect was reflected in a decreased liver DNA content in the rats with PHx receiving liraglutide compared to both Ex4 ($p < 0.001$) and saline group ($p < 0.001$). Laparotomy groups had no significant difference in BrdU labeling and DNA content. Liraglutide treatment in contrast to both saline and Ex4 treatment led after any surgery (PHx, LAP) to an increase in serum urea (LAP-LIRA vs LAP-S: $p < 0.001$; LAP-LIRA vs LAP-Ex4: $p < 0.001$; PHx-LIRA vs PHx-S: $p < 0.05$; PHx-LIRA vs PHx-Ex4: $p < 0.01$). Ex4 did not exert any effect on serum urea. Liraglutide also reduced serum total biliribin ($p < 0.05$), serum triacylglycerols ($p < 0.001$) and liver cholesterol content ($p < 0.05$) in the rats with PHx. Analogues had no significant effect on body weight, liver weight, serum creatinine, serum total cholesterol, serum activities of AST, ALT and ALP, liver triacylglycerols content and mitochondrial respiration.
CONCLUSION: Our results suggest that GLP-1 analogues, exenatide and liraglutide, significantly affect (diminish) early phase of liver regeneration after 2/3 partial hepatectomy and that liraglutide effect is even more pronounced. Interesting finding is an effect of liraglutide on a serum urea level, without a concomitant effect on a serum creatinine.
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Disclosure of Interest: None Declared
Keywords: exenatide, GLP-1, liraglutide, liver regeneration, metabolic parameters, partial hepatectomy

P048 FGF SIGNALING PATHWAY IS PRINCIPAL REPRESENTATIVE FOR HEPATIC SPECIFICATION

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INTRODUCTION: Bmp and Fgf signaling pathways have remarkable role in regulation of hepatic specification based on the investigation from in vitro tissue explant and cell implantation, but additional research for demonstration of this hypothesis especially genetic research is indispensable. Consequently, utilization of zebrafish study model with overexpression of dominant-negative forms of Bmp or Fgf receptors can reveal the main mechanism. Additionally, genetic analysis demonstrated this point that, Foxa gene can regulate the competence of endodermal cells regarding to hepatic inductive signals [1]. Bmp and Fgf signaling have an additional role in the morphogenetic outgrowth of the hepatic endoderm regulation specially, FGF8 [2]. Altogether, this information suggests that, Bmp and Fgf signaling pathways are essential for hepatic specification/gastrulation and lacking of this pathways is observable in defects related to liver specification.
AIMS&METHODS: Embryos were heat shocked for 25 minutes at 40°C and 15 minutes at 37°C via transferring them into a prewarmed plate. Zebrafish line has utilized which overexpress dominant-negative *Bmpr1a*. In this experiment, hemizygous embryos were effortlessly distinguished and has tested for presence of the *hsp70:bmp2b* transgene by PCR technique. In situ hybridizations technics has performed through the *pdx1*, *prox1* and *foxa3* probes [3, 4].
RESULTS: Results reveal the important role of Bmp signaling in hepatoblast specification when was blocked at 30 hpf. In this period, *prox1* expression was reduced compared with wild-type. In embryos with blocked Bmp signaling, *gata6* expression was significantly decreased in the liver. In the heat-shocked hemizygous embryos, *hhex* expression was absent suggesting that Fgf signaling after 16 hpf is essential for hepatoblast specification.
CONCLUSION: Based on the in vitro tissue explant methodologies, Fgf signaling plays two main roles in early liver development. Genetic analysis have demonstrated that, Gdf6a and Alk8 is also expressed in the endoderm at the time of specification. This data have been confirmed the Fgf signaling role together with Bmp and TGF-β in the hepatoblast specification.
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Disclosure of Interest: None Declared
Keywords: Fibroblast growth factor, Liver, Regeneration

P049 GENE EXPRESSION PROFILING AND SECRETOME ANALYSIS DIFFERENTIATE ADULT-DERIVED HUMAN LIVER STEM/PROGENITOR CELLS AND HUMAN HEPATIC STELLATE CELLS

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INTRODUCTION: Adult-derived human liver stem/progenitor cells (ADHLSC) are isolated after primary culture of liver parenchymal fraction. The cells are currently developed as potential alternative to hepatocyte for liver cell based therapies. ADHLSC are of fibroblastic morphology and exhibit a hepatomesenchymal phenotype. Hepatic stellate cells (HSC) isolated from the liver non-parenchymal fraction present a comparable morphology as ADHLSC and are described as liver stem/progenitor cells.
AIMS&METHODS: In the current work, we strived to extensively compare both cell populations and to propose tools demonstrating their singularity.
ADHLSC and HSC were isolated from the liver of four different donors, expanded in vitro and followed from passage 5 until passage 11. Cell characterization was performed using immunocytochemistry, flow cytometry, and gene microarray analyses. The secretion profile of the cells was evaluated using Elisa and multiplex Luminex assays.
RESULTS: Both cell types expressed α-smooth muscle actin, vimentin, fibronectin, CD73 and CD90, in accordance with their mesenchymal origin. Microarray analysis revealed significant differences in gene expression profiles. HSC present high expression levels of neuronal markers as well as cytokeratins. Such differences were confirmed using immunocytochemistry. Both cell types also display distinct secretion profiles as ADHLSC highly secreted cytokines of therapeutic and immuno-modulatory importance, like HGF, interferon gamma and IL-10. Finally, ADHLSC and HSC behave differentially when incubated with specific growth factors involved in hepatogenic differentiation.
CONCLUSION: Our study demonstrates that, even sharing several phenotypic characteristics, ADHLSC and HSC are distinct liver fibroblastic cell populations as they exhibit significant different intrinsic gene expression and secretion profiles.
This study confirms the promising future of ADHLSC in liver regenerative medicine.
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Disclosure of Interest: None Declared
Keywords: hepatic stellate cells, Liver, progenitor cells, secretome

P050 IMPROVED OUTCOME OF HEPATOCYTE TRANSPLANTATION WITH PHARMACOLOGICAL ENHANCEMENT OF DONOR CELL ENGRAFTMENT

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INTRODUCTION: Hepatocyte transplantation is a safe and effective method to treat inherited metabolic liver diseases. However, it only partially corrects the underlying metabolic disorder and therefore limits its application. The number of hepatocytes that engraft during a single procedure is insufficient to fully correct the metabolic disorder, highlighting the importance to enhance donor cell engraftment. Potential barriers that prevent a sufficient engraftment include hepatic sinusoidal endothelial barrier, low sinusoidal blood flow, instant blood mediated immune response and Cyclooxygenase (COX)-mediated inflammation.
AIMS&METHODS: In the present study, we tested the hypothesis that pharmacological modulation ofthese barriers should enhance hepatocyte engraftment in mice and rats, and augment the metabolic benefit of hepatocyte transplantation in the UDP-UGT-1A1 deficient Gunn rat model of Crigler-Najjar syndrome type 1 (CN1). In a first series of experiments recipient C57/Bl6 mice were treated with Dextransulfate, Nitroglycerin, Naproxen, Cyclophosphamide or hepatic X-irradiation (HIR) prior transplantation of hepatocytes from (Rosa)26 C57BL/6 mice. Morphometric quantification of hepatocyte engraftment was performed three days after transplantation. For the second set of series, recipient Gunn rats were pretreated with Cyclophosphamide, Naproxen or Cyclophosphamide+Naproxen prior to transplantation of hepatocytes from

congeneic normal Wistar-RHA rats. Serial serum bilirubin levels were followed for six months.
RESULTS: Recipient mice: Cyclophosphamide, HIR, and Naproxen increased hepatocyte engraftment by 97%, 92% and 52%, respectively compared to control ($p<0.001$). No significant effect was observed with Dextransulfate or Nitroglycerin. Gunn rat recipients: Mean reduction of serum bilirubin levels four months after transplantation compared with sham-treated controls were: (a) no drug: 32.0%, (b) CPA: 54% (c) Naproxen: 44%, (d) CPA + Naproxen 68%.
CONCLUSION: Hepatocyte engraftment in mice was significantly increased by a single preparative dose of HIR, Cyclophosphamide or Naproxen. In recipient Gunn rats Cyclophosphamide or a combination of Cyclophosphamide and Naproxen doubled the hypobilirubinemic effect of hepatocyte transplantation. These findings may be relevant in hepatocyte transplantation-based therapies of CN1 and other liver-based inherited metabolic disorders.
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Disclosure of Interest: None Declared
Keywords: cell engraftment, crigler-najjar-syndrome, hepatocyte transplantation, hereditary liver disease, liver, rat

P051 PREVALENCE OF METABOLIC SYNDROME IN A PROSPECTIVE STUDY OF PATIENTS REFERRED TO A SECONDARY HOSPITAL FOR HYPERFERRITINEMIA

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INTRODUCTION: Nearly 25% of adult population in the western countries have the metabolic syndrome. Hyperferritinemia (HF) is frequently present in patients with this clinical entity.
AIMS&METHODS: To study the prevalence of the metabolic syndrome in patients referred for hyperferritinemia to a secondary hospital.
January to December 2010; prospective study; included 132 consecutive patients, aged 18 years or older, with HF ($> 200\mu g$ / L women,$> 300\mu g$ / L men); Laboratory: serum ferritin, transferrin saturation, serum iron, transaminases, glucose, cholesterol, triglycerides, HBV, HCV, HFE mutations. Blood pressure, weight, height, BMI, alcohol intake, hypertension and/or dyslipidemia treatment, were determined; Radiology: abdominal ultrasound, MRI to determine LIC (liver iron concentration);
The Metabolic syndrome was defined (1) by the presence of waist circumference $\geq$94cm men; $\geq$80 cm women (abdominal obesity). And two of the following factors: Triglycerids$\geq$150 mg/dL or treatment for this dislypemia; HDL $<$40 mg/dL women, $<$50 mg/dL men or treatment for this dislypemia; glucose$\geq$100 mg/dL or type 2 diabetes; hypertension: Blood Presure $\geq$130 mm Hg/ $\geq$85 mm Hg or treatment for elevated blood pressure.
RESULTS: 24 women, 108 men, mean age 54.42 SD 13.47 (range 23-83), Weight: 83.17 SD 15.86 (43-137); Height: 175.28 SD 55.20 (146-186), BMI: 28.80 SD 3.96 (17-39); Waist circumference: 80/97; 17/17 women $\geq$80 cm; 63/80$\geq$94 cm; blood pressure: systolic 139.26 mm Hg, SD 19,93 (100-190); dyastolic 81.19 mm Hg, SD 11,03 (50-105).
AST 41 IU/L, SD 35.33 (4-230); ALT 55.61 IU/L, SD 47.22 (12-371); GGTP 94.83 IU/L, SD 141.47 (8-806); AP 73.32 IU/L, SD 20.71 (34-160); Bilirrubin 0.74 mg/dL, SD 0.38 (0.15-2.71); albumin 4.60 g/L, SD 0.32 (3.50-5.50).
Glucose 106.95 mg/dL, SD 25.03 (73-272); triglycerids 151.75 mg/dL, SD 93.71 (40-477), cholesterol 201.71, SD 42.92 (96-338), HDL 54 mg/dL, SD 17.08 (28-162);
Ferritin 579.54 ng/mL SD 296.575 (206-1668), TRS 43.87% SD14.09 (12-95); Fe 134 µg/dL, SD 49.68 (55-322). Ferritin $>$ 1000, 12 patients (9%), overweight (BMI $\geq$ 25) 48.31%, obesity (BMI$\geq$ 30) 40.44%, 89% overweight or obese.
Hypertension treatment in 50 patients; dyslipidemia treatment in 35. Metabolic syndrome: 44/80 men (55%) and 10/17 women (59%) presented MS. Some of the results of the study were presented last year in UEGW 2012.
CONCLUSION: Metabolic syndrome is associated with more than 50% of patients with hyperferritinemia and is one of the main causes of a raised serum ferritin.
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Disclosure of Interest: None Declared
Keywords: hyperferritinemia, liver diseases, metabolic syndrome

P052 HEPATIC STEATOSIS: PREVALENCE AND PREDICTIVE FACTORS IN A PORTUGUESE POPULATION

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INTRODUCTION: Hepatic steatosis is a multifactorial condition extremely prevalent worldwide. Recently several predictive risk factors have been identified.
AIMS&METHODS: To evaluate hepatic steatosis prevalence and to determine predictive factors for its presence.
Prospective study of 288 assymptomatic individuals submitted to abdominal ultrasound for hepatic steatosis (according to the hepatorenal index), visceral and subcutaneous fat evaluation. Laboratorial evaluation, dietary questionnaires and alcohol consumption (cut-offs: men 30g/women 20g) were also evaluated in the same day. Hepatic steatosis divided in 2 groups: 1) without steatosis/mild steatosis; 2) moderate/severe.
After a descriptive analysis a comparative univariate analysis was performed. Data stratified by gender.
Tests: Chi-square and Man-Whitney Wilcoxon [$p < 0.05$].
RESULTS: Global hepatic steatosis prevalence was 57,6%. In our sample alcohol consumption was not statistically related to hepatic steatosis. After exclusion of the patients with alcohol consumption above the *cut-off* 195 individuals (64,4% male) were evaluated. From those, 37 had moderate/severe steatosis and 92 mild/no hepatic steatosis. Univariate analysis revealed that visceral obesity (RR=3.03; $p<0.001$), BMI$\geq$25 (RR=5.08;$p<0.001$), waist circumference $\geq$94 in men and $\geq$80 in women (RR=5.15; p=0.003) and fasting glucose$>$100 (RR=3.51; $p<0.001$) are risk factors for hepatic steatosis; Gamma-glutamyltransferase ($p<0.001$) and triglycerides (p=0.003) medians were significantly greater in patients with moderate/severe hepatic steatosis.
CONCLUSION: In our sample hepatic steatosis prevalence was 57,6%. Visceral obesity, BMI, waist circumference, fasting glucose, gamma-glutamyltransferase and triglycerides positively related to hepatic steatosis in individuals without excessive alcohol consumption.
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Disclosure of Interest: None Declared
Keywords: steatosis, visceral obesity

P053 FATTY LIVER ÍNDEX – VALIDATION AND ITS APLICATION IN NON-ALCOHOLIC FATTY LIVER DISEASE AND VISCERAL OBESITY

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INTRODUCTION: Although abdominal ultrasound is considered a valid option, liver biopsy is still the *gold-standard* to diagnose hepatic steatosis. Fatty Liver Index[1] (FLI) – a score calculated with triglycerides, body mass index, waist circunference and gamma-glutamyltransferase – revealed a adequate accuracy in the prediction of hepatic steatosis.
AIMS&METHODS: To validate FLI in our sample. Evaluate FLI applicability to predict visceral obesity and hepatic steatosis in individuals without excessive alcohol consumption.
Prospective analysis of assymptomatic individuals submitted to abdominal ultrasound with visceral fat measurement and hepatic steatosis classification according to the hepatorenal índex. Laboratorial evaluation, dietary questionnaires and alcohol consumption (cut-offs: men 30g/women 20g) were obtained. Original *cut-offs* for Fatty Liver Index. Visceral obesity cut-off according to Ribeiro et al. Hepatic steatosis divided in 2 groups: 1) without steatosis/mild steatosis; 2) moderate/severe.
Statistics: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under receiving operator curve (AUROC).
RESULTS: 288 individuals (mean age 60.8 years, 53.8% male), from which 29.0% presented moderate/severe hepatic steatosis. FLI revealed good accuracy to predict hepatic steatosis (73%, specificity 77%, NPV 87%; PPV 57%, AUROC: 0.80); FLI also revealed adequate accuracy to predict visceral obesity (sensitivity 68%, specificity 77%, NPV 83%; PPV 60%; AUROC 0,81). Applying FLI to predict non-alcoholic fatty liver its accuracy is still adequate (sensitivity 68% specificity 81%; PPV 61%, NPV 86%; AUROC: 0,80.)
CONCLUSION: In our sample Fatty Liver Index revealed good accuracy to predict hepatic steatosis and visceral obesity.
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Disclosure of Interest: None Declared
Keywords: steatosis, visceral obesity

P054 ENDOSCOPIC DUODENAL-JEJUNAL BYPASS LINER RAPIDLY IMPROVES NONALCOHOLIC FATTY LIVER DISEASE PLASMA PARAMETERS

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INTRODUCTION: Bariatric surgery reduces obesity, type 2 diabetes, and non-alcoholic fatty liver disease (NAFLD). Recently, the duodenal-jejunal bypass liner (DJBL) has been developed to mimic the bypass component of the gastric bypass in a minimally invasive way. Previous studies with this device have revealed improvement of obesity and type 2 diabetes. We investigated the effect of DJBL treatment on plasma parameters reflecting NAFLD.
AIMS&METHODS: Seventeen subjects with obesity and type 2 diabetes were prospectively included and received the DJBL for 24 weeks. Before, during, and after DJBL treatment, plasma aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyltransferase (γ-GT), albumin, caspase-

cleaved cytokeratin-18 (CK-18), and liver fatty acid-binding protein (L-FABP) were determined.
RESULTS: At baseline, patients had a BMI of 37.0±1.3kg/m^2. AST, ALT, and γ-GT were elevated (AST:35±4IU/L, ALT:54±5IU/L, and γ-GT:66±14IU/L). Caspase-cleaved CK-18 and L-FABP concentrations were 214.4±35.6U/L and 29.3±2.6ng/mL, respectively. Three months after initiation of DJBL treatment, BMI had decreased to 33.6±1.2kg/m^2 ($p<0.05$). Plasma levels of all NAFLD-related parameters had also decreased (AST:28±3IU/L, ALT:32±2IU/L, γ-GT:44±7IU/L, caspase-cleaved CK-18:140.6±16.3U/L, and L-FABP: 18.2±1.5ng/mL, all $p<0.05$). A further decrease of ALT and γ-GT was observed at month six (ALT:28±2IU/L and γ-GT:35±5IU/L) and BMI had decreased to 32.9±1.2kg/m^2 (all $p<0.05$). AST, caspase-cleaved CK-18, and L-FABP levels had stabilized (AST:23±2IU/L, caspase-cleaved CK-18:149.2±23.1U/L, L-FABP:20.2±1.6ng/mL, all p=ns). At month twelve, ALT, γ-GT, and caspase-cleaved CK-18 levels were still diminished (ALT:37±3IU/L, γ-GT:42±5IU/L, and caspase-cleaved CK-18:124.5±12.5U/L, all $p<0.05$). BMI was 34.3±1.5kg/m^2 ($p<0.05$). AST and L-FABP levels had returned to baseline levels (34±3IU/L and 29.5±3.1ng/mL respectively, both p=ns).
CONCLUSION: Weight loss induced by proximal small intestinal exclusion through DJBL positively affects NAFLD.
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Keywords: nafld, obesity, plasma parameters

P055 ENERGY METABOLISM IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE IN COMBINATION WITH ARTERIAL HYPERTENSION

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INTRODUCTION: The increase cases of non-alcoholic fatty liver disease (NAFLD) due to the growth of patients with abdominal obesity. It belongs to the key factors in the development of metabolic syndrome, which is characterized by high rates of cardiovascular disease, particularly arterial hypertension (AH).
AIMS&METHODS: The aim of this study was to investigate violations of energy metabolism in patients with NAFLD/AH.
The study involved 182 patients with NAFLD/AH. For verification of diagnosis the following examinations were done: clinical-laboratory, instrumental, biochemical parameters of liver function, immune status assessment, Fibro-Max test. ATP, ADP and AMP were determined in erythrocytes of peripheral blood by thin-layer chromatography. Cell energy charge (EC) formula EC= ATP/(ADP+AMP) and key enzyme total activity of anaerobic glicolysis – serume lactatdehydrogenase (LDH), were calculated also.
RESULTS: Abdominal obesity was observed in all studied patients. Average BMI was 33,21±1,25 kg/m^2 . Changes of energy metabolism in examined patients consisted in ADP and ATP level reducing, which are the main indicators of energy supply for cells. ATP content in erythrocytes of the patients was 2,6 times lower than in normal group ($p<0,001$). AMP level was increased, which could indicate by ATP decay. It's known that ATP content takes a principal role in aerobic metabolism, while the LDH concentration, as LDH_{4-5}, is an indicator of anaerobic metabolism. LDH content increased in the blood of patients with NAFLD/AH. Exactly the LDH_{4-5} activity was increased, that characterizes anaerobic processes, while the activity of LDH_{1-2} was reduced ($p<0,05$). Coefficient LDH_{1-2}/LDH_{4-5} was reduced in patients with NAFLD/AH 3,8 times, which indicates on significant predominance of anaerobic glycolysis over oxidative phosphorylation ($p<0,001$). EC – 2,4 times lower in patients group than in normal one, which indicates on decreased energy supply of the body ($p<0,001$).
CONCLUSION: The results of the study showed that patients with NAFLD combined with AH had changes in energy metabolism, characterized by decreased ATP level, LDH activity increased and its spectrum shifted, which is caused by reducing the proportion of aerobic fraction – LDH_{1-2} and increasing proportion of anaerobic fraction – LDH_{4-5}. All of this indicates on less effective way of energy metabolism (anaerobic glycolysis) in patients with NAFLD/AH.
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Disclosure of Interest: None Declared
Keywords: Arterial hypertension, Energy metabolism, NAFLD

P056 CLINICAL APPROACH IN WILSON DISEASE USING LEIPZIG SCORING SYSTEM

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INTRODUCTION: Wilson disease (WD) is an autosomal recessively inherited disorder of the copper accumulation and toxicity. It's treatable, if diagnosed early. The recognition is clear in typical clinical presentations. Unexplained liver tests abnormalities are a diagnostic challenge and require more examinations.
AIMS&METHODS: *Aim:* To investigate the clinical features and diagnostic possibilities in WD.
Material and methods: Sixty three patients with WD were analysed (22 female, 41 male), from June 2010 to March 2013, aged at the end of evaluation between 18 and 64 years. Leipzig scoring system was used for diagnosis.
RESULTS: The patients were followed up from 3 months to 21 years from diagnosing. The diagnosis was based on clinical suspicion and findings, parameters of copper metabolism, ultrasonography, ophthalmological examination, liver biopsy, MRI, DNA analysis and assessment of the Leipzig scoring system at the final evaluation. Twenty seven patients (42,9%) were with liver disease alone, thirty one (49,2%) - with hepatic and neurological presentation, three with neurological features without signs of a liver injury and two asymptomatic patients. The hepatic presentation was as follows: steatosis (4/63), hepatitis 38,1% (24/63), cirrhosis in 47,6% (30/53), acute liver failure after a discontinuation of the treatment (2/63), hepatocellular carcinoma in one cirrhotic patient. The average level of the ceruloplasmin was 0,137 g/l. 24-hour urine copper was increased. D-penicillamine challenge test showed mean value 17,69 μmol/24 h of urine copper excretion. According to the Leipzig diagnostic criteria 55(87,3%) patients had a score ≥4 (max.12). Eight patients had score 3, but the exclusion of another etiology and the clinical course of the disease confirmed the diagnosis. 23(36,5%) patients had Kayser-Fleischer ring and 4 – sunflower cataract. Liver biopsy was performed in 23 patients, with rodamine positive staining in 9. DNA analysis was done in 54 patients and were found mutations in 26(48,1%).
CONCLUSION: WD is a treatable inherited disorder. It has to be considered in the liver diseases to prevent the delay of the recognition and the progression of the copper metabolic disorder. Our experience confirms that the Leipzig scoring system with a combination of clinical symptoms, laboratory parameters of copper metabolism, genetic testing and liver biopsy is useful for diagnosing of WD in the clinical practice.
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Disclosure of Interest: None Declared
Keywords: diagnostic approach, leipzig scoring system, wilson disease

P057 GLYCYRRHIZIN ALLEVIATES STEATOSIS AND INDUCES THE PRODUCTION OF REGULATORY T CELLS (TREGS) THAT ATTENUATES NONALCOHOLIC STEATOHEPATITIS (NASH) PROGRESSION

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INTRODUCTION: NASH has been confirmed as the rate-limiting step of non-alcoholic fatty liver disease (NAFLD) progressing to cirrhosis and becomes the main cause of obvious cirrhosis. Recently, high-fat diet (HFD)-induced steatosis was thought to be associated with the depletion of hepatic Tregs and the adoptive transfer of Tregs decreased inflammation in HFD-fed mice. Glycyrrhizin (GL), a natural triterpene in clinical treatment of patients with chronic liver disease, can significantly reduce free fatty acid (FFA)/ HFD induced hepatic lipotoxicity.
AIMS&METHODS: For induction of NASH, mice were fed with a methionin–choline-deficient (MCD) diet for 8 weeks. Control mice received a standard diet containing 10% fat. All diets were γ-irradiated. Development of liver injury was followed by intraperitoneal administration of GL or saline two times a week for the last 4 weeks. We evaluated the therapeutic effects of GL on the progression of NASH, and then the hepatic and splenic CD4+T cells phenotypes were analyzed by flow cytometry. Purified splenic CD4+CD25+T cells from MCD-fed mice or GL treated MCD-fed mice were collected and co-cultured with splenic CD4+CD25-T (Teffs) cells from control mice to explore whether GL can modulate the functions of splenic nTregs and the production of iTregs. Furthermore, specific inhibitor of PPAR-γ (GW9662) or agonist of PPAR-γ was also added along with GL treatment to observe whether the effects of GL were dependent on PPAR-γ signaling.
RESULTS: GL alleviated MCD-induced liver injury, by decreasing ALT and AST levels to normalization nearly in time and dose dependent manners, along with reduced hepatic inflammatory cell infiltrations and lipid overloading. Besides, GL altered the cytokines secretion and proportion of hepatic and splenic CD4+T cells showing the prevalence of Tregs in MCD-fed mice. GL promoted the apoptosis of hepatic and splenic Th1 and Th17 cells but inhibited which of Tregs. PPARγ was enhanced correlating with serum CD4+CD25+T cells positively by GL and in vitro experiment, PPARγ signaling participated in the GL-induced proliferation of splenic nTregs, as well as the enhanced inhibition functions on Teffs. Furthermore, GL promoted the production of iTregs and altered the apoptosis and cytokines secretion of iTregs.
CONCLUSION: GL, which has excellent anti-inflammatory characteristics, amelioration of hepatic injury and definite lipidlowering properties, may alleviate the progression of NASH. The therapeutic effects of GL partly contribute to the induction of Tregs and enhanced modulatory functions of Tregs, and furthermore, PPAR-γ signaling may be involved in the modulatory mechanism of GL.
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Disclosure of Interest: None Declared
Keywords: Glycyrrhizin, NASH, PPAR-γ, Tregs

P058 EFFECT OF GLP-1 ON DIET INDUCE NON-ALCOHOLIC FATTY LIVER DISEASE IN RATS

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INTRODUCTION: The aims of the study were to investigate the effect of glucagon-like peptide-1 (GLP-1) on diet induce non-alcoholic fatty liver disease (NAFLD) in rats.
AIMS&METHODS: A total of 30 male rats were randomly divided into three groups. Each group contained 10 rats, in which they were fed with normal diet (ND), high-fat diet (HFD), high-fat diet with intraperitoneal injection of liraglutide (HFD+GLP-1, first 12 weeks with HFD, later 4 weeks with liraglutide) for 16 weeks respectively. After 16 weeks' feeding, the rats were killed ethically and their blood samples and liver tissues were collected. The levels of

aminotransferase (ALT), aspartate-aminotransferase (AST), triglyceride (TG), total-cholesterol (TC) were detected by biochemistry automatic analyzer. The levels of superoxide dismutase (SOD) and malondial-dehyde (MAD), tumor necrosis factor-a (TNF-a), JNK-1 and P-JNK1 in liver homogenates were detected by RIA, ELISA and Western blot respectively.
RESULTS: The body weight, liver index, serum and liver homogenates levels of TG, TC, ALT and TG, TC, MAD, TNF-a in the HFD group were apparently higher than those in the normal group, while the level of SOD decreased significantly. When compared with the HFD group, the body weight, liver index, serum and liver homogenates levels of TG, TC, ALT and TG, TC, MAD, TNF-a in the HFD+GLP-1 group decreased apparently, while the level of SOD increased. ($P < 0.05$)
CONCLUSION: Liraglutide (GLP-1) has an anti-inflammatory effect on NAFLD rats, which is conducted by decreasing blood lipid and liver homogenate inflammation index level.
Disclosure of Interest: None Declared
Keywords: GLP-1, non-alcoholic fatty liver disease

P059 THE URSODEOXYCHOLIC ACID AS A MONOTHERAPY OF PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE COUPLED WITH METABOLIC SYNDROME

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INTRODUCTION: Non-alcoholic Fatty Liver Disease (NAFLD) is associated with Metabolic Syndrome (MS) frequently and has a tendency to increase in the last few years. NAFLD associated with MS is characterized by hepatic steatosis, inflammation with hepatocyte injury (ballooning) with or without fibrosis, lipid metabolism disorders, abdominal obesity, gastrointestinal dysfunctions and gastrointestinal microbiota lesions. It is need to optimize the therapy of NAFLD associated with MS in that hepatobiliary system is involved in pathological process in the majority of patients.
AIMS&METHODS: The aim was to assess efficacy of ursodeoxycholic acid in treatment of patients with NAFLD associated with MS. 21 patients with NAFLD associated with MS were observed (average age was 41±4,6 years). All patients were treated by ursodeoxycholic acid (UDHA) in dose 15 mg/kg twice a day during 2 months. The serum chemistry, analysis of body mass composition (determination of fat mass, water mass and dry body mass by bioimpedance analysis) and analysis of intestinal microbiota composition were performed before and after the treatment course. The intestinal microbiota composition was assessed by examination of stool culture and by using special microbial identification system based on studying of minor fatty acid profiles in blood samples (gas chromatography and mass spectrometry). Statistical analysis was performed with Wilcoxon test.
RESULTS: Alanine aminotransferase (ALT) rate was reduced by 32,3% (p=0,004), aspartate aminotransferase (AST) rate was reduced by 13,5% (p=0,080), γ glutamyl transpeptidase (γGT) rate was reduced by 5,6% (p=0,070) and lipids metabolism markers had uptrend to decrease after course of the UDHA treatment. Body mass was decreased after treatment in 62% of patients mainly due to fat mass reduction. The reduction of the mean body mass by 0,8 kg ($p = 0,008$) and reduction of the mean fat mass by 0,6 kg ($p = 0,005$) were observed in average in the patients after UDHA therapy. The quantity of *Lactobacterium spp*., *Bifidobacterium spp*. and *Enterococcus spp*. were significantly increased (p=0,006, p=0,005 and p=0,004 respectively) in examination of stool culture after course of UDHA treatment. Analysis of microbial identification by gas chromatography – mass spectrometry was demonstrated prominent elevation of endotoxins amount and total microbial quantity in blood samples before and significant decrease of these indexes after UDHA treatment.
CONCLUSION: The UDHA has beneficial effects on blood chemistry indicators, composition of body mass and intestinal microbiota in patients with NAFLD associated with MS.
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Disclosure of Interest: None Declared
Keywords: Metabolic Syndrome, Non-Alcoholic Fatty Liver Disease, ursodeoxycholic acid

P060 THE PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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INTRODUCTION: According to several epidemiological studies in 24-88% of patients with diabetes exhibit nonalcoholic fatty liver disease (NAFLD). The problem of development and progression of NAFLD at the present time is one of the most important and urgent problems of internal medicine, a general medical and social importance for the leads to poor quality of life, disability and premature death. However, data on the prevalence referred to in the literature is not always true, because in order to diagnose nonalcoholic fatty liver disease, a liver biopsy is needed each of the examined patients, given the danger and pain of this procedure is not always available. Data on research-based on avtopsies was not found.
AIMS&METHODS: The aim of the study was to research the prevalence of NAFLD by histological examination of liver deaths, suffering from type 2 diabetes
The results of the liver histological in patients with type 2 diabetes mellitus who died from various causes in hospitals from 2000 to 2010 were examined. The age of patients ranged from 23 to 87, mean age 65,37 ± 0,66, the men were 93 women 183.For quality control protocols were processed autopsies in 2002 patients who died from various causes in hospital, but not suffering from diabetes. Among them were men 38, women 62. The average age of 69,84 ± 1,94. Standard wiring used drugs with staining sections with hematoxylin-eosin.
RESULTS: NAFLD frequency and its clinical forms in patients with type 2 diabetes often prevailed among the patients in the control group. According 65,6% in patients with type 2 diabetes, and 23% for the control group. Steatosis in patients of the main group was 24.6%, control,- only 14%. Steatohepatitis was diagnosed in 37,3% of patients with type 2 diabetes, while only 16% of patients without diabetes. Fibrosis, 3,6% in the main group and in 2% of the control group.
CONCLUSION: Since the study was based on prevalence avtopsies based protocols, indicating that diagnostic accuracy and eliminates the possibility of unreliable diagnosis, data on the prevalence NAFLDin patients with type 2 diabetes (65,6%) can be considered reliable and informative.
Disclosure of Interest: None Declared
Keywords: Diabetes mellitus type 2, nonalcoholic fatty liver disease

P061 MONITORING OF LIVER FUNCTION IN PATIENTS WITH FATTY LIVER DISEASE IN COMBINATION WITH CORONARY HEART DISEASE AND TYPE 2 DIABETES MELLITUS

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INTRODUCTION: Nonalcoholic fatty liver disease (NAFLD) is diagnosed in a 72% of coronary artery disease and type 2 diabetes patients. However, more attention is paid to early diagnosis of NAFLD by using either special sets of designed formulas with biochemical parameters or respiratory tests with 13C-methacethine (C13-MBT)
AIMS&METHODS: The aim of the study was to examine the liver detoxification function by comparing a 13C- methacethine breath test, with a Forns formula and with liver transaminases in patients with coronary heart disease and type 2 diabetes mellitus in combination with nonalcoholic fatty disease. The study involved 52 patients with type 2 diabetes and coronary artery disease (male 24, female 28, mean age 60,94 ± 0,82 years). Biochemical tests were taken- total bilirubin, AST, ALT, AST/ALT and lipidogram. Studies for the presence of fibrotic changes were conducted by calculating a Forns formula: 7,811-3,131 × ln (platelets) + 0,781 × ln (GGTP) + 3,467 × ln (age) - 0,014 × (cholesterol, mg/dl). To determine the degree of liver injury all patients underwent a 13C-MBT.
RESULTS: Groups were formed based on the ultrasound information. Among them, 20 patients were found with steatosis, 22 - with steatohepatitis, 5 - with fibrosis and in 5 patients NAFLD was not found. Forns formula clearly showed presence of fibrotic changes at a value > 5.26 in patients with fibrosis. A strong negative relationship was marked between the Forns formula and ALT levels (r = -0,944) and bilirubin (r = -0,967) in fibrosis group. As a result of 13C-MBT, patients without NAFLD indexed antitoxic liver function beyond the norm (20,44 ± 0,66%), with steatosis and steatohepatitis- a moderate reduction in liver function, respectively, (10,94 ± 1,22%) and (11,69 ± 0,48%), with fibrosis meant a marked reduction in the liver antitoxic function(6,32 ± 1,47%). Analyse of liver transaminases and data-13C MBT showed a higher metabolic rate correlated with higher cumulative doses 40 and 120 minutes and normal ALT levels ($p < 0,05$). A reduction in the rate of metabolism and cumulative doses 40 and 120 minutes was observed with increasing levels of ALT ($p < 0.05$).
CONCLUSION: When monitoring the hepatic function in patients with coronary artery disease and type 2 diabetes it is desirable to include data from the ultrasound of the liver, the evaluation a 13C-methacetin test which shows a pathological changes in the early stages of NAFLD and positively correlated with the Forns formula which result more than 4.25 diagnose the fibrosis as clinical stage NAFLD. It is likely to find fibrosis of the liver when Forns formula is over 4.25, 13C-breath test at least 10%, lower levels of ALT and bilirubin.
Disclosure of Interest: None Declared
Keywords: 13C- methacetine breathe test, Fibrosis, Forns formula, nonalcoholic fatty liver disease, steatohepatitis, steatosis

P062 METABOLIC GENE POLYMORPHISMS, INTERACTION WITH ENVIRONMENTAL FACTORS AND NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

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INTRODUCTION: Nonalcoholic fatty liver disease (NAFLD) is the most common cause of non-viral chronic liver disease. Even with the large prevalence, only few percentage of subjects with NAFLD develop nonalcoholic steatohepatitis (NASH), the most severe form. The oxidative stress and its interplay with genetic and environmental factors; seems to be the most important step for explaining the progression of liver disease.
AIMS&METHODS: Aim of our study was to evaluate the role of polymorphisms of metabolic genes (GSTT1, GSTM1, SULT1A1, CYP2E1 and 1A1) in NAFLD subjects and the effect of interactions of these genetic variants with environmental risk factors and clinical variables. 294 NAFLD cases and 359 controls were eligible for the statistical analysis. For each subject lifestyle and physical data through a structured questionnaire, venous blood sample for peripheral lymphocytes DNA extraction. A subgroup of NAFLD patients performed underwent liver biopsy. Multiplex-PCR for GSTM1 and GSTT1 null alleles and RFLP-PCR for SNPs analysis of SULT1A1, CYP2E1 and 1A1 were used respectively.

RESULTS: A statistically significant interactions were observed for: GSTM1 and fruit intake ($p<0.001$); GSTT1 and fruit intake ($p<0.001$); CYP1A1 and fruit intake ($p<0.001$); CYP2E1DraI and fruit intake ($p=0.001$); SULTI1A1 and fruit intake ($p<0.001$); GSTT1 and grilled meat or fish intake ($p=0.002$); CYP1A1 and grilled meat or fish intake ($p=0.011$); SULTI1A1 and grilled meat or fish intake ($p=0.002$). CYP1A1 and fruit consumption ($p<0.001$; CYP2E1DraI and fruit consumption ($p=0.001$). Statistical evidence of a difference between subjects with the wild-type form and those carrying a mutation (or with the null form) emerged with regards to: GSTT1 and obesity ($p=0.037$), CYP2E1PstI and diabetes ($p=0.028$); CYP2E1DraI and ALT ($p=0.021$); SULT1A1 and glycaemia ($p=0.025$), HOMA ($p=0.036$), total cholesterol ($p=0.047$), triglycerides ($p=0.027$). We also found a correlation between GSTM1 and inflammation at liver biopsy ($p=0.003$).
CONCLUSION: Some interaction between SNPs of metabolic genes and environmental factors may identify those subjects with potential evolutive NAFLD.
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Disclosure of Interest: None Declared
Keywords: Gene polymorphism, nonalcoholic fatty liver disease

P063 MECHANISMS OF MYOCARDIAL STRESS DEPENDENT ON NON-ALCOHOLIC FATTY LIVER DISEASE: A ROLE FOR FGF21?

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INTRODUCTION: Cardiac events are more common than liver events in causing morbidity and mortality in patients with non-alcoholic fatty liver disease (NAFLD). NAFLD is the hepatic component of the metabolic syndrome an umbrella of pathological conditions including insulin resistance and diabetes. NAFLD encompasses a spectrum of diseases ranging from simple hepatic steatosis to non-alcoholic steatohepatitis (NASH).
AIMS&METHODS: Increased risk of cardiovascular mortality in hepatic steatosis is found in absence of insulin resistance and diabetes in patients, and the mechanisms underlying the onset of left ventricular stress in this context are unknown. We studied these mechanisms in a model of NAFLD/NASH without insulin resistance/diabetes: the MCD mice fed a methionine choline deficient diet that lacks methionine and choline, essential factors for very low-density lipoprotein production.
RESULTS: We found that in the MCD mouse model of NAFLD an altered expression of anti-oxidant genes (SOD1/2, HIF1/2, catalase) was present in the myocardium. Circulating levels of fibroblast growth factor 21 (FGF21), an endocrine factor secreted by the liver that favour glucose metabolism, were increased in MCD mice. FGF21 role in heart is unknown. We found that FGF21-null mice had an increased heart weight and cardiomyocyte area and developed dilatation and cardiac dysfunction in response to isoproterenol infusion.
CONCLUSION: We propose that an increase in liver-generated FGF21 might be a compensatory mechanism of the body to protect against heart oxidative and hypertrophic stresses generated by NAFLD in absence of other metabolic risk factors.
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Disclosure of Interest: None Declared
Keywords: cardiovascular diseases, growth factors, NAFLD, NASH, oxidative stress

P064 WILSON DISEASE: INDICATIONS FOR LIVER TRANSPLANTATION AND RESULTS

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INTRODUCTION: Wilson's disease (WD) is a hereditary disorder associated with decreased biliary excretion of copper, leading to its accumulation in various organs, particularly liver, brain and cornea. Patients often present with liver disease, varying from asymptomatic elevation of aminotransferases or serum bilirubin to acute liver failure (ALF) or liver cirrhosis. Liver transplantation (LT) is often necessary in the presence of ALF or end-stage liver disease (ESLD).
AIMS&METHODS: Between March 1995 and March 2013 1420 LT were carried out in 1233 patients at ''Centro Hepatobiliar e de Transplantação'' of the Curry Cabral Hospital. For this study, we only considered patients with WD. Overall survival was calculated using the Kaplan-Meier method.
RESULTS: Sixteen LT were performed in 12 patients with WD. The ALF was the indication for LT in 6 patients (3 men). One was being investigated for liver disease of unknown etiology and another had a diagnosis of WD for 13 years but had suspended the medication on her own. The mean age of patients transplanted for ALF was 22.8 years. Two patients died early after LT due to acute renal failure and cytomegalovirus infection. One patient was re-transplanted 3 times – due to hepatic artery thrombosis, chronic rejection and hepatic artery thrombosis with multiple liver abscesses. Another patient had to be re-transplanted because of ischemic cholangitis.
The ESLD was the indication for LT in 6 cases (4 men). The mean age at diagnosis was 19.3 years and at the time of transplantation was 30.3 years. The Child-Pugh score was B in 2 and C in 4 patients. Five of the six patients were under medical treatment until transplantation. The mean hospital stay after LT was 36 days.
In the 12 patients transplanted for WD there was no late mortality. The overall survival post-LT was 83.3% at 1, 5 and 10 years and these patients are clinically well and none developed any sign of recurrence.
CONCLUSION: Without treatment, the WD is progressive and invariably fatal. When diagnosed in a timely manner, patients often respond to medical therapy. However, the WD can manifest itself as ALF, observed in 5 patients in our series. In patients diagnosed with WD under medical therapy, there may be a rapid deterioration of liver function with ALF precipitated by discontinuation of therapy, which occurred in 1 patient in our hospital. In cases that do not respond to treatment and progress to ESLD, the LT has a prominent position. Overall survival after transplantation was similar to other series in the literature. WD is a rare indication for LT but when indicated this procedure allows for a good long-term survival.
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Disclosure of Interest: None Declared
Keywords: Liver transplantation, Wilson Disease

P065 CHANGING TRENDS IN LOW-RANGE LIVER ENZYMES ELEVATION; IS NON-ALCOHOLIC FATTY LIVER DISEASE THE ELEPHANT IN THE ROOM?

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INTRODUCTION: There is very little information regarding the most prevalent causes of elevation of liver enzymes in our population and usually is necessary to perform a number of tests and several visits to the specialist to reach a diagnosis. For these reasons, we designed a protocol to streamline the evaluation of patients presenting such elevations in a single-act office visit.
AIMS&METHODS: From March of 2008 until June of 2010 we performed a descriptive study of all patients presenting with an incidental elevation of liver enzymes who were referred by their primary care physicians. At the time of referral, all of these patients had a complete biochemistry analysis, and they got an abdominal ultrasound scan the same day of the office evaluation by the hepatologist.
RESULTS: A total of 427 patients were included. A definitive diagnosis was reached in the first referral visit in 322 (74%) of the cases. The most common cause of transaminase elevation (40%) was Non-Alcoholic Fatty Liver Disease (NAFLD), followed by alcohol intake (17%) and HCV infection (13%). Also NAFLD was the most common cause of isolated GGTP elevation (30%) and combined elevation with AP (21%). A self-limited elevation was seen in 9% and we could not identify a definite cause in 11% of cases.
CONCLUSION: NAFLD was the most common cause of elevated liver enzymes.
The single-act office visit has proven quite efficient, yielding a diagnosis in the majority of cases.
Transaminases elevation must be confirmed prior to initiating a more thorough work-up.
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Disclosure of Interest: None Declared
Keywords: liver enzymes, single-act office visit, non-alcoholic fatty liver disease, transaminases

P066 WILSON'S DISEASE: LONG-TERM OUTCOME SEEMS TO BE INFLUENCED BY PRESENTATION FORM

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INTRODUCTION: Wilson's disease (WD) is a rare inborn disease related to copper storage, leading to liver cirrhosis and neuropsychological deterioration. Limited data are available on the long-term outcome of patients with WD.
AIMS&METHODS: A retrospective analysis of 35 consecutive patients with WD followed in our unit between 1980 and 2011 was performed, to determine clinical presentation and long-term outcome. Four patients were excluded due to absence of clinical data on admission or during follow-up.
RESULTS: Thirty-one patients were included, 58.1% females, mean age at diagnosis 18.4±8.2 years (22.1 in male, 15.5 in female, $p=0.025$), with mean follow-up

of 17.9±11.3 years. Clinical presentation: 32.3% hepatic (H) (mean age: 17.1 years), 25.8% asymptomatic (mean age: 13.6 years), 24.6% neuro-hepatic (NH) (mean age: 25.2 years) and 19.4% neurological (N) (mean age: 19 years). The patients with neurological symptoms were significantly older at the onset of symptoms than patients with hepatic symptoms. Kayser-Fleischer rings (KF rings) and mutations of the coding region of ATP7B were detected in 58.6% and 83% of patients, respectively. Liver biopsy was performed in 74.2% of patients. Histological analysis revealed: steatosis in 44.4%, fibrosis in 100% and cirrhosis in 47.8%.
During follow-up, 6 (19.4%) patients died, 4 (12.9%) required liver transplantation and 10 (32.3%) had clinical decompensation. No patient developed hepatocellular carcinoma.
Clinical presentation positively correlated with WD progression: NH with death (p=0.003), H with liver transplantation (p=0.007) and H+NH with clinical decompensation (52.9% vs. 7.1%, p=0.005). After initiating treatment, most patients (68%) experienced a stable or improved course of disease. Absence of response to treatment was associated with progression to clinical deterioration (p=0.030) and death (p=0.002). No association was found between the degree of fibrosis or steatosis and WD progression.
CONCLUSION: WD is a rare but important cause of chronic liver disease, with generally favourable outcomes for patients who respond to initial therapy. However, patients with hepatic symptoms (hepatic or neuro-hepatic presentation) were associated with a worst prognosis.
Disclosure of Interest: None Declared
Keywords: Clinical presentation, follow-up, Prognostic factors, WILSON'S DISEASE

P067 EFFECT OF THE NAFLD LIFESTYLE EDUCATIONAL PROGRAM (NALEP) IN THE MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE IN CLINICAL PRACTICE

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INTRODUCTION: Non-alcoholic steatohepatitis (NASH) is a chronic and progressive liver disease strongly associated with the metabolic syndrome (MS). The only established therapies are life style intervention and treatment of concomitant metabolic disorders like dyslipidemia and diabetes.
AIMS&METHODS: Patients seen at the Vienna NAFLD outpatients clinic were offered the possibility to join a monthly NAFLD lifestyle educational program (NALEP) especially developed for patients with NAFLD including a detailed nutritional education. Patients were also advised to engage in physical training at least 3 times a week for 30-60 minutes. We prospectively analyzed the data available up to six months after the first intervention.
RESULTS: To date, 48 patients participated in NALEP. Follow-up data are available of 35 patients (17 female, 18 male). Median age was 51 years (26-75), median BMI 29 (21-40). Liver biopsy within 6 months before NALEP was performed in 21 patients (NASH n=19). In fifteen patients NAFLD was diagnosed by ultrasound, presence of MS and/or elevated transaminases after exclusion of other liver diseases.
Thirteen patients had previously or newly diagnosed type 2 diabetes and all patients dyslipidemia. If needed, patients were treated simultaneously with metformin (n=11, 6 de novo) or statins (n=21, 12 de novo).
Median follow-up (FU) was 4.3 months. 35 patients had a FU of 3 months (FU3), 18 also of 6 months (FU6). BMI significantly decreased at FU3 and FU6 (-5%/-3kg;p=0.001). Serum liver parameters decreased and normalized in 78% within the observation period from baseline to FU3 and FU6 (median AST 49/32/34 IU/L; ALT 75/45/45 IU/L; GGT 176/90/75 IU/L; p=0.01). Serum cholesterol and triglycerides also significantly declined from median 213 and 206 mg/dl, respectively at baseline, to 186 and 130 mg/dl at FU 6 (p=0.05).
CONCLUSION: Lifestyle intervention with close and continuous follow-ups effectively improved body weight, liver enzymes and metabolic parameters in patients with NAFLD. In clinical practice this could reduce the number of patients in need of drug interventions. Although a sustained effect has to be proven by longer follow up.
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Disclosure of Interest: None Declared
Keywords: Diet, Fatty Liver, Lifestyle Intervention, NAFLD, NASH, Therapy

P068 DISCONTINUING TERLIPRESSIN POST BAND LIGATION: A FEASIBLE OPTION

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INTRODUCTION: Terlipressin is recommended therapy for 3 to 5 days in the management of bleeding esophageal varices. This is an expensive drug with inherent side effects.
AIMS&METHODS: The aim of this study was to determine the feasibility of administering terlipressin therapy only prior to band ligation in managing bleeding esophageal varices.
61 patients presenting with esophageal variceal bleeding received terlipressin 2mg intravenous bolus followed by 1mg 6 hourly until undergoing endoscopic band ligation. The patients were monitored for the occurrence of re-bleeding for 5 days.
RESULTS: All patients received terlipressin until undergoing endoscopic band ligation. 12 (19.6%) patients underwent band ligation after a single 2mg dose of terlipressin, 15 (24.5%) patients after two doses (6 hours therapy), 10 (16.3%) patients after 3 doses (12 hours therapy), 5 (8%) patients after 4 doses (18 hours therapy), 5 (8%) patients after 5 doses (24 hours therapy) and 14 (22.9%) patients after more than 5 doses (more than 24 hours therapy). Band ligation was done within 12 hours in 37 (60.65%) patients and within 24 hours in 47 (77%) patients. Endoscopy was delayed beyond 24 hours in 14 (22.9%) patients. This delay was due to Sengstaken Blakemore tube placement, encephalopathy and blood transfusion requirements. Rebleeding was seen in 3 (4.9%) patients (p-value >0.05. No statistical significance). Repeat endoscopy on patients who rebled showed ulcers on sites of band ligation with no active ooze in 2 patients. These were managed conservatively. One patient had varices with red signs which required repeat band ligation. Two patients died. One secondary to hepatorenal syndrome and another due to persistent encephalopathy. No drug related adverse effects were noted.
CONCLUSION: Terlipressin is an important part of management of bleeding esophageal varices. Once definitive endoscopic therapy in the form of band ligation is performed, terlipressin may be safely discontinued. This can result in reduction in cost of treatment with no significant increase in morbidity and mortality.
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Disclosure of Interest: None Declared
Keywords: Band ligation, Portal Hypertension, Terlipressin, Variceal bleeding

P069 CIRRHOTIC CARDIOMYOPATHY?,INVESTIGATION OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION (LVDD) WITH ECHOCARDIYOGRAPHY AND QT PROLONGATION WITH ECG

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INTRODUCTION: Cirrhosis is a controversial issue whether it is caused by cardiomyopathy. Echocardiography in patients with cirrhosis of left ventricular diastolic dysfunction (LVDD) and electrocardiogram (ECG) QT prolongation in cirrhotic cardiomyopathy looking to investigate.
AIMS&METHODS: A prospective cross-February-July 2012 period, the cirrhotic patients and the control group were investigated by echocardiography, left ventricular diastolic dysfunction. LVDD was assessed by echocardiography by experienced cardiologists.
RESULTS: In 34 of 60 patients with cirrhosis (56%) were male, mean age 51.78 $\pm$ 15.6 years (range 19-84), 26 serving as the control group, 14 (54%) were male, mean age 51.8 $\pm$ 8.4 years (range, 33 -67), respectively. 33 cirrhotic patients (55%) compensated, and 27 (45%) was decompensated. Patients, 31 of whom (52%) child A, 22 of them (36%) child B, 7 of them (12%) were C child. Etiology 24 (40%), hepatitis B, 14 (23%), cryptogenic, 12 (20%), hepatitis C, 4 (6%) Wilson cirrhosis, hepatitis delta 3, one each cardiogenic, chronic biliary, congenital hepatic fibrosis, respectively. Cirrhotic group, 22 (37%) patients in the control group 4 (15%) patients, QT prolongation ($p < 0.05$). 12 patients with compensated liver cirrhosis (36%) of QT prolongation, whereas patients with decompensated liver cirrhosis in 10 (37%) of QT prolongation ($p > 0.5$). Cirrhotic group, 27 (45%), higher than in the control group 16 (61%) patients had LVDD ($p < 0.05$). 13 patients with compensated liver cirrhosis (40%) of the cases LVDD, whereas 14 patients with decompensated liver cirrhosis (52%) patients had LVDD, the difference was not statistically significant ($p > 0.5$).
CONCLUSION: In cirrhotic patients, QT prolongation, more than 2 times higher than the control group, whereas no significant difference was observed among those with compensated and decompensated. In cirrhotic patients, left ventricular diastolic dysfunction in the control group were determined, to a lesser extent, compensated and decompensated There was no significant difference between those. Whether or not lead to cirrhosis, cardiomyopathy, the more different parameters, the more number of patients investigated.
Disclosure of Interest: None Declared
Keywords: cardimyopathy, cirrhosis

P070 A PROSPECTIVE LONG TERM FOLLOW-UP OF IDIOPATHIC NON-CIRRHOTIC PORTAL HYPERTENSION: SLOW CIRRHOSIS OR NO CIRRHOSIS?

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INTRODUCTION: Idiopathic portal hypertension (IPH) is characterized by a long-standing non-cirrhotic portal hypertension(NCPH) because of the intrahepatic block of small portal vein branches. NCPH is due to various causes that generally are extrahepatic, involving the prehepatic or the post hepatic circulation. INCPH includes Extra Hepatic Portal Vein Obstruction (EHPVO) and Non-Cirrhotic Portal Fibrosis (NCPF). The natural history of INCPH is not clear
AIMS&METHODS: Aim: To determine prospectively the changes in the portal venous system in patients with NCPH.
Method: Patients with a diagnosis of NCPF and EHPVO registered since 2001 were serially followed at an yearly interval for changes in liver size, its echotexture, and in the intra and extrahepatic portal venous system. Baseline

demographic details, LFT, and co-morbid illness including virological profile were noted. Patients with co-morbid illness and those with known etiology of cirrhosis were excluded from the study.
RESULTS: There were 34 patients with NCPF (M: F 1:1.8) and 30 patients with EHPVO (M: F ratio 1.6:1). The mean age was 24.9 yrs and 41.2 yrs respectively. During follow up, 20 out of 34 and 16 out of 30 patients with NCPF and EHPVO respectively had no progression of disease. 14 patients with NCPF progressed to cirrhosis over a mean period of 5.21 years. Eight patients developed ascites and required diuretics. 14 patients with EHPVO progressed to NCPF over the mean period of 8.6 years, 12 patients further progressed to cirrhosis over a mean period of 5.1 years. Overall 40% of patients with EHPVO progressed to cirrhosis over a mean period of 13.7 years.
CONCLUSION: INCPH is a spectrum wherein EHPVO progresses to NCPF and further to cirrhosis over a period of 13.7 years at least in a proportion of patients. Conversely, identifying these changes may suggest to the clinicians the need to work-up a patient for portal hypertension.
Disclosure of Interest: None Declared
Keywords: EHPVO, INCPH, NCPF

P071 CAN TRANSIENT ELASTOGRAPHY,FIB-4, FORNS INDEX AND LOK SCORE PREDICT ESOPHAGEAL VARICES IN HCV RELATED CIRRHOTIC PATIENTS?

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INTRODUCTION: HCV is the most common cause of chronic liver disease in Egypt. Gastroesophageal varices are present in approximately 50% of patients with liver cirrhosis. The current guidelines recommend screening of all cirrhotic patients by endoscopy, but repeated endoscopic examinations are unpleasant for patients and cause significant burden to the endoscopy units and costs to the country.
AIMS&METHODS: The aim of this study is to evaluate liver stiffness measurement (LSM) using transient elastography (TE), Fib-4, Forns Index as potential noninvasive predictors of esophageal varices in patients with HCV related liver cirrhosis. This prospective study included fifty patients with HCV-related liver cirrhosis. All studied subjects underwent routine laboratory tests, TE and gastroduodenoscopy. Serum fibrosis scores were then calculated. The diagnostic performance of the methods were assessed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, likelihood ratios and receiver operating characteristic curves.
RESULTS: The four predictors (LSM, FIB-4, Forns Index and Lok Score) demonstrated statistically significant correlation with the grade of esophageal varices (P values; 0.000, 0.000, 0.003 and 0.008 respectively). For prediction of large varices (grade2, 3), LSM showed the highest accuracy (80%) with a cutoff of 22.4KPa at an AUROC of 0.801. Its sensitivity was 84%, specificity 72%, PPV 84% and NPV 72%.The diagnostic accuracy of FIB-4, Forns Index and Lok Score were 70%,70% and76% respectively at cutoffs of 3.3, 6.9 and 0.7 respectively. The PPV of FIB-4, Forns Index and Lok Score were 79%, 75% and 77% respectively. Adding TE to each of the other diagnostic indices increased their sensitivities and specificities but LR+ or LR- did not show much improvement in combined results. Indeed, this combination decreased the LR- in all tests.
Table. Accuracy of diagnosis of large esophageal varices by serum fibrosis scores alone and after combining LSM with serum fibrosis scores.

Serum fibrosis scores alone						In combination with LSM			
	Best cutoff	sensitivity	specificity	LR+	LR-	sensitivity	specificity	LR+	LR-
Fib-4	≥3.3	72.9%	66.7%	2.2	0.42	100%	56%	2.2	0
Forns	≥6.9	78%	56%	1.8	0.39	97%	44%	1.76	0.07
Lok score	≥0.7	87.5%	55.5%	2	0.23	97%	44%	1.76	0.07

CONCLUSION: Noninvasive predictors can restrict endoscopic screening to patients presenting a high probability of having large esophageal varices. This is useful in clinical settings where resources are limited. Identifying patients at risk of having large esophageal varices may help in early management decisions and justifying health resource allocation.
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Disclosure of Interest: D. Omran : None, E. Medhat : None, M. El Beshlawey : None, M. abdo : None
Keywords: esophageal varices, liver stiffness measurement, Noninvasive predictors, Serum fibrosis scores

P072 EARLY USE OF TIPS DECREASES REBEEDING AND IMPROVES THE SURVIVAL IN CIRRHOTIC PATIENTS OF EVL ULCER BLEEDING: A PROSPECTIVE STUDY

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INTRODUCTION: Endoscopic variceal ligation (EVL) is the recommended method to manage esophageal variceal bleeding with lower variceal ulceration and rebleeding rates compared to sclerotherapy. However, a proportion of patients do develop EVL induced ulcers and present with massive bleeding. In these cases, endoscopic therapy is difficult and often unsuccessful and definitive methods, such as TIPS need to be evaluated.
AIMS&METHODS: Aim: To determine the effectiveness of reduction in portal pressure by polytetrafluoroethylene-covered transjugular stenting (TIPS) for band-induced esophageal ulcer bleeding. **Method:** Following admission within 24 hours, consecutive patients with cirrhosis and EVL induced bleeding ulcers were prospectively treated using standard therapy (endoscopy and vasoactive drugs; Group 1, n=19) or standard therapy plus TIPS (Group 2, n=22). Primary end-point was survival at 6 wks. Secondary end-points were early and late rebleeding.
RESULTS: Results: Out of 488 cirrhotic patients who underwent EVL from 2010-11, 41 (8%) (Median age 42 (range 32-72), 90% males) developed bleeding EVL ulcer. These patients were enrolled and offered either of the two treatments. Baseline parameters including age, presence of ascites, HE, HRS, platelets, PT (INR), HVPG, Child and MELD score were similar in both the groups. After follow-up of 6 wks, 10 patients (62%) in group 1 and 5 (25%) in group 2 died ($p<0.05$). The incidence of failure to control bleed/early rebleed was seen in 9 patients (56%) in group1 and in 1(5%) in group 2 ($p<0.05$). Similarly, the incidence of late rebleeding was seen in 5 patients (45.4%) in group 1 while in 1(5%) in group2 ($p<0.05$). The median time to death was 2.5 (0.5-12) days and 13 (2-21) days in the two groups ($p<0.05$).
CONCLUSION: Conclusion: Around 8% patients develop life threatening EVL induced ulcer bleeding. Portal pressure reduction with the TIPS is significantly superior in the control of bleeding, preventing rebleeding and reduction in mortality.
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Disclosure of Interest: None Declared
Keywords: EVL Ulcer, TIPS

P073 A RANDOMISED CONTROLLED TRIAL ON EFFICACY OF PROBIOTICS ON REVERSAL OF MINIMAL HEPATIC ENCEPHALOPATHY AND ITS CORRELATION WITH IMPROVEMENT IN SMALL INTESTINAL BACTERIAL OVERGROWTH AND OROCECAL TRANSIT TIME IN PATIENTS WITH CIRRHOSIS

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INTRODUCTION: Hepatic encephalopathy (HE) is associated with poor prognosis. Small intestinal bacterial overgrowth (SIBO) and delayed orocecal transit time (OCTT) is associated with systemic endotoxemia and minimal hepatic encephalopathy (MHE). Abnormal intestinal motility may play an important role in increasing the growth of pathogenic bacteria and increased absorption of gut toxins. Probiotics alter gut flora with non urease producing organism with decrease ammonia production.
AIMS&METHODS: Present study assessed effects of probiotics on reversal of MHE and its correlation with improvement in SIBO and OCTT. In a prospective randomised controlled trial, patients with cirrhosis with MHE were divided into: group 1 (Probiotics, $n = 42$, one capsule TDS) (contatining *Bifidobacterium brev, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus paracasei, Lactobacillus bulgaricus, Streptococcus thermophilus*, 110 billion CFU) and group 2 (control, $n = 39$). MHE was diagnosed when psychometric hepatic encephalopathy score (PHES) was ≤5. All patients underwent psychometric tests, critical flicker frequency (CFF), glucose hydrogen breath test (GHBT) for SIBO and lactulose hydrogen breath test (LHBT) for OCTT. Primary end point was reversal of MHE.
RESULTS: 81 patients (age 46.6±13.1 years, M:F 47:28) were included. 13 (16%), 24 (29.6%) and 44 (54.3%) were in CTP class A, B and C respectively. Mean CTP score was 9.72 ± 2.61 and MELD score was 19.22±6.91. Baseline laboratory parameters, CTP score, MELD score, CFF, PHES and OCTT were comparable.22 (48.8%) and 20 (51.2%%) patients in group 1 and 2 had SIBO respectively. OCTT was 135.13±13.95 min in Group 1 as compared to 137.59±14.80 min in group 2(p NS). Mean follow up of Group 1 patients was 38.6 ± 8.80 weeks and Group 2 patients was 34.3 ± 9.8 weeks (p=0.78). 7(8.6%) patients were lost during follow up. 4(9.5%) in Group 1 and 6 (15.3%) in Group 2 died (p=0.67). 5(11.9%) patients in Group 1 and 11(28.2%) patients in Group 2 developed overt HE ($p<0.05$, hazard ratio 2.6, 95% CI,1.30-6.43). 22 (52.3%) patients in Group 1 and 5 (12.8%) in Group 2 had reversal of MHE at 3 months ($p<0.05$). There was significant improvement in arterial ammonia levels, SIBO,

OCTT, PHES and CFF after 3 months of treatment with probiotics. Improvement in SIBO and OCTT were associated with improvement in PHES and reversal of MHE.

CONCLUSION: Probiotics are effective in reversal of MHE. This could be due to improvement in small intestinal bacterial overgrowth and orocecal transit time.

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Disclosure of Interest: None Declared

Keywords: hepatic encephalopathy, minimal hepatic encephalopathy, orocecal transit time, probiotics, small intestinal bacterial overgrowth (SIBO)

P074 ASSOCIATION OF SERUM ARYLESTERASE ACTIVITY WITH THE DEGREE OF SEVERITY OF LIVER CIRRHOSIS AMONG PATIENTS AT THE NATIONAL KIDNEY AND TRANSPLANT INSTITUTE

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INTRODUCTION: Cirrhosis is an important cause of morbidity and mortality in the world. The gold standard in its diagnosis is still liver biopsy. However, this carries substantial risk from complications and sampling error. Thus, assessment of one's liver function requires a battery of tests, such as total bilirubin, platelet count, prothrombin time, and albumin. The enzyme under study, Arylesterase, protects cell membranes from peroxidation, with subtype paraoxonase-1 (PON-1) being exclusively synthesized in the liver. It is then hypothesized that the enzyme activity would be useful as an index of liver function status.

AIMS&METHODS: This prospective study aims to investigate the relationship between serum arylesterase activity and the degree of severity of liver damage in patients with cirrhosis. Subjects consisted of healthy individuals and cirrhotics, the latter being further subdivided according to Child Pugh scoring. Blood extraction and subsequent spectroscopic determination of arylesterase activity were done. Absorbance at 270 nm was used to indirectly measure arylesterase activity.

RESULTS: Ninety-four patients, 47 controls and 47 cirrhotic patients (15 under Child Pugh A, 16 under Child Pugh B, and 16 under Child Pugh C) were matched and evaluated. More than half of the cases attributed their underlying chronic liver disease to Hepatitis (Chronic Hepatitis B/C or previous exposure to these viruses), and comprised 57.4% of the cases. The mean serum arylesterase activity was significantly lower (p-value < 0.01) for cases ($45.9 + 25.0$ kU/L), as compared to that of the control group ($123.4 + 19.6$ kU/L). Further comparing the enzyme activity among Child Pugh A, B, and C patients, we see a statistically significant decrease in activity (p-value < 0.01), with values of $74.6 + 10.4$ kU/L, $40.5 + 12.3$ kU/L, and $22.7 + 10.5$ kU/L, respectively. This is supported by a Pearson correlation of -0.84.

CONCLUSION: Serum Arylesterase levels were significantly reduced in patients with liver cirrhosis. Furthermore, the enzyme activities correlated with Child Pugh Class, and followed an inversely-linear pattern. The ease and reproducibility of the test, as shown in this study, may make it a good alternative for stratifying severity of liver cirrhosis.

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Keywords: Arylesterase, chronic hepatitis, Liver cirrhosis, Liver function tests

P075 UTILITY OF LIVER STIFFNESS MEASUREMENT USING FIBROSCAN IN DIFFERENTIATING ACUTE SEVERE VIRAL HEPATITIS AND ACUTE ON CHRONIC LIVER FAILURE AT ADMISSION

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INTRODUCTION: Liver stiffness (LS) measurement using FibroScan is a reproducible and accurate technique for assessment of fibrosis and portal hypertension. Often it is difficult to differentiate severe acute viral hepatitis (AVH) from patients with acute on chronic liver failure (ACLF) at admission. Aim is to determine utility of LS measurement in differentiating patients from severe AVH and ACLF at admission.

AIMS&METHODS: A total of 90 patients with severe AVH (serum bilirubin > 5 and INR > 1.5) and ACLF as per APASL guidelines of varying aetiologies were recruited prospectively. LS and biochemical tests were performed at admission and liver biopsy was done if needed.

RESULTS: The mean age of the patients (78 men and 12 women) was 37.7 ± 14.9 years. The aetiology of acute hepatitis (n=45) included (HAV,n=12, HEV,n=18, drug induced, n= 3, HBV,n= 3 and unknown,n= 9).Similarly etiology of ACLF(n=45) were HBV with severe reactivation, n=10,Alcoholic with alcoholic hepatitis, n=24, acute viral hepatitis on cryptogenic cirrhosis, n=11. There was no significant difference at baseline between ACLF and AVH in body mass index(26.3 ± 4.3 vs $25.2 \pm 3.6 kg/m^2$,p=0.19) hemoglobulin (12.0 ± 1.9 vs 12.6 ± 1.7 gm%,p=0.13),platelet count(202 ± 88 vs 212 ± 78 thousand/cumm,p=0.22),serum bilirubin(15 ± 8 vs 13 ± 8.5 mg/dl,p=0.18) and INR(1.8 ± 0.4 s 1.8 ± 0.3).However there was significant difference in ACLF and AVH in median AST (123,33-1049 vs 230,54-3721 IU/L,p=0.01) and ALT(118,24-751 vs 246,66-6349 IU/L,p=0.001). Mean LS (53.3 ± 21.5 vs 16.1 ± 9 kPa,p=0.001) were significant more in ACLF compared to AVH. Multivariate analysis showed only LS at admission could differentiate severe AVH versus ACLF(p=0.0001).Taking a cutoff for LS as 28.2kPa sensitivity and specificity for diagnosing ACLF was 84% and 85% respectively.

CONCLUSION: Baseline liver stiffness measurement by fibroscan can differentiate severe acute viral hepatitis from acute on chronic liver failure at admission.

Disclosure of Interest: None Declared

Keywords: ACLF, APASL, AVH

P076 ANTICOAGULATION FOR ACUTE PORTAL VEIN THROMBOSIS IN LIVER CIRRHOSIS IS SAFE AND DOES NOT INCREASE THE MORTALITY

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INTRODUCTION: Portal vein thrombosis (PVT) is caused by liver cirrhosis, inflammatory diseases, cancer, myeloproliferative and coagulation disorders. Acute PVT can be distinguished from chronic PVT. Clinical presentation depends on the onset and the extent of the thrombosis and the development of collateral circulation / portal hypertension. For acute PVT early initiation of anticoagulation (AC) or thrombolytic therapy is recommended. The therapeutic approach in chronic PVT, especially in patients with liver cirrhosis, is controversial.

AIMS&METHODS: Our analysis was designed to validate retrospectively the managment of PVT in patients with different underlying illness. Therefore we reviewed all patients with diagnosed PVT (n=149) in a period of 2005 to 2012 at our Department of Medicine. Patient characteristics, including demographics, acute or chronic PVT, underlying disease, therapeutic managment and complications were analyzed.

RESULTS: PVT occurred in 102 men and 47 women. PVT was common in patients with gastrointestinal cancer, liver cirrhosis, inflammatory diseases, abdominal surgery, myeloproliferative and coagulation disorders. 76 patients had acute and 73 chronic PVT. 36 patients with acute PVT were treated by AC. AC (heparin, marcumar, thrombolytic therapy) could achieve in 20 patients recanalisation. In 7 patients AC caused impairment and 9 patients died. 20 patients with chronic PVT were treated by AC. AC could achieve in 3 patients recanalisation In 1 patient AC caused impairment, 16 patients showed no change and 5 patients died.

CONCLUSION: Patients with acute PVT benefit significantly from AC. AC is safe, especially in patients with liver cirrhosis (CHILD A & B) and had no significant impact on side effects and mortality. Patients with cancer (HCC, pancreatic cancer) and acute PVT have no advantage of AC.

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Keywords: anticoagulation, liver cirrhosis, portal vein thrombosis

P077 CLINICAL, BIOCHEMICAL PROFILE AND PREDICTORS OF EARLY MORTALITY IN PATIENTS WITH ACUTE ON CHRONIC LIVER FAILURE

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INTRODUCTION: Acute-on-chronic liver failure (ACLF) is defined as rapid deterioration occurring in a patient with known or unknown chronic liver disease due to acute insult. We describe the clinical, biochemical profile of ACLF and the effect of acute insult and associated complications on the natural course of patients.

AIMS&METHODS: Patients diagnosed to have ACLF as per APASL guidelines were prospectively enrolled. Patients were evaluated for the clinical presentation, etiology of acute decompensation and underlying chronic liver disease and in hospital mortality. Patients were further classified as ACLF-1 when they had no organ failure except liver, ACLF-2 when they had one organ failure along with liver, ACLF-3 when they had two organ failure along with liver and ACLF-4 with≥ 3 organ failure along with liver.
RESULTS: One thirty four patients with ACLF (mean age 44.2±10.3 years; M/F 128:8) were included. Median serum bilirubin 14.5 (5-45.9 mg%), mean CTP score (10.4±1.9), mean MELD score (25.6±7.7) and median hospital stay was (7,1-35 days). Alcoholic hepatitis (n=79,59%) followed by hepatitis B virus reactivation (n=23,17 %) were the commonest acute events. Underlying chronic liver disease was due to alcohol (n=92,69%),HBV(n=17,13%) and cryptogenic in 20(15%).Ascites was present in 118(88%),hepatic encephalopathy (50,37%),sepsis(11,8.2%),chest infection(22,16%),spontaneous bacterial peritonitis(17,13%),acute kidney injury in 52(39%). Overall mortality during hospitalization was (n=60, 45%).Mortality was 19% in ACLF-1, 45% in ACLF-2, 78% in ACLF-3 and 100% in ACLF-4. Patients who died had significantly lower age but higher CTP score, MELD score, sepsis, lower respiratory infections, acute kidney injury, HE and number of organ failure compared to survivors. On multivariate analysis only loss of >2 organ failure either at presentation or development during hospital stay was predictor of mortality.
CONCLUSION: Alcoholic hepatitis and hepatitis B virus were common acute insults in ACLF patients and loss of more than two organ function either at presentation or during hospital stay is an independent predictor of mortality in these patients. Measures to control sepsis and organ failure should be initiated early in the course of ACLF patients.
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Disclosure of Interest: None Declared
Keywords: ACLF - Acute on chronic liver faliure, HE - Hepatic encephalopathy

P078 DEVELOPMENT AND VALIDATION OF SINHALA VERSION OF THE CHRONIC LIVER DISEASE QUESTIONNAIRE (CLDQ)

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INTRODUCTION: The Chronic Liver Disease Questionnaire (CLDQ) is a validated tool measuring the Health Related Quality of Life among cirrhotics (1). It is designed to measure six domains of QOL; Abdominal symptoms, Fatigue, Systemic symptoms, Activity, Emotional functions and Worry. CLDQ has been translated and validated to different languages around the world and has shown good correlation with severity of liver disease (2,3)
AIMS&METHODS: Aim of this study was to develop and validate a Sinhala version of the CLDQ (sCLDQ) and to test its correlation with the degree of liver dysfunction in a cohort of Sri Lankan patients with cirrhosis.
A standard translation method was used to develop the sCLDQ. Pilot testing was done with relevant cultural and language adaptations. The final version was self-administered to stable CLD patients, together with the WHO Quality of Life-BREF (WHOQOL-BREF) validated Sinhala version, for comparison. sCLDQ was re-administered 4 weeks later to test internal consistency and reliability. The validation was assessed by Cronabach's alpha, intraclass correlation coefficient (ICC) and Pearson's correlation coefficient. ANOVA and Pearson's correlation were used to test correlation with the degree of liver dysfunction.
RESULTS: Validation was done with 214 subjects, mean age 55.6 (SD 10.4) years; male 77.6%. Overall Cronabach's alpha was 0.926. Itra-class correlations varied from 0.431 to 0.912 and all were significant (p 0.000). Retesting was done on a sub-sample of 18 subjects. Test-retest correlation was 0.695 (p 0.008). WHO-BREF was applied on a sub-sample of 48 subjects. There was a significant correlation (Pearson's r=0.391; p=0.004) between sCLDQ and WHOQOL BREF. sCLDQ was significantly associated with MELD (r=-0.13;p=0.038), MELD Sodium (r=-0.223;p=0.002), Bilirubin (r=-0.124;p=0.036), Serum Sodium (r=0.172;p=0.009), Serum Albumin (r=0.201;p=0.003) and Child grade (f=3.687;p=0.027).
CONCLUSION: sCLDQ is a reliable and valid tool to assess QoL of Sri Lankan cirrhotics and correlates well with known indices of disease severity.
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Disclosure of Interest: None Declared
Keywords: Chronic Liver Disease Questionnaire, CIRRHOSIS, quality of life

P079 HIGHER EDUCATIONAL LEVEL PROTECTS AGAINST DRUG AND ALCOHOL ABUSE: A STUDY ON A YOUNG SATURDAY NIGHT DRIVERS POPULATION

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INTRODUCTION: Alcohol consumption is linked to social-cultural aspects in Northeast Italy. Precedently alcohol was consumed daily by all members of the family in North Italy (steady drinking). Young people now seem to prefer binge drinking. Drug use is also on the rise. It has been shown recently hepatic injury by Cocaine and Tetrahydrocannabinol (THC).
AIMS&METHODS: This study aimed to determine the prevalence of alcohol and drug consumption in drivers on weekend nights. As part of the government sponsored "Safe Roads" Program (November 2008 to September 2012) 3150 drivers were stopped in Padua (Italy) by law enforcement officials between midnight and 6. All underwent a preliminary alcohol test. Those who tested positive underwent the Breathalyzer test (710 MK III®) and also to urine test for drugs (RapiScan®, Cozart). Few anamnestic data were collected. Alcohol test >0.5 g/l was considered positive.
RESULTS: 1068 (909 M - 85% - and 159 F -15%; mean age 30.5 yr) drivers underwent the Breathalyzer test. 714 of 3150 (22.6%) were found positive (mean alcohol 0.77 g/l; range 0-2.67). 242 of 1068 (22.6%) were also positive for drugs. 114 drivers resulted positive for cocaine, 66 for THC, in other 26 those two drugs were associated. Drug use was more frequent in those resulting positive to alcohol (23,6% vs 15,4%; p=0.006209). The mean alcohol value was statistically higher (0.90±0.6 SD vs 0.62±0.5 SD, p<0,001) in the subjects positive to drugs as well as in the only cocaine users (1.00±0.6 SD vs 0.62±0.5 SD, p<0,001). The highest mean alcohol value (0.88 g/l) was found between 4 and 5 am (p=0.006509). Positivity rate for drugs and mean blood alcohol content resulted higher in subjects with lower educational levels (30,8% vs 18,0%, p< 0,001 and 0,689 g/l vs 1,027, p=0,00782). At the multivariate analysis drug use is correlated with age, sex, scholar level (OR 1,86 95% CI 1,27-2,73, p=0,001) and alcohol, instead positive test for alcohol is correlated only with scholar level (OR 1,50 95% CI 1,04-2,16, p=0,028) and use of drugs.
CONCLUSION: The prevalence of drugs and alcohol consumption on weekends is high. The most common drug used is cocaine, alone or in association. Drug use is associated to alcohol consumption. This type of behavior, in our opinion, may probably lead in the future to new types of chronic liver diseases. Is encouraging that high educational levels may be protective against the use of drugs and alcohol abuse.
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Disclosure of Interest: None Declared
Keywords: Alcohol, Car driver, Cocaine

P080 NON-ALCOHOLIC FATTY LIVER DISEASE: A SOMERSET SERVICE EVALUATION STUDY

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INTRODUCTION: Non-alcoholic fatty liver disease (NAFLD) is an increasing burden on the NHS. Prevalence is estimated at 20-30% in Western adults[1,2] and fatty liver has now overtaken alcohol as the leading cause of chronic liver disease in many developed countries[3]. This is being reflected in increasing referrals to secondary care. This survey aimed to review the process by which patients with NAFLD were evaluated and managed within West Somerset (350,000 population). It looked at primary care referrals, comparing it with the route outlined in the NHS Map of Medicine[4], the investigation and management of patients with NAFLD, including non-invasive fibrosis risk scoring, and the secondary care decisions made regarding discharge and follow-up.
AIMS&METHODS: We performed a retrospective case note review of all patients with a diagnosis of NAFLD seen in gastroenterology or hepatology clinics between 01/09/10 and 31/08/11. Patients were identified by using the search terms "Non-alcoholic fatty liver disease", "NAFLD", "NASH", "Non-alcoholic steatohepatitis" and "Fatty liver" within our clinic letter database. We excluded cases with additional liver pathology, except for alcohol intake (stratified into <20, 20-50, >50 units per week). We assessed our service against the American Association for the Study of Hepatology (AASLD) guideline on the management of NAFLD[5].
RESULTS: 158 patients were identified, 14 of which were excluded due to additional liver disease and 3 sets of notes were unobtainable, leaving 141 patients for analysis (71 new referral, 70 follow-up). 116 patients (82%) had pure NAFLD; alcohol was implicated in 25 cases (18%, >20 units per week). Non-invasive fibrosis risk stratification was done in 48% (68/141) of patients; 65% (44/68) of those had a low risk score. Liver biopsies were requested in 36 patients (25%), 20 (56%) of which had not been risk-stratified and 8 (20%) had a low fibrosis risk score. 71% (61/100) of patients referred in from primary care had an incomplete non-invasive liver screen (full Map of Medicine guidance was followed in only 2%). 24 (44%) of the 55 newly referred patients with full risk assessment had a low fibrosis score.
CONCLUSION: Non-invasive risk stratification was performed in less than half of secondary care patients with NAFLD and only 2% of primary care referrals. Almost half of newly referred patients with full NAFLD assessment were deemed dischargeable after the first visit; i.e. may not have required referral into secondary care. In the absence of a European guidance on the investigation and management of NAFLD, the Map of Medicine provides an evidence-based pathway for patients with abnormal liver function tests and can be utilised to form local referral pathways for patients with NAFLD.

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P081 BINGE DRINKING, ALCOHOL ABUSE AND DEPENDENCE: SCREENING STUDY IN AN EMERGENCY DEPARTMENT

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INTRODUCTION: Alcohol is associated with many health problems and with 15.000-20.000 death/year in Italy. In Hospital Emergency Departments are examined alcohol related problems as consequence of short-term exposure to alcohol as well as consequences of long term alcohol use. The aims of this study are to investigate: the patterns of alcohol consumption among emergency room patients (risk or hazardous drinking, harmful drinking, alcohol abuse and dependence); the share and the characteristics of alcohol consumption subgroup; the feasibility of screening for alcohol problems in the emergency room.
AIMS&METHODS: The study was carried out at S. Anthony Hospital Department during a period from 8th January 2012 to 16th May 2012, 4 weeks were randomly selected. In three weeks screening was led from 8 am to 8 pm, in one week from 7 pm to 12 pm. Patients $>$ 18 years old were approached after they had been triaged, before or after being visited. AUDIT and CAGE tests were self-administered only to patients who accepted to perform the test in this way, the others were interviewed by the same interviewer. The statistical analysis was carried out with Pearson test.
RESULTS: 1520 patients were evaluated in emergency department during the period of the study. 1000 (65.8%) were examined. 874 (87.4%) were interviewed. 19.5% of interviewed patients had alcohol related problems on the basis of either CAGE or AUDIT. Higher rates were found for men ($p < 0.001$), young people aged 18-20 years ($p < 0.028$), divorced or single ($p < 0.003$), unemployed subjects ($p < 0.001$), homeless ($p = 0.005$), immigrants ($p < 0.001$). There was a lack of significant correlation between positive tests and day of presentation and need of admission.
CONCLUSION: Our data indicate that a large amount of emergency room patients have alcohol-related problems. Emergency Department may be the initial point of healthcare contact for patients with alcohol problems. Social outcast persons present higher risk of alcohol disorders. Screening can be useful to provide the first step of intervention in this group and is needed for early prevention and health care intervention.
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Keywords: Alcohol, Binge drinking

P082 ETHNIC DIFFERENCES IN ALCOHOL-RELATED DISEASES IN SCOTLAND

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INTRODUCTION: Alcohol-related harms, most commonly liver disease-related, are a public health priority in Scotland Previous research has identified variations in liver disease mortality endpoints using country of birth as a proxy for ethnicity in the UK. We report ethnic differences in the incidence of alcohol-related and liver disease using an adequate measure of ethnicity in Scotland.
AIMS&METHODS: Using the Scottish health and ethnicity linkage study (SHELS), linking NHS hospital admissions and mortality to the Scottish census 2001, we explored ethnic differences in incidence (2001-2010) of specific alcohol-related diseases (ARD) (NHS Information Services Division definition for ARD, all liver diseases, alcoholic liver disease) in Scotland. Risk ratios (RR) were calculated using Poisson regression with robust variance and multiplied by 100, by gender and adjusted for age. The White Scottish population was the standard reference population (100). 95% confidence intervals (CI) were calculated to enable comparison and exclude 100 in the results below.
RESULTS: For alcohol-related diseases, White Irish had about a 2 fold higher risk for both men (RR 225; 95% confidence interval [CI] 196 to 258) and women (182; 147 to 224); other British women also had a 25% higher risk (126; 107 to 148). Other White British men had a 10% lower risk (89; 80 to 98), with risks even lower in Pakistani men (66; 55 to 78) and women (49; 30 to 78), and Chinese men (47; 38 to 58).
For alcoholic liver disease, White Irish had about a 50% higher risk of ALD for both men (165; 130 to 209) and women (150; 117 to 193). Other White British men had about a third lower risk of ALD (61; 50 to 75), as did Pakistani men (62; 42 to 90) and a composite of South Asian women (73; 58 to 91).
For all liver diseases, some ethnic groups had about a third higher risk: Chinese men (144; 118 to 175) and women (133; 107 to 165) as well as Pakistani women (140; 112 to 176). Lower risks for all liver diseases occurred in other White British men (72; 62 to 83) and women (77; 69 to 87) and other White women (76; 64 to 90).
CONCLUSION: These findings show persistent differences in incidence by ethnicity for both alcohol-related and liver disease and have important clinical and public health implications. New policy, research and practical action are required to address these differences.
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Disclosure of Interest: None Declared
Keywords: alcohol, Alcohol and Liver disease, ALCOHOLIC LIVER DISEASE

P083 FOSTERING EQUITY: LOCAL ACCESS TO LIVER TRANSPLANT SERVICE

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INTRODUCTION: In the UK, current landscape of service provision for patients with liver disease does not match that of disease burden[1]. Most hepatologists are based in the transplant centres and access to tertiary liver service is not geographically equitable[1]. In an attempt to improve access, we established a liver transplant outreach clinic from the regional liver unit within a large gastroenterology unit. Here, we describe the benefits of this clinic.
AIMS&METHODS: A dedicated monthly joint liver clinic was established in a large gastroenterology unit. Patients with complex liver disease, including pre- and post-transplant are seen by a consultant transplant hepatologist from the regional transplant unit and a local consultant gastroenterologist. Quantitative data was available from the transplant centre. A sample of patients (76) and specialists were asked to complete a written questionnaire on their opinions of the clinic service
RESULTS: Since August 2010, over 400 patients have been seen. In the 4 years prior to establishment of the clinic, there were a median of 3 (1-4) referrals annually for liver transplant assessment. This increased to 9.5 (9-10) in the subsequent 2 years. Patients were satisfied with the clinical service (Table 1) and the majority (95%) preferred local follow up, citing it as more convenient (99%) with easier travel arrangements (99%). Specialists (n=16) agreed unanimously that the clinic was more convenient for patients, easy to refer into and improved both accessibility to liver services and communication with the regional liver unit. Most (83%) felt that it reduced waiting times for specialist opinion.
Table1. Patient questions and mean score 1(low) – 5(high)

Patient Question	Mean Score
Overall quality of care and services	4.5
Access to specialty care, if needed	4.4
Skill, experience and training of doctors	4.5
Respect shown to you by doctors	4.7
Confidence in the doctor you saw	4.6

CONCLUSION: Establishing an outreach clinic has increased referrals for transplant assessment. Patients prefer to be seen locally and do not feel this affects their specialist care. They have confidence in the skill and experience of the clinicians they see and rate the quality of care, highly. Referring clinicians are also satisfied with the quality and accessibility of the outreach clinic. Overall, outreach clinics may serve to improve equity of access to transplant services.
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Disclosure of Interest: None Declared
Keywords: Access, Equity of liver transplantation service, Liver transplantation, Service Development

P084 SPHINCTER OF ODDI DYSFUNCTION: BOTOX VS SPHINCTEROTOMY A LONDON TERTIARY CENTRE STUDY

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INTRODUCTION: Sphincter of Oddi Dysfunction is rare and often difficult condition to treat. It is commonly seen in women post cholecystectomy[1]. The condition is felt to be secondary to sphincter dysmotility, distinct from papillary stenosis in which the obstruction is fixed [2-5]. Sphincter of Oddi Dysfunction is usually classified into three different types using the Milwaukee Criteria. Type 1 are defined as those with abnormal liver biochemistry and a dilated bile duct. Type 2 are classified as one of the above abnormalities and type 3 classified as typical biliary pain with none of the above features. It is therefore necessary to investigate potential Sphincter of Oddi Dysfunction using manometry and ercp.
AIMS&METHODS: Aims: To investigate optimum treatments for Sphincter of Oddi Dysfunction using pancreatic sphincterotomy, biliary sphincterotomy, botox or a combination of the three.

Methods: We followed up pain outcomes in 91 patients treated for Sphincter of Oddi Dysfucntion between January 2008 to March 2013. We recorded the interventions received be it either, botox injection, pancreatic sphincterotomy, biliary sphincterotomy or a combination of the three. Follow up was at 6 months post intervention. Pain outcome were recorded as worse, no difference, some improvement and complete resolution.

RESULTS: There were a total of 103 interventions with 9 patients having 2 interventions and one patient having 4 interventions. Of the 103 interventions 19 had botox only,18 had pancreatic sphincterotomy alone, 24 had biliary sphincterotomy alone, 5 had all three interventions, 23 had pancreatic sphincterotomy and botox, 4 had botox and biliary sphincterotomy and 10 had no intervention.

All patients receiving all 3 therapies recorded a decrease in pain at follow up. The next most successful treatment was biliary sphincterotomy and botox with 75% of patients recording improvement in pain. In the pancreatic sphincterotomy group 50% showed improvement in pain, this is similar to the biliary sphincterotomy group who showed 46% of patients had improvement of pain. In the botox only group 37% of patients showed some improvement in pain with 11% showing complete resolution. Of the patients who received both pancreatic and biliary sphincterotomies 35% demonstrated improvement in pain.

CONCLUSION: Treatment of Sphincter of Oddi Dysfunction remains very difficult with challenges and risks in both diagnosis and treatment. It is well documented that patients with Sphincter of Oddi Dysfunction often have overlapping functional disorders which can make treatment all the more difficult. Our study has shown that all three modalities of treatment have some success and that further larger scale studies may help determine which treatment is best.

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Disclosure of Interest: None Declared

Keywords: botox, sphincter of oddi dysfunction

P085 IS DOUBLE-GUIDEWIRE TECHNIQUE REALLY HELPFUL FOR DIFFICULT BILE DUCT CANNULATION ?

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INTRODUCTION: Needle-knife fistulotomy (NKF) is widely used in failed standard biliary cannulation (BC). But NKF requires experienced endoscopists, contains significant complication risks. Double-guidewire technique (DGT) has been reported to be useful for difficult biliary cannulation and to achieve a success rate of 47–93% in patients who fail BC.

AIMS&METHODS: The aim of this study was to compare the success rate and complications between the DGT and NKF in patients with difficult biliary cannulations. Patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) between January 2009 and September 2012 were eligible for this study. DGT or NKF were performed if deep biliary cannulation was not achieved despite of five minutes of attempted cannulation or more than three attempted unintentional pancreatic cannulations. Patients with unsuccessful DGT underwent NKF as alternative procedure. The success rate of cannulation and the frequency of post-ERCP pancreatitis (PEP) were investigated.

RESULTS: A total 1550 ERCP cases were analyzed, the total success rate of selective biliary cannulation was 94.2% (1460/1550). Of the 302 patients with unsuccessful standard cannulation technique, DGT was performed in 70 patient and NKF was performed in 199. The success rate in the DGT and NKF groups were 41.4% (29/70) versus 81.4% (162/199) ($p < 0.01$). Thirty patients with unsuccessful DGT underwent NKF as alternative procedure, biliary cannulation was achieved in 70.0% (21/30). Three step protocol (traditional cannula with guidewire, DGT, and NKF is performed sequentially) was no signigicant benefit in success rate compared with NKF only group (84.7%, 50/59, $p = 0.453$). The incidence rate of PEP was significantly higher in DGT group (20.0%,14/70) than in NKF group (8.0%, 16/199) ($p < 0.01$). There was no significant difference in bleeding incidence.

CONCLUSION: DGT in patients with a difficult biliary cannulation resulted in a low success rate of biliary cannulation and a high incidence of PEP comparing with NKF. DGT before NKF had no statically additional benefit in cannnulation success. We suggest that NKF should be considered as a first approach in difficult cannulation situations.

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Disclosure of Interest: None Declared

Keywords: cannulation, double-guidewire technique, endoscopic retrograde cholangiopancreatography, Needle-knife fistulotomy, pancreatitis

P086 CHANGES IN CAUSATIVE PATHOGENS OF ACUTE CHOLANGITIS AND THEIR ANTIMICROBIAL SUSCEPTIBILITY OVER A PERIOD OF 6 YEARS

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INTRODUCTION: For the most effective empirical antimicrobial therapy in acute cholangitis, knowledge of prevalence and antimicrobial susceptibility of the institution is essential.

AIMS&METHODS: We evaluated changes of bacteria cultured from bile and blood and their antimicrobial susceptibility over six years at our institution. From August 2006 to August 2012, medical records of patients with acute cholangitis who received biliary drainage were retrospectively reviewed. Acute cholangitis was diagnosed when one or more of the followings were present: 1) purulent bile in gross appearance, 2) leukocytes in bile≥ 50/HPF, 3) positive growth in bile culture. Total of 1589 cases were included. Cases were divided into community-acquired cholangitis (n=201, 12.6%) and hospital-acquired cholangitis (n=1388, 87.4%). Cases were also divided according to time period: Group A (August 2006-December 2008) and Group B (January 2009 - August 2012). Antimicrobial susceptibility were evaluated in each group.

RESULTS: Mean age of the patients was 68.3±13.8 years. There were 905 male patients (53.1%). Of 1589 cases with bile culture, growth was detected in 1513 cases (95.2%). Gram-negative bacteria were isolated in 1422 cases (94%). Most frequently isolated Gram-negative bacteria were extended beta-lactamase (ESBL)-producing *Escherichia coli* (*E. coli*) (n=482, 33.9%), *E. coli* (n=211, 14.8%), *Citrobacter freundii* (n=110, 7.7%), *Klebsiella pneumoniae* (*K. pneumoniae*) (n=99, 7.0%), and ESBL-producing *K. pneumoniae* (n=90, 6.3%). In hospital-acquired cholangitis group, prevalence of ESBL-producing *E. coli* and *Citrobacter freundii* was higher (52.1 vs. 31.4%, p=0.00; 13.5 vs. 6.9%, p=0.002). In Group B, prevalence of E. coli has decreased significantly (p=0.017). Antimicrobial agents with high susceptibility were as follows: amikacin (85.3%), piperacillin-tazobactam (70.3%), cefotetan (77.7%), and imipenem (95.7%). In Group B, susceptibility to piperacillin-tazobactam has decreased significantly (67.9 vs. 73.7%, p=0.027).

CONCLUSION: Prevalence of ESBL-producing *E. coli* and *K. pneumoniae* in cholangitis has increased over six years. In hospital-acquired cholangitis, prevalence of ESBL-producing *E. coli* and *Citrobacter freundii* is higher. Susceptibility to piperacillin-tazobactam has decreased over recent years.

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Disclosure of Interest: None Declared

Keywords: acute cholangitis, antimicrobial resistance, antimicrobial susceptibility, bile culture

P088 MARKED HYPERTRANSAMINEMIA: A NEW PARADIGM?

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INTRODUCTION: In general practice, it is estimated that severe transaminases elevations correspond to ischemic hepatitis, viral or toxic. However, cases of biliary obstruction, increasingly common, have been associated with marked hypertransaminemia. With this study we thus intend to determine the true etiology of increased transaminases in the context of hospital emergency.

AIMS&METHODS: We identified retrospectively all patients going to the emergency unit of Centro Hospitalar Universitário de Coimbra (CHUC) between 1 January 2010 and 31 December 2010 with at least one of transaminases increased more than 15 times. All patient records were analyzed to determine a diagnosis of hypertransaminemia.

RESULTS: A cohort of 273 patients was analyzed. The most frequently etiology found for marked hypertransaminemia was pancreatobiliary acute disease (39.3%), mostly lithiasic, followed by malignancy (20.5%), ischemic hepatitis (17.2%), acute primary hepatocellular disease (13.9%) and muscle damage (6.4%). We could not find a diagnosis in 10 cases (2.7%) after study. There were 27 cases of recurrence in the group of pancreatic-biliary pathology lithiasic, 24 of which had not undergone cholecystectomy ($p = 0.014$). The etiology of hypertransaminemia was influenced by age ($p < 0.001$), by sex ($p = 0.052$), by cholestasis ($p < 0.001$) and by GPT average ($p = 0.022$).

CONCLUSION: The pancreatobiliary lithiasis, often treatable, has been underestimated in the differential diagnosis of hypertransaminemia, and its possibility should always be considered in such situations, in order to improve prognosis. Not performing cholecystectomy early after the first episode predisposes to recurrent biliary obstruction.

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Disclosure of Interest: None Declared

Keywords: Gallstone disease, hypertransaminemia

P089 THE CLINICAL USEFULNESS OF ENDOSCOPIC ULTRASONOGRAPHY ACCORDING TO ASGE PROBABILITY OF CHOLEDOCHOLITHIASIS IN PATIENTS WITH SUSPECTED CHOLEDOCHOLITHIASIS BUT A NEGATIVE CT SCAN

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INTRODUCTION: Endoscopic ultrasonography (EUS) is a minimally invasive technique with low morbidity and proven efficacy in the diagnosis of choledocholithiasis.

AIMS&METHODS: We aimed to investigate the usefulness of EUS in patients with clinically suspected choledocholithiasis but a negative CT scan. Between March 2008 and January 2013, 108 patients with clinically suspected choledocholithiasis and no evidence of CBD stones according to MDCT underwent EUS. Common bile duct stones were confirmed by endoscopic retrograde cholangiography (ERCP) and clinical data were retrospectively collected. The risk of choledocholithiasis was assessed by applying the ASGE guidelines, which provide recommendations for categorizing patients into low, intermediate, and high probability.
RESULTS: The accuracy of EUS findings were confirmed according to ASGE probability of choledocholithiasis. EUS accuracy for common bile duct stones were 88.9% (sensitivity 96%, specificity 72%, positive predictive value 89%, negative predictive value 89%). In patients with high and intermediate probability of choledocholithiasis, the detection rate for CBD stones were 83.9% and 70%. CBD stone in patient with low probability was not detected. On multivariate logistic analysis using significant factors after univariate analysis, EUS finding of CBD stone was the only significant predictive factor associated with the presence of choledocholithiasis (OR, 43.2 CI, 9.3-201.4 $P<0.01$). However, EUS finding (stone, dilation), CBD dilation on CT, fever, abnormal liver biochemical test, and ASGE choledocholithiasis probability classification were not associated with the presence of choledocholithiasis.
CONCLUSION: EUS is recommended for further CBD evaluation in patients with suspected choledocholithiasis despite recent improvements in the accuracy of MDCT. CBD Stone on EUS is useful predictor of diagnosis for choledocholithiasis with negative CT scan, regardless of ASGE probability of choledocholithiasis. But EUS is not necessary in patients of the low probability of ASGE guideline and negative CT scan due to very low stone detection rate.
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Disclosure of Interest: None Declared
Keywords: ASGE, Choledocholithiasis, EUS

MONDAY, OCTOBER 14, 2013 9:00–17:00
PANCREAS I – Poster Area

P090 BASIC AMINO ACIDS CAUSE MITOCHONDRIAL DAMAGE IN RAT PANCREATIC ACINAR CELLS

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INTRODUCTION: Acute pancreatitis (AP) is the sudden inflammation of the pancreas. Large *i.p.* doses of basic amino acids induce AP in rodents, but the mechanisms mediating pancreatic toxicity remain unknown. Mitochondrial injury is thought to play a role in the pathomechanism.
AIMS&METHODS: Our aim was to get insight into the mechanisms through which basic amino acids damage the exocrine pancreas. Pancreatic acinar cells were isolated from rat pancreas with enzymatic digestion. Isolated cells were treated with different concentrations (20-60 mM) of L-arginine, L-lysine or L-ornithine. The morphology of acinar mitochondria was monitored with electron microscopy. We measured intracellular Ca^{2+} concentration ($[Ca^{2+}]_i$) by microspectrofluorometry using the Ca^{2+}-sensitive fluorescent dye FURA-2-AM. The effect of basic amino acids on basal and cerulein-stimulated amylase secretion was tested.
RESULTS: We observed the swelling of mitochondria after incubating the cells for 2 hours with 20-60 mM basic amino acids. However, we did not detect any change in the $[Ca^{2+}]_i$ of cells in response to administration of basic amino acids, whereas marked Ca^{2+} signaling was found in response to 100 μM carbachol. Basal and cerulein stimulated amylase secretion was not influenced by basic amino acids vs the control group.
CONCLUSION: Our data suggest that basic amino acids are unlikely to cause pancreatitis via calcium signaling, they do not alter amylase secretion, but they injure mitochondria. Further experiments are needed to investigate the exact pathomechanism.
This study was supported by OTKA, MTA and NFÜ/TÁMOP.
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Disclosure of Interest: None Declared
Keywords: acute pancreatitis, basic amino acids, mitochondrial injury

P091 MOLECULAR IDENTIFICATION AND REGULATION OF GHRELIN SYSTEM IN THE AR42J CELLS

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INTRODUCTION: Ghrelin (GHRL), is 28-amino acid polypeptide, originally isolated from the stomach and it has also been identified in the pancreas. This peptide is an endogenous ligand for the growth hormone (GH) secretagogue receptor (GHS-R). In animal experiments GHRL protects the gastric mucosa and the pancreas from the acute damage, but the involvement of GHS-R and/or endogenous polypeptide in acute pancreatitis (AP) is still unclear.
AIMS&METHODS: To determine the effect of GHRL and caerulein stimulation of AR42J cells on protein levels of GHS-R1a subtype and of acylated GHRL.
AR42J cells were incubated in standard medium at 37^0C for 48 h, under basal conditions and stimulated with caerulein (10^{-8}M), GHRL (10^{-7}M), or combination of above. Protein expression was assessed employing Western-blot.
RESULTS: GHS-R1a subtype and acylated GHRL have been detected in the pancreatic AR42J cells under basal conditions. Incubation of these cells in presence of GHRL alone resulted in the significant upregulation of both detected proteins. On the contrary, application of caerulein to the cell culture significantly downregulated GHS-R1a, but failed to affect the signal for GHRL. Addition of GHRL reversed caerulein-induced suppression of this protein.
CONCLUSION: Caerulein is able to modify the GHS-R1a subtype in the pancreatic AR42J cells. This effect could be prevented by pretreatment with GHRL and perhaps might be implicated in the mechanism of pancreatic damage induced by caerulein overstimulation.
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Disclosure of Interest: None Declared
Keywords: caerulein, AR42J cells, western-blot, GHRL, GHS-R1a

P092 EFFECT OF TRYPTOPHAN METABOLITE ON PANCREATIC AMYLASE SECRETION IN THE RATS

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INTRODUCTION: The kynurenines, products of tryptophan metabolism, are involved in many physiological processes as well as in regulation of the immune response of the organism. These products have been detected within gastrointestinal system, but their effects on pancreatic amylase secretion have not been investigated yet.
AIMS&METHODS: To assess the effects of intraduodenal (i.d.) infusion of L-kynurenine on pancreatic amylase outputs under basal conditions and following the stimulation of pancreatic secretion with diversion of pancreatobiliary juice (DPBJ) and the role of CCK in that process.
The study was performed on Wistar rats weighing 350g. Under pentobarbitane anesthesia the animals were surgically equipped with silicone catheters, inserted into pancreato-biliary duct, and into duodenum. L-kynurenine (50 or 250 mg/kg i.d.) was given under basal conditions or following stimulation of pancreatic secretion with DPBJ. In the part of the study the lorglumide, the CCK_1 receptor antagonist (1 mg/kg i.d.) was administered 15 minutes prior to application of L-kynurenine. Samples of pancreato-biliary juice were collected to measure the amylase outputs. The blood specimens were taken for determination of CCK employing ELISA.
RESULTS: Intraduodenal administration of L-kynurenine resulted in dose-dependent increase of pancreatic amylase secretion alike under basal conditions as well as during stimulation with DPBJ. These changes in amylase outputs were accompanied by significant increase of CCK plasma levels. Administration of CCK_1 receptor blocker completely abolished the secretory effects of L-kynurenine on pancreatic exocrine function.
CONCLUSION: CCK is involved in the stimulatory effects of tryptophan metabolite, L-kynurenine, on exocrine pancreatic secretion in the rats.
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Disclosure of Interest: None Declared
Keywords: L-kynurenine, amylase secretion, CCK, rats, pancreas

P093 OPEN-LABEL, MULTICENTER, RANDOMIZED CROSSOVER STUDY COMPARING SAFETY AND EFFICACY OF PANZYTRAT 25000 TO KREON 25000 FOR CONTROL OF STEATORRHEA IN CYSTIC FIBROSIS AND EXOCRINE PANCREATIC INSUFFICIENCY PATIENTS >7 YEARS

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INTRODUCTION: Introduction & Objectives: Exocrine pancreatic insufficiency (EPI) affects the majority of cystic fibrosis (CF) patients causing significant morbidity and mortality. Panzytrat®, an enteric-coated pancreatic enzyme product (PEP), has been widely available in Europe and South America for over 20 years for the treatment of EPI; however, its efficacy was not studied in patients with EPI due to CF previously. This study compared the efficacy and safety of Panzytrat® 25 000 Ph Eur Units and Kreon® (an enteric-coated PEP) 25 000 Ph Eur Units for the control of steatorrhea in CF patients with EPI.
AIMS&METHODS: Methods: This open-label, randomized study enrolled patients aged ≥7 years with CF and EPI who were receiving Panzytrat® or Kreon® as their main PEP for ≥30 days. The study employed a crossover design with two 14-day treatment periods. Stools were collected over the last 3 days of each treatment period, and dietary intake was recorded over the last 4 days of each treatment period. The primary end point was the coefficient of fat absorption (CFA%). Stool characteristics and presence/frequency of abdominal symptoms were secondary efficacy end points.
RESULTS: Results: Eighty-seven patients (53 male, 34 female; median age, 12y [range, 7-36y]) were randomized to Panzytrat® then Kreon® (n=42) or Kreon® then Panzytrat® (n=45), with 39 and 42 patients, respectively, completing the study (per protocol population). Both groups had similar baseline nutritional status. Mean study drug compliance was 93-98% during each period. Mean CFA% for patients while taking Panzytrat® was 78.3% (95% confidence interval [CI], 73.2-83.7) and 80.4% (75.2-85.9) for patients on Kreon® (P=0.46, 95% CI, –7.2-4.0 for treatment difference; PP analysis). Thus, Panzytrat® was noninferior to Kreon®.
There were no clinically significant differences in stool characteristics, pain, flatulence or abdominal distention reported between groups. The percentage of patients reporting adverse events (AEs), drug-related AEs (abdominal pain, flatulence or diarrhea) and severe AEs was modestly higher with Panzytrat® than Kreon® (37.2% vs 23.5%, 12.8% vs 4.7% and 18.6% vs 10.6%, respectively). No serious AEs or deaths occurred.
CONCLUSION: Conclusions: Panzytrat® demonstrated noninferiority to Kreon® using CFA% as the primary efficacy parameter in a population of

patients with EPI due to CF. Stool characteristics, abdominal symptoms (pain, flatulence or distention) and AEs did not differ significantly during treatment with Panzytrat® vs Kreon®. Panzytrat® thus provides an efficacious treatment option for CF patients with EPI.
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Disclosure of Interest: None Declared
Keywords: cystic fibrosis, enzyme replacement, pancreatic insufficiency

P094 URSODEOXYCHOLATE AMELIORATES THE TOXIC EFFECT OF CHENODEOXYCHOLATE ON PANCREATIC DUCTAL CELLS

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INTRODUCTION: Recent work by our group has shown that chenodeoxycholate (CDC) at high concentration (1mM) strongly inhibited ion transporters and induced irreversible mitochondrial injury in intact guinea pig pancreatic ducts (*Venglovecz et al. Gut, 2008)*. Previous studies demonstrated that ursodeoxycholate (UDC) and its conjugated forms have antiapoptotic and cell protective effects.
AIMS&METHODS: The AIM of this study was to investigate the effect of UDC on cell damage induced by high concentration of CDC. METHODS: Inta-interlobular ducts were isolated from guinea pig pancreas by enzymatic digestion. Ducts were then pretreated with different concentration of UDC (0.1 and 0.5 mM) for 5 and 24-hours and changes in intracellular Ca^{2+} concentration $[Ca^{2+}]_i$, ATP level $[ATP]_i$ and pH $[pH]_i$ were measured by microfluorometry. Morphological changes of mitochondria were studied by transmission electron microscopy.
RESULTS: 5-hour pretreatment with 0.1 or 0.5 mM UDC and 24-hour pretreatment with 0.1 mM UDC did not significantly influence the effect of 1 mM CDC on duct cells. In contrast, 24-hour pretreatment with 0.5 mM UDC significantly decreased the rate of ATP depletion and mitochondrial injury caused by 1 mM CDC. In addition, 0.5 mM UDC prevented the inhibitory effect of CDC on acid-base transporters.
CONCLUSION: Our results indicate that UDC may represent a novel option against bile acid-induced ductal injury.
This study was supported by OTKA, MTA and NFÜ/TÁMOP
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Disclosure of Interest: None Declared
Keywords: Acute Pancreatitis, chenodeoxycholic acid, mitochondrial injury, ursodeoxycholic acid

P095 CATIONIC ELASTASE AND TRYPSIN ISOFORMS ARE PREMATURELY ACTIVATED UPON DYSBIOSIS IN RATS WITH CHRONICALLY SUPPRESSED GASTRIC ACID SECRETION

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INTRODUCTION: Long-term suppression of gastric acid secretion (LTS-GAS) is associated with a range of negative consequences for the gastrointestinal tract (GIT). One of them is dysbiosis development that leads to colonization of GIT by opportunistic microbiota, thus favouring inflammatory processes both in GIT and associated glands, such as pancreas (Zavros et al., 2002). Premature activation of pancreatic enzymes and self-digestion of the gland are potential consequences. Levels of different pancreatic enzymes in pancreatic tissue, serum and feces are markers of these processes. Cure of dysbiosis with probiotics can help us to elucidate the role of pathogenic microbiota in pancreatic physiology dysregulation.
AIMS&METHODS: The purpose of work was to assess the activity of different pancreatic enzymes and level of α-1-antitrypsin (A1AT) in gland tissue, blood serum and feces, as well as to establish the involvement of dysbiosis in its dysregulation upon LTS-GAS.
The study was performed with white non-strain male rats. Chronical suppression of GAS (second group) was reached by 28-day long abdominal injection of omeprazole (14 mg/kg once a day). Multistrain probiotic "Symbiter" was administrated daily *per os* (third group). Control animals were treated with water.
A1AT level was determined by immunoturbidimetric assay. Trypsin, lipase and pancreatic amylase activities were measured in blood serum and pancreatic tissue with standard spectrophotometric assays. Faecal and pancreatic juice proteolytic profiles were assessed with contact zymography.
RESULTS: Substantial dysbiotic changes in the stomach upon this experimental model were proved by our colleagues (Abdulahad et al., 2012). Significant elevation of serum A1AT (main inhibitor of trypsin and elastase) level and lipase activity was observed; however, serum amylase and trypsin activities weren't changed upon LTS-GAS. Low cationic trypsin activity, as well as slight activation of lipase and amylase were found in rat pancreatic tissue upon LTS-GAS. Subtle activity of cationic (but not anionic) proteases were indicated in few pancreatic juice samples. Enzymography of faecal samples showed increased activity of cationic proteases, which were identified as cationic elastases-1/2 and trypsin-3 starting from 21st day of low gastric acidity. Most of abovementioned parameters weren't deviated form control values upon cure of dysbiosis with multistrain probiotics.
CONCLUSION: Thus, there is evidence of preliminary activation of cationic elastase and trypsin isoforms, as well as important role of GIT dysbiotic changes as causative factor upon long-term suppression of gastric acid secretion.

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Disclosure of Interest: None Declared
Keywords: dysbiosis, elastase, Hypochlorhydria, pancreas, trypsin

P096 ATPI IS A KEY MOLECULE IN THE TOXICITY OF ETHANOL AND ITS NON-OXIDATIVE METABOLITES ON CFTR FUNCTION

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INTRODUCTION: Excessive alcohol consumption causes acute pancreatitis but the mechanism involved is not well understood. Recent investigations suggest that pancreatic ductal epithelial cells (PDECs) are involved in the pathogenesis of pancreatitis. Because the cystic fibrosis transmembrane conductance regulator (CFTR) Cl^- channel plays a major role in PDEC anion and fluid secretion, and that dysfunction of CFTR is often associated with pancreatitis, we therefore tested the hypothesis that ethanol exerts a direct effect on CFTR to impair ductal function.
AIMS&METHODS: The dose- and time-dependent effects of ethanol, its oxidative and nonoxidative metabolites (acetaldehyde (Ac) and palmitoleic acid ethyl ester (POAEE), respectively) and palmitoleic acid (POA) were investigated on CFTR activity on freshly isolated guinea pig PDECs and Capan-1 cell line, using the whole cell configuration of the patch clamp technique. Changes in intracellular ATP (ATP_i) were measured by spectrofluorometry.
RESULTS: Ethanol (10 and 100 mM) significantly increased the basal, but reversibly blocked forskolin-stimulated CFTR currents. The inhibitory effect of ethanol was mimicked by POAEE and POA, the latter being produced by fatty acid ethyl esterase hydrolase. Ethanol, POAEE and POA caused depletion of intracellular ATP (ATP_i) linked to CFTR inhibition, since their inhibitory effects were almost completely abolished if ATP_i depletion was prevented.
CONCLUSION: We propose that ethanol causes functional damage of CFTR through an ATP_i-dependent mechanism. Furthermore, we suggest that the maintenance of ductal ATP_i may represent a therapeutic option in the treatment of the disease.
This study was supported by OTKA, MTA and NFÜ/TÁMOP.
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Disclosure of Interest: None Declared
Keywords: CFTR, Ethanol, Pancreatic ductal cells

P097 THE STRAIN DEPENDENCY OF L-ARGININE-INDUCED ACUTE PANCREATITIS IN MICE

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INTRODUCTION: Acute pancreatitis (AP) is a sudden inflammation of the pancreas. The pathogenesis of AP is not well understood and the disease has no specific therapy. To investigate the pathomechanism of AP, we mainly rely on animal models such as L-arginine-induced AP. The use of L-arginine to induce AP in mice is becoming increasingly popular. However, we found high mortality with the originally published dose (2x4 g/kg) of L-arginine in mice. Thus, we aimed to establish a basic amino acid-induced AP model with a lower mortality rate.
AIMS&METHODS: AP was induced with various intraperitoneal (ip.) doses of L-arginine in FVB/n or C57Bl/6 mice. Control mice were injected with physiological saline. Laboratory (serum amylase and pancreatic myeloperoxidase activities) and histological (necrosis and inflammatory infiltration) parameters were measured to determine AP severity.
RESULTS: Ip. injection of mice with 2x4 g/kg L-arginine resulted in a 82 % mortality rate in FVB/n and 55 % in C57Bl/6 mice, which was independent of AP. Using 4 hourly injections of 2.5 g/kg L-arginine, we found significantly lower mortality (33 % in FVB/n and 10 % in C57Bl/6 mice), and similar degree of AP morbidity compared to 2x4 g/kg L-arginine dose. The pancreatic myeloperoxidase and serum amylase activities and histological parameters were significantly elevated in all L-arginine treated groups compared to control mice.
CONCLUSION: Different mouse strains show various sensitivities to L-arginine and there is a fine borderline between the effective and lethal dose of L-arginine. All laboratories have to precisely determine the effective dose of L-arginine used for the induction of AP.
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Disclosure of Interest: None Declared
Keywords: Acute Pancreatitis, basic amino acids

P098 MANIFESTATIONS OF ENDOGENOUS INTOXICATION IN ACUTE PANCREATITIS-ASSOCIATED LUNG DAMAGE IN EXPERIMENTAL CYTOFLAVIN CORRECTING

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INTRODUCTION: Despite some progress in the diagnosis and treatment of acute pancreatitis, some aspects of its pathogenesis remain poorly understood, which, along with other determining factors impact on fatality rates, which vary between 5-22% [1, 3], when the disease is complicated development of the syndrome of acute lung injury mortality reaches 48-86% [2] without a significant trend towards improvement in recent decades.

AIMS&METHODS: The aim of the study was to examine the effectiveness of multiantihypoxants and antioxidant "Cytoflavin" at different stages of acute pancreatitis-associated lung injury in rats.

The experiment simulated acute pancreatitis in rats by two intraperitoneal injections of 20% L-arginine (total dose of 5 g/kg, with an interval of one hour) by the method of L. Czako. In the comparison group animals within 5 min after simulation acute pancreatitis injected drug "Cytoflavin" in a dose of 0.21 ml/kg body weight. Determined amylase, Medium Molecule MM_{254} and MM_{280} content, the level of malonic aldehyde, diene conjugates in blood, lung and pancreas tissue examined histologically.

RESULTS: In experimental acute pancreatitis indicators of endogenous intoxication significantly increases of over 12-48 h, which is directly dependent on the severity of membrane destruction processes in the tissues of the pancreas against the growing activity of lipid peroxidation. Determined a significant increase in lipid peroxidation, which triggers a similar increase in the content of its products in the blood. However, the medical correction within the first 72 hours, there was reduction of malonic aldehyde and diene conjugates by 3.54 % and 31.25 % compared to similar indicators in the control group ($p < 0,05$).

CONCLUSION: Use of the drug "Cytoflavin" reduces the severity of endotoxemia: reducing MM - 24 h and 72 h, malonic aldehyde and diene conjugates - after 24 hours. He also has a positive impact on the protective components of aero-hematic barriers and reducing their damage in acute pancreatitis-associated lung damage in the experiment by reducing swelling interalveolar barriers and improve microcirculation.

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Disclosure of Interest: None Declared

Keywords: Acute Pancreatitis, acute pancreatitis-associated lung injury, endogenous intoxication, cytoflavin

P099 TRYPTOPHAN METABOLITE; KYNURAMINE ATTENUATES ACUTE PANCREATITIS IN THE RATS AND INCREASES PRODUCTION OF HEAT SHOCK PROTEIN

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INTRODUCTION: Melatonin precursor: L-tryptophan protects the pancreas against acute pancreatitis. The effect of L-kynuremine (KYN), the product of L-tryptophan metabolism, on acute pancreatitis has not been investigated. Heat shock protein (HSP) are intracellular chaperons, guarding the other proteins.

AIMS&METHODS: To assess the effects of KYN on caerulein-induced pancreatitis (AP) in the rats and on HSP60 production in AR42J pancreatic acinar cell line.

AP was induced by subcutaneous caerulein infusion (25 microgr/kg). KYN (25, 50 or 100 mg/k) was given intraperitoneally to the rats 30 min prior to the induction of AP. Lipid peroxidation products (MDA+4HNE) and the activity of an antioxidant enzyme; glutation peroxydase (GPx) were measured in pancreatic tissue. Blood samples were taken for evaluation of amylase and TNF alpha concentrations. HSP60 was determined by Western blot in AR42J cells subjected to KYN (10^{-12}, 10^{-10}, 10^{-8}) without or with addition of caerulein (10^{-8}M).

RESULTS: AP was confirmed with histological examination and by the increases of amylase and TNF alpha blood levels (by 800% and 300%, respectively). In the pancreas of AP rats contents of MDA+4HNE was increased by 300%, whereas GPx activity was reduced by 50%. KYN significantly diminished histological manifestations of AP, dose-dependently decreased amylase and TNF alpha blood levels, significantly reduced MDA+4HNE and augmented GPx in the pancreas of AP rats. In AR42J cells KYN (10^{-10} 10^{-8}) alone or combined with caerulein markedly increased HSP60 protein signal.

CONCLUSION: L-kynuremine significantly attenuated acute pancreatitis. This beneficial effect could be related to the antioxidative effect of: L-kynuremine and, possibly, to the increase of HSP60 in the acinar cells.

Disclosure of Interest: None Declared

Keywords: heat shock protein, L-kynuramine, pancreatic acinar cells, pancreatitis

P100 ETHANOL AND FATTY ACIDS STRONGLY INHIBIT PANCREATIC DUCTAL BICARBONATE SECRETION AND DECREASE THE EXPRESSION OF CFTR CHLORID CHANNEL IN PANCREATIC DUCTAL EPITHELIAL CELLS

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INTRODUCTION: Excessive ethanol (EtOH) consumption is one of the most common causes of acute pancreatitis, which has no specific treatment. Pancreatic ductal epithelial cells (PDEC) secrete HCO_3^- rich fluid via Cl^-/HCO_3^- exchanger (CBE) and cystic fibrosis Cl^- channel (CFTR), which prevents acinar damage. However, no information is available about the effects of EtOH and EtOH metabolites ((fatty acid ethyl esters (FAEE) and fatty acids (FA)) on PDEC.

AIMS&METHODS: In our experiments human pancreatic epithelial cell line (Capan-1), guinea pig and human pancreatic tissue were used. The effects of EtOH, FAEE and FA on intracellular pH (pH_i), Ca^{2+} concentration ($[Ca^{2+}]_i$), ATP [$(ATP)_i$], mitochondrial membrane potential ($\Delta\Psi$) and CFTR Cl^- current were measured. The effect of EtOH and FA on the expression and localization of CFTR were analysed in PDEC, in guinea pig and human pancreatic tissue samples.

RESULTS: High concentration of EtOH (100mM) and palmitoleic acid (POA) (200μM) strongly decreased the activities of the apical CBE and CFTR and inhibited the HCO_3^- secretion of PDEC *in vitro* after 10 min. The administration of 100mM EtOH and 200μM POA induced sustained $[Ca^{2+}]_i$ elevation by releasing Ca^{2+} from the endoplasmic reticulum via IP_3 and ryanodin receptor activation and extracellular Ca^{2+} influx. Moreover 100mM EtOH and 200μM POA depleted the $(ATP)_i$ and decreased $\Delta\Psi$. The prevention of the sustained $[Ca^{2+}]_i$ elevation abolished the inhibitory effect of EtOH and POA. The expression of CFTR was significantly decreased by EtOH and POA after 48h in PDEC. Moreover *ip* injection of EtOH and FA decreased the luminal expression of CFTR in guinea pig pancreas. Importantly, we observed the same decrease in the pancreatic tissue of acute and chronic alcoholic pancreatitis patients.

CONCLUSION: These results suggest that EtOH and FA inhibit pancreatic ductal HCO_3^- secretion via sustained $[Ca^{2+}]_i$ elevation and decrease the expression of CFTR, which can contribute to the development of acute pancreatitis. The restoration of the HCO_3^- secretion may be a potential therapeutic target in alcohol induced acute and chronic pancreatitis.

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Disclosure of Interest: None Declared

Keywords: Acute Pancreatitis, CFTR, Ethanol, PANCREATIC BICARBONATE SECRETION, Pancreatic ductal cells

P101 INFLAMMATORY AND OXIDATIVE STRESS MARKERS IN RAT PANCREAS UPON LONG-TERM GASTRIC HYPOCHLORHYDRIA AND ITS CORRECTION WITH MULTIPROBIOTIC "SYMBITER"

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INTRODUCTION: Long-term usage of medications suppressing gastric acid secretion upon treatment of acid-related disorders is a risk factor for acute pancreatitis development or even pancreatic malignization [1, 2]. But common factors and mechanisms of pancreatic structural and functional reorganization upon long-term gastric hypochlorhydria are still poorly understood. Probiotics are widely used for restoration of gastrointestinal tract homeostasis, since they have a broad spectrum of biological activity.

AIMS&METHODS: The purpose of study was to assess the cytokine profile and intensity of free-radical processes in rat pancreas upon long-term gastric hypochlorhydria and administration of multiprobiotic "Symbiter".

All experiments were carried out on white non-strain male rats. Hypochlorhydria was induced by 28-day long abdominal omeprazole injection (14 mg/kg once a day). The second group of rats simultaneously with omeprazole was treated with "Symbiter" (0.14 ml/kg *per os*). Control animals were treated with water: 0.2 ml abdominally + 0.5 ml orally during 28 days. Studied parameters were determined in pancreatic homogenates with standard assays.

RESULTS: The increased levels of reactive oxygen species in rat pancreas upon long-term gastric hypochlorhydria were observed: superoxide anion and hydrogen peroxide levels were 1.5 and 1.8 times higher than control, respectively. Upon the same conditions, thioredoxin reductase activity, total NO-synthase activity, nitric oxide content and iNOS gene expression were 1.8, 4, 2.3 and 3 times higher than control, correspondingly. Upregulation of IL-1α, IL-6, IL-8, TNF-α and IFN-γ upon these conditions was also observed: their levels were 2.8, 1.5, 4.5, 3 and 1.8 times higher in comparison with the control, respectively. At the same time IL-4 and IL-10 concentrations were decreased in 1.5 and 1.8 times. Joint administration of multiprobiotic «Symbiter» with omeprazole was associated with normalization of studied parameters in rat pancreatic tissue.

CONCLUSION: The intensification of free-radical processes and inflammation development in rat pancreas upon long-term gastric hypochlorhydria were established. Multiprobiotic «Symbiter» exerted antioxidative and immunomodulatory properties upon correction of hypochlorhydria-associated consequences in pancreas.

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Disclosure of Interest: None Declared
Keywords: cytokine profile, free-radical processes, long-term gastric hypochlorhydria, multiprobiotic, pancreas

P102 ATAXIA TELANGIECTASIA MUTATED LOSS DRIVES PANCREATIC CANCER FORMATION VIA EMT INDUCTION

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INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is one of the leading causes of cancer deaths in the developed world, with a 5 year survival rate as low as 5%. In recent years, genetically engineered animal models of pancreatic cancer which recapitulate the human disease have provided a useful means of studying both the morphological and molecular features associated with PDAC.
AIMS&METHODS: The most commonly studied model to date has been the expression of active Kras under the control of an endogenous, pancreas specific promoter which leads to a spectrum of changes in the pancreas recapitulating development of human PDAC. Interestingly, PDAC develops much more rapidly when further oncogenes such as *SMAD4* or p53 are deleted.
RESULTS: In the current study, we address the role of Ataxia Telagiectasia Mutated (Atm) gene in PDAC and describe a loss of ATM protein with advanced UICC stage in primary human tumor specimens. We also found that mutations in the ATM gene are more abundant in large collectives of human pancreatic cancer. Subsequently, we show that loss of Atm enhanced the metastatic potential of the Kras mouse model and decreased survival of mice to 36 and 38 weeks for homozygous and heterozygous Atm deletion, respectively. These mice developed a greater number of pre-malignant pancreatic intraepithelial neoplasias (mPanINs) with a significant increase in proliferation and α-smooth muscle actin positive cells, indicative of activated pancreatic stellate cells (PSCs). This was followed by an increase in large, dysplastic papillary lesions and a significant amount of surrounding fibrosis compared to controls. Our results furthermore establish that the loss of Atm in this mouse model promoted early EMT and a dedifferentiated PDAC phenotype. Moreover, early EMT upon ATM loss was associated with increased invasive properties.
CONCLUSION: Taken together, our data suggests that there may be an intimate link between Atm activity and pancreatic cancer formation, one of the major signalling pathways altered in PDAC and targeting this axis may provide therapeutic potential in the future.
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Disclosure of Interest: None Declared
Keywords: ATM, Mouse model, Pancreatic cancer

P103 OVEREXPRESSION OF P-HSP27, HSP70 AND HSP90A/B IN PANC-1 CELLS IN RESPONSE TO KYNURAMINES. INVOLVEMENT OF 5-HT AND MEL A/B-1 RECEPTORS.

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INTRODUCTION: Kynuramines, metabolites of L-tryptophan and melatonin, are synthetized endogenously by oxygenases or by interaction with free radicals. Previously we have reported that melatonin stimulated expression and phosporylation of HSP27, production of HSP70 and HSP90a/b in PANC-1 cells. Based on above results, we hypothetized that above process could be involved in the mechanism of intrinsic proapoptotic pathway interruption.
AIMS&METHODS: Here in, we would like to present that L-kynurenine (L-KYN) and N^1-acetyl-N^2-formyl-5-methoksykynuramine (AFMK) lead to the overexpresion of HSPs synthesis and that this process is partially abolished by 5-HT_3 or Mel A/B-1 receptors antagonists. PANC-1 cells in culture were treated with L-kynurenine or AFMK, Mel A/B-1 receptors antagonist; luzindole, 5-$HT2_{,3}$ receptor antagonists; ketanserin, MDL72222, or combination of above. After incubation, cells had been harvested, the cytoplasmic and nuclear proteins fractions were isolated for immunoblotting or/and immunoprecipitation analysis of HSP27, HSP70 and HSP90$\alpha\beta$.
RESULTS: Our studies have shown that both L-kynurenine and AFMK significantly decreased cytoplasmic HSP27 content, presumably due to increase of its phosphorylation and consequent translocation, confirmed by immunoprecipitation of phosphorylated HSP27. These changes were accompanied by slight augmentation of HSP70 and HSP90 abundance in cytosolic fraction. Pretreatment of the cell cultures with luzindole or MDL72222 followed by the addition of kynuramines reversed the stimulatory effects of L-KYN or AFMK on HSPs expression in PANC-1 cells, whereas ketanserin failed to affect analyzed protein signal.
CONCLUSION: We conclude that L-kynurenine or AFMK could stimulate phosphorylated HSP27, HSP70 and HSP90$\alpha\beta$ production in PANC-1 cells through interaction with the Mel A/B-1 or/and 5-HT_3 receptors.
Disclosure of Interest: None Declared
Keywords: heat shock protein, kynuramines, melatonin receptor, pancreatic carcinoma

P104 LYMPHOTOXIN-ASSOCIATED INFLAMMATION AS AN ETIOLOGICAL FACTOR OF PANCREATIC CARCINOGENESIS

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INTRODUCTION: Pancreatic inflammation is a well-known risk factor for pancreatic ductal adenocarcinoma (PDAC) development in humans, and its initiation is linked to activating mutations in KRAS oncogene. Recent studies propose a stepwise process starting from acinar cells undergoing ductal reprogramming (acinar to ductal metaplasia, ADM) throughout premalignant PanIN (pancreatic intraepithelial neoplasia) lesions leading to tumor formation. However little is known about the mechanisms how inflammatory damage promotes ADM and PanIN progression.
AIMS&METHODS: Here we establish a new genetic model by intercrossing the commonly used $p48^{+/Cre}$;$Kras^{+/G12D}$ (KP) model for pancreatic tumorigenesis, to a novel transgenic mouse developing spontaneous pancreatic inflammation, due to overexpression of Lymphotoxin (LT). Immunohistochemistry along with RT-PCR were used to obtain an inflammatory signature.
RESULTS: Overexpression of Lymphotoxin in mice harbouring a constitutively active form of Kras mutation in the pancreas (LTKP) dramatically accelerates the development of premalignant PanIN lesions compared to KP animals. Already at the age of 6 weeks we observed highly proliferating cells, development of ADM and PanIN in LTKP mice. This coincided with a significant upregulation of pro-inflammatory cytokines and cell-cycle inhibitors. This type of molecular and phenotypic change was only observed around 16 weeks of age in Kras animals. Similarly, earlier activation of downstream targets of Kras was observed in LTKP mice. Furthermore, in the KP model we detected a significant elevation of ligands and receptors of the LTβR-signalling pathway during PanIN progression.
CONCLUSION: Our data point towards the involvement of LTβR-signalling in the initiation of pancreatic cancer, revealing Lymphotoxin as a critical component of spontaneous and pancreatitis-accelerated PDAC precursor formation.
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Disclosure of Interest: None Declared
Keywords: inflammation, KRAS oncogene, Lymphotoxin, metaplasia, PanIN

P105 NEURAL INVASION IN PANCREATIC CANCER IS CHARACTERIZED BY BETA-1-INTEGRIN- AND L1-CAM-DEPENDENT HETEROTYPIC CELL ADHESION BETWEEN PANCREATIC CANCER CELLS AND NEURAL SCHWANN CELLS

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INTRODUCTION: Neural invasion is one of the most frequent modes of tumor spread in pancreatic cancer (PCa). However, how PCa cells can attach to and migrate along Schwann-cell-covered axons in nerves remains unclear.
AIMS&METHODS: The aim of this study was to investigate the potential heterotypic cell adhesion between PCa cells and Schwann cells (SC) and to identify the surface molecules that enable this interaction. Human SC, PCa cells, human PCa tissue, normal human pancreas and intrapancreatic nerves were investigated for the expression of the cell adhesion molecules beta-1-Integrin, NCAM, L1-CAM and NrCAM via immunoblotting, QRT-PCR and immunohistochemistry. Heterotypic cell adhesion and mutual migration between SC and PCa cells were quantified via a recently established adhesion assay and 3D migration assay by applying neutralizing antibodies against these adhesion molecules.
RESULTS: Expression of beta1-Integrin and L1-CAM were more prevalent in PCa tissues, human SC, intrapancreatic nerves and PCa cells than NCAM and NrCAM. Confrontation of SC with PCa cells led to rapid heterotypic cell adhesion, which could be inhibited by neutralizing antibodies against beta-1-Integrin and L1-CAM, but not against NCAM and NrCAM on PCa cells. Similarly, blockade of beta-1-Integrin on PCa cells diminished the carcinotropic migration of SC. Interestingly, inhibition of these molecues on SC did not influence the adhesion or carcinotropic migration of SC.
CONCLUSION: Neural invasion harbors heterotypic cell adhesion and mutual migration between SC and PCa cells. Therefore, cell-cell-adhesion represents a key pathophysiological mechanism in neural invasion and for the associated local tumor recurrence and neuropathic pain in PCa.
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Disclosure of Interest: None Declared
Keywords: adhesion, neural invasion, pancreatic cancer, Schwann cells

P106 PHOTOACOUSTIC ULTRASOUND IMAGING TO DETECT HYPOXIC AREAS IN A SYNGENEIC, PRECLINICAL MODEL OF PANCREATIC DUCTAL ADENOCARCINOMA

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INTRODUCTION: Preclinical testing of novel therapeutics in mouse models relies on reproducible read-outs to assess treatment efficacy. Non-invasive imaging techniques are thus pivotal to assess orthotopic tumor growth in internal organs, which defy conventional caliper measurements.
To this end, high frequency ultrasound for rodents has been introduced, which allows for conventional B-mode scans, as well as color-coded Doppler imaging of internal organs. As an emerging technology, photoacoustic scanners provide additional functional information such as tissue oxygenation, which can be combined with conventional ultrasound. Here, we applied 3D-photoacoustics to

assess tumor growth and intraparenchymal oxygen saturation longitudinally in a syngeneic, orthotopic model of pancreatic carcinoma in mice.
AIMS&METHODS: Murine pancreatic ductal adenocarcinoma cells (C57BL/6 background) were injected intrapancreatically and subcutaneously using high-frequency ultrasound guidance (Visualsonics Vevo®-LAZR integrated micro-ultrasound/photoacoustic system, VisualSonics, Canada). Tumor development was monitored by trimodal imaging (3D-ultrasound, 3D-photoacoustics, IVIS-Spectrum-bioluminescence). In particular, relative tissue oxygen saturation was determined with a photoacoustic probe (20Hz tunable laser 680-970nm) in 3D and overlaid with B-mode ultrasound data. Specific labeling of hypoxic areas on tissue specimens was achieving using immunohistochemic detection of pimonidazol (hypoxyprobe), which was injected prior to sacrifice when tumors reached the size of 0.8 cm^3.
RESULTS: Conventional ultrasound, photoacoustics and bioluminescence imaging allow monitoring tumor growth at different resolution and accuracy. Photoacoustic imaging can be utilized to monitor the development of hypoxic and necrotic regions in subcutaneous and orthotopic pancreatic tumors. Photoacoustic signatures of tissue hypoxia can be correlated to hypoxic regions as detected in post-mortem analysis.
CONCLUSION: Photoacoustic imaging can be utilized to detect hypoxic and necrotic tumor regions in pancreatic carcinoma mouse models and is a putative novel tool to assess early treatment response in preclinical studies.
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Disclosure of Interest: None Declared
Keywords: Imaging, Mouse, pancreatic adenocarcinoma, Ultrasound

P107 HEAT TREATMENT INHIBITS EPITHELIAL-MESENCHYMAL TRANSITION (EMT) IN HUMAN PANCREATIC ADENOCARCINOMA CELL LINE.

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INTRODUCTION: Pancreatic cancer (PC) is an aggressive malignancy that has a proclivity to lead to early metastasis and relatively poor outcome. Although gemcitabine (GEM) is the standard therapy for PC, survival benefit is insufficient. Recently, it has been reported that epithelial-to-mesenchymal transition (EMT) plays a crucial role in cancer metastasis and is associated with a poor prognosis in patients with PC. And GEM-resistant pancreatic cancer cells have shown to be associated with EMT. We have reported that heat treatment inhibited NF-kB activation, which mediates EMT and resistance to chemotherapy. In this study, we evaluated the effect of heat treatment on TGF-β or GEM-induced EMT in pancreatic cancer cells. Moreover, we evaluated the efficacy of regional hyperthermia (HT) combined with GEM in patients with unresectable locally advanced PC.
AIMS&METHODS: Human pancreatic cell lines (PANC-1, MIAPaCa-2 and BxPC-3) were stimulated by TGF-β or GEM, and evaluated for morphological changes using immunofluorescence and EMT-related factors (i.e. E-cadherin, Vimentin, Snail and Zeb-1) using RT-PCR. To examine the effect of heat on EMT, the cells were treated with heat (43°C) for 1h followed by the stimulation of TGF-β (10ng/ml). Moreover, we retrospectively analyzed 10 patients with unresectable locally advanced PC, who received combination therapy with GEM and HT at our hospital between November 2008 and December 2011. The patients received GEM (1000mg/m2) intravenously on day 1, 8 and 15, and HT (40min/once) weekly.
RESULTS: After treatment with TGF-β or GEM, pancreatic cancer cells changed their morphology from a typical epithelium to mesenchymal spindle-shaped. The expression of vimentin and snail was up-regulated by TGF-β or GEM, and the expression of E-cadherin was down-regulated. These TGF-β-induced changes in morphology and expression of EMT-related factors were attenuated by the heat treatment. As for clinical efficacy of HT, the objective response rate and disease control rate were 20% and 100%, respectively. Median overall survival was 17.3 months. No severe HT-related toxicities were observed.
CONCLUSION: Our results suggest that the heat treatment could suppress TGF-β- and GEM-induced EMT, and HT could improve prognosis of locally advanced PC. These results support the potential of HT as a treatment for cancer metastasis.
Disclosure of Interest: None Declared
Keywords: EMT, pancreatic adenocarcinoma, Pancreatic Cancer

P108 COMBINED SUPPRESSION OF NOTCH AND JAK/STAT IMPAIRS PANCREATIC CANCER PROGRESSION IN VITRO AND IN VIVO AND IS SUPERIOR TO MONOTHERAPIES

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INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive disease with a high rate of metastasis. Recent studies have indicated that Notch and JAK2/STAT3 signaling pathways are both important for the initiation and progression of PDAC.
AIMS&METHODS: The purpose of this study was to determine the outcome of targeting these two tumor signaling pathways simultaneously both *in vitro* and *in vivo*. We assessed the combinational effects of the gamma-secretase inhibitor IX (GSI IX) and JAK2 inhibitor (AG-490) on growth and epithelial plasticity of human pancreatic cancer cell lines, and in a genetically engineered mouse model (Pdx1- Cre; LSL-KrasG12D; p53 $^{lox/+}$) of PDAC.
RESULTS: Dual treatment with GSI IX and AG-490 significantly impaired cell proliferation, migration, invasion, soft agar growth and apoptosis when compared to monotherapies. Most importantly, combinational treatment significantly attenuates tumor progression *in vivo* and suppresses conversion from acinar-ductal-metaplasia (ADM) to PDAC.
CONCLUSION: Our results suggest that targeting Notch and JAK2/STAT3 signaling pathways simultaneously is superior to single inhibitions, supporting combined treatment by GSI X and AG-490 as a potential therapeutic approach for PDAC.
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Disclosure of Interest: V. Palagani: None Declared, P. Bozko: None Declared, M. El Khatib: None Declared, H. Belahmer: None Declared, B. Sipos: None Declared, N. Malek: None Declared, R. Plentz Financial support for research from: DFG, TUI
Keywords: Jak/ STATpathway, notch pathway, PDAC

P109 IDENTIFICATION OF A SUBPOPULATION OF PANCREATIC CANCER PATIENTS WITH MTOR DEREGULATION: NEW CHANCES FOR RAPAMYCIN TREATMENT

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INTRODUCTION: Pancreatic cancer (PC) remains one of the most lethal common malignancies worldwide. Deregulation of several core signaling pathways have been identified in PC and distinct pathways are affected between different patients. Hence, personalized based medicine is an attractive approach in the treatment of PC.
AIMS&METHODS: We aim to identify a subpopulation of PC patients with activation of the Mammalian Target Of Rapamycin (mTOR) pathway by measuring phosphorylated S6 (pS6), a downstream protein of the mTOR pathway, in Endoscopic Ultrasound–Fine Needle Aspiration (EUS-FNA) obtained tissue.
Methods: Immunohistochemical (IHC) staining of pS6 on Formalin Fixed Paraffin Embedded (FFPE) specimens from PC resection was performed. To study mTOR activation and inhibition by rapamycin, PC cell lines were analyzed by means of western blot (cleaved caspase 3, pS6, LC3A/B), cell viability assays and flow cytometry (pS6). Single cell suspensions obtained through EUS-FNA of pancreatic tumors were stained for cytokeratin 8/18 (CK8/18) and pS6 expression and subsequently analyzed using flow cytometry.
RESULTS: The proportion of tissue (n=66) expressing pS6 is 50% in healthy ducts, 67% in PanIN lesions, and 82% in tumor regions. In PC cell lines, rapamycin decreased cell viability in a dose dependent manner and decreased pS6 expression by 30 to 665-fold.
On flow cytometry analysis of cell lines, two hours of incubation with 0.1 μM rapamycin reduced the Mean Fluorescence Intensity (MFI) in CK8/18 positive cells of pS6 by more than 50%. Similarly, in ex vivo analysis of fresh EUS-FNA tissue, rapamycin inhibited pS6 expression in CK8/18+ cells in two out of nine samples (22%). In these potential responders, rapamycin reduced the amount of pS6 expressing cells by more than 90%. Potential responders showed a mean reduction in MFI of 81.3% (±2.7%), while the average MFI change in non-responders was 8.8% (±6.1%) ($p<0.01$).
CONCLUSION: As hypothesized, great variation exists in the expression of pS6 between PC patients. In PC cell lines, rapamycin markedly reduced cell viability and pS6 expression. Validation in ex vivo EUS-FNA biopsies showed a subpopulation of PC patients sensitive for rapamycin. The result of this study shows that in PC patients, the identification of a subpopulation eligible for mTOR inhibition is possible which is a first step towards personalized based medicine in PC.
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Disclosure of Interest: None Declared
Keywords: EUS-FNB, mTOR, Pancreatic Cancer, Personalized medicine, Rapamycin

P110 THE ASSOCIATIONS BETWEEN THE COAGULATION/IMMUNE MOLECULES AND SYSTEMIC TRAFFICKING OF BONE MARROW-DERIVED STEM CELLS IN PATIENTS WITH PANCREATIC NEOPLASMS.

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INTRODUCTION: Recently we have reported that in patients with pancreatic malignancies intensified peripheral trafficking of bone marrow (BM)-derived stem cells (SCs) occurs (*Starzynska et al. JCMM 2013*), and this was associated with activity of the complement cascade. Nevertheless, the mechanisms responsible for selective SCs mobilization in patients with malignancy are not known, and immune system together with coagulation cascade are hypothesized to contribute to this phenomenon.
AIMS&METHODS: In this study we examined a panel of immune-derived chemokines (IL-1, IL-6, IL-8, IL-10, IL-12, IL-17 and IL-23), coagulation molecules (kalikrein 2 and 10, TAT) together with inflammatory molecules (tumor necrosis factor-alpha-TNFα and granulocyte-colony stimulating factor-G-CSF), and verified whether activity of these molecules was associated with abnormal peripheral trafficking of BMSCs in patients with pancreatic neoplasms. 26 patients with pancreatic neoplasms (22 *adenocarcinoma*, 4 neuroendocrine tumors) and 32 control individuals were recruited. Plasma levels of these molecules were measured using ELISA.

RESULTS: Significantly higher levels of IL-6, IL-8, IL-10, TAT, TNFα, and lower of IL-23 were observed in patient with pancreatic neoplasms (in all cases at least $P<0.02$). IL-6, IL-8, TNFα and TAT levels negatively correlated with absolute numbers of circulating hematopoietic and endothelial stem/progenitor cells (in all cases $P<0.05$), and IL-10 was positively correlating with numbers of very small embryonic/epiblast-like stem cells ($P<0.05$). Furthermore, analysis using receiver operating characteristics (ROC) curves demonstrated area under ROC curve values ranging between 0.70-0.83 for IL-6, IL-8, IL-10, TAT and TNFα.
CONCLUSION: Selected coagulation and immune-derived molecules seem to be involved into the orchestration of abnormal peripheral trafficking of BMSCs in patients with pancreatic neoplasms. Clinical significance and predictive value of examined molecules require furthers investigations. Study supported by Ministry of Science and Higher Education grant (402 423038) assigned to TS.
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Disclosure of Interest: None Declared
Keywords: bone marrow-derived stem cells, coagulation cascade, interleukins, pancreatic neoplasms

P111 CLOBENPROPIT ENHANCES ANTI-TUMOUR EFFECT OF GEMCITABINE IN PANCREATIC CANCER

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INTRODUCTION: Histamine is associated with carcinogenesis through activation of its 4 membrane-specific receptors. We evaluated the anti-tumour effect of clobenpropit, which is the specific H_3 antagonist and H_4 agonist, with gemcitabine combination in pancreatic cancer cell line.
AIMS&METHODS: Three kinds of human pancreatic cancer cell lines (Panc-1, MiaPaCa-2, and AsPC-1) were used in this study. Expression of H_3 and H_4 receptor in pancreatic cancer cell was identified with Western blotting. Effects of clobenpropit on cell proliferation, migration and apoptosis were evaluated. Alteration of epithelial and mesenchymal markers after administration of clobenpropit was analyzed. *In vivo* study with Panc-1 xenograft mouse model was also performed.
RESULTS: H_4 receptors were present as 2 subunits in human pancreatic cancer cells, while there was no expression of H_3 receptor. Clobenpropit inhibited cell migration and increased apoptosis of pancreatic cancer cells in combination with gemcitabine. Clobenpropit up-regulated E-cadherin, whereas down-regulated vimentin and matrix metalloproteinase 9 in real-time PCR. Also, clobenpropit inhibited tumor growth and enhanced apoptosis in combination with gemcitabine by up-regulation of E-cadherin and down-regulation of Zeb1 in Panc-1 xenograft mouse.
CONCLUSION: Clobenpropit enhanced anti-tumour effect of gemcitabine in pancreatic cancer cells through inhibition of epithelial-mesenchymal transition process.
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Disclosure of Interest: None Declared
Keywords: Clobenpropit, Epithelial-mesenchymal transition, Histamine receptor, Pancreatic Cancer

P112 INSULIN-LIKE GROWTH FACTOR-I RECEPTOR AS A CANDIDATE FOR A TARGETING MOLECULE IN HUMAN PANCREATIC ADENOCARCINOMA HAVING A MUTATED K-RAS

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INTRODUCTION: Insulin-like growth factor-I receptor (IGF-IR) signaling is required for tumorigenicity and progression of human malignancies, including human pancreatic adenocarcinoma. We have previously reported successful therapy for several gastrointestinal carcinomas using recombinant adenoviruses expressing dominant negative IGF-IR (IGF-IR/dn, Ad-IGF-IR/dn). Mutation (MT) in k-ras plays important roles in both the progression and the resistance for anti-EGFR therapy in gastrointestinal cancers and is detected in around 80% of pancreatic cancer.
AIMS&METHODS: In this study, we sought to evaluate the effect of IGF-IR targeting therapy for human pancreatic adenocarcinoma with k-ras MT. We assessed the effect of IGF-IR blockade on proliferation, survival, and signal transduction in several pancreatic cancer cell lines with or without k-ras MT. Combination effects of anti-IGF-IR and chemotherapy were studied. Then IGF-IR blockades were evaluated in the treatment for pancreatic cancer xenografts in nude mice. To block IGF-IR signals, we used an Ad-IGF-IR/dn and a monoclonal antibody for IGF-IR.
RESULTS: IGF-IR blockades suppressed proliferation and tumorigenicity. Targeting for IGF-IR inhibited survival by itself and up-regulated chemotherapy (5-FU and gemcitabine) induced apoptosis. Anti-IGF-IR blocked autophosphorylation of the receptor and the downstream signals. Moreover, the combination of anti-IGF-IR and chemotherapy was effective against tumors on mice. The effect of IGF-IR blockade was not influenced by the MT stasis of k-ras. IGF-IR targeting reduced peritoneal dissemination and prolonged survival of k-ras mutated tumor bearing mice. The drug did not affect on neither murine body weight nor blood concentrations of glucose, insulin, and IGFBP-3.
CONCLUSION: IGF-IR might be a good molecular therapeutic target for human pancreatic adenocarcinomas even if k-ras is mutated.
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Disclosure of Interest: None Declared
Keywords: insulin-like growth factor receptor, k-ras mutation, molecular targeting, pancreatic adenocarcinoma

P113 ASSESSMENT OF GLUCOSE TOLERANCE, INFLAMMATORY CYTOKINES AND ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH CHRONIC PANCREATITIS AND NEWLY DIAGNOSED PANCREATIC CANCER

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INTRODUCTION: Patients with chronic pancreatitis (CP) and pancreatic cancer (PC) often demonstrate abnormal glucose metabolism. The mechanism of the association between diabetes and these diseases is elusive but is known to results in metabolic, hormonal and immunological alterations that influence tumor growth.
AIMS&METHODS: The aim of the study was to identify the differences in cytokines and parameters of endothelial dysfunction and observe their correlations with the glycemic status in patients with CP and PC. A total of 45 patients were included in the present investigation, 27 with CP and 18 with PC. In addition, the study included 13 age- and body weight-matched healthy subjects served as controls. All subjects underwent oral glucose tolerance test (OGTT) with plasma glucose and insulin measurements. HOMA index and fasting plasma adiponectin, TNF-alfa, interleukin-6 (IL-6), interleukin-1beta (IL-1b), E-selectin, thrombomodulin, adhesion molecules ICAM and VCAM, and endothelin-1 were assessed.
RESULTS: PC and CP patients as compared with controls had significantly greater plasma adiponectin (13292 and 12227 vs 5408 ng/ml; $p<0.0003$), TNF-alfa (22.1 and 23.1 vs 13 pg/ml; $p<0.0002$) and IL-6 (6.6 and 7.3 vs 3.3 pg/ml; $p<0.0001$). Moreover there was significantly higher concentration of ICAM (931 and 492 vs 290 ng/ml; $p<0.005$) and VCAM (1511 and 1080 vs 840 ng/ml; $p<0.01$) in PC and CP patients. The concentration of endothelin-1 was lower in pancreatic diseases compare with healthy (1.81 and 1.7 vs 3.2 pg/ml; $p<0.03$). According to OGTT we diagnosed diabetes or impaired glucose tolerance in 12 patients (44%) from CP group and 5 (28%) from PC group. In the PC and CP patients insulin resistance, as assessed with HOMA was similar with the control group. When PC and CP patients with and without diabetes were considered separately, there was no difference in adiponectin, cytokines and parameters of endothelial dysfunction. No significant differences between serum cytokines and age, gender, BMI, smoking status, and clinical data of patients with pancreatic diseases have been found.
CONCLUSION: These data demonstrate that endothelial dysfunction is present in patients with PC and CP. Moreover, despite absence of insulin resistance, CP and also PC subjects present with clinical markers of subclinical inflammation. Changes in adiponectin, inflammatory cytokines and endothelial dysfunction in patients with CP and PC are not likely related to endocrine disorders.
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Disclosure of Interest: None Declared
Keywords: Chronic Pancreatitis, Diabetes, pacreatic cancer

P114 A CELL AUTONOMOUS EGFR-NFATC1 LOOP PROMOTES ACINAR TO DUCTAL METAPLASIA IN PANCREATIC CARCINOGENESIS

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INTRODUCTION: Recent evidence has shown a crucial role for EGFR activation in $Kras^{G12D}$ -driven pancreatic carcinogenesis. However, the key transcription pathways conferring EGFR signaling in early tumorigenesis are enigmatic.
AIMS&METHODS: To define signaling networks in EGFR driven ADM formation *in vitro* and *in vivo*. $Kras^{G12D}$ mice strains with pancreas specific differential NFATc1 activation ($Kras^{G12D}$-c.n.NFATc1 and $Kras^{G12D}$-NFATc1$^{fl/fl}$) were challenged by chronic pancreatitis. Acinar cells were isolated from $Kras^{G12D}$ or $Kras^{G12D}$-NFATc1$^{fl/fl}$ mice and treated with EGF (20ng/ml). Pancreata and acinar cell explants were analysed by IHC, RT-PCR and immunoblot. ChIP-seq and microarray analysis were performed to identify NFATc1 target genes and co-immunoprecipitation was carried out to identify NFATc1 transcription partners.
RESULTS: We identified a cell-autonomous EGFR-NFATc1 loop in ADM formation. Furthermore, genetic depletion of NFATc1 reduced EGFR expression and signaling and thwarted ADM formation in $Kras^{G12D}$ mice, even in context of chronic inflammation. Mechanistically, EGFR induces NFATc1 and c-Jun transcription complex formation and subsequent Sox9 promoter induction, a key step in ADM formation.
CONCLUSION: Our study uncovers a cell-autonomous EGFR-NFATc1 signaling loop which is required for pancreatic cancer initiation.
Disclosure of Interest: None Declared
Keywords: ADM, EGFR, NFATc1

P115 COMPARISON OF THERAPEUTIC EFFICACY BETWEEN FULL-DOSE GEMCITABINE-BASED CONCURRENT CHEMORADIOTHERAPY (CCRT) AND 5-FLUOROURACIL-BASED CCRT IN LOCALLY ADVANCED PANCREATIC CANCER

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INTRODUCTION: Concurrent chemoradiotherapy (CCRT) is a standard therapeutic option for managing locally advanced pancreatic cancer (LAPC). Although 5-fluorouracil (5-FU) or gemcitabine are recommended as the reference chemotherapeutic agent for CCRT, the optimal dosage for CCRT is still controversial.
AIMS&METHODS: The aim of this study was to compare the therapeutic efficacy and tolerability of full-dose gemcitabine based CCRT (GEM-CCRT) and low dose 5-FU based CCRT (5FU-CCRT) for LAPC. From January 2006 to March 2013, 110 patients with LAPC who received GEM-CCRT (n=90) or 5FU-CCRT (n=20) were included for retrospective analysis. GEM-CCRT included full-dose weekly gemcitabine monotherapy (1000mg/m^2) or combination therapy with cisplatin (70mg/m^2). 5FU-CCRT treated with radiosensitizing low dose of bolus 5-FU (500mg/m^2, weekly) plus leucovorin (20mg/m^2). Concurrent radiotherapy targeted the primary tumor with 5 to 10 mm margin without regional lymph node irradiation. One month after completion of CCRT, response evaluation was conducted by computed tomography scan.
RESULTS: GEM-CCRT had more advanced T-stage at the time of diagnosis (T4 - 86.7% versus 60.0%; $p = 0.005$). Objective response rate (ORR) and disease control rate (DCR) was significantly higher for GEM-CCRT than 5FU-CCRT (ORR – 32.6% versus 5%; $p = 0.013$; DCR – 79.8% versus 50.0%; $p = 0.006$). Both groups showed similar loco-regional control rate (92.2% versus 85.0%; $p = 0.362$) but distant metastasis rate was higher in 5FU-CCRT (17.8% versus 45.0%; $p = 0.017$). Grade 3 or higher neutropenia (34.4% versus 10%; $p = 0.031$) and thrombocytopenia (21.1% versus 0%; $p = 0.021$) was more frequent in GEM-CCRT. The subgroup of GEM-CCRT patients who received gemcitabine monotherapy showed no significant differences in toxicity rate compared with 5FU-CCRT (all $p > 0.05$).
CONCLUSION: Full-dose gemcitabine based CCRT seems more effective on initial local and distant control of LAPC than bolus 5-FU based CCRT. With cautious monitoring on hematologic toxicities, GEM-CCRT can be tolerably conducted. Considering that distant metastasis is one of treatment failure pattern in CCRT of LAPC, full-dose gemcitabine CCRT should be regarded as the first line treatment.
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Disclosure of Interest: None Declared
Keywords: 5-FU, CCRT, chemoradiotherapy, gemcitabine, locally advanced pancreatic cancer

P116 RECURRENCE AFTER SURGERY FOR IPMN WITH LOW (LGD) TO HIGH-GRADE DYSPLASIA (HGD)

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INTRODUCTION: Background: IPMN offers a chance to cure when surgery is performed at an early stage. Nonetheless this may lead to over treating patients with benign lesion.
Objective: To evaluate the long-term outcome of pancreatic resection for IPMN with LGD to HGD.
AIMS&METHODS: Retrospective review of prospectively collected data on all patients operated for IPMN. All 147 patients who had pancreatic surgery between 1994 - 2011 were reviewed. Among them 87 had IPMN with LGD to HGD. All patients had frozen section of pancreatic cut surface and extension of resection was done when needed. There were 41 men and 48 women with a mean age of 60.2±13.1. Surgery included 38 PP-pancreaticoduodenectomies, 21 distal pancreatectomie, 11 PP-total pancreatectomie, 4 duodenum preserving pancreatic head resection, 7 duodenum preserving total pancreatectomies and 6 central pancreatectomies. Postoperative course was uneventful in 41%. Severe complications occurred in 24% including 1% mortality at 90-day. Pathological examination showed LGD in 39 cases, and HGD in 48 cases. All had R0 resections except 3 with LGD on pancreatic margin. 5 patients had incidental NET and 28 had associated chronic pancreatitis. In one case, Pan-In IA was also present. IPMN was a main duct type in 9 cases, a branch duct in 26 cases and a combined duct type in 52 cases. All patients had yearly MRI follow-up (CT-scan before 1998). During follow-up 8 patients died from causes other than pancreatic neoplasms one from PPH, 2 from colorectal cancer, 4 from cardiovascular causes and 1 from cerebrovascular accident.
RESULTS: During follow-up 9 (10.3%) patients had radiological recurrence. Initial pathologies were: Duct types = 3 BD, 1 MD & 5 CD; histology = 2 LGD & 7 HGD. At recurrence duct types were 2 BD, 2 MD, 4 CD and 1 patient died from infiltrating unresectable carcinoma. 2 patients with IPMN recurrence are currently under surveillance. 6 patients had surgery, 5 were confirmed on pathological examination (1 LGD, 3 HGD, 1 Adenocarcinoma pT3) and one was Pan-In IA. DFS was 60±107 months.
CONCLUSION: In our experience, 10% of patients who had pancreatectomy for IPMN with LGD to HGD will present recurrence. Our data suggests that long-term close follow-up is mandatory. Despite initial benign lesion, patient may also develop pancreatic carcinoma.
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Disclosure of Interest: None Declared
Keywords: IPMN with low grade or high grade of dysplasia, lon term outcome, pancreatic resection for IPMN

P117 VISCERAL ABDOMINAL OBESITY AND PANCREATIC CANCER RISK: A CASE CONTROL STUDY

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INTRODUCTION: Recent evidence indicates that obesity and related metabolic abnormalities are associated with increased incidence for a number of cancers including pancreas. However, there are few studies addressing the association between measured values of visceral fat accumulation and pancreatic cancer.
AIMS&METHODS: We assessed the relation between visceral abdominal obesity and pancreatic cancer risk in a Japanese case-control study. Following ethical approval, 149 patients with pancreatic cancer (84 men and 65 women) who had undergone staging computed tomography (CT) between 2006 and 2012 were identified from our database. Abdominal adipose tissue distribution for these 149 patients was compared with that of 547 healthy control subjects (312 men and 235 women), standardized for age, sex, and body mass index. Visceral and subcutaneous adipose tissue volumes were calculated from a single axial CT slice at the level of the umbilicus. A two-sample t test for the difference in volume between the two groups was used. The associations between visceral adipose tissue and pancreatic cancer were estimated with adjusted odds ratio and 95% confidence intervals (CI).
RESULTS: The visceral fat areas (VFA) of pancreatic cancer group were significantly larger than that of controls (104.3 ± 33.8 cm^2 and 75.7 ± 49.4 cm^2, P = 0.012). Compared with participants who had VFA of less than 100 cm^2, the odds ratio for pancreatic cancer was 1.18 (95% CI, 1.00-1.39) for VFA of more than 100 cm^2. There were no statistically significant difference in subcutaneous fat areas (136.8 ± 70.3 cm^2 and 111.3 ± 59.3 cm^2, P = 0.08).
CONCLUSION: Patients with pancreatic cancer have a relatively greater proportion of abdominal visceral adipose tissue compared with controls. Our study adds further evidence to a positive link between visceral abdominal obesity and risk of pancreatic cancer.
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Disclosure of Interest: None Declared
Keywords: OBESITY, PANCREATIC CANCER

P118 JASPAC 03: A PHASE II STUDY OF S-1 PLUS LEUCOVORIN AS FIRST-LINE TREATMENT FOR METASTATIC PANCREATIC CANCER

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INTRODUCTION: S-1 is an oral fluoropyrimidine and one of the current standards for metastatic pancreatic cancer (mPC) in Japan. Leucoborin (LV) is a calcium folinate and enhances cytotoxicity of fluorouracil. Combination of S-1 plus leucovorin showed promising activity for metastatic colorectal cancer.[1]
AIMS&METHODS: We designed a single-arm phase II study to evaluate the efficacy and toxicity of S-1 plus LV as first-line therapy in patients with mPC. Patients with an age of 20-75 years, ECOG PS of 0-1, measurable lesion, and adequate organ function were eligible. S-1 (40 to 60mg based on body-surface area) and LV (25mg) were administered orally twice a day for one week, repeated every 2 weeks until disease progression or unacceptable toxicity. The primary endpoint was response rate (RR) according to the RECIST ver.1.1. Secondary endpoints were progression free survival (PFS), overall survival (OS), and toxicity (CTCAE ver.4.0). Planned sample size of 30 provided 85% power to reject the RR of 20% under the expectation of 40% with one-sided alpha of 0.1.
RESULTS: Between August 2011 and May 2012, 32 patients were enrolled from 8 centers in Japan. Of 31 eligible patients, the median age was 69 years (range, 42-75); male/female 21/10; advanced/recurrence 23/8; ECOG PS 0/1 17/14. Six patients achieved partial response and 11 patients showed stable disease. RR was 19.4% (80%CI, 10.5-31.5%) and disease control rate was 54.8% (41.8-67.3%). With a median follow-up time of 14.2 months, the median PFS and OS were 2.8 and 9.0 months, respectively. The most common grade 3 or 4 adverse events were anorexia (6.5%), fatigue (6.5%), diarrhea (6.5%), mucositis oral (6.5%) and leukopenia (6.5%).
CONCLUSION: The combination of S-1 and LV was well-tolerated but showed modest activity for mPC in the first-line setting. Clinical trial information: UMIN000004958
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Pharmaceutical Co., Ltd., A. Fukutomi Lecture fee(s) from: Taiho Pharmaceutical Co., Ltd.
Keywords: Leucovorin, metastatic pancreatic cancer, Phase II study, S-1

P119 IDENTIFICATION OF RISK FACTORS THAT LEAD TO MALIGNANT TRANSFORMATION OF INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS: A COHORT ANALYSIS OF 91 PATIENTS

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INTRODUCTION: Intraductal papillary mucinous neoplasms (IPMN) are common cystic lesions of the pancreas. IPMNs are considered as premalignant precursors of pancreatic ductal adenocarcinoma (PC). The management of IPMNs is still under debate.
AIMS&METHODS: Our analysis was designed to determine new predictive risk factors for malignant IPMNs. We retrospectively reviewed all patients with radiologically diagnosed IPMNs in a period of November 2005 to August 2012. Comparisons were made between IPMNs with and without malignancy.
RESULTS: A total of 91 patients were analyzed with IPMN during a 7-year period. 15% of the patients developed malignant tumor of the pancreas. The proportion of women was significantly higher in the IPMN group (41.6%) compared to the IPMN+PC group (21.4%). In both groups, the mean age at diagnosis was about 67 years. The mean size of the neoplastic IPMN was 29.6mm. Body mass index (BMI) was higher in the IPMN group (25.1) compared to the IPMN+PC group (22.9). Patients with IPMN+PC were significantly more likely to have diabetes (50%), pain, jaundice and diarrhea (35.7%). The tumor localization was 64.3% in the pancreatic head. Main duct type IPMN was present in 21.4% and a branch duct type IPMN in 28.6%.
CONCLUSION: IPMNs are being diagnosed with increasing frequency. Identification of IPMNs with malignant transformation is challenging and a general resection controversial. Our data analysis revealed the following potential risk factors: Male sex, IPMN lesions> 20mm, low BMI and diabetes.
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Disclosure of Interest: N. Bochon: None Declared, S. Clasen: None Declared, N. Malek: None Declared, R. Plentz Financial support for research from: DFG, TUI
Keywords: IPMN, Pancreatic Cancer, Risk factors

P120 THE MANAGEMENT OF PATIENTS WITH BRANCH-DUCT TYPE INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS BASED ON INITIAL EUS FINDINGS.

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INTRODUCTION: Accumulated evidence has been shown that branch-duct type intraductal papillary mucinous neoplasm (BD-IPMN) usually has a benign clinical behavior unlike main-duct type IPMN (MD-IPMN). However, there are still some cases of BD-IPMN, which has morphological changes afterward and results in having a malignant clinical behavior. It is very important to differentiate malignant BD-IPMN from benign BD-IPMN, while it has yet to be determined. The objectives of the present study were to determine what initial EUS findings were related to a malignant behavior in the future.
AIMS&METHODS: A total of 43 patients with BD-IPMN were enrolled in this study. The EUS findings including tumor location, tumor size, main pancreatic duct (MPD) size, presence of mural nodule (MN) and chronic pancreatitis were initially evaluated and those EUS features were evaluated again over a year later. The significant morphological changes of BD-IPMN could be useful as indicator of developing a malignant behavior in the future. The morphological changes were defined as follows; increased tumor size by more than 2 mm/year, increased size of MPD, appearance of newly MN or increased size of MN. The patients were categorized into two groups; morphologically changed group (CG) and non-changed group (NCG). By comparing two groups, we investigated the initial EUS findings that were associated with morphological changes of BD-IPMN.
RESULTS: Tumor growth more than 2 mm/year was seen in 14 patients. Increase in MPD was observed in 10 patients. Appearance of newly MN or increased size of MN was observed in 10 patients. Some patients overlapped the morphological changes above. As a result, 25 patients were in CG, while the remaining 18 patients were in NCG. In statistical analysis, the initial EUS findings including MPD dilation (P=0.029) and existence of MN (P=0.031) are significantly associated with morphological changes of BD-IPMN later. However, other EUS findings such as tumor location, tumor size and chronic pancreatitis were not related.
CONCLUSION: The initial EUS findings of MPD dilation and presence of MN might be related to developing a malignant clinical behavior in the future. EUS could be a useful modality of choice to differentiate malignant BD-IPMN from benign BD-IPMN. BD-IPMN with MPD dilation or MN should be followed up carefully by EUS.
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Disclosure of Interest: None Declared
Keywords: Branch duct type, EUS, Intraductal papillary mucinous neoplasm

P121 EUS IS MANDATORY FOR DETERMINATION OF PANCREATIC CANCER UNRESECTABILITY

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INTRODUCTION: The salient indication of pancreatic cancer (PC) unresectability is superior mesenteric artery (SMA) and celiac artery (CA) encasement, indicating arterial invasion. Computed tomography (CT) is the gold standard for the evaluation of PC resectability.
AIMS&METHODS: Radiology data were compared with the findings from 51 standard, 58 extended and 17 total pancreaticoduodenectomies; 9 distal resections with CA excision; and 28 palliations for PC. The survival of 11 patients with controversial CT and EUS data with regard to arterial invasion, after R0/R1 procedures (false-positive CT results, Group A), was compared to survival after eight R2 resections (false-negative CT results, Group B) and after 12 bypass procedures for locally advanced cancer (true-positive CT results, Group C)
RESULTS: In all of the cases in group A, operative exploration revealed no arterial invasion, as predicted by CT. The one-year survival in Group A was 88.9%, and the two-year survival was 26.7%, with a median follow-up of 22 months. One-year survival was not attained in groups B and C, with a significant difference in survival (Pa-b = 0.0029, Pb-c = 0.003).
CONCLUSION: Arterial encasement on CT does not necessarily indicate arterial invasion. Whenever PC is considered unresectable, endoUS should be used. In patients with controversial CT and EUS data for peripancreatic arteries involvement radical resection might be possible, providing survival benefit as compared to R2–resections or palliative surgery
Disclosure of Interest: None Declared
Keywords: arteries encasement, Computed tomography, Endoscopic ultrasonography, Pancreatic cancer, resectability

MONDAY, OCTOBER 14, 2013 9:00–17:00
ENDOSCOPY AND IMAGING I – Poster Area

P122 L-MENTHOL SPRAYED ON THE GASTRIC MUCOSA AFFECTS ENDOSCOPIC FINDINGS.

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INTRODUCTION: L-menthol (LM) is useful as a safe antiperistaltic drug for esophagogastroduodenoscopy (EGD) to identify small gastric lesions. However, we realized that LM sprayed on the gastric mucosa frequently caused the specific change, annular and/or reticular edematous thickening, of the distal gastric mucosa.
AIMS&METHODS: Our aims were to evaluate whether LM causes the specific change and whether the atrophic gastritis affects it, and to investigate the impact on the diagnosis of gastric lesions. To enhance the minimal change of the gastric mucosa, indigocarmine (IC) was added to LM. A total of 96 patients scheduled to undergo EGD were randomly assigned to receive LM solution (160mg of 0.8% LM added 2.5ml IC) (n=48; LM group) or decuple diluted IC solution without LM (n=48; nonLM group). Each solution was sprayed into the distal gastric mucosa. We compared the incidence of the specific change on the gastric mucosa, the prevalence of the atrophic gastritis and the difference in endoscopic findings of several gastric lesions between the groups. Additionally, in some gastric lesions that were detected in non LM group, we resprayed LM solution after the study and observed the change induced in them.
RESULTS: The annular-reticular-like mucosal change appeared immediately after administration of LM solution. The change was observed in 71% (34/48 subjects) of LM group compared with 13% (6/48 subjects) of non LM group ($P < 0.01$). The prevalence of the atrophic gastritis did not differ significantly difference between the groups. In the non LM group, the change was observed in 15% (5/33 subjects) of subjects with atrophic gastritis compared with 7% (1/15 subjects) of subjects without atrophic gastritis (P=0.72), whereas in the LM group, the change was observed in 84% (27/32 subjects) of subjects with atrophic gastritis compared with 44% (7/16 subjects) of subjects without atrophic gastritis ($P < 0.01$). The incidence of gastric lesions (hyperplastic polyps, adenomas, cancers, erosions / ulcers) detected in the study did not differ significantly difference between the groups. Most of early gastric cancers, erosions and ulcers became well-demarcated after administration of LM in non LM group. Gastric peristalsis was significantly suppressed in LM group ($P < 0.01$).
CONCLUSION: LM changes a superficial gastric mucosa into an edematous mucosa and the change was more exposed in the atrophic gastric mucosa and less in the pathological lesions. LM may be useful not only to suppress the peristalsis but also to detect easily the demarcation of pathological gastric lesions.
Disclosure of Interest: None Declared
Keywords: esophagogastroduodenoscopy, L-menthol

P123 ENDOSCOPIC OBSERVATION USING MONOCHROME MODE IS USEFUL FOR OBSERVING VASCULAR LESIONS COMPARED WITH THE CURRENT NBI SYSTEM WITH A DISTANT VIEW

A. Imagawa[1,*], H. Terasawa[1], Y. Yoshida[1], K. Takeuchi[1], H. Sakae[1], H. Endo[1], H. Yasuhara[1], H. Jinno[1], E. Kaji[1], H. Hata[1], A. Moriya[1], M. Nakatsu[1], M. Ando[1]. [1]*Gastroenterology, MITOYO GENERAL HOSPITAL, Kan-onji, Japan*

INTRODUCTION: Magnified observation of detailed mucosal structure and blood vessels using the narrowband imaging (NBI) system has become very common in recent years. Implementing the NBI system requires time and cost,

however. On the other hand, a clear image can be obtained of vascular lesions using monochrome mode, which is an endoscopic observation function originally featured in the LUCERA system (CV-260, Olympus co., Tokyo).
AIMS&METHODS: The aim of this study was to evaluate the usefulness of endoscopic observation methods using monochrome mode for vascular lesions compared with the current NBI system. From May 2009 to September 2012, 14 cases (VE: vascular ectasia, 8 cases; GAVE: gastric antral vascular ectasia, 2 cases; RC: radiation colitis, 4 cases) were enrolled in this study. For these cases, 28 images were taken (close view: 14 images, distant view: 14 images) in the same situation using each of normal mode, NBI mode and monochrome mode (MONO mode). Normal mode observation was defined at 5 points. A total of 84 images (28 images for each of three modes) were evaluated by 15 trainee doctors with little experience of endoscopy, on a scale of one to ten, for each of a: Recognition of the lesion, b: Observation of the vessel and c: Observation of the background mucosa.
RESULTS: The scores for NBI mode (a: 5.37, b: 5.50, c: 5.06) and MONO mode (a: 5.33, b: 5.44, c: 5.02) showed almost the same evaluation results, and they were better than in normal mode. In the close view, the scores for NBI mode were better than with MONO mode for recognition of the lesion (a: 5.72 vs. 5.43, $p < 0.05$) and observation of the background mucosa (c: 5.51 vs. 5.17, $p < 0.05$). However, although there was no significant difference in the distant view, better results were obtained for all factors with MONO mode (a: 5.23, b: 5.17, c: 4.86) compared with NBI mode (a: 5.03, b: 5.01, c: 4.62). The brightness of the field of view obtained using MONO mode, even in the distant view, was considered to be a reason for the results. Moreover, MONO mode was effective for observation of remaining blood vessels after APC ablation for GAVE and RC, as an evaluation of endoscopic treatment.
CONCLUSION: Monochrome mode is convenient and useful in endoscopy for observation of vascular lesions.
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Disclosure of Interest: None Declared
Keywords: monochrome mode, NBI, vascular lesion

P124 PROB-BASED CONFOCAL LASER MICROSCOPY (PCLE) FOR THE DIAGNOSIS OF DYSPLASTIC BARRETT'S ESOPHAGUS AND IMMEDIATE RADIOFREQUENCY (RF) TREATMENT

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INTRODUCTION: The miniprobe confocal endomicroscopy (MCE Cellvizio, Mauna Kea Technologies, France) diagnoses in vivo Barret's Esophagus (BE) dysplasia that allows immediate treatment by radiofrequency (RF) with BAARx system (Covidien, U.S.).
AIMS&METHODS: Monocentric retrospective study has been realised from March 2011 to July 2012. About 23 pCLE examinations for 14 patients with known BE has been done. 11 of these examinations,in whom pCLE was followed by RF treatment in the same session, were selected for the final analysis. The probe was passed in the operating channel and placed in contact to the area to be analyzed. This area was previously analyzed with the white light and NBI (Narrow Band Imaging, Olympus GIF 180). For pCLE, glandular architecture, the appearance of cells and vascularization were studied after injection of 2.5 ml of fluorescein IV. Target biopsies on suspected areas for dysplasia allowed a retrospective analysis of concordance.
RESULTS: BE was not nodular in all cases. The average classification of C5M6, follow up to 3.6 years (1-9 years). and age was 58 years. All patients (19H) were under proton pomp inhibitor. 8 patients had been already treated by circumferential RF (HALO 360) and pCLE was performed as a control 2 months before any additional focal treatment. The pCLE exam showed normal cardiac mucosa in 1 patient, intestinal metaplasia IM in 1 patient, LGD in 2 patients, HGD in 4 patients and non-classified dysplasia in 3 patients. No complication related to pCLE was reported. Only the ''normal'' classified exam has not been treated. One RF related complication was reported, retro-sternal pain that developped in one patient but resolved within 48 hours. Assessment of concordance with histology has not been possible in 2 cases (biopsy not performed). The first corresponded to an aspect of intestinal metaplasia and the second to a known HGD. Histological analysis showed a concordance with the MCE in 8 of 9 cases. The discordant case corresponded to a suspicion of non-classified dysplasia pCLE but was not confirmed by histology (which showed intestinal metaplasia). The case of normal mucosa at the gastroesophageal junction cardia was confirmed by histology.
CONCLUSION: The pCLE allows in vivo diagnosis of Barrett's esophagus; And the good concordance with the histology provide an argument for the possibility of the treatment during the same procedure, thus avoiding multiple biopsies and complications from repeated general anesthesia for the patient.
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Disclosure of Interest: None Declared
Keywords: Barrett's Esophagus, Confocal Laser Microscopy, Dysplasia, NBI, radiofrequency ablation

P125 PILOT STUDY OF TRANSESOPHAGEAL ENDOSCOPIC PERICARDIAL RESECTION BY SUBMUCOSAL ENDOSCOPY

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INTRODUCTION: The mediastinal space could be safely accessed by submucosal endoscopy with the mucosal flap safety valve (SEMF) technique. The NOTES approach provides potential access to central structures for minimally invasive surgery.
AIMS&METHODS: Aim of the study is to evaluate the technical feasibility of transesophageal endoscopic pericardial resection by using submucosal endoscopy technique. Acute animal experiment was performed with 3 Beagle dogs. A longitudinal mucosal incision was made on esophageal right wall approximately 25 cm from the incisors. A submucosal tunnel was created at least 5 cm distal to the mucosal incision. Then a myotomy was performed inside the submucosal space, enlarging the incision for insertion of a cap-fitted endoscope and establishing the mediastinum access with IT knife. The mediastinum was endoscopically accessed through the myotomy site along the trachea. After crossing the bifurcation of trachea, pericardium was exposed and pericardial window was created with a hook knife. Then pericardial resection was performed with an IT knife by circumference incision. After the operation, resected pericardium was removed, the myotomy site of the esophageal was covered by the tunnel mucosal flap and the mucosal entry site was closed with clips. A necropsy was performed to study the esophagus, mediastinum, pericardial space and resected locations on the pericardium after the procedure immediately.
RESULTS: Transesophageal access to mediastinum and heart by submucosal endoscopy was achieved in all 3 dogs. Pericardial resection was successfully performed in 2/3 dogs. One dog died during the procedure because of inadvertent injury of pulmonary veins, the other 2 dogs were euthanized immediately after the procedure. The esophageal incision was closed tightly by clips, the trace of endoscopic access could be observed, pericardial space and resected locations on the pericardium were normal in appearance.
CONCLUSION: Transesophageal endoscopic pericardial resection by submucosal endoscopy is feasible technically. It gives us a new choice to the minimally invasive surgery of central structures in mediastinal space. The further survival study and familiarity with local anatomy are required.
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Disclosure of Interest: None Declared
Keywords: animal study, Natural orfice transluminal endoscopy surgery, pericardial resection, submucosal endoscopy

P126 TUMOR LOCALIZATION USING MAGNETIC MARKING CLIP DURING LAPAROSCOPIC SURGERY FOR GASTRIC SUBMUCOSAL TUMOR : A PILOT STUDY

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INTRODUCTION: It is difficult to locate a tumor simply and correctly during laparoscopic surgery for submucosal tumor (SMT). Various methods such as intraoperative sonography, intraoperative endoscopy, etc, are performed in localization gastrointestinal tumor for laparoscopic surgery. However there are limitations of methods, such as discomfort for surgeon, complexity. To overcome these limitation, we devised a simple marking clip with magnet to locate a tumor.
AIMS&METHODS: This study enrolled 11 patients undergoing laparoscopic wedge resection for SMT. Enrolled criterias were intraluminal growing and suspicious of malignancy. We devised 10mm sized ring type magnet (**outdiameter:D10mm, indiameter:4mm, thickness:3mm**, **maximal magnetic force:2660G**), which was coated with silicon and fixed to endoclip using 3-0 nylon. A magnetic marking clip was applied on the center of lesion during preoperative esophagogastroduodenoscopy. During surgery, magnetic body hanged with long thread which was inserted through laparoscopic trocar, was used to find intragastric lesion which marked by magnetic clip. We analized tumor detection rate, detection time, proximal & distal margin from lesion and complication.
RESULTS: In 7 patients, tumors located on the anterior wall of stomach, and 4 located on the posterior wall of stomach. Tumor size ranged from 12.0mm to 18.0 mm. Magnetic marking clips were successfully detected in all 11 patients. The time required for detection ranged from 20 to 85 sec. The resected margin from lesion ranged from 5 to 30 mm. 8/12 of pathology was confirmed GIST, 3/12 was leiomyoma, 1/12 was schwanoma. None of our patients experienced complication s from this marking technique.
CONCLUSION: Magnetic marking clip method was simple and convenient for surgeon, and showed good results for accuracy of tumor localization, and detection rate. Also complication associated with method was not shown. Therefore the magnetic marking clip method may be useful for tumor site detection during laparoscopic SMT wedge resection.
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Disclosure of Interest: None Declared
Keywords: endoclip, laparoscopic surgery, magnet

P127 CHARACTERISTICS OF GASTRODUODENAL EROSIVE AND ULCERATIVE LESIONS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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INTRODUCTION: Chronic obstructive pulmonary disease (COPD) as a systemic disease has an impact on various systems and organs including gastrointestinal tract. Erosive and ulcerative lesions are accompanied by serious complications with a prognostic significance.
AIMS&METHODS: To identify clinical and endoscopic features of erosive and ulcerative lesions 75 moderate and severe COPD patients were included in the study. 50 individuals were treated with inhaled corticosteroids, 25 participants did not receive these medications. The control group covered 65 patients without COPD. Esophagogastroduodenoscopy (EGDS) was performed with endoscope Pentax EG 2990 i (Japan); biopsy was taken from the location of erosive and ulcerative lesions. Helicobacter pylori was detected morphologically and with rapid urease test.
RESULTS: 10 (13,3%) patients from the main group and 27 (41,5%) individuals from the control group complained of the epigastric discomfort, pain and nausea

(χ^2=14,25; p<0,001). Erosions were revealed in 35 (46,7%) patients from the main group (χ^2=4,16; p=0,041 compared to the control group). In 24 individuals with COPD erosions were localized in the stomach (68,6%), in 11 patients (31,4%) they were found in the stomach and duodenum (χ^2=4,66; p=0,031 compared to the control group). Ulcers were detected in 25 (33,3%) participants from the main group and in 10 (15,4%) patients from the control group (χ^2=5,98; p=0,015). In the main group stomach ulcers were observed in 9 (36%) patients, duodenal ulcers were revealed in 16 (64%) individuals (p=0,029 compared to the control group). Patients from the control group had only duodenal ulcers. Multiple ulcerative lesions (2 and more) were seen only in patients from the main group (14,7%, p=0,011 compared to the control group). Erosions (62%, p<0,001) and ulcers (44%, p=0,005) were significantly more often found in COPD patients treated with inhaled corticosteroids. Combination of the atrophic features, detected during EGDS with the i-scan SE function, erosive and ulcerative stomach lesions was disclosed in 23 (30,7%) participants from the main group and in 4 (6,2%) individuals from the control group (p<0,001). A direct correlation was revealed between inhaled corticosteroids intake and development of gastroduodenal erosions (r=+0,75, p<0,001) and ulcers (r=+0,70, p<0,001). There wasn't any confirmed link between Helicobacter pylori contamination degree and development of erosions and ulcers in COPD patients.

CONCLUSION: Erosive and ulcerative lesions in COPD patients are not accompanied by marked clinical picture and can more frequently be seen in those treated with inhaled corticosteroids.

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Disclosure of Interest: None Declared

Keywords: chronic obstructive pulmonary disease, erosions, esophagogastroduodenoscopy, ulcers

P128 SYSTEMATIC NOTES MEDIASTINOSCOPY VS CONVENTIONAL MEDIASTINOSCOPY: A RANDOMIZED LONG-TERM SURVIVAL STUDY IN SWINE.

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INTRODUCTION: Natural Orifice Transluminal Endoscopic Surgery (NOTES) mediastinoscopy through the esophagus has proven to be feasible in the animal model. However, pneumotorax is a frequent complication that could affect the outcome of the surgery. Inflammatory impact of transesophageal mediastinoscopy has never been assessed.

AIMS&METHODS: Aim: to compare the efficacy, inflammatory impact and safety of systematic transesophageal NOTES mediastinoscopy and conventional video-assisted mediastinoscopy (VAM). Methods: 24 pigs were randomly assigned to NOTES or VAM. Animals were kept NPO for 24 hours prior to procedure and pre -op antibiotics were administered. Anti-septic technique was utilized in NOTES whereas VAM was performed in sterile conditions. In NOTES group, the mediastinum was accessed through a 10 cm-submucosal tunnel in the esophageal wall. In VAM group, a transverse cervical incision was made. 30-minute mediastinoscopies were performed with identification of 7 structures (carina, right pulmonary artery, right atrium, vena cava, porcine bronchium, brachiocephalic vein, right vagus nerve). Blood samples were drawn pre and post-operatively for IL-6, IL-1beta, alfaTNF, blood cell count and RCP (1h, 8h, 24h, and 48h). Animals were survived for 7 days. Upon necropsy animals were weighted, adequacy of closure and degree of adhesions were evaluated and interleukin analysis was performed.

RESULTS: Results: 24 animals weighting 31.3+1.9 kg were included in this study (12 NOTES and 12 VAM). Mediastinoscopy was not possible in two animals (1 NOTES and 1 VAM). The mean number of identified organs and total time of surgery was not different in NOTES (6.8+2.2 and 42+7 min) vs VAM (7.7+0.5 and 45+3 min; p=ns). Intrasurgical complications were more frequent in NOTES than in VAM (7 vs 1, p=0.013) being hemorrhage the most frequent (4 and 1, respectively) (see table). 22 animals completed follow-up and 2 in NOTES group had a poor recovery. At necropsy, pathological findings were seen in 11 animals (7 NOTES and 4 VAM; p=ns) (see table). Interleukin levels, blood cell count and RCP were not related with complications.

CONCLUSION: Systematic NOTES mediastinoscopy is possible and comparable to VAM in terms of number of organs identified and inflammatory impact. However, the higher number of complications in NOTES mediastinoscopy raises concern about its potential role as a safe alternative to VAM.

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Disclosure of Interest: None Declared

Keywords: Mediastinoscopy, NOTES

P129 DETECTION RATE OF PHARYNGEAL CANCER DURING ROUTINE UPPER GASTROINTESTINAL ENDOSCOPY USING NARROW BAND IMAGING OBSERVATION: A SINGLE-CENTER EXPERIENCE

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INTRODUCTION: Narrow band imaging (NBI) with non-magnifying observation is useful for detecting abnormal pharyngeal lesions with quite high sensitivity. NBI with magnifying observation enables us to make a precise diagnosis, such as in distinguishing between cancerous and non-cancerous lesions. Thus, NBI including magnifying observation is very useful in detecting pharyngeal cancer at an early stage. Early detection allows for minimally invasive treatment. When NBI is used with the pharyngeal cancer high risk group, it is detected at high frequency. However it is not known how many cancerous lesions can be detected in a routine examination.

AIMS&METHODS: The aim of this study was to evaluate the detection rate of pharyngeal cancer during routine upper gastrointestinal (UGI) endoscopy using NBI. Between January 2009 and December 2012, a total of 11,050 consecutive patients underwent their first UGI endoscopy using NBI at our hospital. Primary endpoint was detection rate of the pharyngeal cancer among all patients, and the detection rate based on patients' initial purpose for the endoscopy. The purposes were divided into 5 groups as follows: screening, pharynx discomfort, surveillance after treatment of head and neck cancer (HNC), pretreatment or after treatment of esophageal cancer (EC), pretreatment or after treatment of gastric cancer (GC). Secondary endpoint was frequency of superficial cancer, in which depth of invasion was defined until subepithelial layer, and treatment procedure.

RESULTS: Detection rate of pharyngeal cancer was 0.26% (29/11,050) among all patients. The detection rate in the HNC group (9.7%, 3/31) and EC group (3.5%, 10/282) were significantly high. The rate in the screening, pharynx discomfort and GC group were 0.11% (10/8,872), 1.1% (3/265) and 0.19% (3/1,600), respectively. Overall, 38 lesions were detected, of which 25 (65.8%) in 20 patients (69.0%) were removed by endoscopic resection or surgical local resection. Pathological examination revealed that the 25 lesions were all superficial. The remaining lesions were treated with chemo and/or radiotherapy. The invasion depths of these lesions were pathologically unclear.

CONCLUSION: Pharyngeal cancers were found in not only the pharyngeal cancer high risk group, but also the screening group although the rate was low. Accordingly, we should consider the use of NBI in a routine UGI endoscopy for the early detection of pharyngeal cancer.

Disclosure of Interest: None Declared

Keywords: Early Detection, Narrow Band Imaging, Pharyngeal Cancer

P130 ASSESSMENT OF STILL AND MOVING IMAGES IN THE DIAGNOSIS OF GASTRIC LESIONS USING MAGNIFYING NARROW-BAND IMAGING: MULTICENTER TRIAL, NBI-SM STUDY

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INTRODUCTION: Magnifying narrow-band imaging (M-NBI) is very useful for the accurate diagnosis of gastric cancer. In a recent trial, M-NBI including moving images was shown to be more accurate than white-light imaging for diagnosing depressed small gastric cancer [1]. However, it is uncertain whether moving M-NBI images have additional effects compared with still images.

AIMS&METHODS: To identify the additional benefits of moving M-NBI images by comparing the diagnostic accuracy of still images only with that of both still and moving images. Thirty-four endoscopists from 10 institutions participated. Still and moving M-NBI images of 40 undiagnosed gastric lesions were recorded by an expert endoscopist. Pathological examination diagnosed 21 cancerous and 19 non-cancerous. Each participant was first tested using the still images only (still test), and then tested a month later using both the still and moving images (moving test). The primary endpoint was to compare the diagnostic accuracy between the still test and the moving test. The secondary endpoint was a subgroup analysis of the characteristics of the participants, including whether or not they were board-certified by the Japan Gastroenterological Endoscopy Society, and their M-NBI experience.

RESULTS: There was no significant difference in the diagnostic accuracy between the still and the moving test (60% vs 61%). However, it was significantly lower in the still test than the moving test in the subgroup of board-certified (63% vs 67%, p=.04), and that of endoscopists who had experienced more than 200 M-NBI procedures (66% vs 69%, p<.05).

CONCLUSION: The addition of moving images to still M-NBI images did not improve the diagnostic accuracy of gastric lesions. However, moving images may have some additional diagnostic benefit for experienced endoscopists.

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Disclosure of Interest: None Declared

Keywords: Gastric cancer, magnifying endoscopy, Narrow-band imaging

P131 ENDOSCOPIC DIAGNOSIS OF EARLY ORAL CAVITY AND LARYNGOPHARYNGEAL CARCINOMA IN PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA USING A TRANSNASAL ULTRATHIN ENDOSCOPE (EG-580NW).

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INTRODUCTION: New diagnostic techniques have dramatically increased the detection of superficial pharyngeal cancer. However, some patients cannot be examined using transoral esophagogastroduodenoscopy (EGD) at otorhinolaryngeal sites due to their gag reflex. On the other hand, Transnasal EGD can be performed comfortably because of its attenuation of the gag reflex. It has some disadvantages compared with conventional endoscopy such as brightness, image solution, and suction ability, so its diagnostic abilities have not been sufficiently evaluated. The procedure has been tremendous progress, and a new endoscope (model EG-580NW, FUJI film, Tokyo, Japan) has been manufactured beginning in September, 2011. The endoscope is a transnasal endoscope that provides of 140°with FICE system.
AIMS&METHODS: We retrospectively assessed the diagnostic value of transnasal EGD in detecting another primary head and neck cancers in patients with esophageal cancer(EC). One hundred twenty one EC patients(male 106/female 15 mean age 68.3 years old) underwent transnasal EGD screening with both a white light and an FICE system between September 2011 and September 2012. The Valsalva maneuver and screening of the oral cavity was also performed.
RESULTS: A total of 23 superficial cancers were found in 18 patients (14.8%) by transnasal EGD. In particular, 15 hypopharyngeal cancers were detected in this study. In addition, six cases of mesopharyngeal cancer, floor of the mouth and larynx in one case were found. Seventeen of those cases were determined to have intraepithelial neoplasia. 5 hypopharyngeal cancers which located at nearby the orifice of the esophagus were detected during the Valsalva maneuver. It hadn't been found among the standard screening. The FICE system enables easily observation of the presense of scattered brown dots to diagnose superficial cancers.
CONCLUSION: Therefore, transnasal endoscopy using the Valsalva maneuver may become the standard examination modality for the screening of the oral cavity, pharynx and larynx.
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Disclosure of Interest: None Declared
Keywords: esophageal cancer, FICE, head and neck cancer, transnsal endoscopy, Valsalva maneuver

P132 RISK FACTORS OF BLEEDING EVALUATED BY FORREST CLASSIFICATION AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR EARLY GASTRIC NEOPLASMS IN JAPANESE POPULATION

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been now standard therapy for early gastric neoplasms in Japan. Although safety of the ESD procedure has been substantiated, complications such as perforation and bleeding are still serious problems.Post-ESD bleeding was considered one of the most major complications related with gastric ESD. Endoscopic hemostasis is effective for stopping post-ESD bleeding in mostly cases, if an emergency endoscopy is properly performed. Therefore, for the presuming appropriate management, it is necessary to beforehand determine the nature and risk factors of the post- ESD bleeding. In our study, we investigated the relationship among backgrounds of patients, characteristics of tumors, and exposed vessel on artificial post-ESD ulcers evaluated by Forrest classification on emergency or scheduled second-look endoscopy.
AIMS&METHODS: Subjects were 200 consecutive patients (145 males and 55 females; mean age, 71.0 years) who underwent ESD for gastric epithelial neoplasms (42 adenomas and 158 adenocarcinomas) between January 2006 and April 2012. Properly preventative coagulation for all exposed vessels on the artificial ulcer with hemostatic forceps was performed routinely at the end of ESD procedure. The vessel types on artificial post-ESD ulcers were evaluated by Forrest classification at the next day after ESD and were divided into two groups, high risk group including Ia, Ib and IIa which are essentially required with endoscopic hemostasis; low risk group including IIb and III which are not required with endoscopic hemostasis. To identify risk factors for possible bleeding after ESD, We analyzed patients and tumor related various factors between the two groups.
RESULTS: Patients with dialysis in the high risk group was significantly higher than those in the low risk group (p=0.03). However, there were no significant differences in patient-related factors (age, gender, comorbidities, use of anticoagulants and antiplatelet drugs) and tumor related factors [tumor location, histological type (adenoma *vs* adenocarcinoma), depth (intramucosal invasion *vs* submucosal invasion), size of the resected specimen, operation time].
CONCLUSION: Patients undergoing dialysis were considered to harbor high risk factor for post-ESD bleeding in gastric epithelial neoplasm, and these patients require carefully observation and optimal management after ESD for avoiding massive bleeding which may consecutively induce unexpected mortality. It is important to prepare to perform emergency or prophylactic endoscopic hemostasis for these patients.
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Disclosure of Interest: None Declared
Keywords: Early gastric cancer, Endoscopic submucosal dissection (ESD), Forrest classification, Post ESD bleeding, Rebleeding, Second-look endoscopy

P133 PILOT TRIAL ON EFFICACY OF SINGLE DOSE PERIOPERATIVE INTRAVENOUS DEXAMETHASONE FOR PAIN RELIEF AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is the gold standard technique for performing en bloc resection of large superficial tumors in the upper and lower gastrointestinal tract. Very little is known about the management of epigastric pain after ESD for gastric neoplasm.
AIMS&METHODS: This study aimed to investigate the utility and safety of single dose perioperative intravenous dexamethasone for pain relief after the operation. This was a double-blind, placebo-controlled trial of intravenous dexamethasone 0.15 mg/kg after ESD for early gastric neoplasm (DM group), comparing with a control group receiving placebo saline only (PL group). Patients completed a questionnaire comprising the present pain intensity and short-form McGill pain (SF-MP) score at immediate postoperative period, 6, 12, 24 hours after ESD. The primary outcomes variable was present pain intensity (PPI) measured at 6 hour after ESD. The secondary outcomes variables included pain medication, McGill pain score, complications, second-look endoscopic finding, and length of stay.
RESULTS: Thirty-six patients receiving ESD for early gastric neoplasm participated. The mean value of 6-hour PPI in DM was lower than that of PL group (1.67±1.21 vs. 2.28±1.56, P=0.003). The total 6-hour SF-MP score, especially in sensory domain, was higher in PL group than in DM group (12.05±4.13 and 9.314±2.12, P=0.026). Tramadol for pain relief was more frequently injected in PL group than DM group (42 % vs. 24%, P=0.041). No difference of length of stay was noted. The distribution of artificial ulcer patterns on second-look endoscopy performed 48 hours following ESD was similar between the groups. There was no difference in complication including acute or delayed bleeding between two groups.
CONCLUSION: Single dose perioperative intravenous dexamethasone after ESD was effective for epigastric pain relief at 6-hour postoperatively.
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Disclosure of Interest: None Declared
Keywords: Endoscopic submucosal dissection, pain relief, perioperative intravenous dexamethasone

P134 PROSPECTIVE STUDY ON ACUTE COMPLICATION RATES AND ASSOCIATED RISK FACTORS IN ENDOSOPIC THERAPY OF DUODENAL ADENOMAS

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INTRODUCTION: Endoscopic therapy of duodenal adenomas has gained importance. However, there are only a few and mainly retrospective studies regarding complications and identificiation of controllable risk factors.
AIMS&METHODS: Determination of complication rates during and after endoscopic therapy of duodenal adenomas and identification of factors that influence the complication rate.
From May 2011 to October 2012, 61 duodenal adenomas of 50 patients have been resected endoscopically. Complications (bleeding, pain, fever, pancreatitis, perforation) have been recorded. Thereafter, the dependence of a bleeding from other factors (gender, age, anticoagulation, adenom location and size, primary internistic disease, lesion type, resection type and performance of a bleeding prophylaxis with APC therapy) has been investigated.
RESULTS: Bleeding was the main complication. Major bleedings appeared in 4 cases (6.5%), minor bleedings in 11 (18%). Furthermore, one occult perforation occured. The dependence of the bleeding probability on the adenoma size was statistically significant (increased size, increased bleeding probability p=0.012). Moreover, the promising trend of APC therapy for bleeding prophylaxis was identified with an odds ratio of 0.31. Because of this measure, the bleeding risk was reduced by two thirds in this study. However, due to the small number of six patients that received bleeding prophylaxis with APC therapy, this result was not statistically significant (p=0.31).
CONCLUSION: Bleeding is the main complication of endoscopic therapy of duodenal adenomas. The bleeding risk increases with adenoma size significantly. The achieved results regarding a prophylactic APC therapy for lowering the bleeding risk are promising. However, the other above mentioned factors seem to play no major role. Due to the relevant rate of complications, endoscopic resection of duodenal adenomas is only recommended under inpatient conditions.
Disclosure of Interest: None Declared
Keywords: duodenal adenoma, endoscopic resection

P135 IS PORCINE STOMACH SUITABLE AS AN ANIMAL TRAINING MODEL FOR GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD)?

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INTRODUCTION: Training using animal model is generally recommended before starting endoscopic submucosal dissection (ESD) in human because of the high-level of its technically difficulty. However, we often experienced discrepancy of maneuverability between a porcine and a human stomach. In fact, few reports have demonstrated these ESD differences using training model.

AIMS&METHODS: To clarify the suitability of isolated porcine stomach as an animal training model for ESD. *Study1*; Six experienced endoscopists who continually practice in gastric ESDs in the human were enrolled to perform ESD for 6 hypothetical lesions located in 6 sites of an isolated porcine stomach (1.Lower third (L)/greater curvature (Gre);2.L/anterior wall (Ant);3.L/posterior wall (Post);4.Upper third (U)/Gre;5.U/Ant;6.U/Post). The size of each lesions were 2cm in diameter. A single-channel endoscope (GIF Q260J; Olympus Co., Tokyo, Japan) with a distal attachment was used. Procedure time for each ESD (sec / cm2) was compared among each site. After the procedure, we asked to the endoscopists the maneuverability of endoscope in three steps of ESD (injection, incision and dissection). A score questionnaire (scoring 1-5) was used to assess the similarity to the L of human stomach. *Study2*; The comparison of histology were investigated between an isolated porcine stomach and resected human gastric specimen of donated body. Thicknesses of mucosal layer were evaluated between above-mentioned 6 sites in porcine (n=3) and human stomachs (n=3).
RESULTS: *Study1*; Procedure times were statistically long in L/Gre and U/Gre of porcine stomach (p=0.016). The survey revealed similarity of maneuverability between human and porcine stomach in L/Ant, L/Post, U/Ant and U/Post during the dissection step (p=0.024). In contrast, discrepancies of maneuverability were showed in L/Gre during the step of injection (p=0.001) and incision (p=0.004). *Study2*; A mucosal layer of porcine stomach was significantly thicker than human stomach in L, especially in L/Gre (L/Gre;2541±363/1029±175μm(p=0.0029), L/Ant;1178±129/768±157μm(p=0.025), L/Post 1164±134/807±80μm(p=0.017), U/Gre;758±240/933±134μm(p=0.34), U/Ant;435±67/932±74μm(p=0.001), U/Post;570±198/836±281μm(p=0.25)). However, the mucosal layer of porcine stomach was thinner than human in U/Gre, U/Ant and U/Post, but the statistical difference revealed only in U/Ant.
CONCLUSION: The maneuverability of ESD and the histological feature were different between a porcine and a human stomach. The porcine stomach may be suitable as animal training model for gastric ESD in L/Ant, L/Post, U/Ant and U/Post.
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Disclosure of Interest: None Declared
Keywords: animal training, ESD, porcine

P136 UTILITY OF ENDOSCOPIC RESECTION FOR THE TREATMENT OF DUODENAL CARCINOID TUMORS

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INTRODUCTION: Few studies have been reported on the safety and efficacy of endoscopic resection in duodenal carcinoid tumors. The aim of this study was to evaluate the utility of endoscopic resection in duodenal carcinoid tumors.
AIMS&METHODS: Between February 2004 and February 2012, 35 patients with sporadic duodenal carcinoids managed by endoscopic resection were enrolled. The endoscopic resection was performed for patients with duodenal carcinoids but no node or distant metastasis. The rate of endoscopic complete resection, histologically complete resection, procedure related complications, and tumor recurrence were retrospectively analyzed.
RESULTS: Twenty-five duodenal carcinoid tumors were resected by endoscopic mucosal resection, four duodenal carcinoids were resected by endoscopic submucosal dissection (ESD), and six ampullary carcinoids were treated by snare papillectomy. The mean patient age was 60.9 years (range 43-82 years). The mean (± standard deviation) tumor sizes were 7.8 ± 2.4 mm (range, 3-12 mm) in nonampullary carcinoids, and 13.6 ± 5.4 mm (range, 5-20 mm) in ampullary carcinoids. The endoscopic complete resection rate was 97.1%: one patient with tumor invading the muscularis propria experienced incomplete resection during ESD. The histologically complete resection was accomplished in 31 of 35 patients (88.6%) on the initial attempt. One patient required 2 sessions for complete resection. With regard to the procedure-related complications, perforation during the endoscopic resection occurred in 3 patients with nonampullary carcinoid (8.6%): two patients were treated by endoscopic closure, and in the other one patient was performed by local excision. After a median follow-up period of 39 months (range 10 to 96 months), local recurrences developed in 1 patients (2.8%) with nonampullary carcinoids, including one from tumor larger than 10 mm. Neither local recurrence nor distant metastasis was detected in patients with ampullary carcinoid after endoscopic papillectomy during a median follow-up period of 40 months (range 18 to 100 months).
CONCLUSION: Endoscopic resection is considered as the safe and effective therapeutic option for small (≤10mm), nonampullary carcinoids without any sign of infiltration to the muscularis propria. For ampullary carcinoids smaller than 20mm and confined to submucosa, minimally invasive endoscopic papillectomy could be considered in particular in patients with a high risk of postoperative complications due to old age or advanced comorbidity.
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Disclosure of Interest: None Declared
Keywords: duodenal carcinoid, endoscopic resection

P137 NEW TECHNIQUES TO IMPROVE THE ENDOSCOPIC VIEW FOR THE HYPOPHARYNGEAL CANCER USING TRANSNASAL ESOPHAGOGASTRODUODENOSCOPY

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INTRODUCTION: Narrow band imaging (NBI) and magnifying endoscopy is thought to be a usefull for hypopharyngeal screening. However circumferential observation of hypopharyngeal mucosa is difficult during conventional endoscopy because of its anatomically closed nature, pharyngeal reflex. Thus it is important to develop procedures for widening and improving the endoscopic field of view of the pharynx. Recently, we applied new transnasal esophagogastroduodenoscopy and modifications of endoscopic techniques for observing hypopharyngeal cancers.
AIMS&METHODS: A total of 69 lesions in 66 patients with hypopharyngeal cancer between January 2011 and October 2012, were retrospectively analyzed. Patient characteristics were as follows: median age, 68 years; range, 51 to 85 years; male:female, 63:3; cStage 0/I/II/III/IV23/15/17/5/9; cTis/T1/T2/T3/T4=23/17/19/7/3. We applied procedures for wide visualization of pharynx to the patients. We employed a transnasal endoscope''EG-580NW'' and ''EG-530NW''(FUJI FILM, Tokyo,Japan). First, after endoscopic inspection of the oral cavity, the patients were asked to bow their head deeply in the left lateral position, and then we put our hand on back of patients' head and pushed it forward by one span of our hand. Then they were asked to lift up the chin as far as possible (lateral sniffing position). Only topical anesthesia was used,the endoscope is passed through the nose with no sedation, and the laryngopharynx is observed. The tip of the endoscope is positioned above the inlet of the larynx, and the patient is asked to blow hard and puff the cheeks with the mouth closed. The endoscopist pulled the patient's chin with the right hand forward. Images were recorded with a digital video cassette recorder during the procedures. Four endoscopists retrospectively observed the recorded video, and the extent of the view of hypopharyngeal opening was classified into 3 caregories (excellent, good, poor) by mutual consensus.
RESULTS: The wide endoscopic view of the pharynx was obtained in a series of the procedures(Excellent, 87.9%; good, 4.5%; and poor 7.6%) This new method is effective for the observation of the postcricoid and posterior wall of the hypoparynx region. We successfully identified 13 small lesions, especially in the hypopharynx, that are usually not detected with the conventional method. Among them, the SCCs were intraepithelial cancer in 6 lesions, had invaded up to the submucosa in 5. Moreover, the excellent visualization of the hypopharynx was demonstrated in 80 per cent (8/10)of the advanced cases(T3+T4).
CONCLUSION: The new procedure for wide visualization of the hypopharynx provided an excellent endoscopic field of view of pharynx.
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Disclosure of Interest: None Declared
Keywords: FICE, Hypopharyngeal cancer, transnasal endoscopy, Valsalva maneuver

P138 UPPER GASTROINTESTINAL MUCOSAL CHANGES IN PATIENTS WITH CONGESTIVE HEART FAILURE

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INTRODUCTION: Congestive heart failure increases systemic venous pressure which is transmitted to the inferior vena cava and the hepatic veins, this may induce gastro-intestinal changes. This research aimed to study gastro-intestinal tract changes in patients with congestive heart failure.
AIMS&METHODS: 120 patients with congestive heart failure (CHF) presenting with gastro-intestinal symptoms underwent upper endoscopy. All patients underwent echocardiography to determine the ejection fraction and the degree of tricuspid regurgitation and pulmonary hypertension. Abdominal ultrasound was done to measure the diameters of the hepatic veins, the inferior vena cava, and the portal vein for which pulsatility index was assessed.
RESULTS: Gastric mucosal changes were present in 106 (88.4%), duodenal mucosal changes in 71 (59.2%), and esophageal mucosal changes in 3 (0.3%) patients.
Gastric mucosal changes were the following: mosaic-like pattern (n = 92, 76.7 %), punctate spots (n = 73, 60 %), thickened folds (n = 20, 16.7 %), watermelon stomach (n = 8, 6.7%), and telangiectasia (n = 35, 29.2%). Duodenal mucosal changes were the following: mosaic-like pattern (n = 58, 48.4 %), thickened folds (n = 17, 14.2 %), and telangiectasia (n = 7, 5.9 %). Gastrointestinal symptoms were significantly associated with gastropathy and duodenopathy (p = 0.000). There was a positive correlation between the degree of gastro-intestinal symptoms and gastropathy and duodenopathy (r value, 0.6 and 0.5 respectively). Patients with gastropathy and duodenopathy had higher mean inferior vena cava (IVC) and hepatic vein diameters than those without gastropathy and duodenopathy. Low EF was associated with increased portal vein, IVC and hepatic vein diameters, (P values = 0.02, 0.008, 0.002) respectively. Moreover it was associated with gastro-intestinal symptoms, gastropathy and duodenopathy (P value = 0.000). There was a positive correlation between the ejection fraction and severity of gastro-intestinal symptoms (r =0.6, P = 0.00). Tricuspid regurgitation was associated with gastro-intestinal symptoms, stomach gastropathy, diameter of hepatic vein and IVC (P value 0.007, 0.019, 0.000, 0.000). Mean pulsatility index in patients in the present study was 0.7 ± 0.53 and there was positive correlation between pulsatility index and Pulmonary Artery Systolic Pressure (PASP) (P = 0.02, r = 0.61). Patients with low ejection fraction have a higher pulsatility index than patients with higher ejection fraction (0.7 ± 0.67, 0.6 ± 0.18, p value, 0.26).

CONCLUSION: CHF is associated with gastro-intestinal changes which are significantly associated with the severity of congestive heart failure.
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Disclosure of Interest: None Declared
Keywords: congestive heart failure, duodenopathy, gastropathy, pulsatility index

P139 DURABILITY COMPARISON OF MUCOSAL APPOSITIONS AND INVERTED SEROSA TO SEROSA CLOSURES FOR REPAIRING LARGE GI WALL DEFECTS USING AN ENDOSCOPIC SUTURING DEVICE.

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INTRODUCTION: Reliable closure of large GI wall defects after endoscopic tissue removal is technically challenging with traditional endoclips. Endoscopic suturing devices have been developed as alternatives to achieve more secure tissue approximation. However, it has yet to be proven that the robust mucosal tissue apposition is durable enough to prevent adverse events.
AIMS&METHODS: Aims of this study were to investigate durability of endoscopic suturing of large GI wall defects after endoscopic submucosal dissection (ESD) and endoscopic full-thickness resection (EFTR) in *in vivo* porcine models. A total of 10 pigs were studied under general anesthesia. In 7 pigs, 2 ESD ulcers over 3 cm in size were made in the lower half of the stomach for each animal. In one of the seven pigs, an additional third ESD ulcer left open without closure was created in the upper corpus as a control. In 3 pigs, 1 full-thickness defect approximately 3 cm in size was made with an assistance of percutaneous anterior gastric wall lifting using tissue anchors. After the endoscopic tissue removals, the both mucosal and full-thickness defects were completely approximated with interrupted stitches placed every 5 to 10 mm with an endoscopic suturing device (Overstitch, Apollo Endosurgery, Austin, USA) mounted on a 2-channel gastroscope (GIF-2T240, Olympus Medical systems, Tokyo, Japan). The post EFTR defects were closed while inverting the serosal edges into the lumenal side. Pigs were survived for one week with an oral administration of proton pump inhibitors and sacrificed following an endoscopic observation of studied sites. A necropsy was performed and the studied sites were sampled for histologic evaluation.
RESULTS: The mean size of sampled ESD specimens in the maximum diameter was 4.27 cm. The defect closure was achieved in 12 of 14 attempts (86%) for the post ESD repair, and in all attempts (100%) for the post EFTR repair. The average number of stitches required to close the defects were 2.41 stitches for post ESD ulcers and 4 stitches for post EFTR defects. All pigs survived for one week without significant complications. At the necropsy, all repaired post ESD ulcers were loosened, although minor deformity of the ulcer edge was observed. Meanwhile, all post EFTR defect closures sustained for one week.
CONCLUSION: The immediate closure of large post ESD ulcers and post EFTR defects could be accomplished using the Overstitch device. The serosa to serosa approximation provides more durable and reliable repair compared with the simple mucosal apposition.
Disclosure of Interest: None Declared
Keywords: Endoscopic full thickness resection (EFTR), Endoscopic mucosal dissection (ESD), Endoscopic suturing device

P140 ONE HUNDRED CASES OF PERCUTANEOUS TRANS ESOPHAGEAL GASTRO TUBING BY ENDOSCOPIC ASSISTANCE

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INTRODUCTION: Percutaneous transesophageal gastrotubing (PTEG) was developed as an alternative route to access the gastrointestinal tract for the patients that Percutaneous Endoscopic Gastrostomy was contraindicated with conditions such as prior gastrectomy, gastric anterior wall malignancies, or massive ascites. PTEG was originally developed to be performed without endoscopy. However, endoscopy may enhance the safety of the procedure.
AIMS&METHODS: The aim of this study is to evaluate the clinical usefulness of PTEG supported by endoscopy. A rupture-free balloon (RFB) catheter is inserted into the lower esophagus. Percutaneous balloon puncture with a specialized needle is then performed from the left side of patient's neck under ultrasonographic control. A guide wire is inserted through the needle into the RFB, followed by a dilator and sheath. A placement tube is then inserted through the sheath, and the sheath is removed. We performed PTEG under endoscopiy in a total of 100 patients (65 men and 35 women, mean age 71.0 years) in whom PEG was not feasible. PTEG was performed for nutrition in 56 patients and for decompression in 44.
RESULTS: Satisfactory results were achieved in all 100 patients. Median follow-up was 60.5 days in patients who received decompression because of the obstruction due to malignancies and 301.0 days in those who received nutrition. Nine patients who were started in the fluoroscopically assisted according to the original method needed endoscopic assistance to complete the procedure. None of the 91 patients in the endoscopic assistance required fluoroscopy. There were no major complications, but one patient had tracheal penetration, which was managed conservatively. Other complications were minor oozing bleeding in five patients that did not require blood transfusion, subcutaneous emphysema in two patients, which were managed conservatively. Eight accidental (four self) tube removals occurred more than 2 weeks after the procedure, without any problem in reinsertion. The overall complication rate associated with PTEG was 12.0%. No patient required surgical treatment or died after PTEG.
CONCLUSION: PTEG supported by endoscopy is as feasible, safe, and useful as PTEG supported by fluoroscopy, the original procedure. The use of endoscopy enhances the safety of the procedure and allows better confirmation of each step involved.
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Disclosure of Interest: None Declared
Keywords: endoscopy, gastrotubing, percutaneous, transesophageal

P141 DIGESTIVE ENDOSCOPIC SUB-MUCOSAL DISSECTION WITH A NEW WATER JET SYSTEM (NESTIS® ENKI II®) USING A BI-FONCTIONAL CATHETER, FIRST PROSPECTIVE TRIAL IN 17 HUMANS INJECTING SALINE SERUM IN SUPERFICIAL TUMORS OF THE ESOPHAGUS, THE STOMACH AND THE RECTUM.

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INTRODUCTION: ESD is the first-intent method to treat superficial neoplasms of the digestive tract at it allows an en-bloc resection. Several tools are necessary to perform ESD with the standard technique. Development of water jet with bi functional catheter allows significant reduction of perforation risk. For this purpose, Nestis introduced the Enki 2 pulsed jet technology with high pressure system to inject efficiently and at any time viscous solutions in direct viewing and retroflexion. In addition, preclinical studies on living pig colon have demonstrated that perforation rates and operating times are significantly reduced compared to a standard electrosurgical knife. The present study was performed to confirm this system capability to perform ESD in humans safely.
AIMS&METHODS: We planed to perform 18 ESD with saline serum injection using Nestis® system. Patients had superficial lesions corresponding to Japanese indications of ESD.
RESULTS: Currently, 18 ESD procedures had been performed in 17 patients (one patient with two LST of the rectum). There were 6 lesions of the esophagus (2 adenocarcinoma on Barrett's, one high grade dysplasia (HGD) on Barrett's, and 3 epidermoid carcinoma), 3 gastric adenocarcinoma and 9 lesions of the rectum (5 granular lateral spreading tumors (LST-G) in HGD and one with sm1 adenocarcinoma, one in Low grade dysplasia (LGD), one LST in histology analysis at the moment, and one polypoid lesions with in situ carcinoma). The mean maximal diameter was 42.2 mm (17-106 mm) with a mean time of procedure of 62.5 min (20-155 min). During the procedures, no case of perforation or delayed bleeding occurred. However, one patient needed clipping of an incomplete muscle dehiscence. All resections were en bloc macroscopically. Currently, histology is available in only seventeen first patients including 15 with microscopically complete resections (R0), one with complete macroscopically resection but with vascular embols (epidermoid esophageal cancer), one with R1 resection in lateral margins and one with indeterminate residual tissue (Rx). 3 months endoscopic control is planed. There were no technical issues during the procedures.
CONCLUSION: Nestis Enki II® system appears to be a safe and effective ESD high pressure water jet system that can be used in clinical practice for superficial lesions of the digestive tract. Moreover, The Enki 2 capability to inject various viscous macromolecular solutions is promising.
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Keywords: endoscopic submucosal dissection (ESD), superficial neoplasia, water jet system

P142 ENDOSCOCOPIC TRAINING IN UPPER GASTROINTESTINAL BLEEDING (UGIB): A UK REGIONAL AND NATIONAL AUDIT

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INTRODUCTION: UGIB frequently requires endoscopic intervention. Training in therapeutic endoscopy for UGIB is not mandatory in the UK. Furthermore UGIB endoscopic experience may be diminished by the European Working Time Directive and a Consultant delivered service. There has been no published data on trainees' opportunities for UGIB endoscopic experience. This study evaluates GI trainee experience in the South Yorkshire (SY) region and nationally.
AIMS&METHODS: Rockall scores for patients requiring an endoscopy for an UGIB (n=622, 5 hospitals) was prospectively collected in SY between Sept-Dec 2011. Trainee experience from this cohort was then compared with a historical SY UGIB cohort (n=274) from 1996. Nationally, all BSG trainees (n=478) were invited to respond to a custom designed web based questionnaire (Nov-Dec. 2012). Information was collected about OGD competency (both diagnostic and

therapeutic) and trainees' confidence of acquiring sufficient endoscopic skills in UGIB prior to completing specialty training.
RESULTS: Regionally, comparison between the 2011 and 1996 SY UGIB cohorts demonstrated comparable 30-day mortality rates (8.5% vs 8.1%, p=0.78), with similar median post-endoscopy Rockall scores (6 v 5). When comparisons were made between trainee and non-trainee performed procedures, no mortality difference was identified (p=0.286). However, when comparing trainee undertaken procedures between the two cohorts, a significant decline was observed with 76% (208/274) of endoscopic procedures for UGIB being performed by trainees in 1996 compared with only 16% (97/622) in 2011 ($p < 0.0001$). Nationally, questionnaires were returned by 51% (245/478) of BSG trainees (median = 4 years registrar training, range 1-9 years). Of these, 42% (104/245) had completed a basic upper GI endoscopy training course and 40% a therapeutic course. Median number of OGD's performed by trainees was 500, with therapeutic exposure <10% in 76% of cases. 23% (57/245) of trainees felt their endoscopic skills in UGIB will be insufficient at the time of specialty training completion.
CONCLUSION: This study objectively demonstrates a decline in regional training for gastroenterology trainees in UGIB endoscopic procedures. Furthermore our regional audit is supported by the National audit, which suggests that trainees across the UK are both limited in their opportunities and concerned that a level of competency may not be attained during registrar training. We advocate reviewing UK endoscopic training provision for UGIB ensuring qualified and confident endoscopists are produced to meet future service needs.
Disclosure of Interest: None Declared
Keywords: Bleeding, training

P143 MANAGEMENT OF BURIED BUMPER SYNDROME – EXPERIENCE FROM ROCHDALE, UNITED KINGDOM

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INTRODUCTION: Buried Bumper Syndrome (BBS) is a rare but major complication of percutaneous endoscopic gastrostomy/jejunostomy (PEG/J) with an incidence of 1.5-1.9%. It is caused by the internal migration of the rigid flange of the gastrostomy tube into the gastrostomy track
AIMS&METHODS: To ascertain the incidence of BBS and to review the methods used in our hospital in the management. Details of all patients (pts.)who had a new PEG/J placed between April 1998 to March 2013 and who developed BBS during this period were obtained from the PEG Register kept in the Endoscopy Unit, Rochdale
RESULTS: Number of new PEG/J- 918. Number of pts. 32 with 33 episodes of BBS. Male 23, Age 22-80 mean age (MA) 51, Female 9 Age 34-87 MA 64. Of the 32 pts. with BBS 20 had their PEG/J placed at Rochdale giving an incidence of 2.17%. Indications for PEG/J : traumatic brain injury 6, CVA 9, Multiple Sclerosis 4, Huntington Chorea 2, Achalasia 1, dementia 1, hydrocephalus 1, syringobulbia 1, benign oesophageal stricture 1, Parkinson's disease 1, Meningioma 1, Anoxic brain injury 1, brain injury following removal of brain tumour 1, unknown 2. Types of PEG: Fresenius 15 Fr -25, Fresenius 9 Fr -3. Types of PEJ: Wilson Cook 20 Fr- 2, Freka -3. After excluding 8 patients in whom we could not get the date of insertion of their PEG/J the mean duration between PEG/J insertion and diagnosis of BBS was 28.4 months (3-65 months). BBS successfully removed at index gastroscopy by: Balloon traction /push technique -in 10 cases (in 9 pts.) out of 33, Forceps pull- 1, Quill technique -1. In 13 pts. 9 Fr and in 1 pt. a 15 Fr Fresenius gastrostomy tube through the bumper track was placed with continuation of feeding. Of the above 14 pts., 8 (57%) had their buried flanges gradually resurfaced and were easily removed endoscopically after a mean period of 4.7 months (1- 20 months). In the remaining 7 pts. - 1 removed by minilap, 4 had side by side PEG placed, 1 jejunal tube placement, 1 died from abdominal wall abscess.
CONCLUSION: Incidence of BBS in our series was 2.17%. 31 out of 33 BBS cases were associated with Fresenius make. Buried flange was successfully removed endoscopically in 20 out of 33 cases (61%). Balloon method has been successful in removing the buried flange at first attempt in 30% of cases. Our experience suggests that in difficult patients, placing a 9Fr or 15 Fr Fresenius gastrostomy tube via the opening of buried bumper may enable the release of the buried bumper and facilitate its easy removal at a later stage.
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Disclosure of Interest: None Declared
Keywords: Buried Bumper Syndrome, percutaneous endoscopic gastrostomy

P144 THE FEASIBILITY OF TRANS-UMBILICAL ROUTE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION OF UPPER GASTRIC LESION AND SINGLE PORT LAPAROSCOPIC LYMPH NODE DISSECTIONS; PORCINE EXPERIMENTAL MODEL

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INTRODUCTION: The complete endoscopic resection of upper gastric lesion is very difficult. The aim of this study was to verify the feasibility of trans-umbilical (TU) route for the endoscopic submucosal dissection (ESD) of upper gastric body lesion compared to trans-oral (TO) route, and to compare the performances of single port laparoscopic lymph node dissections (SPLLND) and conventional multiport laparoscopic lymph node dissections (MPLLND).
AIMS&METHODS: Ten healthy pigs were allocated to two groups: TO/MPLLND (n=5) and TU/SPLLND (n=5) groups. We performed ESD on the anterior wall of gastric high body (HBAW) and fundus via TO or TU route in each group. After ESD, lymph nodes (LN 1, 2, 3, 4sa, 4sb) were resected laparoscopically using multiport in TO/MPLLND and single port in TU/SPLLND group. The complete resection rate, operating time, tissue weight and size, and perforation rate for ESD, and completion rate and operating time for LN dissection were compared between groups.
RESULTS: The operating time for ESD was shorter in TU group than TU group for both HBAW (9.2 ± 0.6 vs 16.2 ± 0.8 min, $p < 0.01$) and fundus (19.4 ± 6.3 vs. 27.0 ± 3.6 min, p=0.04). There was no significant difference in the complete resection rates, tissue weight and size between two groups. The overall perforation rate was 80% (4/5, 2 during procedure and 2 postoperative) in TO/MPLLND group and 20% (1/5, postoperative) in TU/SPLLND group. There was no significant difference in the complete resection rate of overall LN and operating time for LN dissection between 2 groups. MPLLND group had a higher complete resection rate for LN 2 (80%) than SPLLND group (60%).
CONCLUSION: TU ESD had comparable performance to TO route, and showed a shorter operating time and lower perforation rate compared to TO route procedure. TU route could be feasible for safe ESD in the patients with the upper gastric body lesion. SPLLND was also comparable to MPLLND.
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Disclosure of Interest: None Declared
Keywords: endoscopic submucosal dissection (ESD), transgastric NOTES

P145 CLINICAL APPLICATION OF OVERSTITCH FOR TISSUE APPROXIMATION IN GASTROINTESTINAL TRACT – A PILOT STUDY

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INTRODUCTION: Previously we had conducted preclinical studies on Eagle Claw suturing for massively bleeding ulcer and closure of gastrotomy in animal models. This study aimed to investigate clinical application of Overstitch endoscopic suturing for management of complicated gastrointestinal luminal defects.
AIMS&METHODS: We recruited patients with large bleeding ulcers, perforations and luminal defects after POEM and ESD. All procedures were performed under MAC or general anesthesia and CO2 insufflation. The Overstitch device was mounted onto a double channel endoscope and pass to luminal defect through an overtube. Tissue approximation was performed using continuous suturing. The perioperative and technical outcomes were recorded.

Table: P145

Age / gender	Indication Closure of rectal ESD perforation	Technical success	Operative time	Size of luminal defect	No of stitches	Mortality	Complication	Additional procedure
M/73		Yes	30 mins	10mm	2	Nil	Nil	Nil
F/59	Closure of bronchoesophageal fistula	Yes	20 mins	30mm	1	Nil	Nil	1. Thoracotomy for abscess drainage 2. OTSC clip
F/78	Fixation of stent for perforated duodenal ulcer	Yes	30 mins	30mm	2	Yes	Sepsis and wound infection	Nil
M/66	Bleeding duodenal ulcer	Yes	40 mins	20mm	3	Nil	Nil	Nil
M/61	Closure of gastric perforation after failed EUS drainage	Yes	20 mins	10mm	1	Nil	Nil	Nil
F/66	Esophageal perforation	Yes	45 mins	40mm	3	Yes	Mediastinal abscess	1. Thoracoscopic drainage of abscess 2. Stenting
M/78	Bleeding gastric ulcer	Yes	25 mins	30mm	1	Nil	Nil	Transarterial embolization
F/33	Post-POEM closure	Yes	13 mins	30mm	1	Nil	Nil	Nil
F/56	Post-POEM closure	Yes	15 mins	30mm	1	Nil	Nil	Nil
F/73	Post gastric ESD closure	Yes	20 mins	35mm	1	Nil	Nil	Nil

RESULTS: From June 2012 to April 2013, 10 patients received endoscopic tissue approximation using Overstitch (Table 1). Majority of these procedures were indicated as emergency, with 5 patients having perforation of the gastrointestinal tract, 2 had bleeding peptic ulcers and 3 had large mucosal tissue defect. Technical success of endoscopic suturing was achieved in all patients, while two patients succumbed due to severe sepsis. The mean operative time for the procedures was 25.8 minutes, while the mean size of mucosal defect was 26.5mm. All the endoscopic sutures were performed without complication, and most of the tissue approximation required only one overstitch with continuous suturing.
CONCLUSION: Endoscopic tissue approximation using Overstitch is a safe and technically feasible for management of large size gastrointestinal luminal defect. Endoscopic suturing for management of gastrointestinal perforation is limited by difficulty in achieving drainage and debridement of abscess collection.
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Disclosure of Interest: None Declared
Keywords: Bleeding peptic ulcer, Endoscopic suturing, Perforations

P146 ENDOSCOPIC OUTCOMES FOR BARRETT'S RELATED NEOPLASIA HAVE IMPROVED OVER TIME WITH CHANGES IN PRACTICE: FIVE YEAR EXPERIENCE FROM THE UNITED KINGDOM RADIOFREQUENCY ABLATION REGISTRY

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INTRODUCTION: Barrett's esophagus (BE) is the pre-cursor to oesophageal adenocarcinoma (OAC). Endoscopic mucosal resection (EMR) & Radiofrequency ablation (RFA) are alternative treatments to surgery for these patients.
AIMS&METHODS: Aims - Prospective data from 19 centres in United Kingdom (UK) registry
Methods - Before RFA, superficial lesions were removed by EMR. Patients then underwent RFA 3 monthly until all BE was ablated or cancer developed (endpoints). Biopsies were taken at 12 months. Primary outcomes for clearance dysplasia (CR-D) & BE (CR-BE) at 12 months were assessed over two time periods, between 2008-2010 & from 2011 till present day.
RESULTS: 400 patients have completed treatment with 12 month histology over 5 years. CR-D & CR-BE have improved significantly between the former & later time periods from 75% & 56% to 88% & 79% respectively ($p=0.0005$, $p<0.0001$, Chi^2). EMR prior to RFA treatment has also increased significantly from 46% to 59% ($p=0.0163$, Chi^2). Rescue EMR during RFA is used less over the last 2 years compared to the initial time period ($p=0.0011$, chi^2). Progression to OAC although lower in the later time period is not significantly different (2.2% in 2011-2013 versus 5% 2008-2010, $p=0.28$, chi^2).
CONCLUSION: Outcomes have improved over time with improved lesion recognition, & more aggressive EMR of visible lesions before initiating RFA. As a result the requirement for rescue EMR during RFA has reduced. Although the rate of progression is lower in the later part of the registry experience, this is not statistically significant & implies that despite advances in technique with minimally invasive endothepry the rate of progression remains in the region of 2-5% in these high risk patients.
Disclosure of Interest: None Declared
Keywords: Barrett's neoplasia, Oesophageal carcinoma, radiofrequency ablation

P147 DISCRIMINATION BETWEEN SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA AND INTRAEPITHELIAL NEOPLASIA USING NARROW BAND IMAGING WITH MAGNIFICATION

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INTRODUCTION: Superficial esophageal tumors were recategorized in 2011 according to a new Japanese esophagus tumor' classification system. This system is based in part on background coloration, a color change in the area between intrapapillary capillary loops (IPCLs) in superficial esophageal tumors, using narrow band imaging (NBI) with magnification.
AIMS&METHODS: Here, we retrospectively examined superficial esophageal squamous cell carcinoma (SCC) and intraepithelial neoplasia (IN) to determine whether they could be distinguished on the basis of this new classification system. Between June 2009 and July 2012, a total of 24 lesions were diagnosed as SCC or IN on the basis of endoscopic submucosal dissection performed at the Miyazaki University Hospital. These cases were assessed in the current study. Five endoscopic images with white light and NBI were randomly selected. These were then reviewed by 13 specialist or non- specialist endoscopists in a blinded manner to determine whether these lesions were SCC or IN according to the new Japanese esophagus tumor' classification system using NBI with magnification. If the lesion was diagnosed as SCC, the basis for this diagnosis was recorded with respect to 4 characteristic IPCL patterns (dilatation, winding, caliber variation, and non-uniformity).
RESULTS: The overall accuracy with which SCC was distinguished from IN was 60.9%, and the accuracy for diagnosing SCC was 67.0%. The total accuracy achieved by specialists (84.3% ± 14.0%) was significantly higher than that achieved by non-specialists (61.8% ± 15.7%, $P < 0.05$). The accuracy of SCC diagnosis achieved by specialists (71.0% ± 4.0%) was also significantly higher than that achieved by non-specialists (57.9% ± 13.8%, $P < 0.05$). The basis for SCC diagnosis was additional dilatation in 16.9% of casas, winding in 36.9%, caliber variation in 13.8%, and non-uniformity in 32.3%.
CONCLUSION: Specialist' endoscopists could discriminate between SCC and IN according to the new Japanese esophagus tumor' classification system using NBI with magnification with greater accuracy than non-specialist endoscopists. Winding and non-uniformity were the particularly important specific IPCL patterns for diagnosing SCC.
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Disclosure of Interest: None Declared
Keywords: intraepithelial neoplasia, magnification endoscopy, narrow band imaging, superficial esophageal squamous cell carcinoma

P148 SPARSE APPEARANCE OF CRYPT OPENINGS IS A HIGHLY SPECIFIC SIGN FOR DIFFERENTIATED TYPE EARLY GASTRIC CANCER: MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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INTRODUCTION: Discrimination between differentiated and undifferentiated types (according to Lauren's classification, intestinal and diffuse types) of early gastric cancer (EGC) is an indispensable factor for the indication of endoscopic resection. However, this is difficult by an endoscopic examination using conventional white light imaging alone. Recently, we reported that dense-type crypt openings (CO) seen on magnifying endoscopy with narrow-band imaging (ME-NBI) is characteristic for low-grade adenoma.[1]
AIMS&METHODS: In the present study, we aimed to clarify whether the density of CO is a useful finding for discrimination between differentiated-type early gastric cancer (D-EGC) and undifferentiated-type early gastric cancer (UD-EGC). We included patients with EGC (D-EGC, UD-EGC, and mixed type) who had undergone an endoscopic examination in Osaka Red Cross Hospital from January 2010 to October 2011. We evaluated the presence of CO in magnified endoscopic photographs obtained by ME-NBI for each lesion. We then counted the number of CO in a quarter of the area of high power endoscopic field. These lesions were classified as dense-type CO (number of CO $\geq$20), sparse-type CO (number of CO $\geq$1 and $<$20), or absent-type (number of CO=0). We also evaluated the presence of these types of CO and calculated the sensitivity and specificity of the sparse-type CO to discriminate between D-EGC and UD-EGC.
RESULTS: In the present study, 98 consecutive patients with 104 lesions (D-EGC, 83; UD-EGC, 16; and mixed type, 5) were included. CO were observed in 46 (44%) of 104 EGCs. Moreover, CO were detected in 45 (54.2%) of 83 D-EGCs. In contrast, CO were detected in one (6.2%) of 16 UD-EGCs. Thus, the detection rate of CO in D-EGC was significantly higher than that in UD-EGC ($P < 0.001$). The number of CO was significantly larger in the D-EGC group than in the UD-EGC group (3.9 ± 6.9, 95% CI 0.5-7.3 *vs.* 0.1 ± 0.3, 95% CI 2.4-5.4, $P = 0.027$). The sensitivity, specificity, and accuracy of detecting CO for discriminating D-EGC from UD-EGC were 54.2%, 93.8%, and 60.6%, respectively ($P < 0.001$). Dense-type CO were detected in only six (7.3%) of 83 D-EGC. In contrast, sparse-type CO were detected in 39 (47.0%) of 83 D-EGC. The sensitivity, specificity, and accuracy of sparse-type CO for discriminating D-EGC from UD-EGC were 47.0%, 93.7%, and 54.5%, respectively ($P = 0.002$).
CONCLUSION: Sparse-type CO is a highly specific sign for D-EGC. Our data suggest that observation of CO in EGC by ME-NBI contributes to discrimination between D-EGC and UD-EGC.
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Disclosure of Interest: None Declared
Keywords: crypt opening, early gastric cancer, magnifying endoscopy, narrow-band imaging

P149 THE NEW VALSALVA MANEUVER METHOD (MOUTHPIECE AND MOUTH-HOLDING METHOD) IN UPPER-GASTROINTESTINAL ENDOSCOPY EXAMINATION

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INTRODUCTION: Valsalva maneuver has been known as a method to observe the piriform sinus and postcricoid area for the nasal endoscope used by ENT doctors. But Valsalva maneuver wasn't possible because patients couldn't be pooled air in the oral cavity in oral endoscope examination. To solve this problem and observe the endoscope observation difficult part of a larynx and pharynx, we developed the new Valsalva maneuver method (Mouthpiece and Mouth-holding method) for oral endoscope.
AIMS&METHODS: Objects are 434 patients who received oral endoscope with Valsalva maneuver method experienced from March to October in 2011. The mouthpiece method: The Valsalva maneuver method was performed using the mouthpiece with a valve which set up the entrance of mouthpiece to prevent flowing out the breath-air from oral cavity (Sumitomo Bakelite Co., LTD).

After the endoscope insertion to the hypopharynx, patient exhales strongly and breath accumulated in the oral cavity, which was closed with a valve. The mouth-holding method: At the end of the examination, the mouthpiece was removed from the mouth and patient mouthed the endoscope by his lips and performed the Valsalva method. The view of a laryngopharynx was evaluated in four steps. (A: The larynx is completely elevated. The piriform sinus, postcricoid area, and palisade vessels can be clearly observed. B: A larynx is elevated. The piriform sinus can be clearly observed, but only a part of postcricoid area and palisade vessels can be observed. C: The piriform sinus can be clearly observed, but postcricoid area and palisade vessels is unobservable at all. D: Almost the same view without the Valsalva maneuver method.)
RESULTS: The evaluation about the view of a laryngopharynx in 434 patients was as being shown below. The mouthpiece method: A 55.3% B 21.5%. The mouth-holding method: A 49.1%, 29.3%. The whole hypopharynx was observed by about 77% of the patients. There was no adverse event by this method, and it was able to carry out again and again safely and easily. The causes of the evaluations C and D were profound sedation, posttreatment scar, pharyngeal reflex and failed Valsalva maneuver method. By using this method, we found the 6 hypopharygeal superficial type cancers during this study.
CONCLUSION: The Valsalva maneuver method (Mouthpiece and Mouth-holding method) can be performed safely and easily in UGI endoscopy. The method is new technique for improving the view of the laryngopharynx and may lead to the early detection of laryngopharyngeal cancer.
Disclosure of Interest: None Declared
Keywords: laryngopharyngeal cancer, valsalva maneuver

P150 ENDOSCOPIC ULTRASOUND IN STAGING ESOPHAGEAL CANCER AFTER NEOADJUVANT CHEMOTHERAPY – RESULTS OF A MULTICENTER COHORT ANALYSIS

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INTRODUCTION: Endoscopic ultrasound (EUS) is considered a gold standard in the initial staging of esophageal cancer. There is an ongoing debate whether EUS is useful for tumor staging after neoadjuvant chemotherapy (NAC).
AIMS&METHODS: Forty-five patients with esophageal cancer who had undergone NAC were retrospectively analyzed. In all patients EUS was performed after NAC and histological correlation through surgery was available. uT/uN classifications were compared to pT/pN stages. Statistical analysis included calculation of sensitivity, specificity and accuracy rates. Agreement between endosonography and T staging was assessed with Cohen's kappa statistics.
RESULTS: Overall accuracy of uT and uN classification was 29% and 62%, respectively. Sensitivity, specificity and accuracy rates for local tumor extension after NAC were as follows (%): T1: –/97/84; T2: 13/76/53; T3:86/29/46; T4:20/100/91; T1/2: 27/83/56; T3/4: 89/31/56. Cohen's kappa indicated poor agreement (kappa=0.129) between uT classification and pT stage. Relating to positive lymph node detection sensitivity and specificity were 100% and 6%, respectively (kappa=0.06). T stage was overstaged in 23 (51%) and understaged in 7 (16%) of the patients.
CONCLUSION: In routine clinical practice, the initial endosonographic staging results of esophageal cancer may be revised by informations from other diagnostic procedures, such as radiographic imaging (MRI, CT, PET-CT). Nevertheless, our previously published data with analysis of a large patient cohort of esophageal cancer shows convincing results of initial EUS for accurate staging of esophageal tumors thus allowing for adequate further clinical management. In contrast, however, EUS after NAC does not allow for reliable T, N and UICC classification of esophageal cancer and should, therefore, not be used for staging purposes
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Disclosure of Interest: None Declared
Keywords: accuracy, endosonography, esophageal tumor, neoadjuvant therapy, staging

P151 THE MANAGEMENT OF GASTIC LESIONS DIAGNOSED AS ADENOMAS BY ENDOSCOPIC BIOPSY.

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INTRODUCTION: There are no definite clinical criteria for the management of gastric adenomas (Vienna classification category 3) diagnosed by endoscopic biopsy.
AIMS&METHODS: The aim of this study was to evaluate the clinical and endoscopic characterizations of gastric lesions that are preoperatively diagnosed as adenomas using endoscopic biopsy to elucidate how to manage them. We studied 208 consecutive gastric lesions from 171 patients (127 men and 44 women; mean age: 71.6 y.o) that were preoperatively diagnosed as adenomas using endoscopic biopsy during the period from September 2007 to September 2012 at our hospital. All biopsy samples were diagnosed histologically according to the Vienna Classification. All 208 lesions were treated with endoscopic submucosal dissection (ESD) and divided into two groups; adenomas (150 lesions) and carcinomas (58 lesions) with post-resection final pathological diagnoses. We investigated the association between the final diagnoses (adenoma or carcinoma) and the following clinical features and endoscopic findings: age, gender, lesion location, size, color, and macroscopic type.
RESULTS: Age and gender were not different between the two groups. Additionally, there were no significant differences between the two groups in terms of lesion location or macroscopic type. However, lesion size was significantly larger in carcinomas than in adenomas ($p < 0.05$). Carcinomas were significantly more frequently found in 20mm or larger lesions than in 1-9mm and 10-19mm lesions ($p < 0.01$ for 1-9mm; $p < 0.05$ for 10-19mm). Additionally, carcinomas were significantly more frequently found in reddish lesions than in discolored lesions ($p < 0.05$). All lesions that yielded both findings, discolored and a size of 1-9mm in diameter, were adenomas.
CONCLUSION: ESD can be recommended if a gastric lesion that is preoperatively diagnosed as adenoma by endoscopic biopsy has at least one of following factors: a size of 10mm or larger in diameter, or a reddish color.
Disclosure of Interest: None Declared
Keywords: Adenoma, ESD (endoscopic submucosal dossection)

P152 DYSPHAGIA WITH NORMAL ENDOSCOPIC APPEARANCES – COULD WE DO BETTER?

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INTRODUCTION: Dysphagia is an 'alarm symptom' that merits prompt investigation by gastroscopy to exclude cancer. Cases in whom cancer is diagnosed at endoscopy in the UK are 'fast tracked' for multidisciplinary team discussion to plan future management. If endoscopy shows no cancer or intrinsic lesion (peptic stricture, oesophageal ring or web), the cause is usually secondary to oesophageal dysmotility. It is recommended that this group of patients should receive a trial of anti-reflux therapy to exclude reflux-related dysmotility. If no improvement in symptoms is seen patients should be referred for oesophageal physiology studies.
AIMS&METHODS: To assess the number of patients who underwent a gastroscopy for dysphagia that had no intrinsic cause found and to evaluate if these patients were managed in line with recommendations.
A retrospective analysis of all patients who underwent a gastroscopy for an indication that included dysphagia at Chase Farm Hospital over a 3-month period (April-June 2012) was performed. Data was obtained from endoscopy reports via the Unisoft GI Reporting Tool (Middlesex) and clinic outcome letters. Intrinsic oesophageal causes for dysphagia were said to be cancer, benign oesophageal stricture and eosinophillic oesophagitis (EE).
RESULTS: 106 patients (37 male, 69 female), median age 66 years, were investigated. 26 (24.5%) had an intrinsic cause for dysphagia - benign oesophageal stricture 18 (17%), cancer 8 (7.5%) and EE 2 (1.9%). 80 (75.5%) patients had no intrinsic cause – reflux oesophagitis 26 (32.5%), Barrett's oesophagus 2 (2.5%), hiatus hernia 28 (35%), gastritis/duodenitis 39 (48.8%), normal 22 (27.5%) and other 13 (16.3%). 55 (68.7%) of these patients had no follow-up organised after endoscopy. The remaining had clinic review 20 (25%), repeat endoscopy 4 (5%) or referral for oesophageal physiology studies 1 (1.3%). 30 (37.5%) patients with no intrinsic cause were prescribed anti-reflux medication after endoscopy. 19 (63.3%) of these patients had no further follow-up. The remaining had clinic review 9 (30%) or a repeat endoscopy 2 (6.7%); none were sent for oesophageal physiology studies.
CONCLUSION: In this study, 75% of patients with dysphagia had no intrinsic cause identified. The majority of patients are discharged from the service without an accurate diagnosis or management recommendation. Our study highlights important shortcomings in the management of patients with a benign cause of dysphagia. We recommend that patients presenting with dysphagia who at endoscopy have no intrinsic cause, be prescribed acid suppression therapy followed by clinical review, and if symptoms persist be considered for oesophageal physiological studies.
Disclosure of Interest: None Declared
Keywords: dysphagia, Endoscopy, Gastroscopy, strictures

P153 THE ENDOSCOPIC SUBMUCOSAL DISSECTION(ESD), THE FINDINGS OF THE TRAINEES IN OUR HOSPITAL

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INTRODUCTION: In our hospital, the gastric ESD was introduced from 2004. In addition, from 2011, we also started gastric ESD done by trainees who have reached the level ESD enforcement in our hospital. At the present time, there are 4 ESD trainees. We started from the antrum lesion, because it reportedly has fewer complications. And then, we gradually moved on to the body of the stomach lesion, fibrosis lesion, esophageal lesion, and colonic lesion. We evaluated the ESD training system, and the gastric ESD findings of the trainees in our hospital.
AIMS&METHODS: We targeted 120 patients (124 lesions), who underwent gastric ESD done by trainees among the 285 patients(294 lesions) who underwent gastric ESD in our hospital from March 2011 to December 2012. We evaluated how to use devices, guidelines, locations, en block resection rate, and complication rate retrospectively. In addition, we also compared with the result of 165 patients (170 lesions) who underwent gastric ESD done by an expert at during the same period.
RESULTS: Male79, Female41, average age72.9. We used flush knife BT2.0 on all patients. 101 lesions(81.4%) were guideline criteria, 6 lesions(4.8%) were expand criteria, 4 lesions(3.2%) were intra criteria, and 13 lesions(10.4%) were gastric adenoma.

Guideline criteria were the most frequent cases. About location, 8 lesions(6.4%) were in the upper part of the stomach, 27 lesions(21.7%) were in the middle part of the stomach, and 89 lesions(71.4%) were in the lower part of the stomach. Lower part of the stomach lesions were the most frequent cases. En block resection rates were 100%. Perforation was 1 lesion(0.8%), and post bleeding were 2 lesions(1.6%). The device used was the same as used by Expert ESD. 92 lesions(54.1%) were guideline criteria, 50 lesions(29.4%) were expand criteria, 18 lesions(10.5%) were intra criteria. 34 lesions(20%) were in the upper part of the stomach, 86 lesions(50.5%) were in the middle part of the stomach, 50 lesions(29.4%) were in the lower part of the stomach. En block resection rates were 99.4%. Perforation was 1 lesion(0.5%), and post bleeding were 3 lesions(1.7%). When ESD was carried out by the trainees, there were more lower part of the stomach lesions and guideline criteria lesions than when the ESD was carried out by the expert ; however, the result of the trainees for en block resection and complication were equivalent to the expert.
CONCLUSION: The ESD result of the trainees was equivalent to the result of the expert. The result show that the training system in our hospital is effective.
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Disclosure of Interest: None Declared
Keywords: ESD(endoscopic submucosal dossection), training

P154 DOSE CARBON DIOXIDE INSUFFLATION REDUCE MEDIASTINAL EMPHYSEMA AFTER ESOPHAGEAL ENDOSCOPIC SUBMUCOSAL DISSECTION? A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND, CONTROLLED TRIAL.

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INTRODUCTION: Mediastinal emphysema sometimes develops following esophageal endoscopic submucosal dissection (ESD) without perforation because the esophagus has no serosa. Carbon dioxide (CO_2) insufflation during esophageal ESD is expected to reduce the incidence of mediastinal emphysema.
AIMS&METHODS: The aim of this study was to assess the efficacy of CO_2 insufflation for reduction of mediastinal emphysema after esophageal ESD. A total of 46 patients who were to undergo esophageal ESD were randomly assigned to CO_2 insufflation (CO_2 group, n = 24) or air insufflation (Air group, n = 22). The patients and the endoscopists were all blind with regard to the type of gas used. Low-dose computed tomography (CT) was carried out immediately after ESD and the next morning. Abdominal pain and distention were chronologically recorded on a 100-mm visual analogue scale (VAS). The volume of residual gas in the digestive tract was measured on CT images. The amount of sedative drugs, end-tidal CO_2 pressure ($EtCO_2$), oxygen saturation (SpO_2) levels during procedure, and clinical courses were recorded. All participants provided written informed consent prior to study enrollment.
RESULTS: The incidence of mediastinal emphysema immediately after ESD in the CO_2 group was significantly lower than that in the Air group (17% vs. 55%, $p = 0.012$). Mediastinal emphysema on the day after the procedure was 8.3% vs. 32% ($p = 0.066$). The mean severity of pain on a 100-mm VAS was 9.6 mm vs. 11.1 mm immediately after ESD, 22.4 vs. 13.9 one hour after the procedure, 16.7 vs. 14.3 three hours after the procedure, and 10.9 vs. 18.8 the next morning, showing no difference between the groups. Abdominal distention scores on VAS at any post-procedure time points did not differ by group either. The volume of residual gas in the digestive tract immediately after ESD was significantly smaller in the CO_2 group than that in the Air group (808 ml vs. 1173 ml, $p = 0.013$). The dosage of sedative drugs used during the procedure did not differ between the groups. Neither the maximum $EtCO_2$ levels nor the minimum SpO_2 levels during ESD differed by group. The incidence of fever of over 38°C was infrequent and similar in both groups (8.3% vs. 9.1%, n.s.). No serious cardiopulmonary complications occurred.
CONCLUSION: Insufflation of CO_2 during esophageal ESD, as compared with that of air, significantly reduced postprocedural mediastinal emphysema. CO_2 insufflation also reduced the volume of residual gas in the digestive tract, but not the VAS scores of pain and distention.
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Disclosure of Interest: None Declared
Keywords: carbon dioxide insufflation, endoscopic submucosal dissection (ESD), esophageal cancer, mediastinal emphysema

P155 PROPOFOL SEDATION USING A TARGET CONTROLLED INFUSION PUMP DURING COLONSCOPY: A PROPOSAL OF STANDARD OPERATING PROCEDURE

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INTRODUCTION: Many drugs have been proposed for sedation during colonoscopy.For its short onset time and quick recovery propofol is widely used.A safe and standardized protocol of administration is still lacking.
AIMS&METHODS: To demonstrate that propofol infusion using a Target Control Infusion(TCI) pump is safe and well tolerated.From February to April 2013 two endoscopic units enrolled 200 consecutive patients going for colonoscopy.Endoscopies were performed by 6 skilled gastroenterologists(>400 colonsopies/year);anesthesiologists were on call.Standard monitoring(ECG, pulsossimetry, NIBP) and capnography were used.Propofol infusion was controlled by a TCI pump(Syramed®µSp6000,Arcomed AG) set on Schnider protocol. Initial Effect Site Target Concentration(ESTC) was 2,5 µg/ml. After 1 minute from the beginning of infusion, endoscopy began.If the patient felt pain, increments of 0,5 µg/ml were allowed to a maximum of 4 µg/ml.At cecum,ESTC was lowered to 0 µg/ml.Propofol administration and monitoring was performed by a trained nurse.Patients were discharged when Aldrete criteria were met and after a Numeric Visual Scale(NVS) test. Patients underwent telephone interview 24h after endoscopy.
RESULTS: 107(53%) males, 93(47%) females,age 22-84 years,ASA 3-4 18(9%),Mallampati 3-4 62(31%), cardiovascular diseases 99(46%),compromised ventilation 5(2,5%),difficult airway related diseases 1(0,5%).Cecal intubation rate was 98,5% and mean cecal intubation time was 7 minutes.ESTC was 2,5 µg in 26(13%), 3 µg in 75(37,5%), 3,5 µg in 94(47%), 4 µg in 5(2,5%);NVS scale was 1,76±2,62, 0,56±1,60, 0,37±1,13, 0±0, respectively(2,5 µg vs 3,0 µg and vs 3,5 µg,p<0,001;3,0 µg vs 3,5 µg and vs 4,0 µg,p=ns). Hypotension <90 mmHg occurred in 20 pt(10%). Nor treatments or the intervention of the anesthesiologist were needed.199 patients were satisfied and would repeat the exam with the same technique.Discharge criteria were fully met 16,5±12,3 minutes after the end of the procedure.
CONCLUSION: The TCI technique allows a propofol infusion to achieve and to maintain the level of sedation required;this standardized technique is less "operator-dependent" than the titration technique. Furthermore,TCI algorythms decrease the risks of side effects due to initial bolus and guarantee a constant and safe level of sedation.We performed this technique on elderly patients, with severe comorbities and with features of risk of ventilation problems; despite of this, we didn't have any severe complications.We suggest an initial ESTC of 3 µg/ml that can be increased to a maximum of 4 µg/ml.
Disclosure of Interest: None Declared
Keywords: Propofol sedation, target-controlled infusion

P156 SAME-DAY BIDIRECTIONAL ENDOSCOPY WITH PROPOFOL ADMINISTED BY NON-ANESTHESIOLOGISTS: A PROSPECTIVE OBSERVATIONAL STUDY ON ITS ADVANTAGES AND SAFETY

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INTRODUCTION: Same-day bidirectional endoscopy (BDE), including esophagogastroduodenoscopy (EGD) and colonoscopy, have not been evaluated in terms of safety, efficiency and reduction of expenses when carried out with nurse-administered propofol sedation (NAPS) under the supervision of the endoscopist.
AIMS&METHODS: A single-centre prospective registry of consecutive American Society of Anesthetics (ASA) class I-III outpatients undergoing EGD, colonoscopy and BDE was carried out. Propofol was the sole sedative agent used. Adverse events, recovery time and procedure-related expenses were analysed.
RESULTS: Of the 1,500 outpatients (51.5% women) included in the study, EGD, colonoscopy and BDE were carried out in 449, 702 and 349 patients, respectively. All patients were discharged directly from the endoscopy room. Age (mean 54.4, range 18–96 years), body mass index and type of procedure showed no differences among genders or type of procedure. Propofol doses for BDE were 25.9% lesser to both EGD and colonoscopy carried out separately ($p<0.001$). Five different endoscopists assisted by six nurses carried out all the exams; no differences were observed in the results between different explorers. Statistically significant relationships existed among propofol doses, patient' age, weight/BMI and ASA class: the amount of propofol administered directly correlated with patient weight (Spearman's rho=0.135; $p<0.001$) and BMI (rho=0.077; p=0.014) and inversely correlated with age (rho=-0.397; $p<0.001$) and ASA class (rho =-0.336; $p<0.001$). Overall adverse events, including transient O_2 saturation less than 90%, systolic blood pressure <90 mmHg and bradicardia (<50 beats/minute) respectively appeared in 10.7% of single EGD and 8.6% of EGD within BDE. Regarding to colonoscopy, adverse events were documented in 8.6% as single procedures and 9.5% within a BDE (p=ns). However, recovery time to discharge after BDE was 47.9% shorter for BDE than the hypothetical case of EGD and colonoscopy had been carrying our separately ($p<0.001$). Expenses of same-day BDE reduced in 28.1% of that of EGD and colonoscopy as separated procedures ($p<0.001$).
CONCLUSION: If required, same-day BDE with NAPS is resulted in reductions of 25.9% in propofol doses, 47.9% in recovery time, and 28.1% in procedure-related expenses, compared to the case both EGD and colonoscopy would had carried out separately. Adverse events during BDE did not increase regarding EGD and colonoscopy as single procedures.
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Disclosure of Interest: None Declared
Keywords: Bidirectional endoscopy, colonoscopy, Gastroscopy, propofol, sedation

P157 PROPOFOL SEDATION IN OUTPATIENT COLONOSCOPY BY TRAINED PRACTICE NURSES SUPERVISED BY THE GASTROENTEROLOGIST: IS A FORECAST OF ASPIRATION PNEUMONIA POSSIBLE?

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INTRODUCTION: Propofol has several advantages for sedation of endoscopic procedures. Sedation administered by anaesthesiologists is associated with high

costs. In this study the safety of propofol sedation administered by trained practice nurses under supervision of the gastroenterologist in a cohort of outpatients of an ambulatory practice of gastroenterology in Germany is evaluated.
AIMS&METHODS: METHODS: During 21 months all patients referred to colonoscopy were eligible for this prospective observational study. The familiar CRC risk of the individuals, indication, completeness and results of the colonoscopy were registered together with the dose of propofol. Propofol was administered by intermittent intravenous bolus titration by trained practice nurses under supervision of the gastroenterologist. Oxygen saturation, heart rate and blood pressure were recorded constantly during the procedure and adverse cardiopulmonary events were monitored by the endoscopy team. All patients received a questionnaire to be answered at 24 hours following the endoscopy, provide information about the change compared to the day of examination, and send it back via addressed envelope. Aspiration pneumonia was defined as a sum of cough and fever and/or shortness of breath 1 day following the endoscopy.
RESULTS: A total of 24.441 endoscopies were recorded and sedated with propofol (52% mono-sedation, 48% combination with midazolam). Major events (mask ventilation or laryngospasm) occurred in 4 patients. Minor adverse events occurred in 110 patients (hypoxemia, bradycardia, hypotension, bleeding, coughing or vomiting) and correlated to age and propofol dosage. 64% of the patients sent back the questionnaire. Aspiration pneumonia occurred at 130 (0.8%). Special minor events (coughing and vomiting) correlated significantly with aspiration pneumonia ($p < 0.001$). The relative risk of getting aspiration pneumonia in patients with special minor events was 26,2 (95% CI 12.5-54.9).
CONCLUSION: Propofol can be administered safely for ambulatory colonoscopy by trained practice nurses, with careful monitoring under the supervision of the gastroenterologist. Patients with coughing or vomiting during the propofol sedation have a high risk of aspiration pneumonia, which may be prevented by giving antibiotics before symptoms occur.
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Disclosure of Interest: None Declared
Keywords: adverse effects, aspiration pneumonia, Endoscopy, Propofol, Sedation

P158 DOES THE TOPICAL TREATMENT CAN SHORTEN THE DURATION OF TREATMENT WITH APC IN RADIATION PROCTITIS?

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INTRODUCTION: Chronic radiation proctitis is a long-term complication of radiation therapy for pelvic malignancy. This complication requires prolonged and expensive treatment.
AIMS&METHODS: The aim of this study was to compare the efficacy and safety of two treatment regimens, local agents following argon plasma coagulation (APC) vs. APC alone for chronic haemorrhagic radiation proctitis. A single-centre, randomized study was performed on patients with haemorrhagic chronic radiation proctitis after irradiation for prostate (60 patients) and cervical cancer (2 patients). Patients were randomized to 5-aminosalicylic acid compounds/sucralfate /budesonide for 4 weeks plus APC and APC alone. APC was repeated every 8 weeks if necessary after the first session. Using an established scoring system, patients were classified into three groups, with none, mild or severe disease before and at 16 weeks after initial APC treatment (1.5-2 l/min, 25-40 W) and after 48 weeks. Success was defined either as cessation of bleeding or a significant reduction so that further treatment was not required.
RESULTS: 62 patients (mean age 68.4 years). All presented with rectal bleeding, occurring a median 26.8 months (range 7-100 months) after radiotherapy. At baseline there were no significant differences between the local agents plus APC (30 patients) and APC alone (32 patients) groups. At 1 year, a significant improvement in the clinical scale in both groups occurred compared with baseline without statistically significant difference. There were marked differences in the number of sessions (2, 15 vs. 4, 2) and duration of treatment (1, 2 vs. 4, 45) in the group with local agents plus APC (not significant statistically significant). There were no complications related to the procedure
CONCLUSION: APC is safe and effective for the management of chronic radiation proctitis. Additional local agent treatment did not influence the clinical or endoscopic outcome, but could reduce the duration of the treatment. Studies with larger numbers of patients are needed to confirm this.
Disclosure of Interest: None Declared
Keywords: RADIATION PROCTITIS, Treatment response

P159 ENDOSCOPIC MAGNETIC MARKING TECHNIQUE FOR LAPAROSCOPIC COLON TUMOR OPERATION : A PILOT STUDY

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INTRODUCTION: It is difficult to locate correctly and safely a colorectal tumor for laparoscopic surgery. Tattooing is simple, so generally used for localization of colorectal tumor during laparoscopic surgery. However there are limitations, such as incorrect tumor localization due to spread of ink, risk of bowel perforation. To overcome these limitations, we devised a simple magnetic marking technique. We conducted pilot study.
AIMS&METHODS: This study enrolled 12 patients undergoing laparoscopic surgery for early colorectal cancer. We devised 10mm sized ring type magnet (**outdiameter:10mm, indiameter:4mm, thickness:3mm**, **maximal magnetic force:2660G**) which was coated with silicon, and we tied loop using 3-0 nylon. We inserted the marking magnet near lesion with biopsy forcep, and then clipped magnet on target through loop of magnet. A magnetic marking clip was applied on the distal side of lesion during preoperative colonoscopy. During surgery, another magnetic body hanged with long thread which was inserted through laparoscopic trocar, was used to find out the lesion that was marked by magnetic clipping. We analyzed detection rate, detection time, resection margin length from lesion and complication.
RESULTS: 7 of 12 patients' tumor locations were on the rectum, 5 were on sigmoid colon. Tumor size ranged from 10 to 18 mm. Magnetic marking clips were successfully detected in all 12 patients. The time required for detection ranged from 10 to 35 sec. The resection margin from lesion ranged from 40 to 50mm. None of our patients experienced complication s from this marking technique.
CONCLUSION: Magnetic marking technique was simple and convenient for surgeon, and showed good result for accuracy of tumor localization without complication. Therefore, the magnetic marking clip method may be useful for colorectal tumor detection during laparoscopic surgery. And we expect that correct and simple method results in minimizing extent of colon resection.
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Disclosure of Interest: None Declared
Keywords: endoclip, laparoscopic surgery, magnet

P160 THE MANAGEMENT OF COMPLICATIONS FOR COLORECTAL ESD ~ THE USEFULNESS OF CLOSURE OF THE MUCOSAL DEFECTS WITH ENDOCLIPS~

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been applied to the treatment of large colorectal tumors in Japan. However, the rate of complications, such as perforation or bleeding, for colorectal ESD is higher than conventional endoscopic resection. Closure of the mucosal defect may reduce the risk of complications.
AIMS&METHODS: To analyze the usefulness of closure of the mucosal defect with endoclips after colorectal ESD, we retrospective analyzed consecutive 44 patients who underwent ESD for large tumor (≧20mm) in Omori Red Cross Hospital from 2012 April to 2013 March. We closed it by following main three conditions: a muscle layer exposed on the surface (①), thick fibrosis or ulceration (②), or a difficulty with stopping bleed during a treatment (③). There were two groups: patients with closing the mucosal defect (A) and patients without closing it (B). The two groups were compared with respect to their clinical background and the clinical courses.
RESULTS: Median age was 66.6 years. Tumor location was Rt20/Lt12/Rectum12. Tumor size, sample size, median operation time, rate of complete en bloc resection and recurrence were 30.5±16.0mm (15-95), 39.3±17.9mm (20-110), 42.5min, 100%, 0%, respectively. Pathological findings were adenoma26/intramucosal cancer17/submucosal invaded cancer1. The overall rate of perforation and bleeding were 0% and 0%, respectively. 28 of all 44 mucosal defects were closed by endoclips. The reasons of closure (there was some overlapping) were ①8cases, ②6cases, and ③2cases. Average closure time was 8.7min (3-20). Average sample size, operation time, WBC(/μl), CRP(mg/dl), a number of having a high fever(≧38°C), using antibiotic agents and taking a painkiller after ESD were similar: 43.5mm, 48.7min, 7636, 0.85, 1, 5 and 1 in group A, and 35.4mm, 39.0min, 7013, 0.79, 1, 3 and 1 in group B.
CONCLUSION: Reasons for closing the mucosal defect demanded on endoscopic findings during ESD. These selected cases which were needed to close it might be thought to be a higher risk lesions of any complications. As a result of the measures, there was no significant difference between with or without closure and sample size, operation time, clinical data or having any agents. Closure by endoclips does not take much time and will enable to be more safety against complications for colorectal ESD.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, Complications, ESD (endoscopic submucosal dossection)

P161 SPLIT-DOSE POLYETHYLENE GLYCOL PREPARATION IMPROVED POLYP DETECTION RATE: A BACK-TO-BACK STUDY

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INTRODUCTION: Colonoscopy is the current standard method for colon evaluation. Adequate bowel cleanliness is critical for colonoscopy to be safe and effective.
AIMS&METHODS: We assessed the impact of previous day polyethylene glycol (PEG) preparation vs. split-dose PEG preparation on polyp detection rate among patients referred for polypectomy in an academic endoscopic facility. 20 patients (10 male) were included. Median age was 62 years (52-79). All patients underwent two colonoscopies: an index in a private clinic and a second for polypectomy in the endoscopy unit of a University hospital. Median interval period was 5 weeks (1-25). Examinations were performed by two experienced specialist endoscopists, different in each facility. Indications for the index colonoscopies were: 8 screening, 3 blood in stool, 6 abdominal pain and 3 follow-up after resection for colorectal cancer. PEG was administered for bowel preparation in both procedures. Previous day preparation was utilized initially, while split-dose was preferred for the second intervention. Preparation

was characterized as adequate (excellent or good) and inadequate (fair or poor). Based on size, polyps were divided to diminutive (≤ 5 mm), small (6 to 9 mm) and large (≥ 10 mm). We retrospectively compare the polyp detection rate between these procedures and correlate it with the quality of preparation.
RESULTS: Cecal intubation was achieved in all examinations. Adequate bowel preparation was reported in 12 cases with previous day preparation (60%) vs. 15 with split-dose (75%). Respectively, inadequate cleansing was observed in 8 (40%) vs. 5 (25%) patients. A total of 47 polyps were detected during index colonoscopies, while 68 polyps were identified during the subsequent procedures ($p<0,01$). Regarding size, 36 vs. 50 were diminutive ($p<0,05$), 10 vs. 13 small and 1 vs. 5 large. Pathology revealed 23 tubular adenomas with low grade intraepithelial neoplasia (LGIN), 4 tubulovillous with LGIN, 3 serrated, 1 tubular with high grade intraepithelial neoplasia (HGIN), 1 malignant and 36 hyperplastic polyps.
CONCLUSION: Split-dosing resulted in improved colon cleansing compared with preparation taken the day prior to the examination and significantly enhanced total and diminutive polyp detection rate.
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Disclosure of Interest: None Declared
Keywords: bowel preparation, colonoscopy, Polyps detection rate

P162 DOES SUFFICIENT OBSERVATION PRIOR TO TRAINING INFLUENCE COLONOSCOPY PROFICIENCY?

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INTRODUCTION: Little is known of the proper prerequisites for colonoscopy training. The objective of this study was to determine whether the experience of upper endoscopy or the number of cases for colonoscopy observation influence the whole learning process and overall proficiency.
AIMS&METHODS: Starting from March 2011, twenty eight of first-year gastrointestinal fellows were trained in colonoscopy at a single tertiary center up to February 2013. As baseline training, all fellows were board certified in Internal Medicine, but with no experience of full colonoscopy before entering their fellowship training. Endoscopic quality indices like adenoma detection rate (ADR), success rate or withdrawal times prospectively measured throughout the first training year and were compared between two groups, A (14 fellows) with more than 100 cases of upper endoscopy experiences and colonoscopy observations, while B (14 fellows) with less.
RESULTS: A total of 18,263 colonoscopy cases were evaluated and 5,413 of them were screening colonoscopies. Success rate and adequate bowel preparation rate were 97.63% and 84.35%, respectively. There were no significant differences of overall quality index between two groups except for the insertion time (619.2 ± 109.0 vs. 766.4 ± 204.7 seconds, respectively, P=0.012). But the improvement of ADR from the first half year into the latter half was significantly higher for group A when compared to group B (28.8% to 35.5% vs. 31.8% to 28.9%, respectively, P=0.007). However, multivariate analysis showed that withdrawal time was the only significant factor for ADR in the second half year (0.061 ± 0.027 [β±SE], P=0.033).
CONCLUSION: Sufficient observation of colonoscopy before training might facilitate the colonoscopy training for fellows according to this study. However, definite high ADR was related to longer withdrawal times.
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Disclosure of Interest: None Declared
Keywords: adenoma detection rate, colonoscopy, withdrawal time

P163 SPLIT DOSE BOWEL PREPARATION IN DETECTING HIGH RISK PATIENTS FOR COLON NEOPLASIA: A PROSPECTIVE STUDY (PRELIMINARY RESULTS)

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INTRODUCTION: Polyethylene glycol (PEG) solutions are considered the optimal bowel preparation as they achieve better patients' compliance, improve bowel cleansing and have less side effects than other purgatives.
AIMS&METHODS: Our aim in this prospective designed study was to evaluate the number and characteristics of missed polyps due to unsuccessful bowel preparation in routine colonoscopies. Outpatients with unsuccessful bowel cleansing (at least inadequate in Aronchick scale) that received 4 LT of PEG solution the previous day of examination were enrolled in the study. In those patients we advised a split dose of 2 LT the previous and 2 LT on the day of examination and a new colonoscopy within 4 months was scheduled. Moreover, patients were pointed out to perform a 7 day low-fiber diet prior to the repeat examination with only liquid consumption the previous day. Patients with inflammatory bowel disease, familiar polyposis coli and colon surgery were excluded. Complete colonoscopy was considered when cecal intubation was achieved. All detected polyps were removed and recorded. Ottawa and Aronchick score were used for the estimation of the bowel cleansing. Exam indication, comorbidities, drug therapy and bowel habits were also recorded.
RESULTS: Forty-five outpatients were enrolled, 32 (71%) underwent a second endoscopy and 13 were lost from the follow up. Patients' characteristics were: male (65.6%), age (mean value±SD) (61.8±10.3), smokers (30.3%). Parameters compared between exams were: polyp detection rate (PDR) 68.8% vs 78.1%, adenoma detection rate (ADR) 59% vs 48.4%, high risk (HR) patients (≥3 adenomas, 1 adenoma≥1cm, adenoma with villous features or high grade dysplasia) 45.2% vs 29%, withdrawal time 7.25±2.1 vs 9.5±2.64, Ottawa bowel preparation score 0.76±0.17 vs 0.32±0.171, and Aronchick score for endoscopy no 2 was 1.66±0.7. A total of 49 vs 38 adenomas were found with mean size of 6.12 vs 3.9 mm. Among the other measured parameters none was statistically significant except for Ottawa bowel cleansing scale ($p<0.001$) and withdrawal time (p=0.001). Notable is that in 2nd colonoscopy 13 out of 15 patients had at least 1 adenoma in their right colon and that in 3 out of 4 HR patients with villous components, adenomas were located right. Per adenoma miss rate (adenomas 2nd colonoscopy/adenomas 1st +2nd colonoscopy) was 42.7%.
CONCLUSION: Our data enforce the views that consider 4L PEG split dose as the optimal preparation for bowel cleansing in routine base. Split dose has proven its efficacy in right colon cleansing where most exams fall short and dysplasia can be more aggressive.
Disclosure of Interest: None Declared
Keywords: adenoma detection rate, bowel preparation

P164 INVESTIGATION OF RECTAL BLEEDING: IS FLEXIBLE SIGMOIDOSCOPY FAR ENOUGH?

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INTRODUCTION: Current UK guidelines recommend patients with persistent rectal bleeding are referred for further assessment. Choice of investigation is at the discretion of the clinician and is not guideline based. The aim of this study was to ascertain whether a significant proportion of right sided colon cancer might be missed if flexible sigmoidoscopy was undertaken in preference to colonoscopy.
AIMS&METHODS: The St George's endoscopy database was interrogated for all procedures performed in patients presenting with rectal bleeding. Colonoscopies that identified lesions suspicious for cancer were then stratified by age and location of pathology. Lesions confirmed histologically to be adenocarcinoma, or adenomas with high-grade dysplasia (advanced adenomas), were grouped as colorectal cancer (CRC) and included in the analysis. Flexible sigmoidoscopy data over the same period was also analysed.
RESULTS: 6,734 colonoscopies and 5,868 flexible sigmoidoscopies were performed between 1992 and 2012.
At colonoscopy, left-sided CRC was found in 6.24%, but right-sided CRC in only 0.8% of cases overall. The yield of left-sided CRC at colonoscopy increased significantly with each decade of patient age, reaching a maximum of 18.4% in the 71-80 year age group. This rising trend was mirrored in the flexible sigmoidoscopy data, with a maximal yield of 11.4% in the 81+ years age group.
In contrast, the yield of CRC in the right colon did not increase significantly with advancing age, and remained low in patients under age 70 0.45%, those aged 71-80 1.7%, and in those aged 81+ 2.4%. In patients with right-sided CRC, 33.9% had a left-sided adenoma (42.1% of these were over 1cm in size), and 20.2% were found to have an indication in addition to rectal bleeding necessitating subsequent colonoscopy.
CONCLUSION: It has recently been suggested1 that 3% of right-sided CRC would potentially be missed if flexible sigmoidoscopy were undertaken in patients presenting with a history of change in bowel habit, with or without rectal bleeding. Our data provides an estimate of age-specific risk of right-sided CRC in patients presenting with rectal bleeding, and suggests the overall yield of right sided CRC in these patients is low (0.8%). In over half of these patients, left-sided (flexible sigmoidscopy) colonic findings or additional clinical indications would have prompted further colonoscopic evaluation.
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We would therefore advocate flexible sigmoidoscopy as the first line investigation in patients presenting with rectal bleeding, particularly in those aged under 70 years. If applied in clinical practice, this might have significant cost saving and beneficial waiting list implications, without fear of missing significant numbers of CRC.
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Disclosure of Interest: None Declared
Keywords: Age, colonoscopy, colorectal cancer, Detection rate, rectal bleeding, Sigmoidoscopy

P165 COMPARISON OF SPLIT-DOSING VERSUS MORNING REGIMEN FOR BOWEL PREPARATION FOR COLONOSCOPY

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INTRODUCTION: For effective bowel cleansing, the timing of bowel preparation is important. Split-dose preparation is reported better than previous-evening preparation.
AIMS&METHODS: 1. To compare using the Ottawa Bowel Preparation Scale, the efficacy of split versus morning administration of polyethylene glycol (PEG) solution for colon cleansing in patients undergoing colonoscopy. 2. To assess the optimal preparation-to-colonoscopy (PC) interval.
Prospective, randomized, investigator-blind study of 200 outpatient and hospitalized patients requiring elective colonoscopies (mean age 51.5 years, 121 men) between December 2010 and November 2011, assigned to receive one of the two bowel regimens. Exclusion criteria included patients under 18 years of age, creatinine clearance <30 mL/min, pregnant or lactating women, NYHA III or IV heart failure, history of bowel obstruction or resection, known allergies to PEG, refusal to consent or inconvenience to the timing of scopy
RESULTS: Split preparation resulted in better bowel preparation compared to morning preparation (Ottawa score [SD] 5.52 [1.23] vs. 6.02 [1.34]; p=0.017). However, as a result of longer PC interval, afternoon (1-4 PM) colonoscopies had poor bowel preparation compared to morning (11 AM-1 PM) colonoscopies with both regimens. Ottawa score was 4.50 (0.70) vs 7.39 (0.69) in the morning

and afternoon procedures with morning preparation and 4.67 (0.84) vs 7.58 (0.64) with the split preparation, respectively. There was no difference in the tolerability and compliance between the two regimens

CONCLUSION: A PM/AM split-dosing regimen results in better bowel cleansing compared to morning preparation. Preparation-to-colonoscopy interval longer than 6 hours resulted in suboptimal preparation.

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Disclosure of Interest: None Declared

Keywords: bowel preparation, Ottawa bowel preparation scale, split and morning preparation

P166 COMPARISON OF CLINICAL OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION AND ENDOSCOPIC MUCOSAL RESECTION FOR LARGE COLORECTAL TUMORS AT TWO ASIA-PACIFIC EXPERT CENTERS: A PROSPECTIVE COHORT STUDY

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INTRODUCTION: We previously reported short-term outcomes to compare ESD and EMR at two expert centers in DDW 2012. We additionally enrolled cases prospectively and analyzed a one-year follow up data.

AIMS&METHODS: There is few data about the clinical outcomes and cost effectiveness between colorectal ESD and EMR in a multi-country study. The aim of our study is, therefore, to compare the one-year follow-up outcomes and total costs of ESD and EMR at the two Asia-Pacific high volume centers. Prospectively collected data for all attempted resections on colorectal tumors ≧20mm from one with expertise in ESD and the other in EMR was analyzed from September 2010 to March 2012. Data collected included patient and polyp characteristics, en bloc resection rates, complication rates, length of hospital stay, follow up rates, follow up colonoscopy and local recurrence rates.

RESULTS: ESD was performed on 177 lesions and EMR was performed on 273. There was no significant difference between ESD and EMR in patient's age (67.2±9.9 /67.8±11.5; p= 0.575) and mean tumor size (38.2±16.5mm/ 39.3±17.3mm; p= 0.516). Lesions undergoing ESD had significantly higher submucosal invasion rates compared to EMR (18.1% vs. 4.8%; $p<0.001$) but complication rates between two groups were similar and higher en bloc resection rates in ESD compared to EMR (92.7% vs.15.7%; $p<0.001$). Follow up rates was 90.3% (160/177) in ESD and 34.8 % (95/273) in EMR. There was no local recurrence in the ESD group during a mean endoscopic follow up period of 12.6±4.0 months (range: 2-27 months). In comparison, local recurrence occurred in 5.26 % (5/95) in EMR group during a mean endoscopic follow up period of 5.77±3.18months (range: 3-18 months). All recurrences were, however, treated endoscopically without surgery. Limitation of this study was lower follow-up rate in the EMR group, so cost analysis was not carried out.

CONCLUSION: ESD was associated with higher technical success rates than EMR. There were 5% local recurrences in the EMR group, however, all recurrences were managed successfully by repeated endoscopic treatment. Ongoing follow up is being undertaken to assess longer-term outcomes and costs of these two techniques.

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Disclosure of Interest: None Declared

Keywords: colorectal, EMR, ESD

P167 DIAGNOSTIC PERFORMANCE OF MAGNIFYING CHROMOENDOSCOPY COMPARED WITH NBI MAGNIFICATION FOR DEPTH OF INVASION IN EARLY COLORECTAL TUMORS.

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INTRODUCTION: High-grade dysplasia (HGD) and superficial submucosal colorectal cancers can be managed by endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR). Therefore, endoscopic diagnosis for depth of invasion plays an important role in treatment for early colorectal cancer (ECC).

AIMS&METHODS: The aim of this study is to evaluate diagnostic value for submucosal invasion in ECC, using crystal violet (CV) magnifying chromoendoscopy compared with narrow band imaging (NBI) magnifying endoscopy.

Two thousand eight hundred three colorectal tumors were resected endoscopically or surgically between October 2011 and December 2012 at the National Cancer Center Hospital in Tokyo. In these tumors, 314 tumors were retrospectively analyzed: those which were diagnosed by both CV chromoendoscopy and NBI endoscopy before treatment, and those histopathologically revealed as HGD or submucosal invasive cancer. In diagnostic processes, we first observed the lesion with NBI magnifying endoscopy, and after that CV staining with magnifying chromoendoscopy was performed. Endoscopic findings of NBI magnification were graded into Capillary Pattern (CP) type II, IIIA and IIIB as described by Sano. Type V pits were classified into invasive or non-invasive pattern as described by Matsuda. Lesions were diagnosed as deep submucosal invasion when CP type IIIB or type V pits of invasive pattern were observed. We evaluated the accuracy of each endoscopic diagnosis method compared with histopathological results. We assessed the confidence level of diagnosis in each method. Confidence level was defined as a diagnosis with more than 90% certainty.

RESULTS: Among a total of 314 lesions, overall accuracy with NBI endoscopy and CV chromoendoscopy was 85.6% and 87.2%, respectively. In the lesions of HGD or superficial submucosal invasive cancer, the accuracy with NBI endoscopy and CV chromoendoscopy was 90.4% and 92.0%, respectively. In lesions diagnosed with high-confidence, the accuracy with NBI endoscopy and CV chromoendoscopy was 75.8% and 81.4%, respectively.

CONCLUSION: NBI endoscopy and CV chromoendoscopy both showed sufficient diagnostic performance for ECC, especially in HGD or superficial submucosal invasive cancer. In the lesions diagnosed with high-confidence, the accuracy of CV chromoendoscopy seems higher compared with NBI endoscopy. These results suggest that additional observation of CV endoscopy after NBI endoscopy improves diagnostic accuracy in ECC.

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Disclosure of Interest: None Declared

Keywords: chromoendoscopy, diagnostic accuracy, magnifying endoscopy with narrow-band imaging, pit pattern

P168 COMPARISON OF COMPLICATION RATES OF POST-EMR OF LARGE SESSILE POLYPS BETWEEN BOWEL CANCER SCREENING COLONOSCOPIST VERSUS NON-BOWEL CANCER SCREENING COLONOSCOPISTS IN A DISTRICT GENERAL HOSPITAL

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INTRODUCTION: Introduction: EMR for large polyps is a complex procedure and carries significant complication rate. Therefore, experienced endoscopists with special training and interest in EMR should carry out such procedures.

AIMS&METHODS: Methods: 37 patients (25 men and 12 women) undergone EMR for large (≥ 20mm) sessile polyps, over a 2 year period between January 2011 and December 2012 were retrospectively analysed.

RESULTS: Results: Of the 37 polyps removed (one polyp per patient) were either tubulovillous (n=23), or villous (n=14) adenomas.

Mean polyp size was 31.6 mm (range: 20 – 60).

Polypectomy sites were caecum (n=7), ascending colon (n=4), hepatic flexure (n=3), transverse colon (n= 1), sigmoid (n= 11), and rectal (n=11).

Bowel screening Wales (BSW) colonoscopist (n=1) performed 14 (37%) EMRs. Non-BSW colonoscopists (n=4) performed the remaining 23 EMRs.

Comparison between BSW colonoscopist and Non-BSW colonoscopists

	BSW Colonoscopist (n=1)	**Non-BSW Colonoscopists (n=4)**
Mean age of patients	71.5 years	73.7 years
Number of polypectomies	14 (38%)	23 (62%)
Mean polyp size	37.5mm (largest = 60mm)	28mm (largest = 40mm)
Patients awaiting surveillance endoscopy for more than 3 months	1 (7%)	7 (30%)
Recurrence of polyps	None	3 (caecal = 2, rectal = 1)
Peroration	None	1 (requiring surgery)
Major bleeding	None	None
Other major complications	None	None

CONCLUSION: Conclusion: Our data concludes that our post-EMR major complication rates for high risk, large sessile polyps in a district general hospital are very low, and are in keeping with the international standards.

Moreover, in age- and health-matched two groups of patients, there were no complications reported in the BSW colonoscopist group as compared to non-BSW colonoscopist group. This highlights the need for specialising in this field.

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Disclosure of Interest: None Declared

Keywords: endomucosal resection, sessile serrated adenoma/polyp

P169 CLINICAL PROFIL AND NATURAL HISTORY OF SYMPTOMATIC ILEO-CECAL ULCERS

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INTRODUCTION: Ileo-cecal (IC) ulcers represent 15-50% of the total ulcers diagnosed during colonoscopy.Ulcerations in the IC region have a plethora of etiologies and outcomes with a variable natural history.

AIMS&METHODS: Aim of this prospective study was to evaluate the etiology, clinical presentations and natural history of IC ulcers. Patients diagnosed to have ulcerations in the IC region during colonoscopy were enrolled.Their clinical presentation and outcome at first visit were recorded.These patients were followed at every three month interval for presence of symptoms for atleast one year;and colonoscopy was repeated in symptomatic patients.

RESULTS: Out of 1632 colonoscopies performed in a tertiary care hospital from May 2010 to October 2011, 104 patients had ulcerations in the IC region. This population represents the study group. The median age was 44.5 years (range 18-85) and 59% were male. The predominant presentation was lower GI bleed

(55.5%), pain abdomen +/-diarrhea (36.3%)or diarrhea alone (9.9%). Associated fever was present in 32 (31%) patients. The etiology of ulcers was classified into infective causes (43%), non-infective causes (29%), and non-specific ulcers (28%) at first visit. Three patients (3%) died (all had presented with bleed and had non-specific ulcers).These remaining 101 patients were followed at every 3 months for atleast one year.All patients with infective etiology were asymptomatic at one year follow-up.Of the 14 patients with crohn's disease 3 were symptomatic at 1 year follow-up;all were on treatment with steroids.Of the 6 patients with malignant IC ulcers 3 expired;while 3 were asymptomatic.Of the 29 patients with non-specific ulcers;3 were diagnosed as tubercular IC ulcers at follow-up and responded to anti-tubercular treatment ;while 1 was diagnosed as Non-Hodgkins lymphoma and responded well to chemotherpy ;while 2 were diagnosed as Crohn's disease during follow-up and were asymptomatic at end of 1 year on medications.

CONCLUSION: Infection was the most common (>40%) cause of ulcerations of the IC region in the study. Cecal involvement and fever were important clues to infective cause.Majority of the patients(95/101)were asymptomatic at the end of one year;while 3 patients with Crohn's disease were symptomatic at the end of one year. 50% of patient with malignant IC ulcers expirenced mortality at end of one year.While 20%(6/29)patients with non -specific ulcers were reclassified in terms of etiology during the follow-up period of one year.

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Disclosure of Interest: None Declared

Keywords: clinical profile, ileocecal region, natural history, ulcers

P171 NATURAL HISTORY OF DIMINUTIVE COLORECTAL POLYPS: PROSPECTIVE OBSERVATION BY COLONOSCOPY

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INTRODUCTION: Endoscopic removal of colorectal adenomatous polyps effectively prevents cancer. New developments in biomedical optics have enabled the detection of smaller polyps. However, it remains unclear whether the resection of smaller polyps contributes to cancer prevention. To determine whether small polyps should be resected, the natural history of polyps has to be understood.

AIMS&METHODS: The aim of this study was to clarify the natural history of diminutive polyps (≤5 mm) by prospective colonoscopic examinations. A total of 207 diminutive polyps (≤5 mm) detected in 112 patients (73 men, median age 61.9 years) were randomly selected and studied from December 1991 through March 2002 at Niigata University Medical and Dental Hospital, Niigata, Japan. All patients received a detailed explanation of the study protocol and provided informed consent. All polyps were sessile and superficially elevated type with no depressed component and were diagnosed colonoscopically as mucosal low-grade neoplasia (without biopsy). The polyp size was measured by comparison with the diameter of a biopsy forceps placed next to the polyp. To ensure that the same polyp was followed, a site near the polyp was marked with India ink. All patients underwent periodic colonoscopy. If the followed polyp showed clinically significant enlargement (≥10 mm) or the patient desired removal of the polyp, it was resected endoscopically.

RESULTS: During a median follow-up of 86.4 months (range 12.4–223), the mean polyp diameter increased from 3.2 ± 1.0 mm (range 1.3–5.0) to 3.8 ± 1.6 mm (range 1.3-10.0) (p=0.002). Among polyps followed for at least 5 years (134 of 207), 1 polyp (0.7%) grew to more than 10 mm, 28 (20.9%) grew to 6–9 mm, and 105 (78.4%) remained within ≤5 mm at the end of follow-up. Among the polyps followed for less than 5 years, no polyp grew to more than 10 mm. Twenty-four of the 207 polyps were resected endoscopically at the end of follow-up. The histopathological diagnosis was mucosal high-grade neoplasia (Category 4) for 1 polyp, and mucosal low-grade neoplasia (Category 3) for 23 polyps. There was no submucosal invasive carcinoma (Category 5) according to the revised Vienna classification system.

CONCLUSION: Our prospective observations suggest that diminutive polyps grow very slowly. It may not be necessary to resect diminutive polyps for at least 5 years.

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Disclosure of Interest: None Declared

Keywords: colorectal polyp, diminutive colon polyps, natural history, Prospective Studies, surveillance

P172 CLINICAL SIGNIFICANCE OF SMALL AND DIMINUTIVE COLORECTAL POLYPS

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INTRODUCTION: The management of small and diminutive colorectal polyps is not definite. Our aims were to review the clinicopathologic characteristics of diminutive and small polyp and evaluate the risk factors of advanced adenomas.

AIMS&METHODS: The medical records of total 4711 patients who were diagnosed as colon polyp were reviewed retrospectively. Polyp below 0.5 cm defined as diminutive polyp and 0.6≤size≤0.9 as small polyp. The baseline characteristics of the patients, size, location, morphology and histology were assessed. We analyzed the risk factors of advanced adenomas which defined as villous or tubulovillous polyps and/or dysplasia or intramucosal carcinoma histologically.

RESULTS: Male to female ratio was 60.3 : 39.7 and mean age was 56.2±13.0years. Of the 4711 patients, 5058 polyps were detected and polyps below 1cm were noted in 93.0%(4704/5058) and adenoma less than 1cm in size was noted in 54.6%(2761/5058). Diminutive polyp was noted in 75.4%(3549/4704) and small polyp was noted in 24.6%(1155/4704). Diminutive adenoma was noted in 58.2%(1607/2761) and small adenoma was noted in 41.8%(1154/2761). Mean size of polyps was 0.40±0.15. 47.4% of polyp less than 1cm in size was located in right colon. The incidence was most common in sigmoid colon(24.9%). The most common shape was sessile type(56.3%). Advanced adenomas below 1 cm were noted in 0.7%, with villous component(in 19 cases), high grade dysplasia in(3 cases) and adenocarcinoma(in 6 cases). Mean size of advanced adenoma was 0.62 cm, sessile type was most common type and they were most commonly detected in the rectum(28.6%). There were significant differences in age, gender and size of the polyp between advanced and non-advanced adenoma. By multivariate analysis, old age, male gender and size above 0.5cm were risk factors of advanced adenoma of polyps below 1.0cm.

CONCLUSION: The incidence of advanced adenomas below 1 cm was 0.7%. Polyp size, male sex and old age were identified as risk factors of advanced adenoma. Although the size is small, we need more meticulous examination not to miss and active complete removal of the lesion especially with these risk factors.

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Disclosure of Interest: None Declared

Keywords: advanced adenoma, colorectal polyp, diminutive polyp, small polyp

P173 CLINICOPATHOLOGICAL FEATURES OF COLORECTAL POLYPS: COMPARISON WITH 10 YEARS AGO

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INTRODUCTION: As endoscopic examination of colorectum increase in number, detection rate of colorectal polyp is also on the increase. However, comparative studies about the clinicopathologic feature of the colorectal polyps between past and present in Korea are limited. The aim of the present study was to compare the clinicopathologic characteristics of colorectal polyps with 10 years ago.

AIMS&METHODS: The medical records of 4007 patients who underwent colonofibroscope were reviewed retrospectively. The patients were classified into 2002 group and 2012 group. The patients' characteristics, size, gross morphology, location and pathology of all polyps were analyzed.

RESULTS: Mean age of 2002 group was older than that of 2012 group(63.09±13.3 *vs* 52.27±11.9, *p=0.000*). Colorectal polyps were diagnosed in 1816 patients. The numbers of colorectal polyps were 3723 and mean polyp number per one patient was 2.05. Mean polyp size was 0.49 cm and it was larger in polyp 2002 group than that of 2012 (0.60±0.39*vs*0.43±0.32). Sessile type was the most common morphology in both groups. The most common histology was tubular adenoma and more common in right colon in both groups. Although there is no meaningful difference in morphology, distribution and histology between groups, the location of advanced adenoma including villous, tubulovillous adenoma, high grade dysplasia and adenocarcinoma was significantly different between groups(*p=0.010*). Unlike in 2002 group, advanced adenoma was detected more commonly in right side in 2012 group(30.4% *vs*63.6%,*p=0.012*).

CONCLUSION: There was no significant change in distribution of polyp between recent and last decade. However, advanced adenoma was more common in right side recently. Our results suggested that there might be a shift in location of advanced adenomas from left side to right side of the colon. We need to pay more attention not to miss and more active treatment of right side colon polyps.

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Disclosure of Interest: None Declared

Keywords: advanced adenoma, clinical characteristics, colorectal polyp, histology

P174 STUDY COMPARING POLYETHYLENE GLYCOL (PEG) 3350 + SPORTS DRINK + BISACODYL REGIMEN TO PEG-ASCORBIC ACID ON EFFICACY, PATIENT SATISFACTION, TOLERABILITY, EFFECTS ON SERUM ELECTROLYTES & POLYP DETECTION RATE

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INTRODUCTION: Electrolyte-free PEG 3350 (Miralax®), which is only FDA-approved for constipation, combined with 1.9 L of sports drink (SD,Gatorade®) and 2 tablets of Biscodyl (B) (PEG 3350+SD+B) has been increasingly used for bowel preparation (BP) citing patient satisfaction and tolerability. There are no data comparing this regimen to FDA-approved standard split-dose PEG-ascorbic acid (PEG-AA) (MoviPrep®) on bowel prep efficacy in cleansing the colon, patient satisfaction, tolerability and their effect on the electrolytes. Our aim was to assess the efficacy, patient satisfaction, tolerability, polyp detection rate and effect on electrolytes safety of these two PEG-based preparations
AIMS&METHODS: This was a prospective, single-blind, block randomization trial. Patients were randomized to single dose 238 g PEG 3350 + 1.9 L SD + 2 tablets of Bisacodyl(PEG 3350+SD+B) or 2L PEG-AA. The primary outcome was preparation quality using the validated Boston Bowel Prep Scoring (BBPS) system by the endoscopist performing the procedure (E1), nurse assisting the procedure (N) and by a blinded endoscopist (E2) using photos from the procedure. Basic metabolic panels were checked on the day of the randomization and on the day of the procedure. Patients completed a survey on the day of the procedure to assess their experience with the bowel preparation. (NCT 01695863)
RESULTS: We randomized 150 patients (74 PEG 3350 +SD+B, 76 PEG-AA). Patients receiving PEG AA had statistically significantly better BBPS scores for the right side of the colon as rated by E1, N & E2 ($p=0.005$, $p<0.001$, $p=0.001$, respectively) and for the left side and transverse colon as rated by the N ($p=0.004$ and $p=0.026$, respectively) & E2($p=0.000$ and $p=0.006$, respectively) compared to patients receiving PEG 3350+SD+B. After dividing the quality of BP into poor/fair and good/excellent, a significantly higher percentage of patients receiving PEG-AA had good/excellent preparations compared to PEG3350+SD+B ($p=0.03$) group for the right side of the colon (see table below). There was no statistical difference in patient satisfaction, tolerability, polyp detection rate and change in serum electrolytes preceding and following the BP.
Table 1 comparing Movi Prep vs Miralax

Bowel Preparation	Poor/Fair	Good/Excellent	P value
Movi Prep (R)	7.9%	43.3%	0.003
Miralax +SD+B	18.9%	29.9%	

CONCLUSION: Use of single-dose, non-FDA approved PEG 3350+SD+B was inferior in bowel preparation for colonoscopy compared to a split-dose PEG-AA, and thus cannot be recommended for bowel preparation for screening colonoscopy
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Keywords: colonoscopy, POLYETHYLENE GLYCOL

P175 FEASIBILITY OF NARROW BAND IMAGING MAGNIFICATION FOR THE INVASION DEPTH DIAGNOSIS OF EARLY COLORECTAL CANCERS

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INTRODUCTION: Narrow Band Imaging (NBI) magnification is convenient and time-saving method for the endoscopic diagnosis of early colorectal lesions. However, it remains controversial whether NBI magnification is useful for the diagnosis of invasion depth of early colorectal cancers, compared to chromoendoscopic magnification.
AIMS&METHODS: The aim of this study was to clarify the clinical efficacy of NBI magnification for the diagnosis of submucosal massively invasive cancer (SM-M) in the assessment of our modified criteria. The subjects of this retrospective study were 615 early colorectal cancers resected endoscopically or surgically from May 2007 to March 2013. After observation with a conventional image, NBI magnification diagnosis was performed from the standpoint of the shape and arrangement of microvessels according to Sano's classification. Type IIIB, an indicator of massively submucosal invasion with NBI magnification, was determined only by the presence of the following specific irregular findings of microvessels: "caliber change of microvessels", "long irregular vessel" or "decline of microvessel density". Subsequently, chromoendoscopic magnification diagnosis after crystal-violet dye-stain was based on Kudo's classification. VI high-grade and VN pit pattern were defined as indicators of massively submucosal invasion. Histological diagnosis was assessed on the basis of Vienna classification and massively submucosal invasion was defined as an invasion depth $\geqq 1000\mu$m.
RESULTS: 615 colorectal cancers consisted of 449 intramucosal cancers, 69 submucosal slightly invasive cancers and 97 SM-M. Sensitivity, specificity and accuracy of type IIIB for SM-M were 66.0%, 98.8% and 93.7%, whereas those of VI high-grade and VN pit pattern were 76.3%, 98.3% and 94.8%, respectively. There was no significant difference between NBI and chromoendoscopic magnification. The frequency of type IIIB was significantly lower in flat type lesions (39.1%, 9/23) than that in protruded (66.7%, 24/36) and depressed type lesions (81.6%, 31/38, $p=0.0010$). All specific findings of type IIIB had high specificity for SM-M (99.1%, 99.8% and 99.5%, respectively). The "decline of microvessel density" finding was significantly more frequent in depressed type (71.4%) than in protruded (28.1%) and flat type (9.5%, $p<0.0001$).
CONCLUSION: NBI magnification would have the clinical advantage in the diagnosis of submucosal massively invasive cancers. Although diagnostic ability in flat type lesions was not satisfactory, our modified criteria and specific irregular findings of microvessels would be useful for the diagnosis of submucosal massively invasive cancers.
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Disclosure of Interest: None Declared
Keywords: early colorectal cancer, massively submucosal invasion, microvessel, Narrow-band imaging

P176 IMPROVEMENT OF THE FLAT ADENOMA DETECTION RATE WITH PANCOLONIC CHROMOENDOSCOPY WITH INDIGO CARMINE

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INTRODUCTION: The adenoma detection rate (ADR) is one of the independent predictors used to reduce the risk of interval colorectal cancer in screening colonoscopy. Colonoscopic removal of adenomatous polyps decreases the incidence and mortality rate of colorectal cancer. Given that, it is important to improve the ADR in colonoscopy. Several studies have suggested that interval cancer is more likely to be found at the proximal colon than the distal colorectum. Therefore, a bigger emphasis should be placed on detecting precancerous lesions at the proximal colon in advance. Pohl et. al. reported that pancolonic chromoendoscopy (PCC) with indigo carmine markedly improved the ADR and was practicable enough for routine application. The aim of this study is to clarify whether PCC is effective at achieving higher ADR than the conventional method in screening colonoscopy.
AIMS&METHODS: Retrospectively, PCC (with 0.3% indigo carmine spraying during continuous extubation) was compared with conventional colonoscopy (control group) in consecutive patients attending for a routine colonoscopy performed by either of the two endoscopists (T and Y). A total of 7251 examinees received a colonoscopy at our clinic from August 2008 to December 2012. After reviewing their clinical features and endoscopic data, we chose a control population matched for age, gender, and endoscopist by the statistical program R (http://cran.r-project.org). The patients' characteristics, procedure findings including withdrawal time, size, location, morphology and histopathology of the lesions detected were reviewed from medical records and pathological reports of the endoscopic resection or biopsy specimens.
RESULTS: A total of 794 patients were included (397 in the PCC group, 397 in the non-PCC control group) after matching. The patients' demographic characteristics and indications for colonoscopy were similar between the two groups. The proportion of patients with at least one adenoma detected wasn't statistically different between the PCC and the non-PCC group (46.6% vs 43.3%; $p=0.35$). Chromoendoscopy increased the overall detection rate for flat adenomas (23.7% vs 15.4%; $p=0.003$), not for those located at the distal flat adenomas (10.6% vs 10.3%; $p=1.00$) but for those at the proximal colon (19.1% vs 12.8%; $p=0.02$). Mean withdrawal time was slightly but not significantly shorter in the PCC group than the non-PCC group (17.47 min vs 18.73 min; $p=0.40$).
CONCLUSION: Pancolonic chromoendoscopy markedly enhances flat adenoma detection rates, especially at the proximal colon. This procedure may be effective for screening colonoscopy to improve the ADR at the proximal colon and mortality rate of colorectal cancer.
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Disclosure of Interest: None Declared
Keywords: Adenoma, chromoendoscopy, colonoscopy, colorectal cancer screening

P177 ALLOCATION OF TECHNICAL AND HUMAN RESOURCES IN COLO-RECTAL SCREENING PROGRAMS IN NORTHEASTERN ITALY

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INTRODUCTION: Colonoscopic screening for colo-rectal cancer necessitates an important engagement of economic, technical and human resources.
In Italy the main screening protocol consists of the performance of a total colonoscopy in faecal occult blood-test (FOBT)-positive subjects of both sexes - 50-69 or 50-74 years of age - with few scattered centres performing flexible sigmoidoscopy.
Northern and central Italy show a satisfactory coverage of the involved population, whereas Southern Italy is still trailing, with many areas still to be covered by screening campaigns. Preliminary results of a recent and wide survey conducted in northern and central Italy have shown satisfactory data as regards quality in screening colonoscopy, mainly measured through completion of the examination and polyp and adenoma detection rate.
AIMS&METHODS: We hereby report the results of a survey conducted in 2012 and involving 39 secondary level endoscopic centres in North-eastern Italy, all performing second level colonoscopies in FOBT-positive subjects. Reported data relate to the execution of first colonoscopy in first or second round (follow-up colonoscopies are excluded).

RESULTS: 51% of centres reported a standard time slot dedicated to screening colonoscopies, 49% a longer time slot, as compared to colonoscopies done in symptomatic patients.
In 33% dedicated time was 30 minutes; in 15% 40 minutes; in 18% 45 minutes; in 21% 50 minutes; in 13% 60 minutes.
In 15% of centres screening medical staff has been reported to be selected in advance; in 85% no selection has been made.
As regards technical appliances, only 3% of centres declared to care for a selection of instruments and devices for screening colonoscopies; 97 % of centres employed currently used equipment in a random fashion.
CONCLUSION: These data suggest that in Northern Italy management of colonoscopic lists in FOBT-positive subjects recognizes special care in selecting human and technical resources only in a minority of cases.
Time dedicated to screening colonoscopies is longer than in examinations performed in symptomatic subjects in about 50% of cases.
In the absence of recognized standards concerning these issues and considering that these choices do not seem to influence quality of screening colonoscopy, we believe that our data should be taken into consideration for further evaluation both at national and international level.
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Disclosure of Interest: None Declared
Keywords: colorectal cancer screening, Quality of colonoscopy, Resources utilisation

P178 ENDOTICS SYSTEM, A NEW WAY TO UNDERGO THE ENDOSCOPIC VALUATION OF LOWER GI TRACT : OUR INITIAL EXPERIENCE.

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INTRODUCTION: Video-colonoscopy is considered the gold-standard for the diagnosis of colonic diseases, but this diagnostic technique shows some technical limitations, such as invasiveness and patient discomfort, which limit the adherence to the procedure.The *Endotics System* is composed of a disposable probe and a workstation. The probe has a steerable tip, a flexible body and a thin tail.The workstation allows the endoscopist to fully control the disposable probe by means of a hand-held console and to visualize on a screen real time images. This technology thanks its extremely flexible and disposable probe is highly safe and painless.
AIMS&METHODS: This study assessed both the acceptability and efficacy and diagnostic capabilities of this new endoscope. The key primary endpoint was to evaluate diagnostic capabilities in a cohort of patients who wouldn't to undergo conventional colonoscopy without sedation; secondary endpoints were to evaluate the painless capabilities scoring a pain index in a scale ranging from 0 to 10, the cecal intubation rate and the cecum reaching time. A total of twenty patients participated to the study (9 men, 11 women; mean age 55 years). Three patients were excluded: one because of panic syndrome before procedure occurs and two because of inadequate bowel preparation where procedures were stopped on rectum colon. The cecum was reached in 15 patients (cecal intubation rate 100%).
RESULTS: The mean time to reach the cecum was 55 min (range 48-75) and mean pain score was 2. Endoscopic findings were: 4 polyps lesions (mean size x 110 mm), whereof one Ca *in situ*, in 3 people; 7 diverticular disease in 7 people. All findings was confirmed by following conventional colonoscopy procedure with sedation and no additional findings were notice (Sensitivity=100%, Sensibility= 100%). No device-related complications were encountered.Limits of the Endotics System consist on the absence of an instrument channel and procedure time longer than conventional colonoscopy.
CONCLUSION: The Endotics System represents a new painless method to undergo the endoscopic inspection of the lower GI tract, specially, in patients who are not willing to have a conventional colonoscopy procedure without sedation. Endotics System could be useful also for CCR prevention, but the absence of the instrument channel and the longer procedure time represent a limitation for this purpose. Further clinical and comparative studies are warranted.No financial disclosure.
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Disclosure of Interest: None Declared
Keywords: colon polyp, ROBOTIC COLONSCOPE

P179 THE WATER IMMERSION METHOD MIGHT CONTRIBUTE TO COMFORTABLE TOTAL COLONOSCOPY: RANDOMIZED TRIAL

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INTRODUCTION: It is well known that in total colonoscopy (TCS) straightening of the sigmoid colon is important and a basic skill for a comfortable examination. Recently, the water immersion method (WIM) was reported to be better for relieving abdominal discomfort caused by colonoscopy than the traditional air insufflation method (AIM). Additionally, WIM efficiently supports trainees to master TCS skills.
AIMS&METHODS: The aims of this study were 1) to compare insertion times and achievement rates of straight insertion by the WIM with the AIM by TCS experts and to evaluate the efficacy of the WIM in the progress of TCS skills in trainees. 1) A total of 220 patients undergoing TCS were randomized to the WIM or AIM (males, 119; females, 101; mean age, 63.7 years). We used a universal colonoscope with variable hardness, a clear hood, lukewarm water, and normal air, and did not administer sedatives. Cecal insertion time and achievement rates of straight insertion were evaluated in both groups. 2) A total of 113 patients underwent TCS by trainees who had experienced less than 30 cases. These patients were separated into the first 57 patients who underwent TCS (preceding period) and the latter 56 patients (latter period), and were evaluated as in 1).
RESULTS: 1) Nineteen patients were excluded for reasons such as cancerous stenosis of the colon and poor bowel preparation. The overall success rate of cecal insertion was 98.0% (197/201). The success rate was not significantly different between the WIM and AIM (91/93, 97.8% vs. 102/104, 98.0%). Cecal insertion time with the WIM was significantly shorter than the AIM (420±39 s vs. 540±30 s; P=0.0001), and the achievement rate of straight insertion was higher in the WIM than the AIM (64/93, 68.8% vs. 55/104, 52.9%; P=0.022). In the WIM group, there was no difference in cecal insertion time between sexes. However, in the AIM group, TCS in men was faster than that in women (P=0.023). 2) The success rate of TCS was significantly higher in the latter period than in the preceding period (50/56, 89.3% vs. 37/57, 64.9%; P=0.0019). In the latter period, rapid TCS with straight insertion was achieved in many cases.
CONCLUSION: The WIM might support painless and smooth TCS, even in experts. Additionally, the WIM encourages TCS skills in trainees. Popularization of the WIM could contribute to comfortable TCS and lead to early detection of colorectal cancer.
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Disclosure of Interest: None Declared
Keywords: colonoscopy, water immersion method

P180 COLONOSCOPIC POLYPECTOMY PRACTICES IN AUSTRALIA.

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INTRODUCTION: Polypectomy is the mainstay of colorectal cancer prevention [1], however there is little consensus on optimal techniques. This study explores the link between training, experience and case volume on polypectomy practice within Australia.
AIMS&METHODS: A questionnaire to capture relevant demographic, practice history and methods of polyp resection was developed and pre tested. Polyps were categorised as left or right sided and pedunculated or sessile. They were further broken down into 5 different size groups (<5mm, 5-9mm, 10-15mm, 16-20mm and >20mm). Polyp management techniques included cold biopsy, hot biopsy, cold snare, hot snare, submucosal injection with hot snare or referral to tertiary centre. The questionnaire was sent to 140 colonoscopists across Australia. Distribution of surveys commenced in June, 2012 and the final completed survey was collected in November 2012 with the majority of surveys distributed via mail. Data was collected anonymously and analysed using SPSS.
RESULTS: 65 questionnaires were returned. 45 responders were Gastroenterologists, 14 Interventional Endoscopists, 5 Advanced Trainees and one Surgeon. 40 responders had greater than 10 years experience and 28 had trained in ERCP or advanced endoscopy. 36 performed > 500 colonoscopies per year. 44 were from a capital city. Cold snare technique dominated other polypectomy techniques for sessile polyps <10mm (53.8%; p=0.02) and submucosal pre injection and hot snare for sessile polyps ≥10mm (73.3%; p<0.0001). Hot snare was the preferred technique for pedunculated polyps (65.5%; p<0.0001). The chosen technique was not linked to experience (p>0.5), location of practice (p>0.5) or annual volume of procedures (p>0.5). Preparedness to resect sessile right sided polyps >20mm was associated with training in interventional endoscopy (p<0.02). Hot biopsy remains a popular choice for diminutive polyp resection especially in colonoscopists with greater than 10 years experience. 11 (27.5%) of colonoscopists in this group used hot biopsy as their preferred technique for left sided sessile polyps <10mm. This compares to 3 (12%) of those with less than 10 years experience (p=0.2).
CONCLUSION: Polypectomy technique among colonoscopists is highly variable. Location, size and morphology of polyp significantly influence choice of technique. There was no link between experience, location of practice or annual volume of procedures and choice of technique. Despite known safety and inefficacy, [2-3] hot biopsy is still frequently used especially for diminutive polyps. Scope of practice is aligned with previous training as those trained in interventional endoscopy are more likely to attempt removal of large right sided sessile polyps.
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Disclosure of Interest: None Declared
Keywords: Colonoscopy, Polypectomy

P181 COLONOSCOPY IN THE OVER NINETIES: HOW USEFUL AND SAFE IS IT?

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INTRODUCTION: Colonoscopy is accepted as the gold standard imaging modality of the colon for investigation of colonic symptoms including altered bowel habit, anaemia, rectal bleeding and for the detection of colorectal cancer. The incidence of pathological findings within the colon in particular colorectal cancer increases with age, and the detection of these cancers comprise a major role of colonoscopy in the elderly population. However, colonoscopy in the elderly may be more difficult, as elderly patients are more likely than younger patients to have poor bowel preparations. Furthermore, complications of colonoscopy, in particular cardiovascular, maybe higher in this age group. To date no data exist in colonoscopies performed in those over 90 years of age.
AIMS&METHODS: The aim of the study was to assess the diagnostic yield and safety of colonoscopy in the very elderly patients over 90 years of age. A single centre, retrospective analysis of patients over 90 years of age in a district general hospital from north London was performed. The patients were identified using the Unisoft Endoscopy reporting software over a period between June 2006 to March 2013. Data obtained during the study period was scrutinised for indication, sedation administered, quality of bowel prep, findings of procedure, and complications.
RESULTS: During the study period, 66 colonoscopies were performed out of a total 666 endoscopic procedures in patients over 90. The indications for colonoscopy included : abnormal CT scan 5/66, altered bowel habit in 17/66, anaemia 24/66, rectal bleeding 15/66, colonic obstruction 3/66, previous polyp/colon cancer 4/66, abdominal mass 1/66. 18/66 patients had poor bowel prep. Findings included normal in 18/66, colo-rectal cancer in 13/66 patients, colonic polyps in 5/66, ischaemic colitis 1/66, angiodysplasia 2/66, diverticulosis in 31/66. Sedation administered varied from none in 4/66, to midazolam 5mg + pethidine 50mg in 2/66. There were no complications from the colonoscopy in 66 patients within the study.
CONCLUSION: The data from this study demonstrates that colonoscopies can be performed safely in patients over 90years of age with no increase in procedure related mortality. Despite poor bowel preparation encountered in 28%, the diagnostic yield of pathology in patients over 90 having colonoscopy was very high with an abnormality in 48/66 (72% in this study). Colonoscopy in the very elderly is very safe and worthwhile and clinicians should not be reluctant in referring those over 90 years of age for colonoscopic examination.
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Disclosure of Interest: None Declared
Keywords: colonoscopy, Elderly

P182 DIAGNOSTIC FEATURES OF DEPRESSED-TYPE COLORECTAL NEOPLASMS WITH MAGNIFYING ENDOSCOPY AND ENDOCYTOSCOPY

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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 adenoma stage. This theory is called "*de novo*" pathway. It is now available to estimate the histology of colorectal lesions using magnifying endoscopy (Pit pattern classification). And endocytoscopy (EC), using an ultra-high magnification system, can observe not only the structural atypia but also the cellular atypia in living colorectal lesions.
AIMS&METHODS: The aim is to clarify diagnostic features of depressed-type colorectal neoplasms, demonstrating the validity of EC classification together with pit pattern diagnosis.

A total of 19186 colorectal neoplasms excluding advanced carcinomas were resected endoscopically or surgically in our unit from April 2001 to December 2012. Of these, 15925 lesions were low-grade dysplasia, 2345 were high-grade dysplasia and 829 were submucosal (SM)-invasive carcinomas. According to morphological/development classification, they were divided into 3 types: flat, protruded and depressed type. We evaluated the rate of SM invasion, and investigated characteristic findings of depressed-type neoplasms concerning pit pattern and EC classification.
RESULTS: The SM invasion rate of depressed-type lesions reached to 62.8% (170/272), meanwhile that of flat-type and protruded-type lesions was 3.7% (272/7368) and 3.3% (381/11546) respectively. Within under 5mm in diameter, that was 10.7%, 0.00% and 0.02% respectively. Most (90.7% and 88.5%) of the flat-type and protruded-type lesions showed type IIIL or IV pit patterns corresponding to adenomas, whereas 94.2% of the depressed-type lesions were characterized by type IIIs, VI or VN pit pattern corresponding to carcinomas. As for endocytoscopy, the flat-type and protruded-type lesions showed various EC images. In contrast, the depressed-type lesions were presented with EC3a (19/84;22.6%) and EC3b (61/84;72.6%) corresponding to SM invasion.
CONCLUSION: This study revealed the diagnostic features of depressed-type lesions: they present typically type IIIs, VI or VN pit patterns and type EC3a or EC3b in endocytoscopy. These lesions tend to invade the SM layer even when they are small. Therefore, it is important to give a careful consideration to the development and progression of colorectal neoplasms.
Disclosure of Interest: None Declared
Keywords: colorectal cancer, de novo, depressed, endocytoscopy, magnifying endoscopy

P183 RISK FACTORS FOR DELAYED BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL NEOPLASMS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is a safe and effective treatment for superficial colorectal neoplasms, and is becoming a common procedure. The most common serious complication is delayed bleeding; however, the risk factors of delayed post-ESD bleeding are unknown.
AIMS&METHODS: This study aimed to identify the factors associated with the risk of delayed post-ESD bleeding. This retrospective study included 304 lesions in 297 consecutive patients undergoing ESD for superficial colorectal neoplasms at our hospital from January 2009 to April 2013. We analyzed the risk factors for delayed post-ESD bleeding in relation with various clinical factors related patients, lesions, and procedure characteristics.
RESULTS: Delayed post-ESD bleeding was evident in all 13 lesions from 13 patients (4.27% of all specimens, 4.38% of patients). All hemorrhagic episodes were successfully treated using endoscopic hemostatic clips, and none required surgery. Only 1 patient needed blood transfusion (0.33% of all specimens, 0.34% of patients). There were no deaths related to the colorectal ESD procedure. Lesions located in the cecum (odds ratio [OR] 14.13; 95% confidence interval [CI], 3.22-62.08; $p = 0.0005$) and significant bleeding during ESD (OR 19.43; 95% CI, 2.53-149.37; $p = 0.0044$) were significant factors associated with delayed post-ESD bleeding on univariate and multivariate analyses. Lesion size and histology were not risk factors. Submucosal invasive carcinoma was associated with significant bleeding during ESD on univariate and multivariate analysis (OR 9.30; 95% CI, 1.48-58.46; $p = 0.0174$).
CONCLUSION: Lesions located in the cecum and significant bleeding during ESD were highly significant risks for delayed post-ESD bleeding, and submucosal invasive carcinoma was found to be associated with significant bleeding during ESD. ESD for colorectal neoplasms should be done with caution, and it is also desirable to modify the management after ESD under these conditions.
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Disclosure of Interest: None Declared
Keywords: Bleeding, Colorectal cancer, ESD

P184 TELE-ENDOSCOPY ASSISTED DIAGNOSIS OF COLO-RECTAL NEOPLASIA: BRINGING THE PATHOLOGIST CLOSER TO THE ENDOSCOPIC PROCEDURE ROOM – A PILOT STUDY.

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INTRODUCTION: Tissue send to the pathology department for microscopic examination, is accompanied by a short clinical history. Adding information, such as images is rarely done despite the fact that the exchange of information is done electronically. Endoscopic procedures are often documented using images and video. The value for the pathologist of adding footage to the clinical history might be beneficial but cost-effective issues has to be addressed as well.
AIMS&METHODS: Primary aim was evaluate the impact on the histopathologic diagnosis by a-synchronous tele-endoscopy where the pathologist can view video and/or images from the procedure. Secondary aim was to test the possibility of uploading selected macro and microscopic images of the specimen alongside the stored endoscopic images and/or video.
Before performing endoscopic mucosa resection (EMR) of colo-rectal adenomas, video and still images was recorded. Olympus HD/NBI 180 EXERA II or HD/NBI 190 EXERA III endoscopes was used on the EXERA III system with Olympus EndoAlpha Video Management. The recorded footage was stored on the Endoalpha Endobase server on the hospitals network. The resected specimen was send to one senior GI pathologist. An Endobase client was installed on the pathologist desktop PC, making it possible to view the recorded footage (a-synchronous tele-endoscopy). The pathologist either viewed the footage before or after performing the microscopic examination of the specimen. Time used, IT related problems and clinical/diagnostic impact was recorded.
RESULTS: A total of 17 EMR cases were recorded. In 9 cases the footage was viewed *before* microscopic examination with a mean viewing time 10.11 minutes (range 5 to 22). In 7 out these 9 cases, no added value was gained. In 1 case the footage could not be found (spent 22 minutes) and in 1 case the video was to long and skipped. In 8 cases the footage was viewed *after* the microscopic examination with a mean viewing time 9.5 minutes (range 5 to 23). In 7 out these 9 cases, no added value was gained. In 1 case the footage could not be found (spent 8 minutes) and in 1 case problem with file size during viewing (spent 23 minutes). In 5 cases of the 8 viewed after microscopy, a mean of 8 images was uploaded to the server (range 1 to 24). Uploading was found time consuming – up to 18 minutes.
CONCLUSION: Adding a-synchronous tele-endoscopy service to the pathologist, in an un-selected set of clinical cases, did not add value to the final diagnosis.

Average time spent per case was 10 minutes. It was durable to upload and add microscopic images to the endoscopic footage. The value of this feature still needs to be evaluated.
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Disclosure of Interest: S. Meisner Consultancy for: Coloplast Denmark, Olympus Europe, Boston Scientific, A. Glenthøj: None Declared
Keywords: colon, EMR, teleendoscopy

P185 USEFULNESS OF CHROMOENDOSCOPY WITH INDIGO CARMINE DYE SPRAYING FOR DETECTION OF CECAL ADENOMA

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INTRODUCTION: Background: Chromoendoscopy with indigo carmine dye spraying has been shown to be a useful technique for detection of colorectal adenoma. However, application of the staining agent over the entire colorectal mucosa during chromoendoscopy has been reported to be associated with diagnostic difficulties in patients with poor bowel preparation or in areas of the mucosa whose view is obstructed by spray fluid residue. Thus, chromoendoscopy combined with narrow-band imaging (NBI) is currently drawing attention in numerous reports as a useful modality for detection of colorectal adenoma. In this study, we focused attention on the cecum to examine the ability of chromoendoscopy with indigo carmine spraying to detect adenoma.
AIMS&METHODS: Objective: To evaluate the usefulness of chromoendoscopy with indigo carmine dye spraying for detection of adenoma in the cecum.
Methods: Indigo carmine staining was applied to the cecum in a total of 547 patients who underwent chromoendoscopy between March 2012 and March 2013 (indigo group), and routine colonoscopy was conducted in a total of 9,918 patients (routine group) to compare the frequency of detection of adenomas and serrated polyps (SSA/Ps, and TSAs) between the two groups.
RESULTS: Results: Cecal adenoma detection rate was significantly higher at 16.1% (88/547) in the indigo group compared to 5.4% (538/9918) in the routine group, while the detection rate of serrated polyps was not significantly different at 6.8% (6/88) (6 SSA/Ps) in the indigo group compared to 7.2% (42/548) (38 SSA/Ps and 4 TSAs) in the routine group. The mean adenoma size was 6.5 mm in diameter (range, 1-30 mm) in the routine group vs. 4.2 mm (range, 1-18 mm) in the indigo group, with smaller adenomas tending to be detected in the indigo group. By macroscopic appearance, the number of Polypoid type/Non-polypoid type adenomas detected in the routine and indigo groups was 156/389 (0.40) and 5/76 (0.06), respectively, with more Non-polypoid type adenomas tending to be detected in the indigo group.
CONCLUSION: Conclusions: Chromoendoscopy with indigo carmine spraying to the cecum was shown to be more effective than routine colonoscopy in detecting adenomas, which tended to be smaller, non-polypoid type adenomas, while it was not found more effective than routine colonoscopy in detecting serrated polyps.
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Disclosure of Interest: None Declared
Keywords: adenoma detection rate, cecum, chromoendoscopy, indigo carmine

P187 TRAINING IN COLONOSCOPY: THE VALUE OF A STANDARDIZED ASSESSMENT PROGRAM

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INTRODUCTION: Colonoscopy is a practical skill requiring extensive training. There has been little attempt to comprehensively assess both generic and specific technical skills in colonoscopy. Standardized self-assessment during colonoscopy training may provide insight in performance and enable specific intervention to improve skills. On top of that, implementation of an intensified assessment program, where trainees are closely observed during live colonoscopies on regular points in training, provides the opportunity for such interventions. The aim of this study was to assess the value of a standardized assessment program on top of self-assessment of performance.
AIMS&METHODS: We developed a standardized skills training and assessment program for colonoscopy. All procedures were self-assessed. Trainees were systematically evaluated during two colonoscopies after every 50 colonoscopies performed during their formal colonoscopy training. A single expert closely observed the trainee and gave feedback on the trainees' performance. In order to assess the value of this assessment program on top of the self-assessment program, we used a historical control group of trainees as a reference. The historical group only participated in the self-assessment program. The primary outcome parameter was the incremental change in cecal intubation rate (CIR) expressed in a learning curve.
RESULTS: The study group consisted of twelve trainees from different centers. All were included in the standardized skills training and assessment program. The intensified assessment program was additional. The reference group consisted of 18 trainees, all from one center. A total number of 1960 colonoscopies were performed in the study group against 2887 in the historical control group. 55 trainee assessments (range 1-4 per trainee) were carried out by an expert endoscopist. Baseline CIR after 30 procedures was 53.4% versus 65.3% in the reference group ($p=0.004$). The slopes of the two learning curves differed significantly between the study and control group (β 0.18 vs. 0.10, $p<0.001$). Evaluation of the program showed that trainees experienced the assessment program as positive and useful (score of 4.6 on a Likert scale of 1-5).
CONCLUSION: The addition of a standardized assessment program on top of self-assessment in colonoscopy training proves to be useful and results in a steeper learning curve, especially in the early training stage. Trainees experienced this program as very valuable.
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Disclosure of Interest: None Declared
Keywords: Assessment, colonoscopy, learning curve, training

P188 A RANDOMIZED PROSPECTIVE TRIAL COMPARING DIFFERENT REGIMENS OF ORAL PICOSULPHATE AND POLYETHYLENE GLYCOL-BASED LAVAGE IN THE PREPARATION OF PATIENTS FOR COLONOSCOPY

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INTRODUCTION: Adequate bowel cleansing is essential for a high-quality, effective, and safe colonoscopy. There are rare reports that compare directly conventional polyethylene glycol (PEG) intake and picosulphate.
AIMS&METHODS: The aim of this study is to compare the efficacy, safety, and tolerability of different regimens of oral picosulphate and PEG. This study involved 200 adult patients undergoing elective colonoscopy and was single-blinded prospective randomized design in tertiary-care institutions of South Korea. Patients were randomized into four groups with endoscopist was blinded to the regimen. Group A: PEG 4L at 4-6 hours before procedure on the day of the colonoscopy. Group B: PEG 2L at 6:00 PM the day before and 4-6 hours before procedure. Group C: One of 2 sachets of sodium picosulphate at 6:00 PM the day before and 4 hours before procedure. Group D: One of 3 sachets of sodium picosulphate given at 6:00 and 09:00 PM the day before and at 4 hours before procedure.
RESULTS: PEG 4L group (both split and non-split dosage) and 3 sachets of picosulphate produced better mucosal cleansing than 2 sachets of picosulphate. Side effects were more frequent in PEG 4L than picosulphate. Patients' preferences were most high in picosulphate than other goups.
CONCLUSION: Picosulphate is as effective as high-volume PEG-electrolyte solution but has superior tolerance. It has fewer adverse events and is preferred by patients.
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Disclosure of Interest: None Declared
Keywords: colonoscopy, picosulphate, polyethylene glycol

P189 ENDOSCOPIC BALLOON SPHINCTEROPLASTY AS AN ADJUNCT TO ENDOSCOPIC SPHINCTEROTOMY IN REMOVING LARGE AND DIFFICULT BILE DUCT STONES IN THE ELDERLY

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INTRODUCTION: Extraction of common bile duct stones at endoscopic retrograde cholangiopancreatography can be technically challenging when the size of the stone exceeds that of an endoscopic sphincterotomy. These stones are more common in the elderly, with higher risks involved invasive procedures in this population.
AIMS&METHODS: The aim of this study was to evaluate the efficacy and safety of papillary balloon dilation after sphincterotomy for extraction of these difficult-to-remove bile duct stones in the elderly
This was a retrospective study in patients older than 65 years with large common bile duct stones that could not be extracted using a stone retrieval balloon and basket after endoscopic sphincterotomy. Endoscopic balloon dilatation was performed by using standard 12-20 mm Controlled Radial Expansion balloons. The success rate and the complication rate for the papillary balloon dilation technique were assessed
RESULTS: A total of 154 patients (71 men, 83 women; mean age 79, range 65 - 93) were enrolled in this study from January 2008 to march 2013. The mean stone size was 16 mm (range 12 - 20 mm). Stones were removed with sphincteroplasty in first session in 148/154 (96.1%) patients, 6/154 (3.9%) patients in the second session. Six patients (3.9%) required adjunctive mechanical lithotripsy for stone extraction. Surgery was advised for 4 (2.6%) patients because of failure to remove stones by sphincteroplasty. Overall success of endoscopic sphincterotomy and large balloon dilatation in our study was 93.5%
Complications were seen in 24 patients (16.2%). Bleeding was encountered in 5 (3.3%) patients which was controlled by adrenaline injection in 2 patients and all other conservatively. Moderate pancreatitis necessitating admission was seen in 15 patients (9.7%). None of the patients had severe pancreatitis. There were two (1.3) perforation secondary to the procedure, managed with conservative treatment. No patient died as a result of the procedure
CONCLUSION: Papillary balloon dilation after endoscopic sphincterotomy is an effective technique for retrieval of difficult common bile duct stones. The procedure obviates the need for mechanical lithotripsy or surgery in a majority of patients. Although it is a safe procedure, the number of complications in the elderly is higher than those described in the general population.
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Disclosure of Interest: None Declared
Keywords: Elderly, Endoscopic balloon sphincteroplasty

P190 NEW CLASSIFICATION OF BILIARY OBSTRUCTION AFTER LIVER TRANSPLANTATION

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INTRODUCTION: To propose a new classification of biliary obstruction after liver transplantation for selecting appropriate endoscopic treatment.
AIMS&METHODS: we screened out the data of patients after liver transplantation with endoscopic pictures clear enough to reveal biliary imaging, who underwent endoscopic therapy from May 2006 to September 2011 at our Digestive Endoscopic Center. After analyzing the correlation between intrahepatic biliary and anastomotic structure we proposed a new endoscopic classification(Ling classification) of biliary obstruction after liver transplantation. There were four types based on the criteria of Ling classification: type A, normal biliary structure; type B, anastomotic stricture and normal intrahepatic biliary structure; type C, narrow and stiff intrahepatic biliary structure or beaded intrahepatic biliary structure or intrahepatic biliary cast without anastomotic stricture ; type D, narrow and stiff intrahepatic biliary structure or beaded intrahepatic biliary structure or intrahepatic biliary cast with anastomotic stricture. Two endoscopists made a final decision upon mutual agreement through discussion if their separately recorded characteristics were different.
RESULTS: Among the 112 screened patients with jaundice after liver transplantation, 93 qualified patients were selected for the analysis, including 76 males and 17 females. The average age was 50.3years, ranging from 12 to 69 years. type B was the most commonly observed type of biliary obstruction after liver transplantation, accounting for 47.3%(44/93), and type A was the least commonly observed type of biliary obstruction after liver transplantation, accounting for 9.7%(9/93). And type C accounted for 23.7%(22/93)and type D accounted for 19.3%(18/93)
CONCLUSION: A new endoscopic classification of biliary obstruction after liver transplantation is proposed that might help in determining the proper candidates for treatment.
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Keywords: Biliary obstruction, classification, Liver transplantation

P191 ENDOSCOPIC MANAGEMENT OF LARGE BILE DUCT STONES AND COMMON BILE DUCT ROCK PAVING : SUCCESS RATE, COMPLICATIONS, AND ASSOCIATED FACTORS

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INTRODUCTION: Residual lithiasis of the common bile duct is an indication of choice for endoscopic sphincterotomy. Endoscopic treatment provides a clearance of the common bile duct in 90% of cases. However, the presence of a rock paving or a large stone may limit its results. The aim of this study is to evaluate the success rate, associated factors and complications of endoscopic treatment of the rock paving and large stones of the commun bile duct.
AIMS&METHODS: All patients (542) who had undergone endoscopic retrograde cholangiopancreatography for commun bile duct stones from January 2007 to March 2013 were reviewed. We compared the results and complications of ERCP in patients with choledochal rock paving and / or a large stone (group I) versus patients with simple commun bile duct stones: $\leq$ 3 stones, without obstruction (group II). The rock paving was defined by the presence of multiple stones (more than 3) and the large stone by the obstruction of the commun bile duct by a stone that measure more than 15 mm. The success of endoscopic treatment was defined as a complete removal of stones of the common bile duct at the end of procedure
RESULTS: The rock paving and/or large cholelithiasis (group I) represented 32.8% of CBD stones (178 patients). Group II included 364 patients (67.1%). The Success rate was achieved after a single catheterization in 64% of the cases in group I versus 90,2% in group II ($p<0{,}001$). The overall success rate after additional maneuvers and / or recovery the patient was 95.3% in group II versus 89% in group I ($p = 0.006$). The overall rate of early complications was 4.8% in group II versus 7,5% in group I ($p = 0.37$). In multivariate analysis including the factors : age, sex, history of surgery (cholecystectomy, choledochotomy, gastroduodenal surgery), severe acute pancreatitis, cholangitis, stenosis of the common bile duct, diverticulum peri-ampullary, diameter of the bile duct), only the presence of cholangitis, a periampullary diverticulum and / or stenosis of the common bile duct were factors associated with decreased of overall success of endoscopic treatment.
CONCLUSION: Though representing a limit to the endoscopic treatment, in our serial the clearance of the CBD in case of rock paving and / or large stone was obtained after additional maneuvers in 89% of cases without significant increase in early complications. The presence of cholangitis, a periampullary diverticulum and / or stenosis of the CBD appear to be factors associated with decreased overall success of endoscopic treatment.
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Disclosure of Interest: None Declared
Keywords: Complications, Endoscopic treatment, large stones, Rock paving, Success rate

P192 PERI-DIVERTICULAR PAPILLA: CLINICAL SIGNIFICANCE IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY CANNULATION

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INTRODUCTION: An important percentage of patients have a peri-diverticular papilla of Vater (PD). It could hinder the biliary and/or pancreatic cannulation at endoscopic retrograde cholangiopancreatography (ERCP) and might change the outcomes in this procedure.
AIMS&METHODS: Aims: To compare the efficacy and complications rate in biliary cannulation at ERCP in patients with PD vs. patients without PD. **Material and methods:** Through a prospective informatic database were registered all consecutives patients with ''virgin'' papilla that underwent to ERCP from june 2002 to june 2012. The database included demographic data, patients' general status, indications and level of difficulty of the ERCP, anatomic features of the papilla and its localization with regard to the duodenal diverticulum, success and ease of cannulation (number of attempts, Freeman score), biliary cannulation techniques (standard techniques, placement of pancreatic guidewire or stent to assist biliary cannulation, precut ''access'' papillotomy), outcomes of the ERCP and its complications. The data were analyzed using the SPSS 15.0 software.
RESULTS: Between 2337 patients with ''virgin'' papilla (age: 71,7 $\pm$ 15 y; women: 44,7%) 551 (23,1%) had PD (31,4% within; 29,2% in the border and 39,4% adjacent to the diverticulum). In the PD group the cannulation rate was not different from the non PD group (92,3% vs. 92,2%), neither the number of attempts (5,0 vs 5,1) nor the Freeman score. The number of precuts were lesser (14,2% vs 21%; P=0.000) and these were made more frequently starting at the papillary orifice, as compared with ''fistulotomy'' starting above orifice. There were not differences, neither in the guidewire use for biliary cannulation nor in the diagnostic and therapeutic success. In the PD group, complication rate was slightly higher than the non PD group (14,2% vs 11,1%; p=0,035) at the expense of the number of post papillotomy bleeding (8,5% vs 4,6%; p=0,000), even though the most of these were mild (4,9% vs 1,8%) and were resolved during the same procedure. There were not differences between groups regarding pancreatitis, cholangitis, perforations, submucosal injection or abdominal pain.
CONCLUSION: The presence of a peri-papillary duodenal diverticulum does not involve a difficult biliary cannulation or lower cannulation rate. In these patients, complication rate is higher, although mainly represented by mild post-papillotomy bleeding easily solvable.
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Disclosure of Interest: None Declared
Keywords: Biliary cannulation, Peri-diverticular papilla

P193 COMPLEX BILIARY LEAK POST-HEPATECTOMY: IS ENDOSCOPIC TREATMENT EFFECTIVE?

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INTRODUCTION: The ERCP (papillotomy and/or stent) has become the elective treatment for post-cholecystectomy biliary leak (PCBL). Nowadays is unknown if this treatment is equally effective for post-hepatectomy biliary leak (PHBL).
AIMS&METHODS: Aims: To compare the efficacy between endoscopic treatment for PHBL and PCBL. **Methods:** From January 2002 to October 2012 were recorded in a prospective database all patients with post-surgical biliary leak (PSBL) that underwent to ERCP. The database included demographic data: age and sex; type of surgery and indication; PSBL features: localization, debit and associated findings (strictures, biloma/abscess, choledocolithiasis, etc); endoscopic treatment; papillotomy and/or stent, diagnostic success, technical success, efficacy and security. We defined as Diagnostic success: localization of PSBL by ERCP and as Technical success: Endoscopic drainage of PSBL. The sealing of PSBL was confirmed by ERCP and/or clinical evaluation. The data were analyzed using the SPSS 15.0 software.
RESULTS: Between 3785 ERCPs (2002 – 2012) there were 67 patients with PSBL (1,7%): 51 PCBL (67%) and 16 PHBL (33%). Age: 64,79 $\pm$ 15,07 years. Women: 20 (29,9%). In PCBL the surgical indication was cholelithiasis (100%), while in PHBL were liver metastases: 12 (75%), hepatic hydatid disease: 2 (12,5%), traumatism: 1 (6,25%) and gallbladder cancer:1 (6,25%). Cystic duct stump and common bile duct/common hepatic duct were the most frequents localization of PCBL: 58,82 vs. 0,00% (p=0,000) and 25,49 vs. 18,75% (p=0,000), respectively. In PHBL, primary and secondary intrahepatic bile ducts were the most frequents: 31,25 vs. 5,88% (p=0,000) and 37,5 vs. 5,88% (p=0,000), respectively. For PCBL, diagnostic success was higher than PHBL: 96,08 vs. 87,5% (p=0,000). There was not difference in PSBL debits. Strictures (57,14 vs. 22%, p=0,000) and biloma/abscess (87,5 vs. 26%, p=0,000) were more associated to PHBL than choledocolithiasis (7,14 vs. 48%, p=0,000). In regard to endoscopic treatment, there was not difference between both groups: papillotomy and stent was the most frequent procedure and technical success was above 93%. The endoscopic treatment efficacy for PHBL was much lower than for PCBL (25 vs. 84,31%, p=0,000). The complication rate was similar between both groups.
CONCLUSION: The endoscopic treatment efficacy (papillotomy and/or stent) for PHBL is much lower than for PCBL. This is related to their greater complexity: frequently intrahepatic and associated to strictures and biloma/abscess.
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Disclosure of Interest: None Declared
Keywords: Post-cholecystectomy biliary leak, Post-hepatectomy biliary leak

P194 USEFULNESS OF CARBON DIOXIDE INSUFFLATION IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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INTRODUCTION: The purpose of the present study is to clarify whether carbon dioxide insufflation at the time of ERCP is useful for stabilizing patient conditions during or after an operation or for reducing complications.
AIMS&METHODS: 289 subjects of ERCP cases performed consecutively at our hospital during a period from January 2010 through May 2011 were assigned randomly to a normal insufflation group (control group) and a CO_2 insufflation group (CO_2 group). The factors examined are: 1) success ratio of the treatment, 2) enteric tube images before and after the test that were evaluated for the blinded three stages, 3) evaluation of abdominal pain, feeling of abdominal fullness and nausea using the VAS (visual analog scale), 4) vomiting within 24 hours after the test or use of metoclopramide, 5) amount of sedative during the test and 6) status of respiratory circulation and the complications based on the Cotton definition. We conducted a comparative study using these factors.
RESULTS: 149 subjects in the control group consisted of 71 males and 78 females and the average age was 72.8 years old. The 140 subjects in the CO_2 group consisted of 77 males and 62 females and the average age was 71.1 years old. There were no significant differences in the causative diseases or treatment contents or average test times (22.0 minutes in the control group and 24.3 minutes in the CO_2 group. 1) The success ratio of the treatment was 136/149 (91.3%) in the control group and 128/140 (91.4%) in the CO_2 group, which indicated no significant difference. 2) The gas images were significantly less in the CO_2 group ($p=0.00001$). 3) Regarding the symptoms at the end of the test, there was no significant difference in the feeling of abdominal fullness between the two groups. However, abdominal pain and nausea were significantly lower in the CO_2 group ($p=0.0489$ and $p=0.0017$, respectively). 4) Vomiting after the test was found in 19 cases in the control group (12.8%) and 8 cases in the CO_2 group (5.7%) ($p=0.0370$), which indicated significantly lower effect. 5) There was no difference in the amount of use of sedatives.6) Regarding the complications, there were no significant differences.
CONCLUSION: Insufflation of CO_2 at the time of ERCP contributes to improvement in safety without having any influence on the results of the treatment.
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Disclosure of Interest: None Declared
Keywords: Carbon Dioxide, ERCP

P195 EFFICACY OF NOVEL FULLY COVERED SELF-EXPANDABLE METAL STENTS IN POST-LIVER TRANSPLANT ANASTOMOTIC BILIARY STRICTURES NOT RESPONDING TO STANDARD METAL STENT INSERTION

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INTRODUCTION: Anastomotic biliary strictures account for 40% of the complications following liver transplantation. Most strictures are initially treated with plastic stent insertion or balloon dilation with stenting but recent studies have shown that fully covered, self-expandable metal stent (fcSEMS) are effective for benign biliary strictures (90% success) but are associated with a significant migration rate (24%).[1]
Bumpy (6-10cm) and *Short-Bumpy* fcSEMS (4cm, Taewoong Medical, Seoul) have bilateral flared ends and unfixed irregular cell size, which are believed to decrease the risk of migration. The aim of this study was to assess the efficacy and migratory rate of temporary placement of the *Bumpy* and *Short-Bumpy* fcSEMS in post-liver transplant anastomotic biliary strictures when previous treatment with standard metal stent insertion has failed.
AIMS&METHODS: Between July 2010-March 2013, 23 patients with post-liver transplant anastomotic strictures not resolved following metal stent insertion were included in the study. Bumpy stents were kept in place for 12 weeks, after which ERCP was performed to remove the stent and assess biliary morphology. 11 patients with treatment failure following Bumpy removal had a Short-Bumpy stent inserted for a period of 12 weeks. Patients were followed up clinically and with 3 monthly liver function tests following stent removal.
RESULTS: Mean follow up after Bumpy and Short Bumpy removal was 11 months and 9 months respectively. Placement of the stents was successful in all patients with no reported complications after insertion or removal. 12 patients (52%) had endoscopic resolution of the stricture at follow up ERCP after Bumpy insertion with 26% (6 patients) recurrence of the stricture. 10 patients (43%) had spontaneous stent migration and expulsion, including 4 patients (40%) who had treatment success not requiring further interventions after stent loss. 11 patients who had treatment failure with the Bumpy stent were subsequently managed with a Short Bumpy stent which was associated with 90% success (10 patients), 27% recurrence (3 patients) and 0% stent loss.

	Patients (n)	Treatment Success	Stricture Recurrence	Loss of Stent	Success after Stent Loss
Bumpy	23	12(52%)	6(26%)	10(43%)	4(40%)
Short Bumpy	11	10(90%)	3(27%)	0	-

CONCLUSION: Bumpy stents may be used in post-liver transplant anastomotic strictures refractory to treatment with standard metal stents. Short Bumpy stents are associated with very high success rates probably due to its low migration rate.
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Disclosure of Interest: None Declared
Keywords: biliary strictures, metal stent

P196 SYSTEMIC AIR EMBOLISM DURING ERCP: DESCRIPTION OF 3 CASES

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INTRODUCTION: Scattered case reports describe the occurrence of systemic air embolism during ERCP -particularly during highly manipulating procedures- very often with ominous consequences.
The mechanism of action seems to be the escape of air to the portal system and then to hepatic veins, vena cava inferior and right heart, eventually with cardiocirculatory collapse.
AIMS&METHODS: We describe 3 such complications of ERCP experienced at our institution (≈500 ERCPs/year) in the past 3 years.
RESULTS: All patients were males (N.1:70 y;N.2:45 y;N.3:71 y).
N.1 and N.2 were done under propofol with the assistance of a anesthesiology team; N.3 received general anesthesia.
In all cases a choledochal stricture was the main finding. In N.1 and N.2 a biliary sphincterotomy was carried out; in N.1 and N.3 biopsies and brushing samples were obtained. In all pneumatic dilation to 6-8 mm and insertion of multiple plastic stents were performed.
In all cases - during the final part of the examination - a similar sudden onset clinical picture took place: hypoxia, hypotension, bradycardia and dramatic drop of end-tidal CO2, followed by cardiac arrest.
Standardized cardiopulmonary resuscitation maneuvers as well as a trial of aspiration of air through a catheter positioned in the right heart were performed.
In N.2 and N.3 the diagnostic suspicion has been confirmed by emergency cardiac ultrasonography, which revealed –respectively– air in the whole heart and air barrage of the right ventricle.
N.1 and N.3 had a, respectively, delayed and immediate fatal outcome. N.2 had an uneventful recovery.
CONCLUSION: The described cases share common clinical and imaging findings, all in favor of a diagnosis of systemic air embolism during complex ERCP procedures. Sudden onset cardio-vascular collapse, an abnormally distended abdomen, the inefficacy of chest compression in the presence of distended jugular veins all contribute to the clinical suspicion. Trans-thoracic echocardiography has contributed to the diagnosis in 2/3 cases; although not employed in the third case, a trans-esophageal echocardiography has been reported to help in the diagnosis. Such condition deserves in our opinion a note of caution, being probably less infrequent than reported and carrying a very high risk of fatal consequences. The management of complex strictures of the biliary tree may represent a risk factor due to length of the procedure and multiple highly manipulating maneuvers, possibly leading to microtraumas and relevant insufflation of air in the duodenum. To prevent this type of complication, we have decided at our institution to switch to CO2 utilization during ERCP.
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Disclosure of Interest: None Declared
Keywords: ERCP, Systemic air embolism

P198 USE OF A SHORT SINGLE-BALLOON ENTEROSCOPY FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY: PRELIMINARY EXPERIENCES AT A SINGLE CENTER.

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INTRODUCTION: Single-balloon entroscopy (SBE) has been recognised as a useful method for performing endoscopic retrograde cholangiopancreatography (ERCP) in patients with a complex post-surgical anatomy. However, there are a limited number of ERCP accessories that are compatible with SBE because its inner channel diameter is 2.8 mm, and its working length is 2000 mm; this size is smaller and longer than that of a conventional duodenoscope.
AIMS&METHODS: We used a short single-balloon endoscope prototype (SIF-Y0004, Olympus medical systems, Tokyo, Japan), which has an inner channel diameter of 3.2 mm and a working length of 1520 mm, for ERCP in patients with surgically altered anatomy. The aim of this study was to determine the utility of this prototype endoscope.
From January 2012 to April 2013, we attempted 20 ERCP procedures on 13 patients with Roux-en-Y and Billroth II reconstruction using the short single-balloon endoscope prototype. We retrospectively analysed the rate of reaching the blind end, the diagnostic success rate, the therapeutic success rate and the frequency of incidence of related complications.
RESULTS: One case was excluded because of small intestinal stenosis. Thus, we analysed 19 procedures, including Billroth II reconstruction (B-II, $n = 2$), post-gastrectomy with Roux-en-Y reconstruction (RY-G, $n = 12$) and post-choledochojejunostomy with Roux-en-Y reconstruction (RY-CJ, $n = 5$). The rates of reaching the blind end were 2/2 (100%) for B-II, 11/12 (91.7%) for RY-G and 4/5 (80%) for RY-CJ. The diagnostic success rates were 2/2 (100%) for B-II, 8/11

(72.7%) for RY-G and 4/4 (100%) for RY-CJ. The therapeutic success rates were 1/2 (50%) for B-II, 8/11 (72.7%) for RY-G and 4/4 (100%) for RY-CJ. Endoscopic biliary drainage (9 patients), endoscopic sphincterotomy (2 patients), stone extraction (2 patients) and endoscopic papillary large-balloon dilation (1 patient) were performed using conventional endoscopic accessories. The mean procedure time was 56 min. We did not experience any related complications.
CONCLUSION: The blind end could be reached in most of the patients with an altered gastrointestinal anatomy, despite the short length of the prototype endoscope. This prototype endoscopy with a wide inner channel diameter was useful, notably because it allowed the use of the most conventional endoscopic accessories.
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Disclosure of Interest: None Declared
Keywords: ERCP, single-balloon enteroscopy

P199 LONG-TERM FOLLOW UP STUDY OF ENDOSCOPIC PAPILLECTOMY IN TUMORS OF THE PAPILLA OF VATER

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INTRODUCTION: Although Endoscopic papillectomy (EP) has reported to be feasible for the treatment of ampullary neoplasm, there is little data about long-term follow up results after EP.
AIMS&METHODS: The aim of this study was the assessment of local recurrence and late complication after EP. Forty of 129 patients with ampullary neoplasm underwent EP from April 1997 to March 2013, and 27 (68%) of them who were followed up for more than a year were eligible for this study (18 men and 9 women, mean age 64). Histological diagnosis of their tumors were adenoma in 24 and focal carcinoma in adenoma in 3. Twenty of them were placed biliary stent (EBS) and 24 of them were placed pancreatic stent (EPS) for a week after EP. All patients were followed with endoscopic surveillances every 6-12 months.
RESULTS: All 27 patients underwent EP successfully. Twenty-three (85%) patients achieved en bloc resection and the remaining 4 (15%) patients underwent piecemeal resection. Mean follow up time was 60 months (range, 15-144 months). Local recurrence occured in 2 (7%) patients, who received piecemeal resection. One patient had tumor spread to the bile duct 45 month after EP and was treated surgically. Another patient with a recurrence at the time of 14 months was re-treated with EP, although he had a second recurrence 36 months after first EP and ultimately required surgery. Late complication occured in 2 (7%) patients. One patients had scarring and stenosis of the pancreatic duct orifice 36 months after EP and improved by endoscopic pancreatic sphincterotomy and additional EPS. Another patient had focal stent-induced stricture in main pancreatic duct 21 months after EP and was treated with repeated EPS.
CONCLUSION: Although EP is an effective treatment for ampullary tumor, some recurrences or complications may occur even after a year. En bloc resection is important for the prevention of local recurrence. Prophylactic EPS should be placed carefully with an awareness of stent-induced stricture. Long-term follow up is important after EP treatment for ampullary tumors.
Disclosure of Interest: None Declared
Keywords: ampullary tumor, Endoscopic papillectomy, long-term follow up

P200 IMPROVING BILIARY CANNULATION USING A NOVEL SEQUENTIAL PANCREATIC DUCT GUIDEWIRE PLACEMENT TECHNIQUE: A PROSPECTIVE ERCP PILOT STUDY

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INTRODUCTION: Deep biliary cannulation is a fundamental and crucial step in ERCP[ss1]. Although various methods have been developed to facilitate biliary cannulation, the cannulation success rate remains unsatisfactory.
AIMS&METHODS: To compare the performance of sequential pancreatic duct guidewire placement (PDGP) technique and needle knife precut sphincterotomy (NKPS) technique in cases of difficult biliary cannulation.
RESULTS: Sequential PDGP technique had a higher overall cannulation success rate than the NKPS technique (93.7% vs. 70%, p=0.015), as well as a higher initial success rate despite the absence of statistical significance (88.9% vs. 70%, p=0.095). Sequential PDGP technique did not increase difficult cannulation time (7.49mins vs. 10.60mins, p=0.086), and had a comparable rate of post-ERCP pancreatitis as the NKPS technique (12.7% vs.10%, p=1.000)
Clinical outcomes of ERCP procedure

	PDGP group	NKPS group	P value
Initial success rate	56(88.9%)	14(70%)	0.095
Overall success rate	59(93.7%)	14(70%)	0.015
Total cannulation time (mean±SD, minute)	27.03±13.64	34.50±10.47	0.028
Difficult cannulation time (mean±SD, minute)	7.49±5.03	10.60±7.24	0.086
Hyperamylasemia	28(44.4%)	3(15%)	0.018
pancreatitis	8(12.7%)	2(10%)	1.000
Bleeding	9(14.3%)	4(20%)	0.795
Cholangitis	5(7.9%)	0(0%)	0.447
Perforation	0	0	NA

CONCLUSION: Sequential PDGP technique improved the overall success rate in difficult biliary cannulation cases without increasing cannulation time and major complications compared with the NKPS technique. Sequential PDGP technique is a promising method to facilitate biliary cannulation during ERCP.
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Disclosure of Interest: None Declared
Keywords: Difficult biliary cannulation, Needle knife precut sphincterotomy, Pancreatic duct guidewire placement technique

P201 FEASIBILITY OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY RELATED PROCEDURES IN HEMODIALYSIS PATIENTS

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INTRODUCTION: The opportunities of endoscopic retrograde choangiopancreatography (ERCP)-related procedure for hemodialysis (HD) patients have been increasing recently. However, the complication rate of ERCP in HD patients was not evaluated sufficiently.
AIMS&METHODS: We aimed to clarify the feasibility of ERCP-related procedure for HD patients.We retrospectively reviewed 76 consecutive ERCP-related procedures for HD patients between January 2005 and December 2012 in one university hospital and three tertiary-care referral centers. Endoscopic sphincterotomy (EST) was performed in 21 HD patients. We evaluated the incidences and risk factors for complications of all ERCP-related procedures and EST in HD patients.
RESULTS: The incidences of pancreatitis, cholangitis and cardiopulmonary complications for ERCP-related procedures in HD patients were 7.9% (6/76), 1.3% (1/76) and 1.3% (1/76), respectively. The mortality rate was 2.6% (2/76) and it occurred after acute pancreatitis in one patient and pneumonia in the other patient. The incidences of hemorrhage and pancreatitis of EST were 19% (4/21) and 4.8% (1/21), respectively. The duration of HD was significantly longer in the patients with hemorrhage after EST than without (19.5 vs 6 years; p=0.029).
CONCLUSION: ERCP-related procedures except EST were feasible in HD patients. However, EST was inappropriate procedure for HD patients because of high rate of hemorrhage especially for patients with long HD duration.
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Disclosure of Interest: None Declared
Keywords: hemorrhage, complication, endoscopic retrograde choangiopancreatography, endoscopic sphincterotomy, hemodialysis

P202 CLINICAL CHARACTERISTICS, ENDOSONOGRAPHIC FINDINGS AND ETIOLOGIES OF GASTRODUODENAL SUBEPITHELIAL LESIONS: A REFERRAL SINGLE CENTER STUDY.

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INTRODUCTION: Subepithelial lesions are a frequent incidental endoscopic finding. Knowledge is important given the potential for malignancy that associates some types of these injuries.
AIMS&METHODS: The aim of this study was to evaluate the demographic data, endoscopic ultrasonography characteristics, pathology results and complications of the patients with suspected extra luminal compression or subepithelial intramural lesions observed during upper gastrointestinal endoscopy.
From January 2008-march 2013, a total of 310 cases were referred for EUS evaluation due to extra luminal compression or subepithelial intramural lesions. The endoscopic reports, pathology results and the patients' medical records were reviewed
RESULTS: The mean age was 56 (range 25-82). 52% were female. Only 12.6% of the patients had symptoms. The mean size of the lesions was 14.6 mm (range 8-55 mm).The provisional diagnosis of the sub-epithelial lesions, regarding only clinical and endosonographic characteristics were GIST, neuroendocrine tumor, pancreatic rest, lipoma, vascular lesions, polyps, leiomyoma, extrinsic compression and cyst wall (35.6%, 6%, 3.8%, 31%, 2.3%, 3,1%, 15%, 1.6% and 1.6% respectively). All the lesions were diagnosed as GIST originating from either the forth layer (80.5%) or the second layer (19.5%) of gastric or duodenal wall. Fine needle aspiration (FNA) was performed in 85 patients (27.4%), 61 patients with suspected GIST, 15 patients with suspected leiomyoma, 4 patients with suspected cyst wall and 5 patients with suspected pancreatic rest. The positive predictive value, negative predictive value and accuracy of diagnosis of made by endosonographers based on only endosonographic characteristics were 75, 100 and 76% (95% CI: 52.4% > 84.4%) respectively. There were no procedure-related complications.
CONCLUSION: Most of the subepithelial lesions which were referred for EUS evaluation at Gregorio Marañón Hospital were GISTs. The diagnosis of GIST can be accurately made by using the EUS based on only endosonographic characteristics. FNA should be performed in large lesions or when there are diagnostic doubts.

Disclosure of Interest: None Declared
Keywords: endoscopic ultrasonography , subepithelial lesions

P203 PANCREATIC CYSTS CONFOCAL ENDOMICROSCOPY STUDY: A FEASIBILITY STUDY OF NCLE (NEEDLE BASED CONFOCAL LASER ENDOMICROSCOPY) THROUGH FNA NEEDLE

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INTRODUCTION: Probe-based confocal laser endomicroscopy enables *in vivo* real time characterization of the mucosa layer and is a valid tool to differentiate neoplastic vs non neoplastic tissue in upper and lower GI tract.
Despite significant improvements in imaging technology and the advent of endoscopic-ultrasound (EUS)-guided fine-needle aspiration, the diagnosis and management of pancreatic cystic lesions remains a significant clinical challenge. Needle-based confocal laser endomicroscopy (nCLE) is a unique imaging technique, enabling microscopic observation of solid organs and cystic tumors, *in vivo* and in real-time, during an EUS-FNA procedure
AIMS&METHODS: This pilot study evaluates the feasibility of nCLE during EUS-FNA of pancreatic cystic lesions.
Six patients presenting for EUS-FNA of pancreatic cyst were enrolled for nCLE examination. The nCLE procedure was performed using the AQ-Flex 19 preloaded in a 19G needle. In order to obtain images the probe was put in contact with the tissue inside cyst , after IV injection of fluorescein, (2.5 mL of 10% fluorescein). After image acquisition, the probe was retrieved from the needle, and fluid acquisition was performed as appropriate for cytology and tumor markers (FNA).
RESULTS: Six cases included 6 cysts located in head, uncinate,and body of pancreas. No device malfunctions and no technical challenges were encountered. Technical feasibility to perform imaging with nCLE during a pancreatic EUS-FNA procedure was achieved in all of 6 cases with increased agility in probe manipulation. All cases had good to very good image quality. One serious adverse event occurred that required hospitalization for acute pancreatitis.
CONCLUSION: nCLE in the pancreatic cysts is technically feasible via a 19G needle under EUS guidance. Future studies will address identification of structures, diagnostic accuracy, and complication profiles.
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Disclosure of Interest: None Declared
Keywords: Confocal Laser Microscopy, Pancreatic cyst

P204 ROLE OF CONTRAST-ENHANCED ENDOSCOPIC ULTRASONOGRAPHY (CE-EUS) IN THE DIAGNOSIS OF BRUNCH DUCT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM (BD-IPMN)

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INTRODUCTION: The international consensus guidelines for the management of intraductal papillary mucinous neoplasm of the pancreas were revised in 2012. The presence of a mural nodule in BD-IPMN is one of the important criteria for surgical indication.
AIMS&METHODS: The aim of this study was to retrospectively evaluate the ability of CE-EUS to diagnose a mural nodule in patient with BD-IPMN. From March 2009 to October 2012, we performed endoscopic ultrasonography (EUS) in 89 patients with BD-IPMN at our institute. In cases in which we suspected the presence of a mural nodule on EUS, we performed CE-EUS consecutively. Patients diagnosed with a mural nodule on CE-EUS underwent surgery.
RESULTS: CE-EUS was performed in 21 patients. A total of nine patients were diagnosed with a mural nodule on CE-EUS, all of whom underwent surgery. The remaining 12 patients were diagnosed with mucinous clots on CE-EUS, all of whom were observed without malignant findings. The pathological findings revealed mural nodules in all patients who underwent surgery. Seven of the nine patients who underwent surgery were diagnosed with intraductal papillary mucinous carcinoma (IPMC) and two were diagnosed with intraductal papillary mucinous adenoma (IPMA). Three of the seven IPMCs nodules were not detected on any other imaging modalities without CE-EUS. The mean height of the IPMC mural nodules on CE-EUS was 10.7 mm (7-15), and the mean height of the IPMA mural nodules on CE-EUS was 6.5 mm (3-10). With 7 mm taken as the cutoff value for the size of mural nodules measured on CE-EUS, the diagnosis of IPMC had a sensitivity of 100%, a specificity of 50%, and an accuracy of 88%.
CONCLUSION: Evaluating vascularity using CE-EUS is useful for discriminating a mural nodule from mucinous clots in patients with BD-IPMN. The presence of a mural nodule $\geqq$7 mm in size on CE-EUS may be a malignant indicator of BD-IPMN.
Disclosure of Interest: None Declared
Keywords: contrast-enhanced endoscopic ultrasonography, intraductal papillary mucinous neoplasm

P205 NOVEL COMPUTER-AIDED QUANTITATIVE ANALYSIS OF CONTRAST-ENHANCED HARMONIC EUS IN THE DIFFERENTIATION BETWEEN PANCREATIC CARCINOMA AND CHRONIC PANCREATITIS

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INTRODUCTION: Contrast-enhanced harmonic EUS (CH-EUS) has recently emerged as a useful diagnostic modality in the differentiation of pancreatic carcinoma (PC) and chronic pancreatitis (CP). However, discriminating between PC and CP is still challenging.
AIMS&METHODS: The aim of this study was to evaluate the utility of CH-EUS with the newly developed computer-aided diagnostic software (Inspeedia Inc., Kariya, Japan) that was able to quantify the heterogeneity of contrast-enhancement within pancreatic lesion. Consecutive patients with PC or CP with mass lesions who underwent CH-EUS at Jikei University Hospital from February 2011 to February 2013 were retrospectively analyzed. A curvilinear echoendoscope (GF-UCT260), Aloka Prosound α10 processor and intravenous administration of 0.015ml/kg of Sonazoid were used for CH-EUS. Using the software, a region of interest (ROI) which was subdivided into 100 cells could be placed to cover an area within pancreatic mass. The difference of grade of gray scale color between adjoining cells within ROI was detected, and the number of adjoining cells which showed the difference of grade of gray scale color was automatically calculated in each frame rate of CH-EUS (heterogeneity index: HI). The graph of HI curve was also automatically generated to depict the changes in HI over time. The mean HI from start to one minute after injection of Sonazoid in each patient was calculated. The final diagnosis of PC was based on the results of surgery or EUS-FNA and CP on the results of EUS-FNA, clinical course and other imaging tests.
RESULTS: Fifteen patients with PC and 12 patients with CP were analyzed. Isovascular pattern was observed in all patients with CP and 9 with PC, and hypovascular pattern in 6 with PC. The mean HI in patients with PC after injection of Sonazoid was significantly higher than CP (15.4 vs. 6.6, $p<0.0001$). On the basis of ROC curve data, the optimal cut-off value of mean HI to differentiate PC from CP was 11.17. The sensitivity and specificity were 86% and 100%, respectively, and area under the curve was 0.88. Moreover, the combination of vascular pattern and mean HI yielded the sensitivity and specificity of 100%.
CONCLUSION: CH-EUS with this novel diagnostic tool to quantify the heterogeneity of contrast-enhancement within pancreatic lesions might dramatically improve accuracy in the differential diagnosis between PC and CP.
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Disclosure of Interest: None Declared
Keywords: Chronic Pancreatitis, Contrast-enhanced endoscopic ultrasonography, pancreatic carcinoma

P206 HISTOPATHOLOGICAL DIAGNOSIS OF BOTH LEFT AND RIGHT LESIONS BY ENDOSCOPIC ULTRASOUND-GUIDED ASPIRATION BIOPSY WITH A LARGE CALIBRE NEEDLE

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INTRODUCTION: Adrenal masses are occasionally detected in clinical practice. Although most of these masses are benign adenomas, adrenal metastases are occasionally noted in patients with lung cancer; moreover, adrenal lymphomas are also not uncommon. In certain cases, it is difficult to accurately diagnose such masses using only the findings of imaging tests; therefore, pathological diagnosis is often required. The left adrenal gland is readily visible on endoscopic ultrasonography (EUS), and EUS-guided aspiration (EUS-FNA) has often been attempted in such patients. However, the right adrenal gland has been believed not as easily visible on EUS, and only a few studies have reported the use of EUS-FNA for the right adrenal gland. Furthermore, a diagnosis obtained using EUS-FNA with conventional (22- or 25-gauge) needles is usually based on cytological assessment. However, histopathological assessment is often required for the accurate diagnosis of adrenal lesions.
AIMS&METHODS: To evaluate the utility of EUS-guided aspiration biopsy (EUS-FNAB) using a large-calibre (19-gauge) needle for histopathological assessment of left and right adrenal lesions, we retrospectively reviewed patients in our EUS database who had undergone EUS-FNAB for the diagnosis of an adrenal lesion between April 2004 and April 2013. The patients' baseline characteristics, EUS findings, FNAB results, and follow-up data were assessed.
RESULTS: EUS-FNAB was attempted in a total of 45 adrenal lesions (left, 34; right, 11) in 38 patients. In all cases, the procedure was successful. The adrenal lesions were detected by CT in 22 patients and were incidentally detected during lung cancer staging, by EUS, in 16 patients. Thirty-four patients had extra-adrenal malignancies, including lung cancer in 24, lymphoma in 7, pancreatic cancer in 1, cervical cancer in 1, and gastric cancer in 1 patient. The median largest diameter of the lesions was 23 mm (range, 7–108 mm). Histopathological samples were successfully obtained from all lesions, and histopathological analyses provided diagnoses of adenoma in 19, adenocarcinoma in 9, diffuse large B-cell lymphoma in 11, small cell carcinoma in 3, and myelolipoma in 3 lesions. The final diagnoses were lung cancer metastasis in 12 (adenocarcinoma in 9 and small cell carcinoma in 3), diffuse large B-cell lymphoma in 11, adrenal myelolipoma in 3, and adrenal adenoma in 19 lesions. No significant complications developed in the patients who underwent EUS-FNAB.
CONCLUSION: Thus, we believe that EUS-FNAB, using a 19-gauge needle, is safe and useful for diagnosing both left and right adrenal lesions.
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Disclosure of Interest: None Declared
Keywords: adrenal gland, EUS, EUS-FNA

P207 USEFULNESS OF ENDOSCOPIC ULTRASOUND (EUS) ELASTOGRAPHY FOR THE DETECTION OF MALIGNANCY OF MEDIASTINAL AND ABDOMINAL LYMPH NODES (LN)

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INTRODUCTION: EUS-elastography allows analyzing tissue stiffness during a standard EUS examination, which may be of help in the differential diagnosis of solid lesions. Detection of malignant infiltration of LN is highly relevant to define the optimal therapeutic strategy for different tumors. We hypothesized that EUS-elastography may provide with additional information to the conventional EUS B-mode for the detection of malignancy in mediastinal and abdominal lymph nodes (LN).
AIMS&METHODS: **Aim** of the study was to evaluate the usefulness of EUS-elastography in this setting. **Methods**: Prospective study including consecutive patients who underwent EUS for the evaluation of LN. EUS-elastography was performed under conscious sedation by using the linear Pentax EUS (EG-3870-UTK) and the Hitachi-PREIRUS processor. Final diagnosis was based on surgical histopathology or, in non-operated cases, on imaging assessment; EUS-guided fine needle biopsy and clinical follow-up. Elastographic pattern of the different LN are described. Probability of malignancy according to the EUS-elastographic pattern was calculated.
RESULTS: 140 patients (mean age 61 years, 19-82, 94 males) with a total of 140 LN were evaluated. Size of LN was 22.3 mm as a mean (range 4-59mm). 115 LN were located in the mediastinum, and 25 in the abdomen. Malignancy was confirmed by reference methods in 82 cases, whereas the remaining 58 LN were finally considered as benign. Three different elastographic patterns were identified: 1) a heterogeneous blue-predominant pattern (n=62), 2) a heterogeneous green-predominant pattern (n=30), and 3) a heterogeneous mixed green-blue pattern with geographical appearance and no color predominance (n=48). Malignant LN showed a blue-predominant pattern in 59 cases (72%) and mixed green-blue pattern in 23 cases (28%). On the contrary, benign LN showed a green-predominant pattern in 25 cases (43%), a mixed green-blue pattern in 30 cases (51.2%) and a blue-predominant pattern in 3 cases (5.2%). The probability of malignancy in a LN showing a green-predominant pattern was of 0%, and of 95.2% in case of a blue-predominant pattern. Finally, the probability of malignancy in a LN showing a mixed green-blue pattern was of 47.9%.
CONCLUSION: EUS-elastography is a very useful tool for the differential diagnosis of mediastinal and abdominal LN. It provides with specific colour patterns supporting the malignant or benign nature of the LN
Disclosure of Interest: J. E. Dominguez-Muñoz Consultancy for: SIM Pentax, D. de la Iglesia-García: None Declared, J. Lariño-Noia: None Declared, J. Iglesias-García Lecture fee(s) from: Coock, N. Vallejo-Senra: None Declared
Keywords: elastography, Endoscopic Ultrasound

P208 ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION FOR GASTRIC SUBMUCOSAL TUMOR SMALLER THAN 2 CM

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INTRODUCTION: Diagnosis and treatment of gastric submucosal tumor (SMT) smaller than 2 cm is very difficult. EUS-guided fine needle aspiration (EUS-FNA) is a promising technique to obtain tissue samples with minimal risks.
AIMS&METHODS: The aim of this study was to evaluate the efficacy and accuracy of EUS-FNA in the diagnosis of gastric SMT smaller than 2cm. From February 2003 to October 2012, 90 consecutive EUS-FNAs of gastric hypoechoic solid SMT smaller than 2 cm diagnosed by standard EUS were evaluated prospectively. The reference standards for the final diagnosis were surgery (n=43), and/or clinical follow-up (mean 30 months, follow-up only: n=47) including EGD, CT, and/or US. Additionally, immunophenotyping of specimens obtained by EUS-FNA and surgical resection specimens were compared.
RESULTS: In one case puncture was not performed because of severe intratumoral calcification. The diagnostic rate of the gastric hypoechoic solid SMT smaller than 2cm was 74% (66/89). Histological diagnosis of gastric SMT smaller than 2 cm by EUS-FNA were 47 (53%) malignant SMTs (44 GISTs, 1 Glomus tumor, 1 SMT like cancer, and 1 malignant lymphoma), 19 (21%) benign SMTs (14 leiomyomas, 4 ectopic pancreas, and 1neurinoma), and 23 (26%) undeterminated SMTs. In 43 surgically resected cases, the diagnostic accuracy of EUS-FNA using immunohistochemical analysis of gastric hypoechoic solid SMT smaller than 2 cm was 100% (43/43). No major complications were encountered. After surgery, there was no recurrence in 47 malignant SMTs. Appropriate management, including surgery, chemotherapy, and follow-up were performed in all 66 SMTs diagnosed by definitive EUS-FNA.
CONCLUSION: EUS-FNA with immunohistochemical analysis is an effective and accurate method in the pretherapeutic diagnosis of gastric SMT smaller than 2cm. Aggressive use of EUS-FNA for gastric SMTs smaller than 2cm is a promising way to improve its prognosis .
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Disclosure of Interest: None Declared
Keywords: EUS-FNA, GIST, SMT, Stomach

P209 THE COMBINATION OF EUS-FNA AND EUS-FNB IMPROVES THE DIAGNOSTIC ACCURACY COMPARED WITH EUS-FNA ALONE IN DIFFICULT LESIONS - A RANDOMISED COMPARATIVE STUDY

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INTRODUCTION: EUS-guided tissue sampling can be performed either by fine needle aspiration (FNA) for cytology or fine needle biopsy (FNB) for histological analysis. Tissue sampling is still challenging in lesions like GIST, cystic tumours and lymphomas.
AIMS&METHODS: The goal of this study was to examine the diagnostic accuracy of EUS-guided FNA, FNB and the combination of the two methods.
From March to October 2012 we asked patients referred for EUS to be enrolled in the study. Further enrollment is on-going. All EUS-procedures were performed by one experienced endosonographist (RS). Punctures were performed using FNA-needles (Cook Medical, Olympus, Boston Scientific) and FNB-needles (Pro-Core™, Cook Medical). A cytotechnician was present on-site. We aimed at performing both FNA and FNB in each case. Cases were randomised to either FNA first followed by FNB or vice versa. No puncture was performed if lesions were obviously benign. FNB was not performed in areas close to large vessels or to the papilla. We experienced prior to the study one severe pancreatitis after puncturing the papilla with a 22 gauge biopsy needle. One experienced cytopathologist (AD) and one experienced pathologist (ON) separately reviewed the majority of the samples. Histopathology after surgery or autopsy and clinical follow-up were used as end point.

RESULTS: 83 patients (mean age 62) were enrolled. 64 lesions were punctured. FNA and FNB were performed in 45 cases and FNA only in 19 cases. Mean lesion size was 35 mm. A total of 35/45 (78%) of cases punctured with both FNA and FNB had a malignant final diagnosis. The combination FNA/FNB had a higher sensitivity, 94.2 %, compared with FNA alone, 62.9 %, p =0.001. The overall diagnostic accuracy was also higher for the combination FNA/FNB versus FNA alone; 95.6% versus 68.9 %, p = 0.001. Sensitivity and overall accuracy for FNB alone was 88.6 % and 86.7 % respectively and showed no significant difference compared with the combination FNA/FNB. FNA however correctly diagnosed 3 lesions that could not be diagnosed by FNB. No complications were observed.

	Location (n)	Location (%)
Submucosal lesions	20	44
Pancreas (cystic and solid)	13	29
Paraintestinal lesions	7	16
Mediastinal lesions	3	7
Lymph nodes	2	4

CONCLUSION: The combination of EUS-FNA and EUS-FNB shows higher sensitivity and diagnostic accuracy compared with EUS-FNA alone. This combination can be considered in cases with an expected low sampling quality such as GIST or previously sampled lesions.
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Keywords: cytology, EUS-FNA, EUS-FNB, MALIGNANCY, Submucosal tumor

P210 DOUBLING TIME (DT) OF GASTROINTESTINAL SUBMUCOSAL TUMORS

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INTRODUCTION: We retrospectively analyzed the Doubling Time (DT) of gastrointestinal submucosal tumors (SMT) by using sequential findings of endoscopic ultrasonography (EUS) to identify the growth rate.
AIMS&METHODS: A total of 297 patients with SMT in the gastrointestinal tract were underwent surgical resection or EUS-FNA and given a pathological diagnosis in Kitasato University Hospital and Kitasato University East Hospital from 1987 to March 2013. Forty-six patients (34: surgical resection, 12: follow-up after FNA) which were performed EUS more than twice during follow-up were enrolled. Each DT was calculated by using tumor diameter visualized by EUS.

RESULTS: We included forty-six patients (21 male / 25 female, mean age: 65 years old). They located in esophagus (three), stomach (forty-one), duodenum (two). Histological diagnosises were 34 GISTs, five Leiomyomas, three Schwannomas, one ectopic pancreas, one hamartoma, one cyst, one Brunner adenoma. The median of follow-up period was 31.7 months (range: 6.6-210). The median of times of EUS was three (range: 2-13). Compared with the median DT of GIST was 17.2 months, Leiomyoma / Schwannoma / ectopic pancreas / hamartoma / cyst / Brunner adenoma were 231.2 / 104.7 / 274.9 / 61.2 / 49.0 / 134.7 months. DT of GIST, high / intermediate / low, was 3.9 / 17.1 / 27.6 months. DT of the high and intermediate risk grade GIST (mean: 8.2 months) was significantly shorter than that of the low risk grade GIST (mean: 27.6 months) ($p<0.05$). DT of GISTs (mean: 17.2 months) was significantly shorter than that of the median of the total of Leiomyomas and Schwannomas ($p<0.05$).
CONCLUSION: We conclude that DT of GIST is shorter than that of other SMT such as Leiomyoma, Schwannoma, etc. And DT of the high and intermediate risk grade GIST which has more malignant potential is shorter than that of the low grade GIST.
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Disclosure of Interest: None Declared
Keywords: doubling time, GIST, Submucosal tumor

P211 SMALL BOWEL CAPSULE ENDOSCOPY IN PATIENTS WITH UNEXPLAINED ANAEMIA / GASTROINTESTINAL BLEEDING AND CHRONIC KIDNEY DISEASE

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INTRODUCTION: The use of small-bowel capsule endoscopy (SBCE) has revolutionised investigating the small-bowel. However, there are only few reports [1-3] on the Diagnostic Yield (DY) of SBCE in patients (pts) with chronic kidney disease (CKD) and unexplained anaemia and/or obscure gastrointestinal bleeding (OGIB).
AIMS&METHODS: Retrospective study; our SBCE database was searched (March 2005 to August 2012) for pts with estimated glomerular filtration rate (eGFR) $<60ml/min/1.73m^2$. Subsequently, electronic case notes of pts with low eGFR who underwent SBCE for anaemia and/or OGIB were retrieved and abstracted. A mean eGFR value -for up to **5** years prior to SBCE- was calculated for each case. Severity of CKD was defined according to Renal Association recommendations as: **stage 3** (eGFR: 30-59); **stage 4** (eGFR: 15-29); and, **stage 5** (eGFR <15 or on dialysis). Numerical values were expressed as mean±SD or median (range).
RESULTS: In the aforementioned period, 69 pts with eGFR <60 were referred for SBCE. 65/69 (92.8%) had CKD stage 3 (eGFR: 49±7.9) and 4/69 (7.2%) stage 4 (n=3) or stage 5 (n=1). 51/65 (78.5%) of stage 3 CKD pts were referred for SBCE due to unexplained iron deficiency anaemia and/or OGIB [43 (66.1%) & 8 (12.3%), respectively]. 25/51 (49%) had normal SBCE, while 17/51 (33.3%) had angioectasias; other findings were active bleeding (n=2), non-specific fold oedema (n=2), ileal erosions (n=1), adenocarcinoma (n=1) and inconclusive/ videos not available (n=3). All pts (n=4) with CKD 4 or 5 were referred due to unexplained anaemia. 3/4 (75%) had angioectasias and 1 normal SBCE. Faecal calprotectin (FC) was measured in 12 pts with CKD stage 3 and unexplained anaemia prior to SBCE; No sinister pathology or significant small-bowel inflammation was found in this subgroup.
CONCLUSION: SBCE has limited DY in CKD pts referred for investigation of unexplained anaemia. The most common finding is angioectasias, while sinister small-bowel pathology is rare. Furthermore, FC measurement pre-SBCE is not associated with increased DY.
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Keywords: anaemia, capsule endoscopy, chronic kidney disease, obscure gastrointestinal bleeding, small-bowel

P212 THE USE OF OESOPHAGEAL CAPSULE ENDOSCOPY IN PATIENTS WITH HAEMOPHILIA; EXPERIENCE FROM A TERTIARY CENTRE

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INTRODUCTION: A great proportion of patients with haemophilia are considered at risk of being co-infected with hepatitis C (HCV) and variant Creutzfeldt-Jakob disease (vCJD) [1] .Chronic hepatitis C leads to liver cirrhosis, which in turn causes portal hypertension and varices [2]. Alternative endoscopic modalities have been developed for the investigation of the upper gastrointestinal (GI) tract, such as oesophageal capsule endoscopy (OCE). However, OCE is widely accepted and its indications are still under evaluation. 3 Our aim was to evaluate the use of OCE in a tertiary referral centre for GI problems in Lothian, Southeast Scotland, giving a special focus on OCE in patients with haemophilia.
AIMS&METHODS: A retrospective review of the OCE database from May 2005 to March 2012. Electronic case notes and OCE reports were reviewed. Demographics and clinical background, in particular haemophilia, hepatitis C, HIV and cirrhosis, reason for referral and OCE findings were abstracted.
RESULTS: A total of 65 OCEs (50 patients; 27 M/23 F; mean age: 52.7 ±13.7 years) were carried out in the aforementioned period. 32% pts had haemophilia (16/50 patients/all male; mean age: 51.6 ± 9.8 years; range 31-78 years; 28 OCEs); 5 pts had repeat OCEs (1 pt: 1 repeat, 2 pts: 2 repeat, 1 pt: 3 repeat & 1 patient: 4 repeat OCEs). All haemophiliacs were infected with HCV; 2 pts were co-infected with HIV. 3/16 (18.75%) of haemophiliacs had established cirrhosis, 5/16 (31.25%) probable cirrhosis. In haemophiliacs, indications for OCE were: variceal surveillance (OCEs **group A**: 17/28; 60.7%) and/or other upper GI symptoms (OCEs **group B**: 11/28; 39.3%). PillCam®ESO1 was used in 15/28 (53.6%) occasions and PillCam®ESO2 for the rest (13/28; 46.4%). The overall diagnostic yield (DY) of OCE in haemophiliacs was 78% (21/28). The DY was similar in OCEs group A: 64.7% (findings in 11/17) and OCEs group B: 54.5% (findings in 6/11), P =1.0. Oesophageal transit times were mean: 166s; range: 3-1171s. All capsules reached the stomach, but only 8/28 (28.5%) capsules entered the duodenum.
CONCLUSION: OCE is a useful and acceptable alternative to conventional endoscopy in selected groups of patients. In particular, OCE in haemophiliacs has a high DY and should be considered a first line investigation to guide further endoscopic intervention.
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Keywords: cirrhosis, Creutzfeldt-Jakob Disease, haemophilia, Hepatitis C virus, oesophageal capsule endoscopy

P213 NEGATIVE FAECAL CALPROTECTIN (FC) IS A STRONG PREDICTOR OF NEGATIVE SMALL BOWEL CAPSULE ENDOSCOPY

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INTRODUCTION: Capsule Endoscopy (CE) is a standard investigation in the diagnosis of small bowel disease. Increase in CE activity has inevitably increased the frequency of negative CE. Patients having CE frequently undergo other diagnostic tests such as CT Enterography (CTE), MR Enterography (MRE) and Faecal Calprotectin (FC), a non-specific marker of bowel inflammation.
AIMS&METHODS: Our aim was to retrospectively analyse our small bowel CE data to see if CTE, MRE or FC predicts result of a CE study.
144 patients (67M, 77F) were investigated with CE over 2yrs. Referral indications included Iron Deficiency Anaemia (75), Crohn's assessment (28), GI Bleed (13), Chronic diarrhoea and Malabsorption (13), Abdominal pain and weight loss (11), others (4). 78 of 144 (54%) were also investigated with CTE (44), MRE (12), CTE&MRE (3) and FC (19).
RESULTS: 92 of 144 (64%) had positive findings on CE. 16/59 scanned patients had positive findings on CTE (8) and MRE (8). 11/19 patients tested strongly positive for FC. 4/8 (50%) of CTE+ and 5/8 (62%) of MRE+ also had significantly positive findings on CE. 6/11 (54%) of FC+ had significant positive findings on CE. However, 100% of FC negative patients had negative CE. Sub-group analysis showed that 2/4 CTE+ and CE+ patients were tested for FC and both were positive. Only 1/5 MRE+ and CE+ patient was tested for FC and proved positive.
CONCLUSION: CTE, MRE and FC individually predicted positive CE result in roughly 50% of cases.
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In a small sample, combined FC and CTE or MRE positivity predicted positive CE result in 100% of cases.
Negative FC is a strong predictor of a negative CE in IBD setting.

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Disclosure of Interest: None Declared
Keywords: capsule endoscopy, CT enterography, Faecal Calprotectin, MR enterography

P214 CAPSULE ENDOSCOPY: THE EFFECTS OF BMI AND WAIST CIRCUMFERENCE ON LOCATION PICK UP SENSORS

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INTRODUCTION: Capsule endoscopy is an extremely valuable non-invasive tool to examine the entire gastrointestinal tract in particular the small bowel. A variety of reasons for technical failure has been reported [1, 2] like gaps in recording, battery malfunction, failure of sensor localization and failure in downloading images obtained. In a review of 733 cases, the authors reported 8.46% of patients had technical failure or clinical complications which prevented or hampered diagnosis.
AIMS&METHODS: This retrospective analysis looked at the effect of BMI and waist circumference on the location sensors during capsule endoscopy. The data were collected retrospectively from the notes of 143 patients who had capsule endoscopy at Ipswich Hospital during 2006-2011. Patients were divided in two groups one with location sensor signal failure (Group A) and other with detected signal (Group B). In twenty two (15%) patient's location sensor failed to pick up the signal (Group A). Two patients died in the follow up period so the notes were unable to be retrieved. In three out of 20 patients notes BMI were not recorded at the time of procedure and in 10 patients we were unable to obtain the waist circumference. To decrease selection bias we randomly selected 20 case notes from group B. In this cohort, all patients had their BMI noted but we were unable to obtain the waist circumference of nine patients.
RESULTS: The two groups had an equal gender spread (52.6% female and 47.4% male), median age of 58 (18-89 yrs.) with a 99% Caucasians ethnicity. In group A, no one had normal BMI, eight were overweight (BMI 25-29), eight were obese (BMI 30-39) and one patient was severely obese (BMI > 40). Out of eleven patients, three patient had normal waist circumference, two were high (female > 80-88cm and male > 94-104 cm) while the remaining seven were even higher (female > 88cm and male > 104 cm). In group B nine patients had normal BMI, seven overweight, two obese and 2 were very obese. Out of eleven patient, seven had normal (< 80 cm female/< 94 cm male) and four had higher waist circumference. The average BMI of the group A and B were 32.22 (median 35.1) vs 28.49 (median 26.15) kg/m2 and the average waist circumference 95.58cm (median 99.05) vs 85.48 (median 86.4) cm.
CONCLUSION: The results would suggest that the localization sensors may find it difficult to pick up images in patient with either a relatively high BMI or high waist circumference during capsule endoscopy. Further prospective studies are needed to evaluate this further and to determine whether there is a threshold BMI or waist circumference by which the location sensors may be rendered inadequate.
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Disclosure of Interest: None Declared
Keywords: BMI, capsule endoscopy, Waist circumference

P215 FINDING THE SOLUTION FOR INCOMPLETE SMALL-BOWEL CAPSULE ENDOSCOPY

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INTRODUCTION: Capsule endoscopy (CE) is an established technology for the evaluation of small bowel diseases, including obscure gastrointestinal bleeding. An important technique limitation is incomplete examination of the small bowel, which occurs in approximately 20% of the procedures. This means that the capsule did not reach the cecum within the recording time.
AIMS&METHODS: The aim of our study was to assess the benefit of prokinetics, in association with *Real Time Viewer* (RTV), in decreasing the rate of incomplete examinations.
Between June 2012 and February 2013 capsule's location was determined, 1h after its ingestion, through RTV included in the new Given ® recorder (DR3). If the capsule was still in the stomach the patient received 10 mg of domperidone *per os*. The results of this group were compared with CE carried out between January 2009 and May 2012. Statistics were performed with SPSS v 17.0.
RESULTS: Between January 2009 and May 2012, 307 CE were performed, in 15,6% (n=48) the procedure was incomplete. The group analyzed prospectively included 82 CE, with three IE (3,7%). The difference between the rates of IE between the two groups was statistically significant (p=0,003). The two groups were similar with regard to age, sex, indications for performing CE, inpatient status and surgical history. In the first group the average gastric time was significantly longer in patients with IE than in patients with complete examination (77 minutes vs 26 minutes, p=0,003).
In the second group 14 patients received domperidone (17%). There was no difference in mean small bowel transit time in those who received or did not receive prokinetic (247 minutes vs 290 minutes), p=0,15.
CONCLUSION: The administration of prokinetic, in association with RTV, with the aim of decreasing gastric transit time reduces the rate of IE with no effect on small bowel transit time.

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Disclosure of Interest: None Declared
Keywords: capsule endoscopy, incomplete examination

P216 VALIDATION THE LEWIS SCORE – INDISPENSABLE INSTRUMENT IN EVALUATING MUCOSAL ACTIVITY IN ISOLATED SMALL-BOWEL CROHN'S DISEASE

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INTRODUCTION: The Lewis Score (LS) was devised to measure mucosal disease activity using capsule enteroscopy (CE). However this score has not been prospectively validated in daily practice.
AIMS&METHODS: The aim of this study was to verify interobserver agreement for LS.
We performed a retrospective, single-center, double-blind study including patients with isolated small-bowel Crohn's disease (CD) submitted to CE. The LS based on three endoscopic parameters: villous edema, ulcer and stenosis/stricture calculated for which tertile. For each CE, LS was calculated by the coordinator and by one of the investigators. The interobserver correlation was measured by the Pearson test and the interobserver agreement was calculated by the Kappa score.
RESULTS: Forty two CE were included, the cecum was reached in 76% and 81% of examinations according to investigators and coordinator, respectively, (p>0,05). The average global LS was 1385 and 1291, for the coordinator and investigators, respectively. We verified a strong correlation between the investigators and the coordinator either in scores obtained by tertile (first tertile r=0,752, second tertile r=0,768 and third tertile r=0,769) or in total LS (r=0,774), p<0,0001. The interobserver agreement, calculated by Kappa score, taking into account the classification: normal (LS<135), mild disease (LS between 135 and 790) and moderate to severe disease (LS≥790), was good (0,737), (p<0,001).
CONCLUSION: This study has demonstrated a strong interobserver agreement to the LS, validating this score in reporting small-bowel inflammation. The LS might be used in staging, follow-up and therapeutic assessment in patients with isolated small-bowel CD.

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Disclosure of Interest: None Declared
Keywords: capsule endoscopy, Crohn's disease, Lewis Score

P217 UPPER GASTROINTESTINAL FINDINGS DETECTED BY CAPSULE ENDOSCOPY PERFORMED FOR OBSCURE GASTROINTESTINAL BLEEDING

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INTRODUCTION: Patients with Obscure Gastrointestinal Bleeding (OGIB) with a previous negative workup on esophagogastroduodenoscopy (EGD) and colonoscopy need comprehensive evaluation, including Capsule Endoscopy (CE). Sometimes, during the observation of CE images we can see potential bleeding lesions from stomach and duodenum which were overlooked by first EGD.
AIMS&METHODS: The aim of our study was to evaluate the frequency of lesions identified in the upper gastrointestinal tract and to analyze their significance in terms of its role in reducing unnecessary CE studies. We retrospectively study 152 consecutive patients who underwent CE for OGIB at our center, with a normal initial EGD. Patients with a definite cause of bleeding within reach of conventional EGD were identified. For the statistical analysis SPSS18.0 was used. A p value $<$ 0,05 was considered as significant. Percentages were used for categorical variables and mean±SD were used to summarize data for continuous variables.
RESULTS: The most common indication for CE was occult OGIB (76.3%). CE results showed gastrointestinal lesions in 66 (43.4%) patients. In 11 (7.2%) patients, CE showed relevant gastric or duodenal lesions not previously noted during initial EGD. In 9 (5.9%) of these 11 patients gastroduodenal lesions were the only pathological finding discovered in the digestive tract. In the remaining 2 (1.3%) patients found synchronous potential bleeding lesions in the upper tract and small bowel. Nine (81.8%) of patients with upper gastrointestinal findings had a duodenal lesion. All upper gastrointestinal lesions were angioectasias. In patients which CE showed upper gastrointestinal lesions the commonest indication was occult OGIB (63.6%). A second EGD was performed in 10 patients, in all of these patients CE findings were confirmed and treatment with argon plasma coagulation was performed.
CONCLUSION: CE provided information about upper gastrointestinal findings that was considered sufficient to explain the OGIB etiology and recommended a second-look EGD in 7,2% of patients. In 5,9% patients the upper gastrointestinal findings were the only findings that explain the OGIB, so in these cases a second EDG previous to CE should avoid an unnecessary procedure
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Disclosure of Interest: None Declared
Keywords: Capsule Endoscopy, Obscure Gastrointestinal Bleeding

P218 COLON CAPSULE ENDOSCOPY: CAN MOVIPREP® BE USED AS BOWEL PREPARATION AS WELL AS BOOSTER? OBSERVATION STUDY IN 95 PATIENTS.

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INTRODUCTION: Pillcam colon capsule endoscopy (CCE) enables colon visualization without the need of general anesthesia (Given Imaging, Ltd, Yoqnéam, Israel). The study goal was to observe and assess the quality of the colon preparation with 2L of Moviprep® (PEG + ascorbic acid + ascorbate and Na sulfate) as well as its efficacy when used as a booster when substituted to Fleet® to perform a CCE in 95 consecutive patients.
AIMS&METHODS: Patients were prepared according to two consecutive protocols:
Protocol #1 (70 patients): low-residue diet (D5 to D2), pursenide (D2), clear liquid diet and 2L of Moviprep® on D1, capsule ingestion at 8.00 a.m., booster #1 with 45mL of Fleet® 2 hours later and booster# 2 with 22.5mL of Fleet® 6 hours after ingestion if the capsule had not been egested.
Protocol #2 (25 patients): low-residue diet (D5 to D2), pursenide (D2), clear liquid diet on D1, 2L of Moviprep® the morning of the examination, capsule ingestion at 11.30 a.m., booster #1 with 500mL of Moviprep® 2 hours later and booster #2 with 500mL of Moviprep® 6 hours after ingestion if the capsule had not been egested.
RESULTS: In protocol #1, 60 examinations (85.7%) were complete, 10 (14.3%) were incomplete including 5 cases of sigmoid retention, 4 cases of dark rectal residual liquids and one case of premature recording termination. Preparation was rated adequate in 59 patients (84.2%). Mean colic and oro-caecal transit times were respectively 2 hours 47 min and 3 hours 22 min.
In protocol #2, 13 examinations (52%) were complete, 12 (48%) were incomplete including 7 cases of sigmoid retention and 5 cases of dark rectal residual liquids. Preparation was rated adequate in 14 patients (56%). Mean colic and oro-caecal transit times were respectively 3 hours and 6 hours 07 min.
CONCLUSION: Thanks to the bowel preparation with 2 liters of Moviprep® the day before, the quality of the examination was good with 84.2 % of adequate preparations and a complete colic examination in 85.7%, when associated with Fleet® as a booster. When used as a booster, Moviprep® was less efficient on the colic peristalsis than Fleet®, with twice as long colic transit times.
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Disclosure of Interest: L. Jean Christophe : no conflict of interest to declare, A. L. patrick : no conflict of interest to declare, C. michel : no conflict of interest to declare
Keywords: colon capsule endoscopy, preparation

P219 PILLCAM COLON2 AFTER INCOMPLETE COLONOSCOPY-FIRST PRELIMINARY RESULTS OF A MULTICENTER STUDY

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INTRODUCTION: Colonoscopy is the gold standard for colorectal diseases but may be incomplete e.g. in case of redundant colon, severe inflammation or intolerance of sedation. PillCam Colon1 has been used to complement colonoscopy. We report preliminary data from a multicenter study using colon capsule endoscopy (CCE) with PillCam Colon2 after incomplete colonoscopy.
AIMS&METHODS: This prospective multicenter study (supported by Given Imaging) included patients after incomplete colonoscopy without stenosis performed by an experienced gastroenterologist. Primary endpoint was the ability of CCE to visualize missed colon segments. CCE was performed either on the day after colonoscopy with additional cleansing solution (Moviprep) in the morning. Alternatively, CCE was performed within 30 days using new bowel cleansing (Clear liquids day before + split-dose Moviprep). Additional boosts consisted of 0,75 or 0,25 l Moviprep and NaP only as additional rescue boosting if capsule was not excreted after 9 hours.
RESULTS: Data of 45 patients could be analyzed. In 71% CCE was performed the day after colonoscopy. Cleansing levels were adequate in 69%. CCE visualized the entire colon in 80%. CCE visualized missing colonic segments in 87%. In 16/45 (36%) polyps were detected, in 8/45 (18%) polyps were located in segments not reached by colonoscopy. In one case an adenocarcinoma was diagnosed after detection of a 26 mm cecal polyp. Other findings at CCE were detected in 58% (26/45). One capsule was retained in the small bowel (2%). Surgical resection lead to the previously unknown diagnosis of stenosing and fistulating Crohn's disease. In one case (2%) recording failed due to technical problems.
CONCLUSION: In our study complementation of incomplete colonoscopy with PillCam Colon2 and Moviprep regimen was in concordance with previous data for PillCam Colon1 and for device assisted colonoscopy, also showing a relevant amount of additional findings. Previously described low volume cleansing protocol was also effective in our setting. Slow transit due to functional stenosis or motility disorder may be a risk factor for incomplete CCE. Generally the procedure was tolerated well. In one case retention lead to a relevant diagnosis affecting treatment.
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Keywords: Capsule colonoscopy, colon capsule endoscopy, Incomplete colonoscopy, PillCam Colon2, polyp detection, preparation

P220 DOMPERIDONE IMPROVES COMPLETION RATE IN SMALL BOWEL CAPSULE ENDOSCOPY

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INTRODUCTION: The completion rate (CR) of small bowel capsule endoscopy (SBCE) has been reported at 81.3-84.8% [1]. Incomplete examinations can be due to delayed gastric emptying, strictures, intestinal dysmotility and/or capsule battery life. Prokinetic agents are used to increase CR and theoretically SBCE diagnostic yield (DY). Domperidone, an antidopaminergic agent, has not been widely used in SBCE [2,3]; unlike Metoclopramide, it lacks extrapyramidal adverse effects.
AIMS&METHODS: Retrospective study; to assess gastric transit time (GTT), small-bowel transit time (SBTT) and the CR of SBCE when using Domperidone. Furthermore, we aimed to compare the CR of 2 different SBCE systems (MiroCam® , PillCam®). Consecutive SBCE examinations from 2008 to 2012 from a tertiary referral centre in Scotland were analysed; in the first 203, no prokinetics were used; Domperidone was given orally to the subsequent 449, reflecting changes in clinical practice.
RESULTS: In the aforementioned period, a total of 652 SBCE examinations were performed [265 (40.6%) men & 387 (59.4%) women]; 385/652 (59%) were performed with PillCam® and 267 (41%) with Mirocam®. The most common indications for SBCE were obscure gastrointestinal bleeding, anaemia, Crohn's disease (known and/or suspected) and abdominal pain. In 449/652 (68.9%) liquid Domperidone (5 mg) was administered for capsule ingestion, while in 203 (31.1%) the capsule was ingested without any Domperidone.
In our series, the overall CR of SBCE was (86.7%). The 2 SBCE systems showed equivalent CR (PillCam® 87.5%, MiroCam® 85.4%; P=0.43). The use of liquid Domperidone increased CR (88.6% vs. 82.3%, P=0.027). A higher CR was noted when Domperidone was used with PillCam® than with MiroCam® (82.2 vs. 92.5%; P=0.002 and 83.3 vs. 85.5%, respectively; P=0.8). Furthermore, the median GTT and the median SBTT did not differ between the two groups (GTT/SBTT with Domperidone 27.0'/222.0' and without Domperidone 30.5'/228.0', respectively; P=0.436 / P=0.477).The median age of patients who received Domperidone was higher compared with patients who did not receive (58y vs. 48y, P=0.009), although CR was not affected by patient's age (complete: 55y, incomplete: 61y, P=0.331).

CONCLUSION: The use of Domperidone in SBCE increases the CR particularly with PillCam®, although does not affect the median GTT and SBTT and should be routinely used to improve CR in SBCE.

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Keywords: capsule endoscopy, completion rate, domperidone, prokinetic

P221 PREDICTING THE PRESENCE OF INTESTINAL ANGIOECTASIAS: IS THAT POSSIBLE?

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INTRODUCTION: Angioectasias are the most common vascular anomalies found in the gastrointestinal tract. When localized in the small bowel (SB) they can cause obscure gastrointestinal bleeding (OGIB) and in this setting, wireless capsule endoscopy (WCE) is currently an important diagnostic tool.

AIMS&METHODS: This study aimed to identify predictive factors for the presence of SB angioectasias, detected by WCE. We retrospectively analyzed the results of 284 WCE performed consecutively between April 2006 and December 2012, whose indication was OGIB. From these, 47 cases with SB angioectasias and 53 controls without identifiable lesions were chosen. For each selected patient demographic, clinical and laboratorial information on the exam date was collected. Statistical analysis was performed using SPSS v17.0.

RESULTS: The mean age of subjects with angioectasias (70,9±14,7) was significantly higher than in controls (53,1±18,6; $p<0,05$). Angioectasias were found in 56,1% of men and in 40,6% of women, although this difference did not reach statistical significance. The presence of angioectasias in SB was significantly higher when the indication for the exam was overt OGIB ($p<0,05$). From past medical history, hypertension and dyslipidemia were the most significantly associated factors with the presence of SB angioectasias ($p<0,05$), while smoking and chronic kidney disease were only marginally associated (p=0,084; p=0,145). Diabetes, aortic stenosis, chronic liver disease, previous abdominal surgery, and use of antiplatelet or anticoagulant drugs were not significantly associated with SB angioectasias. There was no relationship found with platelet count.

CONCLUSION: In OGIB, factors such older age, overt OGIB, dyslipidemia or hypertension are predictive for the presence of SB angioectasias found by WCE.

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Disclosure of Interest: None Declared

Keywords: angioectasia, obscure gastrointestinal bleeding, wireless capsule endoscopy

P222 WIRELESS CAPSULE ENDOSCOPY IN OBSCURE GASTROINTESTINAL BLEEDING - NORMALCY IS NOT REASSURING.

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INTRODUCTION: Wireless capsule endoscopy (WCE) is currently a fundamental tool in the etiological study of obscure gastrointestinal bleeding (OGIB). However, the impact of a negative exam and the rebleeding risk are not consensual in different studies.

AIMS&METHODS: The aim of this study was to describe the follow up of patients with OGIB and a normal WCE examination, and assess the presence of rebleeding and possible associated factors. We analyzed 79 patients who consecutively underwent WCE examination for the study of OGIB between April 2006 and December 2011, whose results excluded potentially bleeding lesions. Pre- and post-WCE information was collected, including follow up interval and presence of rebleeding (defined as admission to the hospital for symptomatic anemia, need for blood transfusion, decrease in hemoglobin value of >2g/dL, or evidence of melena or hematochezia).

RESULTS: Of the 79 patients initially selected, 4 were excluded because there was no available information. Of the remainder, 61,3% were female and the mean age was 52 years. The indication for the examination was occult OGIB in 59 patients (78,7%) and overt OGIB in 16 patients (21,3%). 68 patients (90,7%) had hospital follow up, with a mean follow up interval of 32 months. From these, 39 patients (57,4%) were posteriorly subjected to further investigation and a diagnosis was established in 11 of them. Rebleeding was documented in 16 (23,5%) of the 68 followed up patients, having occurred on average 15 months after WCE. From the analyzed factors (age, gender, indication for OGIB, past medical history, and hemoglobin value), only male gender was significantly associated with rebleeding (p=0,007).

CONCLUSION: Approximately a quarter of patients with OGIB and normal WCE examination will suffer from rebleeding, which is more significant in men. This result should imply a more regular medical surveillance, and possibly a more exhaustive attempt to clarify the etiology of the OGIB.

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Disclosure of Interest: None Declared

Keywords: follow-up, obscure gastrointestinal bleeding, rebleeding, wireless capsule endoscopy

P223 COMPARISON OF CAPSULE ENDOSCOPY READING MODE: CONCERN ABOUT EFFICIENCY AND TIME SAVING

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INTRODUCTION: Capsule endoscopy is a useful method of detecting and diagnosing small-bowel diseases such as obscure gastrointestinal bleeding, small-bowel tumors, and inflammatory bowel disease. In a survey of 530 members of the American College of Gastroenterology, 23.7% used Singleview, 40.0% used DualView, and 54.5% used Quadview. Each physician should decide the reading settings based on his own experience with CE. These different reading methods may account for some of the reported discrepancies in diagnostic yield and interobserver agreement on capsule interpretation.

AIMS&METHODS: . The aim of this study was to investigate evaluation times and false negative rates in three different reading modes to find the most appropriate mode for evaluation of capsule endoscopy.

Three trainee endoscopists reviewed capsule endoscopy studies performed at our institution from 5/2007 to 6/2012. Each trainee endoscopist read a total of 30 capsule endoscopy videos. Three endoscopists compared three different capsule endoscopic software modes: automatic view at a speed of 20 frames per second (fps) and automatic quadview at a speed of 20 fps, quickview at a speed of 4 fps. Each endoscopist read the same capsule endoscopic record by using one of three different software modes. Capsule endoscopic reading time was recorded, and the number of detected lesions was counted.

RESULTS: The mean evaluation time using quickview was significantly shorter than with automatic view (automatic single view: 18 min 48 sec, quadview: 19 min, quickview: 2 min 7 sec). The false negative rates of ulcers, erosions were higher when reading in quickview compared with reading in automatic view. However, the detection rate of bleeding was similar when reading in quickview compared with automatic view. Automatic quadview 20fps has minimal diagnostic miss rates and can safely replace slower modes in clinical practice. A theoretical advantage of quadview is a longer single frame exposure time compared with singleview

CONCLUSION: Quickview can be used confidently in small bowel bleeding and can be performed in a short time. However, quickview mode has a high false negative rate for the other lesions, such as ulcers or erosions. Selection among time-saving methods should be made on the basis of the clinical indication for the capsule endoscopy.

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Disclosure of Interest: None Declared

Keywords: Capsule endoscopy, Detection rate, Evaluation time

P224 DIAGNOSIS AND QUANTITATIVE ASSESSMENT OF DUODENOGASTRIC REFLUX IN PATIENTS AFTER CHOLECYSTECTOMY

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INTRODUCTION: Symptoms of duodenogastric reflux as heartburn, eructation, feeling of bitterness in the mouth and etc. are often observed in patients after cholecystectomy. X-ray and endoscopic examinations are used for the diagnosis of this condition. However, quantitative characteristics of these methods is rather subjective.

AIMS&METHODS: The aim of the research was to give a quantitative assessment of the duodenogastric reflux (DGR) in patients after cholecystectomy. 98 patients (11 men and 87 women, aged 24-82 years) after cholecystectomy were x-rayed, underwent endoscopic examination of upper gastrointestinal tract and hepatobiliary scintigraphy. To estimate the bile passage a radionuclide tracer 99 mTc HIDA was used, with fatty meal ingestion after 45 minutes. The degree of DGR was defined by a percentage ratio of total radioactivity in a stomach area to radioactivity in the duodenal area which exceeded 15% of the background radiation. DGR was distributed to 4 degrees: I - from 16 to 35%; II - 36-55%; III - 56-75%; IV - more than 75%.

RESULTS: DGR was revealed in 47 (47.9%) post-cholecystectomy patients. The I^{st} degree was revealed in 22 (46.8%), II^{nd} - in 7 (14.9%), III^{rd} - in 13 (27.7%), IV^{th}- in 5 (10.6%) patients. Intensity of DGR correlated with radiological data of the duodenal antiperistalsis (Rs=0.45; $p<0.05$) and regurgitation of contrast substance from the duodenum to the stomach (Rs=0.54; $p<0.05$). The stage of DGR had an association with endoscopic signs of pyloric sphincter function decrease (Rs=0.45; $p<0.05$). Moreover, the patients with the III^{rd} and IV^{th} degrees of DGR had gastroesophageal reflux disease manifestations. Gastroesophageal reflux, determined by x-ray examination, was confirmed during endoscopy by reflux esophagitis manifestation.

Patients with DGR more often demonstrated symptoms of duodenal antiperistalsis ($p<0.001$) and incompetence of the cardia (p=0.02) than those who did not have isotope reflux to the stomach. Pyloric incompetence ($p<0.001$) and a bile reflux ($p<0.001$) of the patients with DGR were more often revealed during endoscopy procedure. Sensitivity of the endoscopic diagnostic procedures of DGR made up 81%, specificity – 72%.

CONCLUSION: Hepatobiliary scintigraphy may be accepted as an informative diagnostic method and quantitative assessment of DGR in patients after cholecystectomy. On an increase of bile regurgitation to the stomach the reflux extends and reaches the gullet, forming "a double reflux". The findings of this method can be used in anti-reflux treatment selection.

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Disclosure of Interest: None Declared

Keywords: cholecystectomy, duodenogastric reflux, esophagogastroduodenoscopy, hepatobiliaryscintigraphy

P225 DIFFUSION-WEIGHTED IMAGING IN THE FOLLOW-UP OF PATIENTS AFTER PRIMARY SURGICAL AND NON-SURGICAL TREATMENT FOR RECTAL CANCER

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INTRODUCTION: Accurate detection of recurrent disease after primary rectal cancer treatment is crucial to allow for curative salvage surgery. Standard imaging is known to experience difficulties in differentiating between post-treatment effects (inflammation and fibrotic scar tissue) and recurrent disease. Diffusion-weighted MRI (DWI) is a technique that analyses differences in tissue cellular density to differentiate between hypercellular (tumour) and low or normocellular tissues (fibrosis and inflammation).
AIMS&METHODS: Aim of this study was to evaluate the value of DWI in the follow-up of patients after primary surgical or non-surgical treatment for rectal cancer. The study group (n=117) consisted of 36 patients who had previously undergone rectal cancer treatment, consisting of either standard surgical resection with or without neoadjuvant (chemo-)radiotherapy (n=36), a local transanal excision (n=40, of which 15 after chemoradiotherapy) or a non-operative 'wait-and-see'-policy (n=41). During clinical follow-up (FU) patients underwent on or more FU-MRIs (1.5T) including DWI (highest b-value b1000), as part of routine FU or because of a suspected local recurrence after surgery. Two readers in consensus evaluated each MRI and scored the b1000 DWI-images as 'no high signal', 'high signal suspected of recurrence' or 'not adequately assessable due to artefacts'.
RESULTS: Patients underwent a mean number of 3 FU-scans (range 1-11) with a mean FU-time of 44 months (4-144). 27/117 patients developed a local recurrence, of which 23 (85%) were accurately detected on DWI. The other 90 patients (without recurrence) together underwent a total of 261 FU scans, of which 194 (74%) remained consistently true negative (no high signal) on DWI. 57 DWI-scans (19%) could not adequately be assessed due to artefacts. 14 DWI-scans were false positive (mainly at the first FU-scan after surgery/local excision), of which 50% again normalised during further FU.
CONCLUSION: DWI is a useful tool in the follow-up of patients after primary rectal cancer treatment. False positives may occur immediately after surgery, but the DWI signal normalises again during follow-up.
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Disclosure of Interest: None Declared
Keywords: follow-up, MRI, Rectal cancer, recurrence

P226 ACCURATE IDENTIFICATION OF COMPLETE RESPONDERS AFTER CRT FOR RECTAL CANCER WITH ENDOSCOPY AND MRI

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INTRODUCTION: Chemoradiotherapy (CRT) for rectal cancer leads to complete tumour response (CR) in up to 15-25%. Accurate identification of a CR is necessary to allow for less invasive treatments (i.e. local excision or wait-and-see policy). Standard imaging cannot accurately identify a CR. Other techniques, such as functional MRI (diffusion-weighted MRI 'DWI') or endoscopy may prove more valuable.
AIMS&METHODS: Aim was to evaluate the accuracy of [1] endoscopy and [2] MRI including DWI for identification of a CR and compare it to standard MRI. Forty-nine patients who underwent CRT followed by response evaluation by means of MRI including DWI and endoscopy 8 weeks after completion of CRT were retrospectively included. One experienced reader scored [1] the standard (T2-weighted) MR images, followed by [2] the MR images including DWI. A second reader scored the endoscopy images. Scoring was performed with a confidence level score (0=definitely residual tumour, 4=definitely CR) and results were compared with histology (CR vs non-CR). Readers were blinded for histology and each others' results.
RESULTS: Of the 49 patients, 31 had residual tumour and 18 had a CR. The AUCs for standard MRI, standard MRI + DWI, and endoscopy were 0.71, 0.78, and 0.88 respectively. Corresponding sensitivities and specificities were 39% and 87% for standard MRI, 39% and 93% for standard MRI + DWI, and 67% and 97% for endoscopy.
CONCLUSION: Although the addition of DWI improves the performance of MRI in identifying a CR, endoscopy provides superior results. With a higher sensitivity, endoscopy corrects for understaging of a CR with MRI. However, MRI remains crucial to evaluate the presence of any extramural residual tumour and/or involved nodes. A combination of endoscopy and MRI + DWI is therefore recommendable to identify patients with a CR after CRT, making less invasive treatments after CRT feasible.
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Disclosure of Interest: None Declared
Keywords: Complete remission, Endoscopy, MRI, Rectal cancer, staging

P227 LONG-TERM OUTCOME IN PATIENTS WITH BENIGN ESOPHAGEAL REFRACTORY STRICTURES TREATED WITH SINGLE OR SEQUENTIAL BIODEGRADABLE STENT: A PROSPECTIVE FOLLOW-UP STUDY.

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INTRODUCTION: Management of benign esophageal strictures refractory to standard dilation therapy (BERS) is challenging. Plastic or metal stents (MS) have been used with inconclusive results. Biodegradable stents (BDS) have recently been described in BERS.
AIMS&METHODS: Long-term outcome and safety of BDS in patients with BERS. Data from consecutive patients with BDS placement for BERS between 2008 and 2012 were prospectively included. Technical/clinical outcomes and complication rates were recorded. Clinical/endoscopic follow-up was scheduled at 1, 3, and 6 months and in case of dysphagia recurrence. Stricture etiology was: caustic 5(18%), post-radiotherapy 5(18%), surgery 12(43%), mixed 6 (21%). Previous treatment included MS in 7 (25%) patients and mechanic or pneumatic dilation in the rest, for a median time of 169 days (range 15-864).
RESULTS: 46 BDS (median 1, range: 1-5) were placed in 28 patients (17 male; median age 58y, range 21-75) and were followed for a median of 354 days (range 19-1611). A single BDS was placed in 19 patients (68%), two BDS in 9 patients (32%), four patients (14%) received a third and a fourth BDS, one (3.5%) received 5 BDS. Technical success rate was 98%. Severe post-stenting thoracic pain requiring analgesia occurred in 3 patients (11%). Median dysphagia-free period (DFP) was 111 days (range 33–341), 183 days (range 15-1209), 121 days (range 85-176) and 74 days (range 70-134), after the placement of the first to fourth BDS respectively. No significant differences, in terms of DFP, were observed when patients were stratified according to etiology or stricture length. At the end of follow-up, 11 patients (39%) were dysphagia free. Recurrence of dysphagia was treated with MS in 5 patients (18%) and periodic mechanic/pneumatic dilation in the rest. Four patients (14%) underwent surgery. An esophagotracheal fistula was developed in two patients (7.1%) after 103 and 134 days from BD placement. One of these patients died of surgical complications related to the treatment of the fistula and the other refused surgery and is treated periodically with metal stents. BDS migration occurred 3 in 3 pts (6.5%).
CONCLUSION: BD stent placement in patients with BERS is associated with high technical success rate and acceptable early complication rate. Two patients (7.1%) developed a major late adverse event. Long-term efficacy of this treatment for refractory strictures remains unsatisfactory with only 39% of patients free of dysphagia at the end of follow-up period.
Disclosure of Interest: None Declared
Keywords: benign oesophageal stricture, biodegradable stents, dysphagia, esophageal dilatation

P228 EFFECTIVENESS OF ENDOSCOPIC PNEUMATIC DILATATION IN THE TREATMENT OF DYSPHAGIA AFTER FUNDOPLICATION

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INTRODUCTION: Fundoplication is used for the treatment of gastro-esophageal reflux disease. Dysphagia is common after surgery, being usually transient and related to postoperative edema. However, in 3-24% of cases, dysphagia may persist and is associated with dysmotility or stricture of the esophagus. Although pneumatic dilatation is done in these cases, there are not many studies that evaluate its effectiveness.
AIMS&METHODS: The aim of this work is to evaluate the efficacy and possible complications of endoscopic pneumatic dilatation in the treatment of dysphagia after fundoplication surgery. Study between January 2007 and December 2012 of the patients who developed dysphagia after fundoplication surgery and required endoscopic therapy. We analyzed the endoscopic data, interval and number of dilations, dysphagia severity before and after dilatation and need for surgical reintervention. Dysphagia was evaluated using the Mellow-Pinkas Scale, by telephone survey.
RESULTS: We included 20 patients with a mean age of 54 ± 13 years, mostly female (80%). The average time between surgery and the first dilatation was 18 months (minimum - 1, maximum - 84). The total number of dilatations performed per patient was: fifteen patients - 1; one patient - 2; four patients - 3. The maximum caliber reached was, on average, 16 mm (minimum - 15; maximum - 20). None of the patients were re-operated. Prior to pneumatic dilatation, seven patients had dysphagia for solid food, seven to semi-solid, two to liquids and four, total dysphagia. After dilation, thirteen reported no dysphagia, five had dysphagia for solids and two for semi-solids. In the subjective assessing by patients, 75% reported improvement in symptoms and 25% remained with the same degree of dysphagia. There were no immediate complications related to the procedure.
CONCLUSION: The endoscopic pneumatic dilatation in cases of dysphagia after fundoplication surgery is a safe procedure with an appreciable success rate, representing a gain in our therapeutic armamentarium.
Disclosure of Interest: None Declared
Keywords: Dysphagia, Fundoplication, Pneumatic dilatation

P229 A NEW FULLY COVERED METAL STENT (HANARO-UTRECHT STENT) FOR THE TREATMENT OF MALIGNANT ESOPHAGEAL STRICTURES: A PROSPECTIVE FOLLOW-UP STUDY

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INTRODUCTION: Insertion of self-expandable metal stents (SEMS) provides effective palliation in patients with malignant dysphagia. Although fully covered SEMS are increasingly used to prevent tissue ingrowth, they are prone to migration. In order to reduce migration, the HANARO-Utrecht stent was developed, a fully covered 20-mm diameter SEMS combining bilateral flared ends and three rows of anchoring silicone flaps on the stent body. Our aim was to evaluate the clinical efficacy and safety of the HANARO-Utrecht stent for the palliation of malignant dysphagia.
AIMS&METHODS: Consecutive patients who underwent HANARO-Utrecht stent placement for palliation of malignant dysphagia in four centers from 6/11 - 10/12 were included. Patients were contacted after 2 weeks and monthly thereafter until death. Intervention- or stent related major complications were defined as complications for which repeat endoscopic intervention or admission was required.
RESULTS: Forty patients (29 men (73%), mean age 68±11 years) were included. Malignant dysphagia was caused by esophageal cancer(n=32), malignant extrinsic compression(n=5), tumor recurrence after esophagectomy(n=2) and gastric cancer(n=1). Four patients (10%) had a fistula and 26 patients (65%) had undergone previous radiation and/or chemotherapy (RCT). Stent placement was technically successful in 39 patients (98%) while in 1 patient the stent collapsed during repositioning for which a second stent was inserted. Thirty-two patients (80%) remained dysphagia-free until end of follow up (median 59 days, range 2-223). Eight patients (20%) had recurrent dysphagia after a median of 46 days (range 9-132), due to tissue overgrowth (n=2) and stent migration (n=6), including partial migration in 5 patients for which successful endoscopic repositioning was performed. In total, 17 intervention- or stent related major complications occurred in 14 patients (35%), including hemorrhage(n=6), aspiration pneumonia(n=2), nausea/vomiting(n=3), fistula formation(n=2), severe pain(n=2), tracheal compression(n=1) and stent migration resulting in an unsealed fistula(n=1). No association was found between prior RCT and increased risk of major complications (p=0.53, OR0.64[95%CI, 0.157–2.603).
CONCLUSION: Our results demonstrate that the HANARO-Utrecht stent is effectively palliating dysphagia with a major complication rate in the same range as seen with other stents. Although the overall recurrent dysphagia rate was low, stent migration, although partially in the majority of patients, still occurred.
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Disclosure of Interest: None Declared
Keywords: dysphagia, esophageal cancer, SEMS

P230 CLINICAL OUTCOME OF SELF-EXPANDING METAL STENTS FOR ACUTE COLONIC OBSTRUCTION BASED ON RADIOLOGICAL POSITION: A SINGLE-CENTRE COHORT STUDY

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INTRODUCTION: Self-expanding metal stents (SEMS) are used to resolve colonic obstructions. The correct placement of a SEMS remains a difficult endoscopic procedure and is not always successful. In addition, complications such as perforation may occur. Data evaluating function and complications of SEMS in relation to the radiological position during or shortly after the procedure are very limited.
AIMS&METHODS: Patients receiving SEMS between June 1998 and August 2012 were retrospectively analyzed in this single-centre study. We analyzed radiological symmetry of deployment and position in relation to the stenosis, angulation, minimal/maximal lumen ratio and number of stents. The primary endpoint was non-elective surgery (NES) within 21 days after SEMS placement. Secondary endpoints were immediate endoscopic relief of feces, production of feces within 24 hours, perforation and bleeding. Using multivariate logistic regression, outcomes were corrected for type of obstruction (benign/malignant/extrinsic), location in the colon and intent (bridge to surgery (BTS) or palliation).
RESULTS: In total 137 patients were included (BTS n=75, palliative n=62). In 39 patients (28.5%) the stent was placed proximal to the splenic flexure. A total of 18 patients (13.1%) underwent NES (unresolved ileus n=15, perforation n=2, invagination n=1). Four out of 5 patients with a benign obstruction and 3 out of 6 patients that received a second stent for elongation (n=1) or malposition (n=2) underwent NES. A more symmetrically placed SEMS was associated with direct endoscopic relief (p=0.007) and a straight position of the stent with at least moderate defecation after 24 hours (p=0.004). None of the radiological features were associated with the risk of NES in univariate analysis. Logistic regression confirmed that the placement of two stents (p=0.007) and benign obstructions (p=0.034) were associated with NES, but none of the radiological parameters. There were no associations between radiological parameters and perforation or bleeding.
CONCLUSION: Although a more symmetrically and straight positioned stent is associated with direct endoscopic relief and defecation within 24 hours, we could not detect a statistically significant association between radiological position of SEMS and occurrence of emergency surgery or complications. Patients with two SEMS or benign obstructions are at higher risk for non-elective surgery.
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Disclosure of Interest: None Declared
Keywords: Colonic strictures, Complications, Endoscopy, Non-elective surgery, Radiological position, Self Expanding Metal Stent

P231 EFFICACY OF GASTRIC HYDROSTATIC DILATION IN THE FUNCTIONAL OBSTRUCTION AFTER SLEEVE GASTRECTOMY

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INTRODUCTION: After sleeve gastrectomy, some patients report postprandial dysphagia and epigastric pain, that is relieved by vomiting. The aims of this study are 1/to identify a food stasis using perprandial videofluoroscopy or barium meal, defining a functional obstruction 2/to estimate the efficacy of a gastric hydrostatic dilation in these patients
AIMS&METHODS: Nine patients (1 men and 8 women ; age: 45.6 ± 4.8 years) were referred for postprandial dysphagia and epigastric pain, that was relieved by vomiting in 7/9 patients after a mean of 14.3 months after surgery. All patients had a gastric endoscopy that did not identify any stenosis, then a barium meal or perprandial videofluroscopy to assess barium stasis. A mediogastric and pyloric hydrostatic dilation was made by using a Boston Scientific CRE Balloon of 20 mm, using the pressure of 6 atmospheres for one minute. Patients symptoms (dysphagia, epigastric pain and vomiting) were evaluated before and 6 months after dilation with a pain visual analog scale (0-10)
RESULTS: A food mediogastric and/or pyloric stasis was identified in all the patients. At 6 months, the score of dysphagia (8.7 ± 0.5 vs 3.0 ± 1.0 ; $p<0.01$), epigastric pain (7.0 ± 1.4 vs 1.6 ± 0.9 ; $p = 0.02$) and vomiting (6.7 ± 1.3 vs 2.2 ± 0.9 ; p=0.02) was improved by hydrostatic dilation (only one session per patient). At the end of the follow up, no patient had regained weight following the dilation. An epigastric pain was reported in 4 patients, that disappeared within 48 hours after dilation. No severe complication was noted.
CONCLUSION: In the patients reporting postprandial dysphagia and epigastric pain relieved by vomiting after sleeve gastrectomy, a functional obstruction is worth to be assessed using a barium meal and/or a perprandial videofluoroscopy. The mediogastric and pyloric hydrostatic dilation is an therapeutic option with an efficacy that lasted over 6 months. This phase I study should be further confirmed on the long term and using randomized trials.
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Disclosure of Interest: None Declared
Keywords: functional obstruction, hydrostatic gastric dilation, sleeve gastrectomy

P232 USEFULLNESS OF COVERED SELF-EXPANDABLE METAL STENT INSERTION FOR THE TREATMENT OF ANASTOMOTIC LEAKS AND TRACHEOESOPHAGEAL FISTULAS AFTER UPPER GI SURGERY.

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INTRODUCTION: Anastomotic leaks and tracheoesophageal fistulas (TEFs) are severe complications of upper gastrointestinal surgery with serious morbidity and mortality. Endoscopic placement of covered self-expandable metal stent (cSEMS) is emerging as a less-invasive alternative to surgery for the treatment of leaks and TEFs.
AIMS&METHODS: The aim of this study is to investigate treatment success rate of cSEMS, removal rate of successful cSEMS and complications of procedure.
Patients with postsurgical gastrointestinal leaks and TEFs treated with cSEMS (fully covered, CHOO/HANARO) between September 2009 and September 2012 were retrospectively reviewed. Treatment success was defined as complete and persistent closure of leaks or TEFs after cSEMS removal (primary closure) or after complementary endoscopic treatment (reposition or reinsertion).
RESULTS: 19 patients were treated with covered self-expandable metal stent (cSEMS). Included patients had anastomotic leaks or TEFs after total gastrectomy(9), esophagectomy(6) and etc(4, esophageal diverticulectomy, submucosal tumor enuclation, transcervical mediastinal drainage, primary esophageal closure). Overall treatment success rate of the leaks or TEFs occurred in 89 % (17 out of 19, including multiple procedures). Repositioning was done in 26% (5 out of 19, due to migration) and successful repositioning was done in 4 out of 5. (additional reinsertion was needed in 1 case and was successful.) Reinsertion was done in 16% (3 out of 19, due to migration) and 2 out of 3 were successful.(1 case was failed due to stent site erosion.) Stent removal after successful treatment was done in 94% (16 out of 17, average 30.6 days, range 11 ∼ 43 days, 1 was lost to follow-up.)
There was no procedure-related complication including perforation or death.
CONCLUSION: cSEMSs are a minimally invasive, safe and useful alternative for treating postsurgical leaks and TEFs in the upper gastrointestinal tract and can be easily removed after successful insertion.
Migration is a major problem, but most of cases can be cured by complementary endoscopic procedure (reposition or reinsertion).
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Disclosure of Interest: None Declared
Keywords: Anastomotic leak, COVERED SELF EXPANDING METAL STENT, upper gastrointestinal surgery

P233 RISK FACTORS FOR UNSUCCESSFUL SURGICAL OUTCOMES AFTER COLONIC STENTING AS A BRIDGE TO SURGERY IN ACUTE LEFT-SIDED MALIGNANT COLORECTAL OBSTRUCTION

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INTRODUCTION: Although self-expanding metal stents (SEMS) as a bridge to surgery (BTS) is an alternative to emergency surgery in patients with malignant colonic obstruction (MCO), risk factors for unsuccessful surgical outcomes after stenting as a BTS is uncertain.
AIMS&METHODS: The aim of our study was to identify risk factors predictive of poor postsurgical outcomes for SEMS as a BTS. The medical records of patients who underwent SEMS insertion in colorectal obstruction between February 2004 and August 2012 were retrospectively reviewed. A total of 181 patients underwent SEMS insertion during the study period, 68 patients who underwent SEMS insertion as a BTS in acute left-sided MCO were included.
RESULTS: The mean age was 64.9 years (range, 38-89), and 70.6% (48/68) were male. The most common obstruction site was in the rectosigmoid area (25/68, 36.8%). Covered SEMS were used in 33/66 (50.0%) of patients with technical success. The technical and clinical success rates of SEMS were 97.1% (66/68) and 88.2% (60/68), respectively. 85.3% (58/68) of patients underwent primary tumor resection and primary anastomosis, with a mean interval of 11.3 days (range, 0-26) between SEMS insertion and surgery. Surgical success rate of SEMS as a BTS was achieved in 77.9% (53/68). On multivariate analysis, multiple SEMS [$\geq$2 stents or $\geq$2 stent insertion sessions (OR, 28.872; 95% CI, 1.939-429.956; p=0.015)] was a significant independent risk factor for surgical failure of SEMS as a BTS.
CONCLUSION: Although SEMS is an effective BTS therapy in most patients, the possibility of surgical failure should not be ignored. Multiple SEMS, turned out to be a risk factor for surgical failure, should be able to help clinicians decided to appropriate treatment strategy in subgroup of patients with acute left-sided MCO.
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Keywords: Colorectal neoplasms, Endoscopy, Intestinal obstruction, Risk factors, Stents

P234 FUNCTIONAL OUTCOME FOLLOWING SUCCESSFUL ENDOSCOPIC RECONSTITUTION OF PATIENTS WITH RADIATION-INDUCED COMPLETE ESOPHAGEAL OBSTRUCTION

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INTRODUCTION: Combined anterograde - retrograde (CARD) endoscopic recanalization is safe and effective in restoring an esophageal lumen in patients with radiation-induced complete esophageal obstruction. In the few small case-series subsequent removal of a gastrostomy feeding tube is feasible in approximately 50%.
AIMS&METHODS: To investigate the long-term functional outcome and factors predictive of failure of clinical success in patients with radiation-induced complete esophageal obstruction after successful endoscopic lumen recanalization performed in a tertiary center. A retrospective chart review was performed. In 35 patients treated from August 2001 to February 2013 (median age 65 years, 23 males) recanalization was technically successful.
RESULTS: Procedural-related adverse events occurred in four patients (11.2%); three were perforations, all managed conservatively. The mean number of total dilations, including the recanalization procedure was 4.9. A mean esophageal dilation of 16mm was achieved. Only 6 patients (19%) were dysphagia-free after the final treatment, 2 patients had dysphagia to solids, 3 to semi-solids, 6 to liquids and 13 (42%) had complete dysphagia. Of 11 patients that had some ability to swallow the feeding tube could be removed in 7, though 6 were dilation-dependent. Only 4 (11%) patients were treatment free and 20 (57%) patients remained with gastrostomy feeding tubes. Head and neck cancer surgery was predictive of clinical success ($p = 0.05$). A trend towards clinical success was seen when the duration between radiation therapy and onset of dysphagia was longer (9.5 months vs. 1.2 months, $p = 0.07$). Mean follow-up was 1.8 years.
CONCLUSION: The ability to swallow after successful endoscopic recanalization of radiation-induced complete esophageal obstruction is low. A predictive factor for clinical success is a history of surgery for head and neck cancer.
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Disclosure of Interest: None Declared
Keywords: esophageal dilatation, Long term outcome, Obstruction, Rendezvous, strictures

P235 VIOLATION OF THE "RULE OF THREE" DOES NOT INCREASE THE RISK OF PERFORATION FOLLOWING ESOPHAGEAL DILATION

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INTRODUCTION: The "rule of three" for esophageal dilation applies to rigid dilators and was arbitrarily proposed to prevent overaggressive dilation and consequent perforation. However, there is no evidence to support its utility.
AIMS&METHODS: To investigate whether violation of the "rule of three" increases adverse events (AEs) following esophageal dilation. Retrospective chart review of 300 patients (median age 63 years, 59% men) who underwent esophageal dilation between December 1991 and February 2013 at a tertiary hospital was performed. Demographics, indication, stricture and procedural characteristics, AE's and follow-up data were recorded. Adherence to the "rule of three" was defined for rigid dilators as passage of only 3 consecutive dilators in increments of 1 mm in a single session after moderate resistance was encountered and for balloon dilators as the dilation diameter was $\leq$ 3 mm than the initial diameter of the esophageal lumen as assessed endoscopic.
RESULTS: In 2,225 rigid or balloon esophageal dilations performed, 22 (1.0%) major AE's occurred, of which 11 perforations (0.5%), 4 fistulas, 3 admissions for pain management, 2 bleedings, 1 fever and 1 leaking tracheoesophageal voice prosthesis. The majority of dilated strictures were benign (n = 277, 93%) and complex (n = 201, 67%). The "rule of three" was not adhered to in 622 dilations. Of the 16 AEs occurring after over-the-wire rigid dilation the "rule of three" was violated once ($p = 0.17$). No correlation was found between AEs and complex strictures ($p = 0.69$), over-the-wire rigid dilators ($p = 0.10$), non-adherence to the "rule of three" ($p = 0.15$), diameter of dilation >3 mm ($p = 0.09$) and another maneuver performed during dilation ($p = 0.48$). No significant difference in perforation rate was seen when the "rule of three" was violated or not (8 vs. 3, $p = 0.15$). Likewise no correlation was found between perforations and complex strictures ($p = 0.39$), over-the-wire rigid dilators ($p = 0.49$) or diameter of dilation > 3 mm in one session ($p = 0.14$). However, a trend towards more perforations was seen when an additional maneuver was performed during dilation ($p = 0.065$). The percentage of AEs and perforations were equally distributed to the number of dilation sessions per patient.
CONCLUSION: Non-adherence to the "rule of three" does not appear to increase the risk of AEs, particularly perforation, following esophageal dilation using rigid dilators. Nonetheless, it needs to be determined whether other factors, like stricture etiology, affect the risk of developing an AE in esophageal strictures.
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Disclosure of Interest: None Declared
Keywords: adverse events, esophageal dilation , rigid and balloon dilators, rule of three

P236 SAFETY AND EFFICACY OF A BIODEGRADABLE STENT DURING NEOADJUVANT THERAPY IN PATIENTS WITH ADVANCED OESOPHAGEAL CANCER (ESNEBIO).

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INTRODUCTION: An increasing number of patients with locally advanced esophageal cancer undergo treatment with chemoradiotherapy prior to surgery. This neoadjuvant therapy often causes acute inflammation and edema of the esophageal mucosa which could increase dysphagia symptoms and potentially jeopardize nutritional status. Initial data on self-expanding plastic stents placement prior to neoadjuvant treatment have shown promising results with regard to improvement of dysphagia and safety, but major drawbacks include stent migration and the need for stent removal prior to surgery. We hypothesized that placement of an uncovered biodegradable (BD) stent (SX-ELLA BD stent, Ella-CS, s.r.o., Czech Republic) might refute these problems while the improvement of dysphagia persists.
AIMS&METHODS: This is a prospective 2-center feasibility study aiming to include 16 patients with resectable esophageal carcinoma scheduled for neoadjuvant chemoradiotherapy and complaints of dysphagia for solid food (grade $\geq$ 2 [scale 0-4]). The BD-stent is placed prior to the start of neoadjuvant treatment. The primary outcome is safety, defined as the absence of intervention-related major complications (perforation, bleeding and pain requiring IV analgesics). Secondary outcomes include technical success, clinical success, other intervention related complications and weight change.
RESULTS: Nine patients have been included until May 1st 2013 (7 male, mean age 68 $\pm$ 8.1, median dysphagia grade 3 [range 2-4], 8 adenocarcinoma, 1 squamous cell carcinoma). No procedure-related or stent-related major complications were seen. Technical success rate was 100%. Clinical success was achieved 100% as well. Adverse events included pain after stent placement (n=6) and stent obstruction (due to necrotic tissue) (n=1). Weight loss occurred in 5 patients (relative median weight loss 6.5% [range 0.4-11.3]) despite additional nasogastric feeding tube placement through the stent in 4 patients after a median of 56 days (range 41-82). One patient had a relative weight gain of 5.6% after 8 weeks of follow-up. In the remaining 3 patients follow-up is still too short to report weight changes.
CONCLUSION: Preliminary results of this study do not reveal major complications and good technical and clinical success rates. Post procedural pain and persisting weight loss after BD stent placement are features which may hamper its future use during neoadjuvant chemoradiotherapy in patients with locally advanced esophageal cancer. We will complete the study as planned in order to draw firm conclusions.
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Disclosure of Interest: None Declared

Keywords: biodegradable stents, dysphagia, Neoadjuvant chemoradiation, Oesophageal carcinoma

P237 SAFETY AND EFFICACY OF A FULLY COVERED LARGE DIAMETER STENT (HANARO CCI STENT) FOR THE TREATMENT OF OESOPHAGEAL PERFORATIONS, ANASTOMOTIC LEAKS AND FISTULA.

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INTRODUCTION: Oesophageal perforations, fistula and anastomotic leaks are severe conditions with high morbidity and mortality rates. Temporary placement of fully covered self expanding metal (fSEMS) or plastic stents has emerged as a treatment option. A high stent migration rate is a major drawback of the self-expandable stents currently used for these indications. In general, migration is often attributed to a relatively too small stent diameter. Therefore this study aimed to investigate the safety and efficacy of a large diameter fSEMS with a 24 mm body and 32 mm flares (Hanaro CCI stent, M.I.Tech, South-Korea) for treatment of these conditions.
AIMS&METHODS: Data were retrospectively collected from medical records of all patients who received the Hanaro CCI stent in the Netherlands between July 2009 and August 2012. The primary outcome was the number of severe stent(-placement)-related complications. Secondary outcomes were non-severe complications, technical and clinical success. Severity of complications was graded according the American Society for Gastrointestinal Endoscopy grading system.(1) Clinical success was defined as sufficient closure of the lesion as confirmed by endoscopy or X-ray with oral barium contrast without the need for an additional stent or surgical intervention.
RESULTS: Stent placement was performed in 21 patients (males 13 [62%], mean age 57 ± 10.4) for the following indications: perforation (n=3), anastomotic leak (n=16) and fistula (n=2). The technical success rate was 95%. Severe stent-related complications did not occur. However, 3 patients died because of persistent intrathoracic sepsis (n=2) and pre-existent bowel ischemia (n=1). A total of 12 patients (57%) experienced 13 non-severe stent-related complications, which consisted out of stent migration (partial n=4, complete n=5), bleeding (n=2), aspiration pneumonia (n=1) and tissue overgrowth (n=1). The overall clinical success rate was 52% (11/21). Median time to stent-removal following clinical success was 39 days (interquartile range 33-56). Clinical failures were caused by technical failure (n=1), premature death (n=3), stent migration (n=5) and insufficient sealing of the lesion (n=1). The 4 partial migrations were treated with endoscopic repositioning and were not considered clinical failures.
CONCLUSION: Placement of the Hanaro CCI stent is an easy to perform and safe treatment for oesophageal perforations, fistula and anastomotic leaks. However, efficacy is still hampered by stent migration despite the relatively large stent diameter.
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Disclosure of Interest: None Declared
Keywords: Anastomotic leak, fistula, oesophageal, Perforations, Stent

P238 HIGH PROXIMAL MIGRATION RATE OF A PARTIALLY COVERED BIG CUP DUODENAL STENT (HANARO DPC-STENT) IN PATIENTS WITH MALIGNANT GASTRIC OUTLET OBSTRUCTION.

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INTRODUCTION: Enteral stent placement has emerged as a safe and effective palliative treatment option for patients with malignant gastric outlet obstruction (GOO). However, long term efficacy of conventional duodenal stents is hampered by stent dysfunction. The most frequently observed causes of dysfunction are tumour ingrowth in uncovered stents and stent migration in covered stents. We hypothesized that a newly designed partially covered big-cup enteral stent (Hanaro, M.I. Tech, Ltd., Seoul, Korea) would refute these problems. The objective of the covered part of the stent is to withstand tumour ingrowth while the proximal uncovered big cup should prevent distal migration by anchoring the stent at the pylorus.
AIMS&METHODS: This study was designed as a prospective two-center single-cohort study aiming to evaluate safety and efficacy of the Hanaro DPC stent in 40 patients with incurable malignant gastric outlet obstruction. Stent placement was performed through-the-scope under endo-fluoroscopic guidance. The primary outcome was stent patency, defined as the time between stent placement and re-obstruction caused by an endoscopically proven stent dysfunction. Secondary outcomes included technical success, clinical success (improvement of GOO-symptoms one week after stent placement) and complications. Follow-up continued until death or stent-dysfunction requiring a second stent, whichever came first.
RESULTS: Six patients (4 pancreatic cancer, 1 cholangiocarcinoma, 1 gastric cancer) were included (4 males, median age 63 [range 47-83], median follow-up 49 days [range 2-228]). Technical success rate was 100%. Clinical success was achieved in 4/6 patients (67%). Clinical failure in 2 patients was caused by proximal stent migration after 2 and 4 days respectively and another proximal stent migration occurred in a third patient, 29 days following stent placement. These 3 patients were treated with endoscopic removal of the Hanaro DPC stent and placement of a conventional uncovered stent. Other complications included biliary obstruction 45 days after duodenal stent placement (n=1) and obstructive symptoms most likely caused by a motility disorder (n=1). The high number of proximal migrations occurring after a relatively short time interval after stent placement made us deciding to stop the study prematurely. One patient is still alive with a functional stent after 228 days of follow-up.
CONCLUSION: The Hanaro DPC-stent is associated with a high proximal migration rate in patients with malignant GOO and can therefore not be recommended in this clinical setting.
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Disclosure of Interest: None Declared
Keywords: duodenal obstruction, MALIGNANCY, Stent

P239 BIODEGRADABLE STENTS FOR CAUSTIC ESOPHAGEAL STRICTURES : DO THEY WORK ?

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INTRODUCTION: Refractory esophageal strcitures present challenging situatuions to the endoscopist. Biodegradable stents curcumvent the tissue reaction and tissue embedment issues seen with metallic stents known to be useful in malignant strictures. There is an upcoming role for biodegradable stents in the management of benign refractory esophgageal strcitures.
AIMS&METHODS: ***Aims*** : To study the response of biodegradable stents(BD)(ELLA, Chech Republic) in patients with refractory caustic esophageal strictures(CES).
Material and methods : 13 patients(18-72 yr, 9males) of refractory CES were subjected to placement of BD stents. Patients were followed up every week for 1 month and then every month for six months. Periodically endoscopy was repeated. Immediate and delayed complications were noted.
RESULTS: The BD stent was placed successfully in all 13 patients with no immediate complication of bleeding, or perforation or migration. 1 patient had retention of the olive of the stent in the stomach which was removed the next day. The size of the stent was 23mm in width in all with 80 mm of length in 12 patients and 115 mm of length in 1 patient. Pain in retrosternal area was reported by all the 13 patients post-procedure. It persisted till 1 week in 10 patients, till 2 weeks in 6 patients and till 8 weeks in 2 patients. 1 patient had stent migration at 4 weeks. Tissue hyperplasia was noted in 6 patients at the proximal end at 3-4 weeks. Stent disintegration was complete by 12 weeks in all the 12 patients with stent in-situ. 9/13 patients had restenosis at 3 months, 10/12 at 6 months and 11/13 at 1 year. Patients with recurrence of stricture were subjected to dilatation (n=9) or surgery (n=2). At esophagectomy, in one patient, no residue of the stent or tissue reaction was found. 2 patients(16%) were free of symptoms at 1 year including the one with migration of stent.
CONCLUSION: Biodegradable stents do not provide long term relief in a majority of patients with CES. Stents with longer time to degradation may be more effective.
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Disclosure of Interest: None Declared
Keywords: biodegradable stents, strictures

P240 EVALUATION OF NINE PERFORATED CASES RELATED TO SELF EXPANDING METAL STENT PLACEMENT WITH MALIGNANT GASTRODUODENAL OBSTRUCTION.

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INTRODUCTION: Self expanding metal stent (SEMS) placement is a useful palliative method for the patients with malignant gastrointestinal obstructions. But etiologies of the adverse events are still unclear. Perforation should be mentioned in particular as a one of most severe events related to SEMS.
AIMS&METHODS: We focused on the perforated cases and evaluated risk factors and conformation of SEMS after insertion. One hundred and forty seven patients of gastroduoedenal obstruction with SEMS placement were enrolled this study. We performed with an over the wire technique for Ultraflex (Boston Scientific) and HANARO stent (Diagmed healthcare) and a through the scope technique for Niti-S (Taewoong medical) and WallFlex (Boston Scientific).
RESULTS: Perforations were occured in 9 patients (6.1%) related to SEMS treatment. Three patients were treated with radiotherapy before SEMS placement. Two of two patients with urothelial cancers resulted in perforation and they were treated with neither chemotherapy nor radiotherapy. Radiotherapy increased perforation risk with significance (OR 6.40, 95% C.I:1.3886-29.4983, p=0.008). Four autopsies were carried out and all perforations were confirmed in oral side edge of SEMS. All stents extend in stenosis, and SEMS with fixed braid tend to be stiff under the incomplete expansion.
CONCLUSION: From our result, a radiotherapy before SEMS placement and urothelial carcinomas are one of most critical factors predicting perforation. Furthermore, we speculate that conformation change of SEMS and peristalsis might cause perforation.
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Disclosure of Interest: None Declared
Keywords: gastrointestinal stenosis, perforation, Self Expanding Metal Stent

MONDAY, OCTOBER 14, 2013 9:00–17:00
SURGERY I – Poster Area

P241 GASTROINTESTINAL SAFETY OF LONG-TERM PEG-J USED FOR CONTINUOUS INFUSION OF LEVODOPA-CARBIDOPA INTESTINAL GEL

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INTRODUCTION: Motor complications observed in patients with advanced Parkinson's disease (PD) on oral medications might be due to impaired gastric emptying and fluctuating drug plasma levels. A new treatment for PD involves the use of a percutaneous endoscopic gastrostomy with jejunal extension tube (PEG-J) to provide continuous delivery of levodopa-carbidopa intestinal gel (LCIG) directly to the jejunum.
AIMS&METHODS: An independent adjudication committee of 3 gastroenterologists reviewed GI procedure- and device-related adverse events (AEs) from long-term, integrated safety data from Phase 3 LCIG studies (total N=395). After elimination of redundant AE coding, the rate, clinical significance, and relationship to procedure/device for the AEs were determined by a comprehensive adjudication process.
RESULTS: The median exposure to PEG-J was 480 days; 180 subjects had ≥540 days, 113 of whom had ≥730 days. At end of year 1, 91.3% of subjects retained the original PEG tube and 62.9% retained the original J-tube. 4.3% of subjects discontinued treatment due to a GI procedure- or device- related AE. Nonserious AEs occurring in ≥5% of subjects: abdominal pain (31.1%), procedural pain (23.0%), postoperative wound infection (20.0%), excessive granulation tissue (18.0%), incision site erythema (15.9%), procedural site reaction (10.1%), and postprocedural discharge (10.1%). Serious AEs (SAEs) occurred in 17.0% of subjects. 41.9% of SAEs occurred during the first 4 wks of treatment.
Table 1. Major and minor SAEs occurring in ≥1% of patients

Major SAEs	Incidence[a]	Procedural Incidence[b]
Abdominal pain[c]	6(1.5%)	1.3%
Peritonitis	9 (2.3%)	1.9%
Pneumonia	7 (1.8%)	1.5%
Minor SAEs		
Abdominal pain	7 (1.8%)	1.5%
Pneumoperitoneum	7 (1.8%)	1.5%

[a]Incidence (%) = proportion of all patients who received a PEG-J (N = 395). [b]Procedural incidence (%) = proportion of all the PEG-J procedures performed (N = 468). [c]Major abdominal pain required hospitalization without other diagnosis.
CONCLUSION: PEG-J longevity exceeded committee expectations. The incidence of PEG-J AEs with the LCIG delivery system was within ranges quoted in the PEG literature. A low discontinuation rate suggests acceptable procedural outcomes and complication rates in this advanced PD patient population. Support: AbbVie
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Disclosure of Interest: M. Epstein Lecture fee(s) from: AbbVie, Consultancy for: AbbVIe, Other: AbbVie, D. Johnson Consultancy for: AbbVie, Other: AbbVie, R. Hawes Consultancy for: AbbVie, Other: AbbVie, N. Schmulewitz Lecture fee(s) from: AbbVie, Consultancy for: AbbVie, A. Vanagunas Consultancy for: AbbVie, Other: AbbVie, R. Gossen Consultancy for: AbbVie, Other: AbbVie, S. Eaton Shareholder of: AbbVie, Other: AbbVie, J. Dubow Shareholder of: AbbVie, Other: AbbVie, K. Chatamra Shareholder of: AbbVie, Other: AbbVie, W. Robieson Shareholder of: AbbVie, Other: AbbVie, J. Benesh Shareholder of: AbbVie, Other: AbbVie
Keywords: clinical trial, endoscopic complications, jejunostomy tube, PEG, PEJ, percutaneous endoscopic gastrostomy

P242 BPC 157 FISTULA-HEALING EFFECT CLOSES TRACHEOTOMY WOUND IN RATS

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INTRODUCTION: BPC 157 is an original anti-ulcer peptide (GEPPPGKPADDAGLV, M.W. 1419) stable in human gastric juice more than 24 hours, successful in trials for inflammatory bowel disease, phase II, wound treatment, no toxicity or side effects were reported, LD1 was not achieved, effective alone without carrier. BPC 157 also closes gastrocutaneous, colocutaneous and esophagocutaneous fistulas. Thereby, we investigate whether BPC 157-fistulas healing may be relevant in tracheotomy wound healing.
AIMS&METHODS: Rats were underwent to standard horizontal tracheotomy, trachea opened horizontally, no cannula was inserted and edges of the trachea were sutured on to a skin. BPC 157 (10 μg/kg, 10 ng/kg) was applied (i) in drinking water until the animals were euthanized, or (ii) once a day intraperitoneally (first application 30 min following surgery, last 24 h before euthanization, at 3rd postoperative day. With 3 mm diameters, trachea was opened on the opposite side of the tracheotomy wound and inner part of the wound was also measured.

RESULTS: BPC 157 administered parenterally or perorally accelerated healing of tracheotomy wound and showed functional, macroscopic and histological healing improvements. In average, with respect to initial size, both outer and inner part of the tracheotomy wound were improved: i.e., 10 ug/kg of BPC 157 in drinking water improved healing by 40 -100% for the outer part (skin), and by 60-100% for the inner part (trachea) of the wound. Contrary, controls showed only poor by 0-37.5% for the outer part (skin), and by 0-50% for the inner part (trachea) of the tracheotomy wound. Further, animals treated with BPC 157 showed slower weight loss than the control.
CONCLUSION: BPC 157 fistula-healing effect may close tracheotomy wound.
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Disclosure of Interest: None Declared
Keywords: BPC 157, fistula, healing, rats, tracheotomy

P243 MEDIUM TERM OUTCOME FOLLOWING 3D ROBOTIC HELLER'S CARDIOMYOTOMY (HC) WITHOUT AN ANTI-REFLUX PROCEDURE (ARP) FOR THE TREATMENT OF ACHALASIA.

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INTRODUCTION: Robotic surgery allows precise and accurate surgery. Mucosal breaches occur in up to 12% of patients with conventional laparoscopic HC and recurrent symptoms are not uncommon (Boeckxstaens et al, 2011). Accuracy and precision is essential when performing HC to avoid incomplete myotomy and mucosal breach. The need for ARP at the time of HC remains controversial. HC with anterior or Toupet fundoplication is common practice, despite lack of evidence from published studies (Andreollo & Earlam, 1987). We present a single centre experience with performing robotic HC for achalasia.
AIMS&METHODS: Retrospective analysis of patients who underwent robotic HC for achalasia between 2009 - 2013 was performed. HC was performed using a Da Vinci robot (Intuitive Surgical Inc.) with 4 laparoscopic ports. Anterior mobilization of the oesophagus was performed leaving the posterior component of phreno-oesophageal ligament intact. A longitudinal myotomy was made extending into the proximal stomach. 3D vision facilitated accurate division of all fibres up to the mucosa. Outcomes were assessed with regards to mucosal integrity, hospital stay and symptom improvement.
RESULTS: 15 patients underwent surgery (8 male) with a median age of 45 years (range 19-67). 2 had simultaneous ARP for; small hiatus hernia (1), early in the series (1). Two cases were for recurrent dysphagia following laparoscopic HC at different centres. Median length of myotomy was 6cm (5-10). No mucosal breaches were identified at surgery, and there were no postoperative leaks. Median length of hospital stay was 1 day (1-28). One patient with multiple comorbidities developed a chest infection and had a prolonged hospital stay. Median follow up was 36 weeks (3-146). All patients had symptomatic improvement in dysphagia, resuming normal diets. None of the patients developed recurrent dysphagia or clinically significant reflux.
CONCLUSION: Robotic surgery offers superior visualization and definition of the oesophageal muscle fibers, along with improved dexterity and ergonomic comfort. This allows precise and complete division of the muscle fibers which is more difficult to achieve with conventional laparoscopy. This may explain the absence of both oesophageal perforation or recurrent dysphagia following surgery in our series. Anterior mobilization of the oesophagus alone may preserve some antireflux mechanisms which may reflect the absence of reflux symptoms following HC such that an additional ARP may not be necessary. Long-term studies are required to evaluate this further.
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Disclosure of Interest: None Declared
Keywords: Achalasia , heller's myotomy, robotic surgery

P244 PARA-OESOPHAGEAL HERNIA REPAIR IS ASSOCIATED WITH IMPROVEMENT QUALITY OF LIFE AND RESOLUTION OF ASSOCIATED ANAEMIA.

H. P. Siriwardana[1,*], N.V. Jayanthi[1], H. Winter[1], C.-B. Tang[1], M. H. Harvey[1], S. S. Kadirkamanathan[1]. *[1]Upper GI Surgery, Broomfield Hospital, Chelmsford, United Kingdom*

INTRODUCTION: Para-oesophageal herniae (PEH) present with varying symptoms including shortness of breath, post-prandial epigastric pain, vomiting with or without haemetemesis. Recent studies have described associated anaemia in these patients.
AIMS&METHODS: Our aim was to evaluate the prevalence of anaemia in patients with PEH and assess the effect of surgery on this alongside changes to quality of life.

All patients who underwent PEH repair between March 1997 and October 2012 were included. All anaemic patients (Haemoglobin [Hb] <13gm/dl in males, <12gm/dl in females) were investigated appropriately. Blood tests were compared pre and post operatively (Hb, Mean Corpuscular Volume [MCV], Haematocrit [Hct]). Physical and mental health components of quality of life (QoL) were also measured pre and post operatively with SF 36 questionnaire. Statistical analysis was performed with Student's t test.

RESULTS: A total of 64 patients had PEH repair (37 male). Median age was 68yrs (40–88). Over half of patients were ASA III or IV (54%) and majority had Type III or IV PEH (76%). Laparoscopic repair was performed in 42 patients. One elderly patient (88yrs) died with aspiration pneumonia. There were no other major complications. 39 (62%) were anaemic at presentation, 8 (13%) being symptomatic from this and incidentally diagnosed with PEH on endoscopy. Preoperative endoscopy revealed oesophageal or gastric ulceration/erosions in 21 patients (54%). Pre and post-operative blood tests are shown in Table 1. Treatment for anaemia consisted of oral iron supplements (33), intravenous iron infusion (1) and blood transfusion (5). In those with preoperative anaemia, detailed follow-up was available in 33 (85%) with a median of 49 months (3-114). Anaemia resolved in 26 (78%). Anaemia improved in the remaining 7 who continued on oral iron supplementation. The median follow-up in these patients did not differ from those with resolution of anaemia ($p = 0.14$). Recurrent hernia was found in 2 of these 7 patients.

There was no significant improvement in Hct. No patients required transfusion or intravenous iron infusion after PEH repair.

Repair of PEH was also demonstrated to significantly improve quality of life as assessed by SF 36 questionnaire ($p < 0.05$).

CONCLUSION: Our data suggests that PEH repair is safe and effective in high anaesthetic risk patients. Anaemia appears to be common in patients with PEH and surgical repair can be seen to improve Hb levels significantly. In addition to this, improvements in quality of life after surgical repair of PEH have been demonstrated.

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Disclosure of Interest: None Declared

Keywords: Anaemia, hiatal hernia, Quality Of Life, surgical treatment

P245 CLINICAL OUTCOMES OF UNDIFFERENTIATED EARLY GASTRIC CANCER WITH HISTOLOGIC DISCREPANCY AFTER ENDOSCOPIC RESECTION

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INTRODUCTION: Endoscopic resection (ER) has become an important curative option for early gastric cancer (EGC). However, the application of ER for undifferentiated EGC, including histologic discrepancy (HD), remains controversial.

AIMS&METHODS: The aim of this study was to evaluate the clinical outcomes for undifferentiated EGC with HD. From October 2002 to June 2011, 59 lesions in 59 patients were finally enrolled (42 poorly differentiated adenocarcinoma (PD) & 17 signet ring cell carcinoma (SRC)). The therapeutic efficacy of ER was assessed according to en bloc resection rate, complete resection rate, and recurrence rate during follow-up.

RESULTS: Of 59 undifferentiated EGCs, 48 cases (81.3%) showed HD (pre-ER biopsy: differentiated cancer (n=39) and atypical gland and/or high grade dysplasia (n=9)). The mean size of lesions was 2.1 cm (range 0.1 to 5.2 cm). The rates of en bloc resection and CR were 94.9% and 76.3%, respectively. The en bloc resection and CR rates in PD were 95.2% and 78.6%, and those in SRC were 94.1% and 70.6%, respectively. There were no significant differences between two histologic subtypes. Of 59 cases, 38 cases (26 mucosal lesions and 12 submucosal lesions) with HD were resected by surgical gastrectomy. In surgical specimen, no case showed lymph node metastasis. Of 15 cases not undergoing surgery, no recurrence occurred during median follow-up of 27.5 months (range 8 to 109 months).

CONCLUSION: ER might be a feasible local treatment in selective cases of undifferentiated EGC with HD

Disclosure of Interest: None Declared

Keywords: endoscopic resection, histologic discrepancy, undifferentiated adenocarcinoma

P246 ROLE OF SENTINEL NODE IN ESOPHAGECTOMY FOR ESOPHAGEAL CANCER: A SYSTEMATIC REVIEW

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INTRODUCTION: Sentinel node (SN) biopsy might provide surgeons an extra tool to limit unnecessarily extended lymphadenectomy. In esophaeal surgery this might be applied to early cancer of the esophageal gastric junction.

AIMS&METHODS: The aim of our study was to review all the available literature data about the use of SN biopsy in esophageal surgery for malignancy.

The review was conducted according to the PRISMA guidelines. A systematic search was performed in the PubMed, EMBASE, and Cochrane database to identify all original articles on the role of SNB in esophageal cancer. Data on methodologies used, tumor stage and localisation, and results were summarized and used to address relevant clinical questions related to the application of the SNB technique in esophageal cancer.

RESULTS: Twelve studies were included with a total of 492 patients. Different methods for SN identification were used (radionuclide, blue-dye, CT lymphography). The pooled values estimated using the random effects model were, respectively: for Tc99m overall detection rate (DR) 0.970 (95% CI: 0.814- 0.996), accuracy (ACC) 0.902 (95% CI: 0.736- 0.968), sensitivity (SE) 0.860 (95% CI: 0.814- 0.895) and negative predicting value (NPV) 0.811 (95% CI: 0.745- 0.863); for blue-dye DR 0.971 (95% CI: 0.890- 0.993), ACC 0.790 (95% CI: 0.681-0.870), SE 0.811 (95% CI: 0.669- 0.901) and NPV 0.673 (95% CI: 0.476-0.824); for CT lymphoscintigraphy DR 0.970 (95% CI: 0.814- 0.996), ACC 0.902 (95% CI: 0.736- 0.968), SE 0.831 (95% CI: 0.452- 0.967) and NPV of 0.938 (95% CI: 0.742- 0.987).

CONCLUSION: Based on these results, the concept of SN in esophageal cancer is technically feasible with an acceptable detection rate and accuracy. Further studies focused on a single tumor type and localisations are needed in order to predict the correct utilisation of this concept in esophageal cancer.

Disclosure of Interest: None Declared

Keywords: esophageal cancer, esophagectomy, sentinel lymph node

P247 PREDICTING POSTOPERATIVE OUTCOME AFTER ESOPHAGECTOMY FOR CANCER: NUTRITIONAL STATUS IS THE MISSING RING IN THE CURRENT PROGNOSTIC SCORES

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INTRODUCTION: Several preoperative prognostic scores based either on physiology of the patient or on the operative findings were designed in order to give a good estimation of the risk of postoperative adverse events. Preoperative nutrition status received minor interest in risk analysis; none of the above mentioned scores includes a parameter linked to nutrition (albumin, percentage of weight loss or BMI). These parameters had already been included in some prognostic scores [1-4] but they had never been used for esophageal cancer.

AIMS&METHODS: The aims of the study were the validation of risk-adjusted models for early outcomes after esophagectomy and to develop a score for severe complication prediction with special consideration regarding nutritional status. A comparison of POSSUM and its derivates, ASA, Charlson score and nutritional indexes was performed on 171 patients undergoing esophagectomy for cancer. A new prognostic score was created for severe morbidity prediction using all the significant components of the mentioned scores and a model.

RESULTS: Postoperative mortality (1.8%) was best predicted by O-POSSUM score. Overall morbidity was 36.3% (62 cases), severe complications (grade III-V) occurred in 23 cases. All the scores had a low discriminatory ability for severe complication prediction (AUC<0.66). Stepwise selection identified four independent predictors of severe morbidity: pulse (OR 8.77; 95%C.I. 2.91-26.44), altered pulmonary status (OR 3.44; 95%C.I. 1.19-9.95), albumin (OR 0.89; 95%C.I. 0.80-0.98) and neoadjuvant therapy (OR 7.43; 95%C.I. 0.84-65.88). The score based on those variables was internally validated using standard bootstrapping techniques and showed a good discrimination (AUC=0.81) and calibration (goodness-of-fit test: p=0.44).

CONCLUSION: Nutrition is an independent risk factor for major complications and an improvement of the current prognostic scores used in oncologic surgery can be made through the introduction in the formulas for the calculation of different physiological scores of a nutritional status coefficient.

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Disclosure of Interest: None Declared

Keywords: esophageal cancer, esophagectomy, nutritional status, postoperative complications, prognostic scores

P248 PET-CT AFTER NEOADJUVANT CHEMORADIOTHERAPY CAN PREVENT NON-CURATIVE SURGICAL INTERVENTIONS FOR ESOPHAGEAL CANCER PATIENTS

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INTRODUCTION: Esophageal cancer is notorious for its rapid dissemination. Accurate staging at the time of diagnosis is essential to identify patients eligible for curative treatment. For the majority of these patients the preferred strategy consists of neoadjuvant chemoradiotherapy (nCRT) followed by esophagectomy. Given the aggressive nature of esophageal tumours, it is conceivable that in a significant portion of patients treated with nCRT, dissemination becomes manifest during this preoperative course. Since metastatic disease is a contraindication for esophagectomy, we added a post-neoadjuvant therapy PET-CT to the standard work-up of patients with potentially resectable esophageal carcinoma.

AIMS&METHODS: The aim of this study was to determine the value and diagnostic accuracy of PET-CT after nCRT in identifying patients with metastases preoperatively.

From January 2011 until February 2013 all esophageal cancer patients deemed eligible for a curative approach with nCRT and surgical resection underwent a PET-CT after completion of nCRT (median interval 18 days). Initial staging consisted of endoscopy with biopsy, EUS, external ultrasonography of the

neck and a thoracoabdominal CT scan. A PET scan was not part of the initial staging. Neoadjuvant therapy consisted of 5 cycles of carboplatin/paclitaxel and concurrent radiotherapy (41.4 Gy). If abnormalities on PET-CT were suspect of metastases, histologic proof was acquired. We designed a clinical decision model to assess the cost-effectiveness of this diagnostic strategy.
RESULTS: During the study period 173 patients underwent a PET-CT after nCRT. In 37 patients (21.4%) PET-CT showed abnormalities suspicious for dissemination requiring additional imaging and/or biopsy, resulting in 20 cases of proven metastasis (11.6%) and a risk of false-positive results of 9.8%. Of the patients without proven metastases 147 patients have been operated at this time. In 7 of these 147 cases distant metastases were detected intraoperatively, leading to a risk of false-negative results of 4.8%. The introduction of a post-neoadjuvant therapy PET-CT has led to a reduction of overall health care costs per patient in comparison with the scenario in which no restaging occurs (€26880 vs. €28970).
CONCLUSION: In 11.6 percent of esophageal cancer patients distant metastases are seen on PET-CT after neoadjuvant chemoradiotherapy. To avoid non-curative resections we advocate post-neoadjuvant therapy PET-CT as a cost-effective part of the standard work-up of candidates for surgery.
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Disclosure of Interest: None Declared
Keywords: Esophageal cancer, Esophagectomy, Interval metastases, Neoadjuvant chemoradiation, PET-CT scan

P249 SENTINEL NODE NAVIGATION SURGERY FOR GASTRIC CANCER BY USE OF INDOCYANINE GREEN

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INTRODUCTION: The sentinel node (SN) is the first lymph node to receive drainage from the primary tumor. In order to detect the sentinel node, there are various kinds of tracers (radiolabeled particles and vital dyes). The prediction of node status in breast cancer or malignant melanoma has been reported to exceed 95 %. However, it is not clear whether sentinel node navigation surgery is applicable to gastric cancer surgery or not. We investigated the feasibility of sentinel node staining and its accuracy in predicting the lymph node status in patients with gastric cancer.
AIMS&METHODS: 45 gastric cancer cases who underwent curative surgery from April 2001 to December 2011 at Japan Railway Tokyo General Hospital (Male 33 cases, Female 12 cases, 62.3 ± 10.0 years (45-80) IA 38 cases, IB 5 cases, II 2 cases). In all patients, the absence of cancer invasion to the serosal layer of the stomach was macroscopically confirmed. [Method] After laparotomy, a fine needle (26-gauge) was inserted into the subserosal layer around the primary tumor and ICG was injected. Total amount of injected ICG was 25 mg (5 ml) for each patient. SN were defined as lymph nodes those were stained green within 5 minutes after ICG injection and were removed before therapeutic surgery with extended lymph node dissection (D2 procedure according to the Japanese classification of gastric carcinoma). Stained nodes (SN), unstained nodes (non-SN), and resected stomach were fixed in 20 % formalin and embedded in paraffin, and 5-micrometer sections were cut to be stained with hematoxylin and eosin for histologic examination. We compared the location and numbers of SN and histological diagnosis of SN and non-SN. We calculated patient survival by Kaplan Meier mehod and compared between sentinel node navigation surgery and standard surgery.
RESULTS: The rate of staining of SN was 97.5 % (44/45). The number of SN was 3.6 ± 2.4 (1-8), and that of non-SN was 19.2 ± 8.5 (13-37). The number of cases with LN metastasis was 20.5 % (9/45). Five year patient survival in Stage IA group was 95.5 %, which revealed no significant difference to 96.7 % among Stage IA gastric cancer patients who underwent standard surgery in the same time.
CONCLUSION: In 44 cases (97.8 %) out of 45 patients, SN could be found by use of ICG staining method. In 9 cases, LN metastasis were histopathologically diagnosed. In all the 9 cases, we found metastasis also in SN. SN status can predict the lymph node status accurately in patients with T1 and T2 gastric cancer. When you find no metastases in SN in T1 or T2 gastric cancer patients, you can perform partial resection of stomach with more limited lymph node dissection. Sentinel node navigation surgery was comparable to standard surgery for relatively early stage gastric cancer patients.
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Disclosure of Interest: None Declared
Keywords: gastric cancer, sentinel lymphnode

P250 NEW CONCEPT OF MINIMALLY-INVASIVE GASTRECTOMY FOR EARLY GASTRIC CANCER: FEASIBILITY OF NON-EXPOSED ENDOSCOPIC WALL-INVERSION SURGERY (NEWS) WITH SENTINEL NODE NAVIGATION SURGERY (SNNS) IN A PORCINE SURVIVAL MODEL

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INTRODUCTION: Non-exposed endoscopic wall-inversion surgery (NEWS) has been invented as endoscopic full-thickness resection without transluminal communication to avoid contamination or tumor seeding into the peritoneum[1)].
AIMS&METHODS: In this porcine survival study, we aimed to investigate feasibility and safety of NEWS with sentinel node navigation surgery (SNNS)[2)], which could minimize the area of lymph node dissection for early gastric cancer (EGC), as a new surgical concept of minimally-invasive gastrectomy. The study protocol was approved by the institutional ethical review board of the laboratory in advance. NEWS with SNNS was performed in three live female pigs weighing 25-35kg. After marking around a simulating lesion on both the mucosal and serosal surfaces, 0.5ml of indocyanine green (ICG) fluid (5mg/ml) was endoscopically injected into the submucosa at four points around the lesion. Subsequently, sentinel nodes basin stained with ICG were identified and dissected laparoscopically, followed by circumferential seromuscular incision and suturing around the lesion. Finally, circumferential mucosubmucosal incision was made endoscopically followed by endoscopic handsuturing of the mucosal edges. The pigs resumed feeding from the day after the operation. Antibiotic with cefazolin sodium hydrate, 0.5g once daily, was administered intramuscularly on the day of operation and perorally on the following three days. They were monitored daily over a period of seven days and sacrificed for necropsy.
RESULTS: Each lesion was created on the anterior wall, the posterior wall and the greater curvature of the gastric body in the three pigs respectively. The procedure was successfully completed without complications and survived without adverse events during the observatory period in all cases. The median of the specimen size and the procedure duration was 35 (range, 25-50) mm and 203 (range, 189-253) min, respectively. Necropsy revealed mild adhesion of the suture site to surrounding organs, but no anastomotic leak or peritonitis.
CONCLUSION: This study demonstrated that NEWS with SNNS was feasible in a live animal model. It can provide patients with early gastric cancer out of the indication for endoscopic resection a minimally-sized gastrectomy and minimally-ranged lymph node dissection without the risk of contamination or tumor dissemination.
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Disclosure of Interest: None Declared
Keywords: endoscopic full thickness resection (EFTR), gastrectomy, minimally invasive, non-exposed endoscopic wall-inversion surgery (NEWS), sentinel lymph node

P251 LONG-TERM POSTOPERATIVE EVALUATION OF JEJUNAL POUCH INTERPOSITION RECONSTRACTION AFTER TOTAL GASTRECTOMY IN TERMS OF FUNCTIONAL PRESERVATION AND QUALITY OF LIFE

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INTRODUCTION: Jejunal pouch interposition (JPI) reconstruction has been chosen for preserving the function of the stomach after total gastrectomy, but the long-term results have not yet been determined.
AIMS&METHODS: The aim of this study is to evaluate the functional preservation and QOL of Jejunal pouch interposition reconstruction in patients after total gastrectomy for the long term. We studied 94 patients with gastric cancer who underwent total gastrectomy. Thirty eight patients were reconstructed with JPI (Group J) and 56 patients with Roux Y (Group R). Dietary intake (compared to preoperative condition), body weight (compared to preoperative condition), gastroesophageal reflux, and dumping syndrome were evaluated by means of a QOL questionnaire. Dietary intake and body weight after 1 year of surgery were compared between the two groups. The nutrition status and the QOL questionnaire were assessed annually for 22 patients of Group J who were investigated more than 3 years (until 10 years) after surgery.
RESULTS: % dietary intake in Group J (83.4±13.0%) (mean±SD) was significantly higher than that in Group R (69.8±18.1%) ($p<0.05$). The ratio of the patients under 80 % body weight compared to preoperative condition is significantly lower in Group J (13.1%) than in Group R (32.1%). In 22 patients of Group J with more than 3 years observation, dietary intake, body weight, total protein, albumin and total cholesterol was significantly decreased one year after surgery, but there were no more significant decreases in these levels later. There was no chronological difference in lymphocyte count over the observation period. There was no deterioration in gastroesophageal reflux or dumping syndrome for the observational period either.
CONCLUSION: JPI is more beneficial to maintain dietary intake and body weight than Roux Y reconstruction after total gastrectomy. Dietary intake, body weight and nutrition status were significantly decreased for the first year after surgery, but after one year has lapsed, the levels remain constant in the JPI group.
Disclosure of Interest: None Declared
Keywords: gastric cancer, jejunal pouch interposition reconstruction, total gastrectomy

P252 VISCERAL ADIPOSE TISSUE CD4+CD25+FOXP3+ REGULATORY T CELLS - A NOVEL TISSUE-SPECIFIC PREDICTOR FOR EARLY WEIGHT LOSS FOLLOWING SLEEVE GASTRECTOMY

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INTRODUCTION: Adipose tissue has been recognized as an inflammatory active organ, which plays an important role in local and systemic inflammation.

Regulatory T cells (Tregs) have been identified as major regulatory components in adipose tissue inflammation. Metabolic changes after sleeve gastrectomy (SG), such as improvement in insulin resistance, may appear early after surgery, prior to significant weight loss. A favorable inflammatory cells' milieu within the adipose tissue may predict clinical outcomes following SG.
AIMS&METHODS: AIM - To evaluate the correlation between Tregs within the visceral adipose tissue and weight loss in obese patients undergoing SG
METHODS - Peripheral blood samples and intra-operative visceral adipose tissue biopsies were collected form consenting female patients undergoing elective SG (n=9). Weight loss was measured as excess weight loss (%EWL). Lymphocytes were isolated from each sample, counted and stained for flow cytometry analysis (FACS). CD4+CD25+FOXP3+ markers were used for Tregs identification. FACS analysis results were then correlated with %EWL at post-operative follow up.
RESULTS: The mean study group's age, weight and BMI were 34.7 years, 111.22 kg and 42.99 respectively. All patients underwent SG without complications. Follow up evaluation was performed 3 times: after 9.4, 76 and 164.1 days (n=5, 4 and 8 respectively), with %EWL of 10.5, 31.8 and 49.7 respectively. The percent of Tregs within the peripheral blood and visceral adipose tissue was 4.34% and 4.23% respectively. A strong correlation was demonstrated between the visceral adipose tissue Tregs and %EWL at the second follow up ($r = 0.9$). However, this correlation was not demonstrated in the third follow-up.
CONCLUSION: Baseline levels of Tregs in the intrinsic visceral adipose tissue, may predict early weight loss following SG. This correlation, emphasizes the value of the local inflammatory milieu within the adipose tissue in predicting early clinical outcomes following SG, and may indicate their potential as future therapeutic targets.
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Disclosure of Interest: None Declared
Keywords: regulatory T cells, sleeve gastrectomy

P253 TNM STAGING IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA AFTER ESOPHAGECTOMY WITH EXTENSIVE LYMPHADENECTOMY : PROGNOSTIC VALUE OF STAGE AND PROGNOSTIC GROUPING

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INTRODUCTION: The 7th edition of the TNM Classification (TNM7) uses tumor location and histologic grading with conventional T, N (number of the positive nodes), and M category for stage or prognostic grouping of esophageal squamous cell carcinoma (ESCC). However, the prognostic value of TNM7 in esophageal cancer after esophagectomy with extensive lymphadenectomy remains unclear.
AIMS&METHODS: The aim of this study was to evaluate the prognostic value of TNM7 in patients with ESCC who underwent transthoracic esophagectomy with 2- or 3-field lymphadenectomy. A total of 268 patients with pT3 ESCC underwent esophagectomy with extensive lymphadenectomy, between 1988 and 2010, and are included in this study. The survival rates at each stage or prognostic group of pT3 ESCC patients were evaluated using the log-rank method. Three-field dissection was performed for patients with a cancer in the upper or middle esophagus who were aged 70 years or younger. The median follow-up was 98 months.
RESULTS: 249 patients (93%) received R0 resection, and 152 patients (57%) had 3-field dissection. The median number of resected lymph nodes was 61 (range, 17-150). The numbers of patients at Stage IIA/IIIA/IIIB/IIIC/IV were 65/68/67/35/33, and those in Group IB/IIA/IIB/IIIA/IIIB/IIIC/IV were 18/33/14/68/67/35/33. The overall 5-year survival rate for all patients was 45.5%. The 5-year survival rate for Stage IIA, IIIA, IIIB, IIIC and IV was 71.6%, 51.4%, 42.8%, 20% and 15.2% (IIA vs IIIA, $P = 0.0265$; IIIA vs IIIB, $P = 0.1388$; IIIB vs IIIC, $P = 0.0183$; IIIC vs IV, $P = 0.3056$). The 5-year survival for Group IB, IIA and IIB was 77.8%, 65.1% and 78.6% (IB vs IIA, $P = 0.5807$; IIA vs IIB, $P = 0.8353$). The survival rate was not affected by either histologic grade or tumor location in the T3N0 ESCC patients.
CONCLUSION: Overall, introduction of a third tier for nodal involvement in TNM7 has good performance in survival stratification for T3 ESCC patients after transthoracic esophagectomy with extensive lymphadenectomy. Findings suggested that histologic grade and tumor location in prognostic grouping had no significant influence on survival in T3N0 ESCC patients with extensive lymphadenectomy.
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Disclosure of Interest: None Declared
Keywords: esophageal cancer, Esophagectomy, lymph node dissection, prognosis, TNM

P254 CHOICE OF RADICAL GASTRECTOMY MODALITY IN MIDDLE ONE-THIRD GASTRIC CANCER

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INTRODUCTION: In cases with resectable gastric cancer, distal or total gastrectomy is recommended. However, there remains controversy for choice of gastectomy modality in middle one-third gastric cancer. This study analyzed the differences between total gastrectomy (TG) and distal gastrectomy (DG).
AIMS&METHODS: To evaluate the rationality of radical distal and total gastrectomy in middle one-third gastric cancer. A total of 293 cases with middle one-third gastric cancer undergoing radical dissection in Gastrointestinal Department of Sun Yat-sen University from Aug. 1994 to Jan. 2008 were divided into distal gastrectomy(DG, n=94) and total gastrectomy group(RTG, n=199). The clinicopathological features, information of surgical procedure, operation complications, postoperative quality of life and prognosis were compared between 2 groups.
RESULTS: No significant difference had been found in gender, age, tumor histological type, and serum CEA level between 2 groups(all $P > 0.05$). Tumor size, infiltration depth, ratio of lymph node(LN) metastasis, distal metastasis, TNM stage IV and Borrmann infiltration type was significant higher in TG than that in DG (all $P < 0.05$). No significant difference existed in number of LN dissected, surgical complications between 2 groups(all $P > 0.05$). Postoperative hospital day, operation duration, volume of blood transfusion, ratio of combined organ dissection increased significantly in TG than in DG (all $P < 0.05$). Ratio of postoperative normal diet in DG(88.7%) was significantly higher than that in TG (68.8%)($P < 0.05$). Logistic regression analysis showed that tumor size, Borrmann type, and adjacent organ invasion were the major influencing factors of gastectomy modality. Multivaritate analysis showed that LN metastasis, distal metastasis, Borrmann type, and tumor size were independent prognostic factors for all cases. Prognosis of RDG group was significantly better than that of RTG group($P < 0.05$). Stratified analysis(stratified by tumor size, organ invasion, LN metastasis, distal metastasis, Borrmann type) showed that prognosis in TG was not better than that in DG.
CONCLUSION: For cases with resectable middle one-third gastric cancer, radical distal gastrectomy should be considered as first-line choice. Compared with radical distal gastrectomy, radical total gastrectomy had more serious surgical trauma, and no beneficial to the postoperative quality of life and prognosis.
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Disclosure of Interest: None Declared
Keywords: Digestive system surgical procedure, Gastrectomy, Middle one-third gastric cancer, Prognosis

P255 EVALUATION OF CURRENT T STAGE OF TRANSVERSE MESOCOLON INVASION IN ADVANCED GASTRIC CANCER

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INTRODUCTION: There remains controversy for T classification of transverse mesocolon invasion in advanced gastric cancer(AGC). This study was performed to evaluate the appropriate T stage for transverse mesocolon invasion in AGC.
AIMS&METHODS: To evaluate T stage of transverse mesocolon invasion in advanced gastric cancer. According to status of transverse mesocolon invasion, 808 cases of gastric cancer with T4a+b stage undergoing surgical treatment(form Jan. 1996 to Jan. 2008, cases were screened form data base of Gastric Cancer Center of Sun Yat-sen University) were divided into group of Non-organic invasion(T4a stage, NOI, n=638), Non-transverse mesolon invaded (T4b stage, NTMI, n=126), TMI (Transverse mesocolon invaded, n=44). The clinicopathological features, surgical procedure and prognosis were compared in three groups.
RESULTS: No significant difference were found in gender, age, lymph nodes metastasis, heptic metastasis, tumor's Borrmann type, histological type, differentiation degree, value of serum CEA among 3 groups(all $P > 0.05$). In group of NOI, NTMI and TMI, significant difference had been found in tumor size, distal metastasis, peritoneal metastasis, TNM IV stage, ratio of radical resection ($P < 0.01$), and pairwise comparisons showed these parameters with significant difference between NOI and TMI group($P < 0.05$), but without significant difference between NTMI and TMI group($P > 0.05$). Significant difference existed in median survival time in 3groups ($P < 0.05$), and pairwise comparisons showed the prognosis with significant difference between NOI and TMI group($P < 0.05$), but without significant difference between NTMI and TMI group($P > 0.05$). In cases received radical resection, the median survival time in 3 groups had significant difference($P < 0.05$), and pairwise comparisons showed the prognosis with

significant difference between NOI and TMI group($P<0.05$), but without significant difference between NTMI and TMI group($P>0.05$).

CONCLUSION: The major clinicopathological features, surgical procedure and prognosis of gastric cancer with transverse mesocolon invasion was similar to that of T4b gastric cancer, but was significant different from that of T4a gastric cancer. Gastric cancer with transverse mesocolon invasion should be regarded as T4b stage.

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Disclosure of Interest: None Declared

Keywords: Stomach neoplasms, TNM classification, Transverse mesocolon

P256 ASSISTANT-BASED STANDARDIZATION OF PRONE POSITION THORACOSCOPIC ESOPHAGECTOMY

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INTRODUCTION: In recent years, the popularity of thoracoscopic esophagectomy in the prone position is increasing because of the excellent exposure of the surgical field and ergonomic advantages for the surgeon. Solo-surgery is also possible in most cases requiring resection of the esophagus and surrounding lymph nodes. However, no consistent approach that can be used for all cases of extensive lymphadenectomy (as conducted in Japan) has been described. In April 2012, we developed the standardization of assistant-based procedure for exposure of the surgical field during thoracoscopic esophagectomy in the prone position. The purpose of the present study is to introduce and evaluate this technique.

AIMS&METHODS: We performed thoracoscopic esophagectomy in the prone position on 65 patients (62 males, 3 females) at our facility from June 2011 to September 2012. The preoperative diagnosis was squamous cell carcinoma in 61 patients, adenocarcinoma in 2, and mixed squamous cell carcinoma combined with neuroendocrine tumor in 2. Preoperative adjuvant chemotherapy was administered to 45 patients. Three patients underwent salvage surgery following radical chemoradiotherapy. Patients were divided into two groups: a pre-standardization group ($n = 35$) that was operated before April 2012 and a post-standardization group ($n = 37$) that was operated after April, 2012. We examined the thoracoscopic operative time and the clinical outcomes of these two groups.

RESULTS: The thoracoscopic operative time was significantly lesser ($P = 0.0037$) in the post-standardization group (after April 2012; $n = 28$; 266.8 ± 31.3 min) than in the pre-standardization group (before April 2012; $n = 37$; 301.0 ± 52.5 min). The learning curve analysis using the moving average method showed the stabilization after the standardization. No significant differences were found in the number of mediastinal lymph nodes dissected, blood loss during thoracic surgery. There were no significant differences in the overall complication rate and incidence rate of pneumonia or recurrent nerve palsy between the 2 groups.

CONCLUSION: Thoracoscopic esophagectomy in the prone position decreased the operative time even in patients requiring extensive lymphadenectomy by an excellent and safe surgical field maintained by assistant-based surgery and standardization of procedure.

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Disclosure of Interest: None Declared

Keywords: Prone position, Standardization, Thoracoscopic esophagectomy

P257 PROCEDURE TIME ONLY AFFECTS THE ULCER HEALING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: In recent years, the technique of gastric endoscopic submucosal dissection (ESD) has markedly improved. However, major complications, especially delayed bleeding, occur in approximately 5% of all patients who undergo gastric ESD. For prevention of delayed bleeding, it is necessary to accelerate healing of the artificial ulcer. Several reports showed the accelerated effect of acid-suppressive drugs or mucosal-protective agents and the delayed effect of ulcerative or scarring lesion. However, the effects of these factors on artificial ulcers that occur after ESD remain unclear. Therefore, we investigated the diminution rates of the ulcers 4 weeks after ESD to clarify the factors regulating artificial ulcer healing.

AIMS&METHODS: Between January 2009 and February 2013, 282 early gastric neoplasms in 315 consecutive patients who underwent gastric ESD, performed by a single physician, were enrolled in this study. All patients were divided into 2 groups: A) $<90\%$ diminution group and B) $\geq 90\%$ diminution group, and retrospectively investigated by univariate and multivariate analysis in terms of location/size/depth of tumor, daily use of gastric mucosal injury drugs, procedural time, sufficient post-ESD coagulation, drugs administered (PPI or PPI+mucosal-protective agents), and *Helicobactor pylori* status.

RESULTS: The average ($\pm$SD) procedure time was 74.60 ± 53.45 min; the rate of en bloc resection was 99.29%; and the rate of complete resection was 93.26%. Perforation complications were 0%, while the rate of delayed bleeding was 2.86%. The diminution rate after 4 weeks was $95.43 \pm 8.12\%$. In the $<90\%$ diminution group and $\geq 90\%$ diminution group, it was 12% and 88%, respectively. Only longer procedural time ($P = 0.042$; OR, 0.45; 95% CI, 0.20–0.97) was independent factors, indicating a diminution rate of $\geq 90\%$.

CONCLUSION: Our results showed that gastric ulcer healing after ESD was regulated by only procedural time, not others. Procedural time under technical stability means difficulty of vascular treatment and/or dissection itself. Therefore, it indicates that electrical injury of ulcer bed during the ESD procedure only affects ulcer healing.

Disclosure of Interest: None Declared

Keywords: gastric ESD, procedure time, ulcer healing

P258 STOOL CALPROTECTIN LEVELS IN PRETERM INFANTS WITH AND WITHOUT NECROTISING ENTEROCOLITIS

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INTRODUCTION: Necrotising enterocolitis (NEC) remains the most devastating disease of the gut of preterm infants. Early signs can be non-specific and present diagnostic challenges. Faecal calprotectin (FC) is an established marker of intestinal inflammation, but its role in the management of NEC is uncertain. We assessed this as a diagnostic tool for preterm infants with NEC.

AIMS&METHODS: We recruited infants <32 weeks gestation and <1.5Kg birth weight within week 1 of life from 3 Neonatal Units. NEC was confirmed by an external observer and radiologist, with staging according to Bell's Criteria. Weekly FC measurements were performed by ELISA (PhiCal, Norway).

RESULTS: N=56 (61% female). 32 were diagnosed with NEC (56%). 20 had $\geq$Bells' 2a. 8 required surgical intervention.

There were no significant differences in FC levels between each week in infants with or without NEC, although the former illustrated a trend to lower levels by week 4 (p=0.096). Many NEC infants developed concurrent ileus with lower stool production. There were no significant differences in NEC before and after clinical signs were apparent (p=0.1179), or in those before NEC and after stoma formation for stage 3b NEC (p=0.3026). However, significantly lower FC levels were noted in stage 3b NEC requiring ileostomy post-operative compared to the immediate sample before (p=0.0327).

Table 2: FC Values (μg/g)

Parameter	NEC (20) [n with samples]	Non-NEC (24) [n with samples]	P value
Week 1 (med, r)	285.6, 113 – 699 [10]	291.2, 49 – 2011 [22]	NS
Week 2 (med, r)	275.1, 81.7 – 2003 [13]	207.1, 89 – 2249 [24]	NS
Week 3 (med, r)	274.2, <5 - 968.3 [15]	273.1, 74 – 2414 [23]	NS
Week 4 (med, r)	220.5, 5 - 587.4 [13]	378.1, <5 – 2413 [22]	NS

CONCLUSION: FC levels were high in those with and without NEC, and the only significant change noted was lower levels after ileostomy formation. A limitation was the onset of severe NEC resulting in prolonged paralytic ileus with low stool production.

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Disclosure of Interest: None Declared

Keywords: calprotectin, necrotising enterocolitis, Preterm

MONDAY, OCTOBER 14, 2013 9:00–17:00

IBD I – Poster Area

P259 ENDOSCOPIC SUBMUCOSAL INJECTION OF ADIPOSE-DERIVED STEM CELLS AMELIORATES TNBS-INDUCED COLITIS IN RATS

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INTRODUCTION: TNBS-colitis is a well studied model resembling inflammatory bowel disease. Adipose-derived mesenchymal stem cells (ASC), due to their immunomodulatory properties have a potential role in IBD therapy.
AIMS&METHODS: Aim: To evaluate the feasibility, safety and efficacy of endoscopic administration of expanded human ASC (h-eASC) in a TNBS-induced colitis model in rats.
On day 0, colitis was induced in SD-OFA male rats (375-400 g) by rectal instillations of 0.5 ml of Trinitrobenzensulfonic acid (TNBS) 30 mg/ml in 50% ethanol. On day 1 a colonoscopy was performed with a 5.9 mm endoscope (GIF-XP160, Olympus Optical Co). Rats were randomly assigned to treatment group (ASC: 10^7 cells, endoscopically injected divided in 4 spots in the submucosa using a 22 G endoscopic needle) or placebo (phosphate buffered saline, PBS). h-eASC were provided by Tigenix SAU (Tres Cantos, Spain), isolated and cultured from healthy donors and characterized as usual. Superficial markers were: HLA-II, CD40, CD80, CD86, CD34, CD14, CD18, CD45 negative; HLA-I, D90, CD105 positive. On day 11 another colonoscopy was performed and rats sacrificed.
The following variables were analysed: a)Daily weight (% from day 0); b)Endoscopic score (day 1-11) including inflammation degree (0-6), length (0-10), ulcer appearance (0-5), stenosis (0-2), colon thickening (0-3) and bleeding (0-1); c)Colon length; d)Macroscopic appearance in necropsy scored 0-3 for each: colon vascularisation, wall thickening and adherences.
RESULTS: Colitis was induced in 46 rats: 25 e-hASC group/21 PBS group. 26 rats were used as healthy controls.
Injection was successful in all rats, with visible submucosal bleb formation. No significant adverse events nor mortality due to the procedure occurred.
Weight recovery was significantly better in ASC group on day 9 (-8.45% vs -3.66%, p 0.034), 10 (-8.42% vs -1.94%, p0.013) and 11 (-6.72% vs -0.84%, p0.037).
Colon length significantly recovered (ASC 222 mm vs PBS 193 mm vs healthy controls 235 mm) ASC vs PBS p0.000.
Endoscopic score change between day 1 and 11 improved in ASC group -6.65 points vs -3.53 in PBS group p0.011.
Correlation between endoscopic score and weight loss was excellent r0.75 on day 1 p0.000 and r0.77 on day 11 p0.000.
Stenosis more frequently developed in PBS group (41.2% vs 4.8%) p0.01
Macroscopic necropsy score showed a trend towards less inflammation although it didn't achieve statistic signification. There were no differences in mortality.
CONCLUSION: h-ASC submucosal endoscopic injection is feasible, safe and ameliorates TNBS-induced colitis.
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Disclosure of Interest: E. Martin Arranz Consultancy for: Cellerix SA, M. D. Martin Arranz: None Declared, T. Robredo: None Declared, P. Macheño Other: Employee Tigenix SAU, R. Menta Other: Employee Tigenix SAU, J. Diez: None Declared, E. Lombardo Other: Employee Tigenix SAU, F. de Miguel Pedrero: None Declared
Keywords: colitis, Endoscopic therapy, IBD, Stem Cells, TNBS

P260 IDENTIFICATION OF CD68+ NEUTROPHIL GRANULOCYTES IN IN VITRO MODEL OF ACUTE INFLAMMATION AND INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: CD-68 is widely regarded as a selective marker for human monocytes and macrophages and is commonly used in human pathology studies. The purpose of this study was to investigate the expression of CD-68 in human peripheral blood mononuclear cells (PBMCs), neutrophil granulocytes (NGs) and in inflamed intestinal tissue samples for comparison
AIMS&METHODS: PBMCs and NGs were isolated from heparinized human blood samples. Intestinal biopsies were obtained during routine endoscopic procedures from patients with inflammatory bowel disease (IBD), e.g. ulcerative colitis and Crohn's disease. Gene and protein expression was analyzed by real-time RT-PCR, Western blot and immunohistochemistry.
RESULTS: Both PBMCs and NGs preparations contained cells that were positive for CD-68 and either neutrophil elastase (NE), or myeloperoxidase (MPO). $CD\text{-}68^+/NE^-/MPO^-$ cells were regarded as monocytes. CD-68 mRNA expression was detected in PBMCs and NGs preparations. With Western blot and by performing immunoprecipitation of cell lysate, we could clearly detect CD-68 in NGs, U-937, THP-1, Hep-G2, Jurkat cells and PBMCs. Identification of inflammatory cells in acutely inflamed colonic mucosa obtained from patients with IBD revealed a strong accumulation of $CD\text{-}68^+/MPO^+$ cells compared to normal colonic mucosa. The uptake of the marker by phagocytosis was excluded by performing a double staining with CD-163/NE and CD-163/MPO in PBMCs, NGs cultures and in inflamed colonic mucosa.
CONCLUSION: These results identify $CD\text{-}68^+$ neutrophil granulocytes in peripheral blood and inflamed colonic mucosa from patients with inflammatory bowel disease. CD-68 is not only a marker for the macrophages-monocytes but also for NGs. The presence of $CD\text{-}68^+$ neutrophils could be an index of the disease inflammatory activity in patients with inflammatory bowel disease.
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Disclosure of Interest: None Declared
Keywords: CD-68, inflammatory bowel disease, neutrophil granulocytes, peripheral blood mononuclear cells

P261 BENEFICIAL THERAPEUTIC EFFECTS OF INTRAVENOUSLY ADMINISTERED FREE-CIRCULATING DNA OF COLITIC ORIGIN IN DSS-COLITIC MICE

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INTRODUCTION: Inflammatory bowel diseases (IBD) are characterized by aberrant innate and adaptive immune responses to commensal bacteria. The presence of free-circulating DNA (fcDNA) sequences in the serum is an established phenomenon in IBD. A close correlation between the quantity of fcDNA and the course or prognosis of several pathologic conditions has already been described. Diagnostic, prognostic, and therapy monitoring roles of fcDNA in regards to chronic colonic disorders have also been examined, however, its biological function still remains unclear.
AIMS&METHODS: The immunobiological effects of isolated, intravenously administered fcDNA of normal and colitic origin were assayed in both a murine model of DSS-colitis and in control mice. After disease- and histological activity evaluations, the changes in Toll-like receptor 9 signaling and the pro- and anti-inflammatory cytokine profile were assayed in isolated immune cells of the lamina propria by real-time quantitative PCR array cards.
RESULTS: Intravenously administered colitis-derived fcDNA has a more prominent beneficial effect on the clinical and histological severity of DSS-induced colitis in mice than fcDNA of normal origin. The systemic administration of colitis-derived fcDNA alters both TLR9-related signaling (i.e. Tollip, IRAK, TRAF6, IkB) and the pro-inflammatory cytokine profile (IFN-A, -B) in a favorable manner, while it has no significant effect on anti-inflammatory interleukin 10 expression.
CONCLUSION: Our study unveiled a novel function of intravenously administered fcDNA in a murine model of DSS-colitis. Induction of colitis itself may result in producing fcDNA with a potential to down-regulate inflammation, hence intravenous administration of fcDNA appears to be a promising novel approach in the treatment strategies of colitis.
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Disclosure of Interest: None Declared
Keywords: DSS-colitis, innate immunity, Toll like receptor-9

P262 MODULATION OF VIPERGIC PHENOTYPE OF ENTERIC NEURONS BY COLONIC BIOPSY SUPERNATANTS FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASES: INVOLVEMENT OF IL-6 IN CROHN'S DISEASE

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INTRODUCTION: Neuroplastic changes in the enteric nervous system (ENS) observed during inflammatory bowel diseases (IBD) might participate in physiopathological process. The involvement of mucosal microenvironment in these changes remains unknown
AIMS&METHODS: Colonic biopsies and their supernatants (SUP) (obtained following 25 min incubation of biopsies in Krebs solution) were collected in inflamed (I) and non-inflamed (NI) area of patients with Crohn's diseases (CD; n=12), Ulcerative Colitis (UC; n=6) and in healthy controls (HC; n=12). ENS primary cultures were incubated with SUP or cytokines and VIP concentration in ENS was measured by ELISA and RT-qPCR. VIP and cytokines profile were quantified in biopsies by RT-qPCR
RESULTS: In biopsies, VIP mRNA expression was lower in patients with CD than with UC ($p = 0.006$), but was similar to HC. VIP mRNA and protein expression were significantly lower in ENS incubated with SUP-CD than with SUP-UC ($p = 0.002$ and $p < 0.01$, respectively). Disease differentially modulated VIP in ENS as a function of inflammation. In particular, SUP-CD-I reduced VIP concentration in ENS as compared to SUP-CD-NI ($p = 0.03$) while SUP-UC-I tended to increase VIP concentration in ENS compared to SUP-UC-NI ($p = 0.07$). In biopsies, VIP mRNA expression was correlated to IL-6 mRNA expression ($r = 0.429$, $p = 0.009$). In the ENS, IL-6 dose dependently reduced VIP mRNA and protein expression and the effects of SUP upon VIP expression were blocked by anti IL-6 antibody.
CONCLUSION: Our study demonstrates that colonic mucosal soluble factors differentially modulate neuroplastic changes observed in IBD according to the disease. IL-6 was responsible for reduced VIP expression in CD. Therefore, approaches aimed at blocking IL-6 might restore normal VIP level and thereby enhance barrier functions as well as reduce inflammation
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, enteric nervous system, IL-6, ulcerative colitis, vaso intestinal peptide

P263 ACTIVATION OF TOLL-LIKE RECEPTOR (TLR) 5 BY FLAGELLIN INDUCES A PRO-FIBROGENIC PHENOTYPE IN HUMAN INTESTINAL FIBROBLASTS (HIF) – A NOVEL PATHWAY MEDIATED BY MYD88 AND CASPASE 1

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INTRODUCTION: Intestinal fibrosis is caused by excessive extracellular matrix deposition by myofibroblasts. Activation of TLRs and Nod-like receptors (NLRs) by gut bacteria mediates an abnormal innate immune response in inflammatory bowel disease (IBD).

AIMS&METHODS: We investigated whether TLR or NLR ligands also induce a fibrogenic response in HIF.

HIF from Crohn's disease, ulcerative colitis and control normal mucosa were exposed to ligands for TLR2/6, 4, 5, Nod1, TGF-β1, BzATP (extracellular ATP), *S. typhimurium* and its flagellin-negative *FljB/FliC* variant, and supernatants assessed for fibronectin (FN), collagen I (Col1), TGF-β1 and IL-6 content. TLR signaling, VCAM1 and ICAM1 expression were investigated and inhibition of TGF-β1, MyD88 and p38MAPK signaling or inhibition of caspase-1 activation was performed using siRNA and blocking agents, immunoblotting, flow cytometry and immunoprecipitation.

RESULTS: All TLR and NLR ligands failed to induce FN or Col1 production by HIF except for flagellin which, alone or combined with Nod1, TLR2/6 or TLR4, significantly increased FN and Col 1 production. This TLR5-mediated response was independent of TGF-β1 signaling. Combined with TGF-β1, TLR5 augmented FN secretion and sensitized HIF to the subsequent action of TGF-β1. All TLR and NLR ligands induced IL-6 secretion, and while flagellin-positive *S. typhimurium* induced FN production by HIF, its flagellin-negative variant failed to do so. Interestingly, the inflammasome activator BzATP enhanced TLR5-induced FN production by HIF. The TLR5 ligand-induced FN secretion was dependent on MyD88, p38MAPK signaling and caspase-1 activation.

To investigate additional effects on fibrogenesis, we found that flagellin, alone or in combination with other TLR or NLR ligands, upregulated VCAM-1, but not ICAM-1, expression by HIF. This enhanced the ability of HIF to bind primary human monocytes, the predominant source of TGF-β1. In fact, monocyte-derived TGF-β1 appeared to be critical for activation of HIF.

CONCLUSION: Activation of TLR5 by flagellin induces a fibrogenic response by HIF that is dependent on MyD88, p38MAPK and caspase-1, but independent of TGF-β1. TLR5 activity on HIF could be boosted by the inflammasome activator BzATP. This direct fibrogenic response is distinct from the inflammatory response, but flagellin also induces fibrogenesis indirectly by promoting HIF-monocyte binding. These results suggest a functional network among bacterial immunity, the inflammasome and excessive matrix production in IBD-associated fibrosis.

Disclosure of Interest: None Declared

Keywords: Collagen, Crohn's disease, Fibrosis, Innate Immunity, Toll like receptor

P264 SUCCESSFUL PREVENTIVE INTRAVENOUS ADMINISTRATION OF FREE-CIRCULATING DNA OF COLITIC ORIGIN IN DSS-COLITIC MICE

G. Mű zes[1,*], F. Sipos[1], I. Fűri[1], B. Wichmann[1], S. Spisák[1], T. M. Germann[1], M. Constantinovits[1], Z. Nagy[1], G. Valcz[1], T. Krenács[2], Z. Tulassay[1], B. Molnár[1]. [1]*2nd Department of Internal Medicine,* [2]*1st Department of Pathology and Experimental Oncology, Semmelweis University, Budapest, Hungary*

INTRODUCTION: Inflammatory bowel diseases (IBD) are characterized by aberrant innate and adaptive immune responses to commensal bacteria. The presence of free-circulating DNA (fcDNA) sequences in the serum is an established phenomenon in IBD. A close correlation between the quantity of fcDNA and the course or prognosis of several pathologic conditions has already been described. Diagnostic, prognostic, and therapy monitoring roles of fcDNA in regards to chronic colonic disorders have also been examined, however, its biological function and preventive immunobiologic effects still remains unclear.

AIMS&METHODS: The colitis preventive immunobiological effects of isolated, intravenously administered fcDNA of normal and colitic origin were assayed in both a murine model of DSS-colitis and in control mice. DSS-colitis was induced 5 days after intravenous fcDNA administration in C57bl/6 mice. After disease- and histological activity evaluations, the changes in Toll- like receptor 9 signaling and the pro- and anti-inflammatory cytokine profile were assayed in isolated immune cells of the lamina propria by real-time quantitative PCR array cards.

RESULTS: Intravenously administered colitis-derived fcDNA has a more prominent preventive effect on the clinical and histological severity of DSS-induced colitis in mice than fcDNA of normal origin. The systemic administration of colitis-derived fcDNA alters TLR9-related signaling (i.e. Myd88, IRAK, TRAF6, IkB), the pro-inflammatory (i.e. IL-6, TNF-alpha) and the anti-inflammatory cytokine (i.e. IL-10) profile in a favorable manner.

CONCLUSION: Our study unveiled a novel function of intravenously administered fcDNA in DSS-colitic mice. Preventive intravenous administration of fcDNA appears to be a promising novel approach to the treatment modalities of colitis.

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Disclosure of Interest: None Declared

Keywords: cytokine, DSS-colitis, Innate Immunity, prevention, Toll like receptor-9

P265 CD24-BASED ASSESSMENT OF NOD2-INFLUENCE ON PANETH-CELL NUMBERS USING INTESTINAL STEM CELL CULTURES AND GENETIC ASSOCIATION ANALYSIS OF CD24 IN IBD

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INTRODUCTION: Environmental conditions, notably co-housing with WT littermates, and mouse genetic background influence NOD2-dependent defensin production.[1] An increase in the number of Paneth-cells, could compensate for a NOD2-dependent reduction in the level of defensin-production in Paneth-cells. CD24, a marker of intestinal crypt stem cells and Paneth-cells, is upregulated in Inflammatory Bowel Disease (IBD).[2, 3] A deletion polymorphism (rs3838646) in the 3' Untranslated Region, which reduces the stability of CD24mRNA, has been associated with susceptibility to Crohn's Disease(CD) (OR 1.61) plus protection against chronic Hepatitis B Virus infection, systemic lupus erythematosus and multiple sclerosis.[4, 5]

AIMS&METHODS: Our aims were to assess the influence of NOD2-status on Paneth-cell numbers (by CD24-based flow cytometry) using mouse intestinal stem cell cultures (organoids), and to determine the role of the CD24 gene polymorphism (rs3838646) in the genetic susceptibility to IBD, in the high incidence Scottish population characterized by a low allelic frequency of the "common" CD-associated NOD2 variants.[6]

Small intestinal stem cell crypts were isolated from C57BL/6 NOD2WT and NOD2KO mice, housed separately in specific pathogen-free conditions.[2] Intestinal crypts were cultured in Matrigel and organoid medium containing R-Spondin, murine recombinant Noggin and Epidermal Growth Factor.[2] We performed a genetic association analysis of the rs3838646 polymorphism in 1038 adult IBD patients, 351 childhood onset IBD and 940 healthy controls.[7]

RESULTS: There was no difference in Paneth-cell numbers (CD24hi, Side Scatter +) between NOD2WT and NOD2KO intestinal organoids using flow cytometry(3.83% vs. 3.9%). Due to the presence of a CD24-pseudogene on the Y-chromosome, only female IBD patients (n=737) vs. female controls (n=498) were analysed to avoid non-specific amplification of the TaqMan assay. Our study had 80% power to detect association with OR 1.46 and OR 1.62 (with IBD and CD, respectively). Genotype frequencies and allelic frequency did not differ between IBD/CD and controls ($p > 0.5$).

CONCLUSION: Using intestinal stem cell cultures from NOD2WT and NOD2KO, we have demonstrated by means of CD24-based flow cytometry that NOD2-status does not influence Paneth-cell numbers. In the high-incidence Scottish IBD population, the CD24 gene polymorphism (rs3838646) is not an important determinant of genetic susceptibility to IBD/CD.

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Disclosure of Interest: None Declared

Keywords: genetics, inflammatory bowel disease, intestinal stem cells, NOD2, Paneth cells

P266 GENETICS DO NOT DRIVE P-ANCA EXPRESSION IN TWINS WITH ULCERATIVE COLITIS

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INTRODUCTION: Inflammatory bowel disease (IBD) is believed to be caused by an inappropriate immune response to gut microbiota in genetic susceptible individuals. Several serologic markers to microbial antigens have been observed in Crohn's disease. In contrast, ulcerative colitis has been associated with perinuclear antineutrophil cytoplasmic antibodies (pANCA) only. The significance of pANCA in the pathophysiology of ulcerative colitis remains largely unknown. Early observations reported an increased presence of pANCA in first-degree relatives of patients with ulcerative colitis, indicating that shared environment or genetic predisposition might play a role. However, these findings have not been replicated in all subsequent studies.

AIMS&METHODS: We aimed to determine whether genetics predispose to presence of pANCA in an European collaborative twin study. In total, 48 twin pairs with ulcerative colitis (Leuven, Belgium n=4, Maastricht, The Netherlands n=5 and Örebro, Sweden n=39) participated: (concordant monozygotic n=3, discordant monozygotic n=15, concordant dizygotic n=1, discordant dizygotic

n=28 and one monozygotic twin pair with both CD and UC). pANCA was analyzed by ELISA and indirect immunofluorescence as previously described. The intraclass correlation coefficient (ICC) was used to assess agreement in concentrations of ANCA within twin pairs.
RESULTS: pANCA was present in 16/52 (31%) twins with UC compared with 4/43 (9%) healthy twin siblings (p=0.01). Consistently, mean (range) concentrations of ANCA were higher in twins with UC [18.7 (1.5-91.1) EU/ml] than in their healthy twin siblings [7.5 (0-30.5) EU/ml], ratio for mean concentrations 2.1 (95% CI 1.5-3.0). However, pANCA was not more frequently present in healthy monozygotic- [1/15 (7%)] than healthy dizygotic twin siblings [3/28 (11%)] (p > 0.99). Similarly, no agreement was observed in monozygotic- or dizygotic discordant twin pairs with UC, ICC=0.11 and ICC=-0.22, respectively.
CONCLUSION: pANCA was more often present in twins with UC than in their healthy twin siblings, reflecting that pANCA status has a specificity for UC. However, pANCA was not more often present in healthy monozygotic- than in healthy dizygotic twin siblings. No agreement in concentration of ANCA was observed in monozygotic or dizygotic twin pairs with ulcerative colitis. Thus, genetic factors do not seem to drive pANCA expression, whereas disease status/phenotype does.
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Disclosure of Interest: None Declared
Keywords: genetics, inflamatory bowel disease, Serology

P267 CO-INHIBITION OF COX-1 AND COX-2 IS PREREQUISITE FOR CHEMOPREVENTION OF COLITIS-ASSOCIATED CANCER

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INTRODUCTION: Cyclooxygenase-2 (COX-2) inhibition has known to be very efficient way of preventing colitis associated cancer because COX-2 is principally engaged as an inflammatory or carcinogenic mediator in colitic cancer. However, there has been reported to the incomplete prevention with COXIBs, for which we investigated the effects of inhibition of COX-2 only and both COX-1 and -2 on the colitis-associated carcinogenesis.
AIMS&METHODS: Mice were exposed to 10 mg/kg AOM followed by 2.5% DSS in drinking water for 7 days with or without aspirin or celecoxib. To further verify the role of COX-2 in the colon carcinogenesis, we compared the incidence and the multiplicity of AOM plus DSS induced colon carcinogenesis in the COX-2 wildtype and knockout mice. After 16 weeks, all mice were sacrificed by cervical dislocation for further analysis.
RESULTS: The 84% mice developed colorectal carcinoma after AOM plus DSS treated mice at the 16 weeks. The expression of COX-2 was markedly elevated in the colon tumors. COX-2 inhibition using celecoxib or genetic ablation using COX-$2^{-/-}$ mice could attenuate colon cancarcinogenesis. Administration of celecoxib lowered incidence and the multiplicity of colon carcinogenesis, and attenuated expression of COX-2 and iNOS as well as activation of NF-κB. However, inhibition of COX-1 and COX-2 with aspirin showed much more inhibitory effects on the expression of inflammatory and carcinogenic markers, the tumor incidence and multiplicity of colon cancer than the only inhibition of COX-2 with celecoxib or COX-$2^{-/-}$ mice. Chemoprevention of colorectal cancer is already possible with celecoxib, but it is still not the ultimate drug of choice.
CONCLUSION: Since COX-1 or COX-2 inhibition achieved 60% of chemoprevention, COX-1 should also be inhibited as well as COX-2 to achieve optimal chemoprevention of colitis-associated colon carcinogenesis.
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Disclosure of Interest: None Declared
Keywords: chemoprevention, colitis-associated cancer, COX-1, COX-2

P268 THE ROLE OF NALP3 INFLAMMASOME IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Traditionally, inflammatory bowel disease (IBD) is considered a state of hyper-inflammation of the gut mucosa. In the present abstract, we challenge this concept by investigating cytokine production by peripheral mononuclear cells (PBMCs) of the patients.
AIMS&METHODS: PBMCs were isolated from 11 healthy controls, 12 patients with Crohn disease (CD) and 10 patients with Ulcerative Colitis (UC) after gradient centrifugation of heparinized whole blood over Ficoll. PBMCs were stimulated with the TLR4 ligand lipopolysaccharide (LPS) and with the NLRP3 ligand monosodium urate (MSU). After 24-hour incubation, cytokine concentrations were measured in supernatants; after 4-hour incubation PBMCs were lyzed for measurement of mRNA transcripts of interleukin (IL)-1β by RT-qPCR.
RESULTS: As shown in the table, cytokine production was lower among patients with IBD than healthy controls (*indicates significant differences compared to controls) and this was most prominent in CD. Activation of NLRP3 is expressed as the % increase of IL-1β production in the presence of MSU. Mean relative IL-1β copies in PBMCs of controls, of UC and of CD were 3.12, 16.3 and 55.3 (p=NS).

	IL-1β (Mean ± SE)	IL-6 (Mean ± SE)	TNFα (Mean ± SE)	NLRP3 (Mean ± SE)
Controls	4720.5 ±1674.8	33134 ± 10519.7	3519.1 ± 1310.9	12.3 ± 22.7
CD	*1327.9 ± 434.3	*6560 ± 1578.6	*212 ± 75.3	*-24.9 ± 14.47
UC	*1110.85 ± 409.1	9940.5 ± 1883.03	624 ± 246	*143.84 ± 88.29

CONCLUSION: Cytokine production by PBMCs is significantly modulated in IBD. Main characteristics are down-regulation after LPS stimulation and activation of NLRP3 inflammasome.
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Keywords: IBD, NALP3 INFLAMMASOME

P269 T CELL EXPRESSION OF CD25 AND TNF RECEPTOR 2 AND IL-1B RELEASE MAY PREDICT ANTI-TNF THERAPY RESPONSE IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: Anti-tumor necrosis factor (anti-TNF) agents are effective treatment options for patients with ulcerative colitis (UC). However, not all patients respond to treatment and cellular mechanisms leading to therapy response are incompletely known. Also, biomarkers which can predict if patients are responders or non-responders before therapy start are needed.
AIMS&METHODS: The overall aim of this study was to identify immunological mechanisms involved in anti-TNF therapy in patients with UC in order to predict therapy response.
UC patients treated with anti-TNF (infliximab) were followed from start to evaluation of treatment efficacy. Blood samples were obtained before the first treatment and cells were stimulated ex vivo with influenza vaccine with and without anti-TNF. Cells and supernatants were analysed using flow cytometry. Disease activity was assessed by Mayo score before treatment start and at an evaluation visit prior to the fourth treatment dose. Response was defined as a decrease in Mayo score of ≥3.
RESULTS: We have included 28 UC patients into the study. Sixteen patients responded to anti-TNF therapy, whereas twelve patients did not respond. Presence of anti-TNF at stimulation induced a more pronounced reduction in the frequencies of $CD4^+CD25^+$ (61.9 (34.7-81.2) vs. 74.9 (61.7-96.1) %; p=0.006) and $CD3^+TNFR2^+$ (51.8 (21.4-69.8) vs. 66.3 (53.9-92.6) %; p=0.03) T cells in therapy responders as compared to non-responders. The same trend was seen for $CD4^+$ T cells expressing the gut homing receptor a4b7. The reduction of activated T cells in responders was accompanied by a reduction of IFN-g expression when comparing stimulated cells with and without addition of anti-TNF (33.2 (0-469.1) vs. 174.4 (0-479.1) pg/ml; p=0.02). However, no reduction of IFN-g was detected in non-responders. In addition, stimulation of blood cells with vaccine alone resulted in increased levels of the pro-inflammatory cytokine IL-1b in non-responders as compared to responders (27.7 (0-118.3) vs. 0 (0-38.1) pg/ml; p=0.04).
CONCLUSION: This study indicates that suppression of the frequencies of $CD25^+$ T cells and $TNFR2^+$ T cells cultured in the presence of anti-TNF may be used as biomarkers to predict therapy response to anti-TNF treatment in IBD patients. Also, therapy non-responders have a higher production of IL-1b upon antigen stimulation which may counteract the anti-inflammatory effects of anti-TNF.
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Disclosure of Interest: None Declared
Keywords: ANTI-TNF-ALPHA THERAPY, Predictive factors, T cell, ulcerative colitis

P270 TELOMERE LENGTH IN NON-NEOPLASTIC COLONIC MUCOSA IN ULCERATIVE COLITIS AND ITS RELATIONSHIP TO THE SEVERE CLINICAL PHENOTYPES

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INTRODUCTION: Telomere shortening occurs with human aging in many organs and tissues and is accelerated by rapid cell turnover and oxidative injury.
AIMS&METHODS: To clarify the clinical importance of telomere shortening in colonic mucosa in ulcerative colitis (UC), we measured average telomere length using quantitative real-time PCR in non-neoplastic colonic mucosa in UC patients and assessed its relationship to various clinical subtypes. Colonic biopsies were obtained from rectal inflammatory mucosa from 86 UC patients. Paired non-inflammatory proximal colonic mucosae were also collected from 10

patients. Relative telomere length in genomic DNA was measured by determining the ratio of telomere repeat copy number (T) to single copy gene (S) copy number(T/S ratio) in individual samples relative to a reference pooled DNA from healthy blood samples.
RESULTS: In 10 cases, average relative T/S ratios of rectal inflammatory mucosa and adjacent normal proximal colon were 3.62+/-2.16 (Mean+/-SD), 2.29+/-1.88, respectively, and were reduced in rectal inflammatory mucosa among 8 out of 10 cases (p=0.01). Relative T/S ratios were also reduced in cases that needed surgery due to toxic megacolon or cancer occurrence (2+/-0.16 *vs*. 0.75+/-0.69: p=0.04). When the severe clinical phenotype was defined as having at least one of following phenotypes; more than two times of hospitalization, steroid dependent, refractory, or needing operation, average relative T/S ratio was significantly reduced in severe phenotypes than the others (2.22+/-0.23 *vs*. 1.57+/-0.21: p=0.04).
CONCLUSION: Telomere shortening is associated with more severe clinical phenotypes of UC, reflecting severe inflammatory state in the colonic mucosa.
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Disclosure of Interest: None Declared
Keywords: Telomere length , ulcerative colitis

P271 IL-7 PROMOTES LONG-TERM IN VITRO SURVIVAL OF UNIQUE LONG-LIVED MEMORY SUBSET GENERATED FROM MUCOSAL EFFECTOR MEMORY CD4+ T CELLS IN CHRONIC COLITIS MICE

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INTRODUCTION: We have reported that colitogenic memory $CD4^+$ T cells, which can survive even in remission for life-long, play an important role for the perpetuation of inflammatory bowel disease (IBD). Memory T cells are heterogeneous and can be divided into subpopulations. Recently, memory stem cells (T_{SCM}), with high potential for survival, self-renewal and multi-differentiation, were identified in both mice and humans. However, it is unclear whether a similar subset is present in IBD.
AIMS&METHODS: We sought to identify and purify a long-lived subset of colitogenic memory $CD4^+$ T cells, which may be ultimate target for the treatment of IBD. First, we checked the role of each subset of memory $CD4^+$ T cells in IBD model mice. Second, a long-lived subset of colitogenic memory $CD4^+$ T cells was purified using a long-term culture system and the characteristics of these cells were assessed.
RESULTS: In multiple IBD model mice, there was no T_{SCM} and most of $CD4^+$ T cells in each organ were effector memory T cells (T_{EM}), which are believed as short-lived terminally differentiated cells. In addition, T_{EM} induced severe colitis to the same extent as central memory T cells (T_{CM}), which are believed as long-lived highly proliferative cells, when they were transferred into new SCID mice. Therefore, we though that hierarchy of memory T cells previously reported cannot apply to IBD model mice, and that T_{EM} in colitic mice are not short-lived cells but include long-lived cells. Next, we tried to purify long-lived subset from colitic lamina propria (LP) $CD4^+$ T cells by culturing with IL-7, which is the most important factor for the maintenance of memory $CD4^+$ T cells.
Colitic LP $CD4^+$ T cells could be maintained *in vitro* with IL-7 for more than 8 weeks, while normal $CD4^+$ T cells could not be maintained. During culture, these cells were quiescent and divided intermittently, which is very similar to their maintenance *in vivo*.
After the culture, LP $CD4^+$ T cells expressed high level of Bcl-2, which suggests these cells are long-lived. Cultured-LP $CD4^+$ T cells expressed unique surface markers, which were different from any memory subsets, and produced large amount of IL-2, which is similar to T_{CM}. Finally, LP $CD4^+$ T cells obtained from colitic mice and cultured with IL-7 for 8 weeks induced more severe colitis than LP $CD4^+$ T cells cultured for 4 weeks.
CONCLUSION: We here developed for the first time long-term culture system to purify long-lived and highly pathogenic memory subset from activated LP $CD4^+$ T cells. IL-7 promoted long-term *in vitro* survival of this subset in a quiescent state.
Disclosure of Interest: None Declared
Keywords: IL-7, inflamatory bowel disease , memory CD4+ T cells

P272 THE ROLE OF IL-9 AND ITS RECEPTOR IN ULCERATIVE COLITIS

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INTRODUCTION: It is currently assumed that the pathogenesis of ulcerative colitis (UC) is due to an altered Th2/Th17 response. However, various aspects of disease development are incompatible with this model. IL-9 has been described as the key cytokine of a new $CD4^+$ T cell population, referred to as Th9 cells. The role of IL-9 in inflammatory bowel disease (IBD) has so far not been investigated.
AIMS&METHODS: In this study we addressed the function of IL-9 in UC. qPCR of colonic biopsies for IL-9, IL-9R, IL-6, IL-17A, IL-21, IRF4, PU.1, S100A8, STAT1, STAT3, STAT5a, STAT5b and TNFα mRNA. IL-9 and IL-9R immunofluorescence (IF) single stainings and IL-9 + IRF4/PU.1/CD3 IF double stainings on gut surgical specimens and biopsies. Histological classification of the inflammation score (IS) 0-3. IL9-R and IL-9 FACS staining of intestinal epithelial cells. Western blot (WB) of colonic biopsies for claudin-2. TEER-measurement of Caco-2 cells after stimulation with IL-9 and WB of the cells for claudin-2.
RESULTS: IL-9 mRNA was expressed by UC patients with active colitis. The IL-9 level strongly correlated with the inflammation marker S100A8 and IL-9 dependent transcription factors. UC patients with active colitis showed a higher number of $IL\text{-}9^+$ cells in the IF. IL-9 was expressed by $CD3^+$ cells in the lamina propria. In patients with active colitis, IL-9 expression correlated to a high degree with its transcription factor PU.1. Apart from that, a high correlation between PU.1 and IRF4 was shown. The colocalization of IL-9 and PU.1 as well as IL-9 and IRF4 in the lamina propria was detected by IF. The number of $IL\text{-}9^+PU.1^+$ and $IL\text{-}9^+IRF4^+$ increased with IS. Using IF and FACS, the expression of the IL-9R on intestinal epithelial cells could be shown. IL-9R expression increased in UC patients with IS. The stimulation of Caco-2 colon epithelial cells with IL-9 resulted in a disturbed barrier function of the epithelium by a STAT- and claudin-2-dependent mechanism.
CONCLUSION: Our data show for the first time that IL-9 produced by $CD3^+$ and $PU.1^+/IRF4^+$ cells is decisively involved in the pathogenesis of UC through the direct damage of the barrier function of the colon epithelium. The modulation of this signaling pathway could represent a further valuable treatment option for UC.
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Disclosure of Interest: None Declared
Keywords: IL-9, inflammatory bowel disease, IRF4, PU.1, ulcerative colitis

P273 COMMD10, AN NF-KAPPAB INHIBITOR, IS REDUCED IN IBD PATIENTS AND IN PRO-INFLAMMATORY INFILTRATING MONONUCLEAR PHAGOCYTES OF COLITIC MICE AND IBD PATIENTS.

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INTRODUCTION: The COMMD proteins family is involved in NF-kB ubiquitination, thus "switching off" transcription of pro-inflammatory genes[1]. In the inflamed mouse intestine, a subset of mononuclear phagocytes (MPs), expressing $Ly6C^{hi}$ and $CX3CR1^{int}$, dominates the macrophage (MF) population. These cells are highly responsive to TLR/NOD2 activation and exhibit upregulation of NF-kB stimulated genes and pro-inflammatory cytokine secretion[2]. A similar dominant population expressing CD14 was identified in human IBD[3].
AIMS&METHODS: Aims: To investigate the expression pattern of COMMD10 in subsets of intestinal MPs in health and IBD in both mouse models and humans.
Methods: Ileocolonic biopsies, circulating leukocytes as well specific blood MP subtypes were isolated from IBD and control patients. MP populations were sorted from the colon of mice with DSS-induced acute and chronic colitis. COMMD10 expression was determined by qRT-PCR. COMMD10 was silenced by siRNA in intestinal epithelial cells and the expression of NF-kB induced pro-inflammatory genes was determined by qRT-PCR and western blot in response to LPS treatment.
RESULTS: Our findings in a wide cohort of patients demonstrate the broad decrease of *COMMD* gene expression in intestinal tissue and circulating leukocytes of both Crohn's disease and ulcerative colitis patients. Contrary to our expectations, this decline did not correlate well with disease severity and could be observed in uninvolved areas of the intestine as well as inflamed areas. Interestingly, we show that the CD14+ MPs, which become dominant in IBD, but not CD16+ MPs, exhibit decreased COMMD10 expression. In correlation with the human data, the infiltrating MFs that express $Ly6C^{hi}$ and $CX3CR1^{int}$ show reduced COMMD10 expression relative to residents MFs both in acute and chronic DSS-induced colitis. Intestinal epithelial cells expressing lower COMMD10 levels *in vitro* are more pro-inflammatory and express higher levels of TNFa, IL-6, IL-32 and ICAM-1.
CONCLUSION: COMMD10 is reduced in the setting of inflammation, specifically in infiltrating MFs in both mice and humans. An acquired state of "COMMD10 deficiency" in infiltrating MFs may unleash NF-kB signaling and participate in the induction and maintenance of IBD. Therefore restoring COMMD10 levels in this specific MF subtype may help to control the inflammatory state in IBD patients.
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Disclosure of Interest: None Declared
Keywords: COMMD, Intestinal mononuclear phagocytes, NF-kappaB

P274 EXPERIMENTALLY PROVOKED RECURRENT INFLAMMATION IMPROVES MUCOSAL HEALING AND RESTORATION OF IMPAIRED MORPHOLOGY OF MYENTERIC NEURONS IN A RAT MODEL OF CROHN'S DISEASE

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INTRODUCTION: Crohn's disease (CD) is a chronic relapsing inflammatory bowel disease (IBD) associated with marked abnormalities in intestinal motility suggesting that impairment in the enteric nervous system (ENS) underlines some of the functional abnormalities observed in patients with IBD. Although there have been numerous studies of the ENS in inflammation, the structural and molecular changes to the ENS under the repetitive relapsing inflammations (RRI) has not been studied yet.
AIMS&METHODS: We aimed to establish a rat model of chronic colitis suitable to investigate the ENS and its intestinal microenvironment in RRI. Colitis was induced by an enema of 2,4,6-trinitrobenzenesulfonic acid (TNBS, 10 mg) in 25% ethanol. RRI was provoked by repeated TNBS treatments. Tissue samples were taken from control, as well as 1x, 2x and 3x treated rats from the ulcered, and also proximal and distal to the ulcered segments of the colon in different timepoints between 2 and 120 days. The quantitative and morphometrical features of myenteric neurons under RRI were investigated by immunohistochemistry using HuC/D as a pan-neuronal marker. The expression of endogenous antioxidant enzyme, heme oxygenase-1 (HO-1) was determined by real time PCR.
RESULTS: Severe mucosal inflammation, decreased myenteric neuronal density and shrinkage of neuronal cell bodies were demonstrated in the acute phase of inflammation induced by the first TNBS treatment. Nevertheless, after the second and even more after the third TNBS treatment the measure of ulcerousness decreased markedly and the soma sizes of myenteric neurons were nearly the same as in the controls. The length of the acute phase of inflammation was also reduced. Mucosal healing was completed 8 days after the first treatment, while complete mucosal recovery was noticed already 6 and 4 days after the second and third treatment, respectively. HO-1 mRNA level was elevated in the acute phase of the inflammation in all three colonic segment, and remained high until day 120th.
CONCLUSION: This study demonstrates for the first time that experimentally provoked RRI in rat model of CD develops preconditioning effect by speeding up mucosal healing and restoring impaired morphology of myenteric neurons. Decreased severity of TNBS induced inflammation in RRI might be associated with the persistent upregulation of HO-1 expression throughout the 120 days experimental period. Therefore, targeted induction of HO-1 might be of therapeutic interest.
Disclosure of Interest: None Declared
Keywords: Crohn's disease, heme oxygenase-1, myenteric neurons, recurrent inflammation

P275 NATURAL KILLER CELLS REGULATE THE EARLY STAGE OF PATHOGENIC T CELL DEVELOPMENT IN AN IBD MODEL

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INTRODUCTION: We previously reported that mice lacking IL-7 and RAG ($IL\text{-}7^{-/-}$ $RAG^{-/-}$) receiving naïve T cells failed to induce colitis. Such abrogation of colitis may be associated not only with incomplete T cell maintenance due to the lack of IL-7, but also with the induction of colitogenic T cell apoptosis at an early stage of colitis development. Natural killer (NK) cells may be associated with the suppression of autoimmune diseases and may induce apoptosis of $CD4^+$ T cells, although the mechanisms have not been well described. We therefore focused our analysis of this phenomenon on NK cells.
AIMS&METHODS: To further investigate these roles of NK cells, $RAG^{-/-}$ and $IL\text{-}7^{-/-}$ $RAG^{-/-}$ mice receiving naïve T cells were depleted of NK cells using anti-asialo GM1 or anti-NK1.1 antibodies.
RESULTS: NK cell depletion at an early stage, but not at a later stage, during colitogenic effecter/memory T cell (T_{EM}) development resulted in elicited colitis in recipient mice even in the absence of IL-7. The isolated NK cells derived from $RAG^{-/-}$ and $IL\text{-}7^{-/-}$ $RAG^{-/-}$ mice indicated that the lack of IL-7 does not affect the differentiation and cell-mediated cytotoxicity of NK cells either in vitro or in vivo. Increased $CD44^+$ $CD62L^-$ T_{EM} and unique $CD44^-$ $CD62L^-$ (double negative, DN) T cell subsets were observed in the T cell-reconstituted $RAG^{-/-}$ recipients when NK cells were depleted. Fas, DR5, which are the specific receptors of Fas-L and TRAIL, respectively, and IL-7R expressions in the DN T cell subset differed from that in T_{EM} subset, indicating that the mechanism by which NK cells suppress the DN T cells is different from that by which they suppress the T_{EM} cells, which is due to the apoptosis via Fas and/or DR5.
CONCLUSION: These results suggest that NK cells suppress colitis severity in the T cell-reconstituted recipient mice through targeting of T_{EM} and, possibly, of the DN subset present at an early stage of pathogenic T cell development.
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Disclosure of Interest: None Declared
Keywords: colitis, effecter T cells, NK cells

P276 EFFICACY OF SELECTIVE MYELOID LINEAGE LEUCOCYTE DEPLETION IN PYODERMA GANGRENOSUM AND PSORIASIS ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE.

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INTRODUCTION: A minority of patients with inflammatory bowel diseases (IBD) develop pyoderma gangrenosum (PG) or psoriatic skin lesions, but this is now increasing significantly by the appearance of new onset psoriasis associated with anti-tumour necrosis factor-alpha therapy (Cullen G, et al. Aliment Pharmacol Ther 2011). The conditions are life-long neutrophilic inflammatory disorders, which do not respond well to pharmacologicals. We thought that patients with PG and psoriasis should respond favourably to selective depletion of myeloid lineage leucocytes by adsorptive granulocyte/monocyte apheresis (GMA) with the Adacolumn.
AIMS&METHODS: A 19-year-old patient developed exacerbated Crohn's disease (CD) complicated by PG while on conventional medication. His symptoms included severe anal pain, bloody diarrhoea more than 20 times/day, and fever. Laboratory variables included C-reactive protein (CRP) 19.9mg/dL, erythrocyte sedimentation rate (ESR) 55mm/hr and leucocyte count $17.9x10^6$/mL. GMA was decided at a flow rate of 40mL/minx90min = one GMA session. Following this case, a study in 15 patients with drug refractory generalized pustular psoriasis (GPP) was undertaken with 5 GMA sessions over 5 consecutive weeks.
RESULTS: In the CD case, after 5, once a week GMA sessions, there was a striking improvement of the PG lesions. The outcomes encouraged us to proceed with a second course of 5 GMA sessions. After the second course, pustular lesions re-epithelialized and colonoscopy showed no active ulcer, but ulcer scars covered by regenerated mucosa in the anal canal, rectum and the sigmoid colon. Stool frequency was 2-3/day, CRP 0.6mg/dL, leucocyte count $4.7x10^6$/mL and normal ESR. The therapeutic outcomes in the 15 patients with GPP were encouraging as well. After 5 GMA sessions, the overall GPP scores improved (n=14, P=0.0027), and the area of erythroderma (P=0.0042), pustules (P=0.0031), and oedema (P=0.0014) decreased. Likewise, Dermatology Life Quality Index improved (P=0.0016), reflecting better daily function, and quality of life.
CONCLUSION: Regarding the mechanisms of clinical efficacy of GMA in patients with PG or psoriasis, post treatment data indicate that GMA down-modulates the expression of the chemokine receptor, CXCR3 (CD183) on leucocytes. CXCR3 is known to have a major role in neutrophilic skin lesions. The outcomes indicate a major role for neutrophils in the immunopathogenesis of PG and psoriasis.
Disclosure of Interest: None Declared
Keywords: Pyoderma gangrenosum, Psoriasis, Granulocytapheresis, Pyoderma gangrenosum, Psoriasis, Granulocytapheresis, Neutrophilic dermatitis

P277 AUTOPHAGY IS INDUCED BY ERSTRESS MAINLY THROUGH IRE1ALFA IN HUMAN COLON CANCER CELLS AND IT PLAYS A CYTOPROTECTIVE ROLE.

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INTRODUCTION: X-box binding protein1(XBP1), which is activated by ER stress, and ATG16L1, Immunity-related GTPase family M protein(IRGM) , which are proteins related to induce Autophagy , are also identified as disease susceptibility genes of Crohn's disease in genome wide association study.
AIMS&METHODS: In colon epithelium, the relation between Unfolded Protein Response(UPR) and Autophagy is unknown, so we intended to elucidate about "Do ERstress induce Autophagy? ", "Which way in three canonical UPR pathway(PERK, IRE1α, ATF6 pathway) is most reliable for Autophagy indumed by ERstress?"and "How do this pathway contribute to cell survival? " We used three kinds of human colon cancer cell lines,HT29,SW480 and Caco-2. They are treated by tunicamycin(tm) or thapsigargin(tg) to activate UPR. We studied phosphorylation of PERK, cleavage of ATF6, splicing of XBP1 and CHOP as a marker of UPR by Western blotting or Polymerase Chain Reaction and LC3II as a marker of Autophagy by Western blotting ,and dots in GFP,RFP-LC3 transfected cells by confocal microscopy. A number of apoptotic cells is studied by flow cytometry.
RESULTS: The up-regulation of UPR and Autophagy was observed in Cells treated by tm or tg. Knock-down of IRE1α gene by RNA silencing inhibited the up-regulation of Autophagy in chemically treated cells while knockdown of PERK and ATF6 did not influence. The inhibitor of Autophagy, 3-methyl-adenine, augmented apoptotic cells, in chemically treated cells.
CONCLUSION: In human colon cancer cell lines, UPR-mediated Autophagy is mainly passed through IRE1α, and UPR-mediated Autophagy plays a cytoprotective role. In future, ERstressor of colon epithelium in human body should be clarified. It is our concern that how the functional disorder of UPR, Autophagy or both influence the Crohn's disease.
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Disclosure of Interest: None Declared
Keywords: autophagy, ER stress

P278 THE EFFECT OF MELATONIN TREATMENT ON DSS INDUCED COLITIS AND PROBABLE MECHANISM BY MICROARRAY: AQUAPORIN8 AND ADIPONECTIN PATHWAY

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INTRODUCTION: There are complex and various causes in the pathogenesis of inflammatory bowel disease. Stressful condition has reported aggravation or reactivation of inflammatory bowel disease. Thus, we tried to investigate the effect of stress caused by sleep deprivation(SD) on DSS induced colitis model. Also, we designed to evaluate the mechanism of melatonin on such condition by gene expression after melatonin treatment.
AIMS&METHODS: We used the 5 groups of C57BL/6 mice. Group I: control, Group II: 2% DSS induced colitis for 7days, Group III: 2% DSS induced colitis and melatonin treatment, Group IV: 2% DSS induced colitis with sleep deprivation(SD, 20hr/d) and Group V: 2% DSS induced colitis with SD and melatonin treatment. Specially designed modified multiple platform water baths for sleep deprivation were used. Melatonin(10mg/kg) or saline was injected daily by intraperitoneal route. The mice were sacrificed after finishing administration of melatonin or saline for 4 days.
We checked body weight and stool color daily. Degree of colitis was evaluated after H&E stain. Also proinflammatory cytokines from serum were checked using Bio-Plex Pro Mouse Cytokine assay kit (Bio-Rad, Hercules, CA, USA). RNA was isolated from the colon of mice in each group and collected to analyze by microarray and ontology. We confirmed significant changes of expression of important genes by RT-PCR and immunohistochemical staining
RESULTS: Sleep deprivation worsens body weight reduction of mice and exacerbate the severity of colonic inflammation. Administration of melatonin reduced the rate of weight loss and severity of mucosa injury compared with saline injection group. Increased expression of pro-inflammatory cytokines such as IL-6, TNF-α, IFN-γ was significantly reduced with melatonin supplementation.
About 68 genes were significantly changed by 2% DSS, sleep deprivation and melatonin in microarray. In real time PCR there are significant change of adipoq and Aqp8 gene, which are related with adiponectin and aqaoporin-8 protein. We also performed immunohistochemical stain of adiponectin and aqaoporin-8.
CONCLUSION: Sleep deprivation acts as an aggravating factor, whereas melatonin acts as an improving factor of inflammation. This study shows melatonin affects both inflammation and sleep control. Especially genetic microarray study revealed that melatonin may regulate inflammation by modulating adiponectin and aquaporin pathway in DSS induced colitis.
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Disclosure of Interest: None Declared
Keywords: adiponectin, aquaporin, DSS induced colitis, melatonin

P279 RISK OF SKIN CANCER IN IBD; A NATIONWIDE STUDY IN FINLAND

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INTRODUCTION: Recent studies have shown an increased risk of non-melanoma skin cancers (NMSCs) in IBD patients, especially in those using thiopurines. An increased incidence of melanoma has also been suggested.
AIMS&METHODS: Our aim was to assess the risk of skin cancer overall among patients with IBD diagnosed between 1987-1993 and 2000-2007 in Finland. In the register of the Social Insurance Institution of Finland, separate codes for Crohn's disease (CD) and ulcerative colitis (UC) were available for IBD patients from 1986-1993 and 2000-2010. The 21,964 patients with IBD (16,649 with UC and 5,315 with CD) were followed until the end of 2010 (236,129 person-years) in a linkage with the nationwide database of the Finnish Cancer Registry. The observed numbers of skin cancers were assessed, and compared to those expected, and standardized incidence ratio (SIR) given
RESULTS: The risk of basal cell carcinoma of the skin was increased in UC (SIR 1.21; 95% CI 1.02-1.40 in males and SIR 1.22; 95% CI 1.01-1.45 in females) and in CD (SIR 1.68; 95% CI 1.19-2.29 in males and 1.60 95% CI 1.15-2.15 in females) in both genders. The risk of basal cell carcinoma of the skin was most pronounced in ages 30-44 over three years after the diagnosis of UC (SIR 3.12; 95% CI 1.64-5.54 in males and SIR 2.07; 95% CI 1.04- 3.71 in females) and in CD over three years after the diagnosis of CD among males in ages 30-44 (SIR 3.84; 95% CI 1.05-9.83) and among females in ages 45-59 (SIR 2.90; 95% CI 1.59- 4.86). A slightly increased risk of melanoma was also seen among male CD patients (SIR 2.33 95% CI 1.12-4.28), especially in ages 30-44 over three years after the diagnosis of CD (SIR 5.70; 95% CI 1.17-16.65).
CONCLUSION: Increased risk of basal cell carcinoma of the skin was found among CD and UC patients and risk of melanoma was increased among males with CD.
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Disclosure of Interest: None Declared
Keywords: basal cell carcinoma of the skin , CD, skin cancer, UC

P280 RISK OF COLORECTAL CANCER IN CD PATIENTS WITH COLONIC INVOLVEMENT AND STENOSING DISEASE 1977-2012. RESULTS FROM A POPULATION-BASED STUDY

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INTRODUCTION: Data are limited.
AIMS&METHODS: Our aim was to study the risk of colorectal cancer (CRC) in patients Crohn's disease (CD) presenting with stenosing colonic lesions in the population-based, Veszprem province database, which included incident patients diagnosed between January 1, 1977 and December 31, 2011.
The data of 640 incident CD patients were analyzed (m/f: 321/319, age-at-diagnosis: 31.5, SD: 13.9 years). Both hospital and outpatient records were collected and comprehensively reviewed.
RESULTS: CRC was diagnosed in total 6 CD patients (total follow-up: 7759 person-years) during follow-up. 62 patients presented with colonic/ileocolonic disease and a stenotic lesion in the colon. The total follow-up was 702 person-years (mean: 11.3 SD 8.1 years). CRC developed in 6.5%, equalling 0.57 /100 person-years and an increased SIR (6.53, 95%CI: 2.45-17.4) with 4 patients observed and 0.61 expected. In a Kaplan-Meier analysis the probability of developing CRC was 5.5% after 5-years and 7.5% after 10-years of disease duration. In a sensitivity analysis, we included all patients who presented with colonic/ileocolonic disease and a stenosing colonic lesion at diagnosis or during follow-up (n=91, total follow-up: 1180 person-years, mean: 12.9 SD 8.8 years). The prevalence of cancer was overall 4.4% (0.34/100 person-years). In a Kaplan-Meier analysis the probability of developing CRC was 3.6% and 4.9% after 5- and 10-years of disease duration.
CONCLUSION: The risk to develop CRC in colonic CD patients presenting with or developing a stenotic lesion in the colon is high already after relatively short disease duration suggesting the need for careful surveillance of these patients.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, Crohn's disease, stenosis

P281 IRRITABLE BOWEL SYNDROME-TYPE SYMPTOMS IN INFLAMMATORY BOWEL DISEASE PATIENTS IN REMISSION: A CROSS-SECTIONAL SURVEY

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INTRODUCTION: Several studies have reported that patients with inflammatory bowel disease (IBD) may report symptoms compatible with irritable bowel syndrome (IBS). Patients who report these symptoms may have therapy escalated, due to concerns about ongoing disease activity. Few studies have examined patient characteristics that may be associated with the presence of IBS-type symptoms.
AIMS&METHODS: This was a prospective cross-sectional survey conducted among consecutive patients with Crohn's disease (CD) or ulcerative colitis (UC) attending an IBD clinic in a single teaching hospital. All patients completed questionnaires and provided a blood sample for C-reactive protein (normal CRP defined as <5.0mg/L). Presence of IBS-type symptoms was defined according to the Rome III criteria. Remission was confirmed using the Harvey-Bradshaw index (HBI score ≤ 4) for CD, and the simple clinical colitis activity index (SCCAI score ≤ 4) for UC. Participants also completed the patient health questionnaire-15, a validated somatisation score, and the hospital anxiety and depression score. Demographic data, including previous surgery and Montreal distribution of IBD, were collected for all patients. The effect of all these patient characteristics on presence of IBS-type symptoms was examined by univariate analysis, with results expressed as odds ratios (ORs) with 99% confidence intervals (CI).
RESULTS: 161 patients with IBD in remission were recruited (75 (46.6%) female, 87 (54.0%) CD, mean age 48.4 years). In total, 42 (26.1%) reported symptoms compatible with IBS (13 (8.1%) diarrhoea-predominant, 3 (1.9%) constipation-predominant, 26 (16.1%) mixed stool pattern). Mean age was not significantly different among those meeting criteria for IBS (45.5 years vs. 49.5), but mean CRP was slightly lower (5.6mg/L vs. 7.7mg/L, $P = 0.06$). Gender, smoking status, alcohol use, previous surgery, and type or Montreal distribution of IBD were not significantly associated with presence of IBS-type symptoms. However, prevalence of co-existent anxiety (OR 3.86; 99% CI 1.10-13.5), depression (OR 10.3; 99% CI 1.18-90.2), or somatisation (OR 5.32; 99% CI 1.13-25.1) were significantly greater among those meeting criteria for IBS.
CONCLUSION: One-in-four IBD patients in remission reported symptoms compatible with IBS. These were commoner in those with co-existent anxiety, depression, or somatisation. This, together with the fact that mean CRP levels were lower among those with IBS-type symptoms, suggests this may not necessarily be related to ongoing disease activity. Strategies for dealing with these types of symptoms in IBD patients are required.
Disclosure of Interest: None Declared
Keywords: Crohn's disease, Inflammatory bowel disease (IBD), Irritable bowel syndrome, remission, ulcerative colitis

P282 PREVALENCE OF SOMATISATION IN INFLAMMATORY BOWEL DISEASE PATIENTS: A CROSS-SECTIONAL SURVEY

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INTRODUCTION: Inflammatory bowel disease (IBD) may be associated with psychological illness, such as anxiety or depression, and reduced quality of life. However, few studies have examined the prevalence of somatisation in patients with IBD, or patient characteristics that may be associated with such behaviour.
AIMS&METHODS: This was a prospective cross-sectional survey conducted among consecutive patients with Crohn's disease (CD) or ulcerative colitis (UC) attending an IBD clinic in a single teaching hospital. All patients completed questionnaires and provided a blood sample for C-reactive protein (normal CRP defined as <5.0mg/L). Participants completed the patient health questionnaire-15, a validated somatisation score, with a score of ≥ 15 used to define presence of somatisation, and the hospital anxiety and depression score. Demographic data, including previous surgery and Montreal distribution of IBD, were collected for all patients. The effect of all these patient characteristics on presence of somatisation was examined by univariate analysis, with results expressed as odds ratios (ORs) with 99% confidence intervals (CI).
RESULTS: 287 patients with IBD were recruited (148 (51.6%) female, 160 (55.7%) CD, mean age 46.3 years). In total, 48 (16.7%) met criteria for somatisation. Mean age was significantly lower among those meeting criteria for somatisation (41.9 years vs. 47.2, $P = 0.02$), but mean CRP was not different (7.2mg/L vs. 9.0mg/L). Females (OR 2.95; 99% CI 1.20-7.3), smokers (OR 3.77; 99% CI 1.49-9.51), those who did not drink alcohol (OR 5.74; 99% CI 2.27-14.5), and those with co-existent anxiety (OR 12.25; 99% CI 3.80-39.5) or depression (OR 12.9; 99% CI 4.41-37.9) were more likely to meet criteria for somatisation. Ethnicity, educational level, previous surgery, and type or Montreal distribution of IBD were not significantly associated with presence of IBS-type somatisation.
CONCLUSION: One-in-six IBD patients reported symptoms compatible with IBS. These were commoner in females, smokers, those who did not drink alcohol, and those with co-existent anxiety or depression. Whether this relates to ongoing disease activity, extra-intestinal manifestations of IBD, or true somatisation remains unclear.
Disclosure of Interest: None Declared
Keywords: crohn's disease, Inflammatory bowel disease (IBD), Irritable bowel syndrome, somatisation, ulcerative colitis

P283 NATURAL HISTORY OF NON-SEVERE INFLAMMATORY BOWEL DISEASES AT DIAGNOSIS

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INTRODUCTION: Crohn's disease (CD) and ulcerative colitis (UC) are progressive diseases characterized by the occurrence of complications requiring immunomodulators and surgery. Few data are available for the prevalence and the factors associated with long-term non-severe (NS) inflammatory bowel diseases(IBD) .
AIMS&METHODS: Our aim was to assess the natural history of NS CD and NC UC at diagnosis and to identify predictive factors of mild evolution over the long term.
A retrospective study of the IBD patients registred in the database of the university hospital of Liège, Belgium. NS CD was defined as the absence of stricturing, penetrating or perianal disease, no treatment with immunomodulators and anti-TNF, no need for surgery in the course of the disease. NS UC was defined as no requirement for immunomodulators, anti-TNF and colectomy. Patients were assessed at 1 year, 5 years and at the maximum follow-up. Patients with less than 5 years of follow-up were excluded.
RESULTS: Among 887 patients, a subgroup of 439 CD and 173 UC were included with a mean follow-up of 19 and 15 years respectively. One year after the diagnosis 147 CD patients had NS CD. At 5 years and at the maximum follow-up respectively, 83/147 (56%) and 15/147 (10%)of the patients still had NS CD. Complications were strictures (29%), fistulizing disease (18%), perianal disease (37%). Immunomodulators and anti-TNF were required in 79% and 54% of patients respectively. Prognostic factors for persistent NS CD were older age at diagnosis (38 vs 26 years, p=0.005), no corticosteroid during the first year (p=0.036). In UC, 142 patients had NS disease one year after the diagnosis. 102/142 (72%) and 62/142 patients (44%) had NS UC after 5 years and at the maximum follow-up respectively. Surgery occurred in 19 patients (13%) after a mean time à 164 months. Immunomodulators were needed in 66 patients (47%) and anti-TNF in 37 patients (26%). NS UC was associated with absence of hospitalization for active UC over the first 5 years (p=0.009) and during the total course of UC ($p<0.0001$), no intake of corticosteroid during the first year (p=0,03).
CONCLUSION: In our cohort representing referral centre recruitment, nearly all CD patients and 2/3 of UC with NS disease at diagnosis became severe with time. Old age at diagnosis was associated with NS CD outcome while absence of hospitalisation during the first year was associated with NS UC outcome. Absence of steroid use during the first year was associated with NS outcome in both diseases.
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Disclosure of Interest: None Declared
Keywords: good prognosis factors, natural history, non-severe IBD

P284 THE RELATIONSHIP BETWEEN MICROSCOPIC COLITIS AND DRUG INTAKE: AN OPEN ISSUE

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INTRODUCTION: Microscopic colitis (MC), including collagenous colitis and lymphocytic colitis, has now emerged as a common cause of chronic diarrhoea, but its aetiology remains unknown. Some studies suggest that it may be trigger by some commonly prescribed drugs.
AIMS&METHODS: To evaluate the prevalence of drug intake in patients with MC compared to chronic diarrhoea controls. We performed a case-control study with all adult consecutive patients attended for chronic diarrhoea at the Department of Gastroenterology of our hospital from April 2008 to December 2011. Complete colonoscopies with mucosal biopsies were carried out in all patients. MC was diagnosed on the basic of commonly accepted histopathological criteria. Patients with normal colonoscopy including biopsies were considered as control group. Detailed history of drug consumption was documented in every recruited patient.
RESULTS: 46 consecutive new cases of MC (25 female/21 male; median age 50.2±20.2y) and 317 consecutive chronic diarrhoea controls (196 female/ 121 male; median age 48.6±17.8y) were included. There were no significant differences regarding to age, gender, prevalence of co-morbidities, family history, smoking habit and fulfilment of the Rome III criteria for irritable bowel syndrome (IBS) among MC cases and control group. MC was more frequently associated with the presence of autoimmune diseases than in control patients (19.6% *vs.* 9.8%; $p<0.05$). Particularly, the prevalence of celiac disease was 10-folds higher among MC patients (13% *vs.* 1.3%; $p<0.05$). Some drug had been prescribed in most of patients (77.1% in MC group and 67.8% in control group; p=ns). Overall, no differences in the intake of drugs were documented between MC and control group. However, the intake of non-steroidal anti-inflammatory drugs (NSAIDs) was significantly associated with MC in the subgroup of patients aged <50 y who fulfilled Rome III criteria for IBS, compared to controls (38.5% *vs.* 10.8%; $p<0.017$), with a higher prevalence of metamizol intake among patients with MC.
CONCLUSION: MC showed association with autoimmune diseases, but not with drug intake. Only in a sub-group of patients fulfilling diagnostic criteria for IBS a significant association between MC and NSAIDs intake was documented.
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Disclosure of Interest: None Declared
Keywords: Drug intake, Microscopic colitis, Risk factors

P285 TREATMENT INFERRED NATURAL COURSE OF IBD IN A SOUTH EUROPEAN IBD REFERRAL CENTER.

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INTRODUCTION: The increasingly frequent appearance of inflammatory bowel disease (IBD) in people of all age groups has caused great concern within the scientific community since their etiology still remains unclear. So far, there is lack of studies bringing to light data on the natural history of IBD in southern Europe. We aimed to describe the treatment inferred natural course of IBD in a well-defined southern European IBD referral center.
AIMS&METHODS: We retrospectively reviewed all clinical data of our IBD patients from 1981 to 2011 (30 years) in order to overview IBD natural course, hospitalisations and pharmaceutical treatment during relapses. In our area the population is approximately 430,000 inhabitants and the migration rate is below 5%.
RESULTS: The study included data on 529 IBD patients (303 males) of whom 373 were diagnosed with UC (ulcerative colitis) and 148 with CD (Crohn's disease). We clearly recorded a CD upward trend in incidence over the past thirty years while UC incidence seems quite stable, the ratio UC:CD being currently 2.8:1. During the cumulative 30-year follow up, the majority of patients experienced 1 to 3 relapses per year (median 1.7) and these relapses were mainly treated with corticosteroids (30%), shifts to biologicals (11%) and surgeries (10%). Men relapsed more frequently compared to women (2.1 vs 1.8 relapses/year) and 36.7% of UC and 52.7% of CD required at least one hospitalization during follow up. Extraintestinal manifestations were more frequent in CD compared to UC (29.7% VS 8.8%) patients. A remarkable reduction of relapses during the last decade was observed. By contrast, in the last decade we observed a trend for more complicated and more severe CD patient cases compared to the past two decades.
CONCLUSION: In this south European IBD center UC and CD seem to have shared a rising trend for the last 30 years with a CD increasing preponderance and severity. By contrast, the number of relapses was markedly decreased during the last decade and this was probably related to the use of biologicals.
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Disclosure of Interest: None Declared
Keywords: Inflammatory bowel disease (IBD), natural history

P286 TIME-RELATED BIAS IN STUDIES OF INFLAMMATORY BOWEL DISEASE INCIDENCE USING ADMINISTRATIVE HEALTH DATABASES

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INTRODUCTION: Administrative databases are used extensively to describe the epidemiology, burden of disease and health outcomes of chronic diseases such as inflammatory bowel disease (IBD). Time-related biases may have been introduced in studies using administrative databases to estimate the incidence of IBD.

AIMS&METHODS: To illustrate and quantify the impact of time-related bias on estimates of IBD incidence rates using multiple validated case definitions.

A population-based cohort study was conducted using the administrative databases of the Régie de l'Assurance Maladie du Québec to identify all people with an IBD diagnosis code associated with physician billings or hospital admissions during the period 1996-2009. The IBD cases occurring during follow-up were identified using 5 different case definitions validated for use with IBD administrative databases. The definitions had as criteria varying combinations of physician claims and hospital discharge summaries with an IBD diagnosis code. Two of the definitions further specified a fixed time period to meet all criteria. Age and sex standardized incidence rates for IBD were calculated for 2 distinct time periods: 1996 to 2004 and 1996 to 2009.

RESULTS: A total of 240937 Québec residents had at least one diagnosis code of IBD during 1996-2009. When disease diagnosis was considered at the first IBD contact in the data, the incidence in 2001 calculated for the 1996-2004 period using the case definitions without a fixed time to meet criteria ranged from 22 to 56 cases/100,000 person-years (p-y). Using the 1996-2009 period, the incidence in 2001 increased by 10 to 23% (range: 27 to 62 cases/100,000 p-y). The use of a two year IBD free period prior to the first IBD contact in the data slightly reduced IBD incidence but did not influence the time-related bias. The bias was significantly reduced when using the two case definitions which specified a fixed time period for meeting the criteria. There was no time-related bias in estimates for the 1996-2004 period when disease diagnosis was considered at the time all criteria were met.

CONCLUSION: Time-related bias in estimates of disease occurrence can be minimized in administrative health database research when disease diagnosis is considered at the moment when all criteria are met, regardless of the case definition used. Implementing a disease free period is recommended to avoid overestimating the incidence rates.

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Disclosure of Interest: None Declared

Keywords: administrative database, bias, epidemiology, inflammatory bowel disease (IBD)

P287 THE PRESENCE OF PERIANAL DISEASE IN PATIENTS WITH OROFACIAL GRANULOMATOSIS INCREASES THE RISK OF DEVELOPING INTESTINAL CROHN'S DISEASE

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INTRODUCTION: Orofacial Granulomatosis (OFG) is a rare chronic inflammatory condition of unknown aetiology, characterised by lip swelling, orofacial erythema and ulceration. A proportion of OFG patients present with perianal disease in conjunction with their oral disease ('top and tail' disease). Perianal disease occurs in approximately one-third of Crohn's Disease (CD) patients and is associated with significant morbidity and a more severe disease course[1]. Perianal disease has been shown to occur in 12% of patients with ileal CD (L1), 41-92% of colonic CD (L2) and 15% of ileocolonic disease (L3)[2].

AIMS&METHODS: We retrospectively analysed a database of OFG patients. Patients with perianal disease were identified and compared to patients without perianal disease. The Montreal classification was used to classify the sites of patient's CD. We set out to determine how many of our OFG patients had concurrent perianal disease and how many of them developed intestinal CD.

RESULTS: 263 patients with OFG were identified, of which 208 patients (79.09%) had OFG only and 55 patients (20.91%) had concurrent intestinal CD. 36 patients (13.69%) had intestinal CD and no perianal disease. 19 patients ((7.22%) 13 male, median age 38 (IQR 25-49)) had intestinal CD and concurrent perianal disease.

Within the perianal group, all patients had concurrent intestinal CD. The commonest sites were colonic (L2)(8/19; 42.11%) and ileocolonic (L3)(8/19; 42.11%). The ileum (L1) was affected in 1 patient (1/19; 5.26%) and 2 patients had concomitant upper gastrointestinal CD with ileocolonic disease (L3+L4)(2/19; 10.53%).

The presence of OFG and perianal disease significantly increased the chances of developing intestinal CD (OR = 222, p = 0.0002, 2-tail Fisher Test).

In the perianal group, 11/19 patients (11/19; 57.89%) were diagnosed with CD prior to developing OFG. The median time to diagnosis of OFG was 10 years after the diagnosis of intestinal CD.

CONCLUSION: Perianal disease in Crohn's disease is common and is associated with a more severe disease course.[1] Perianal disease in OFG patients is less common, however, where it does occur it is always associated with intestinal CD in our cohort. Therefore, these patients should be investigated accordingly.

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The diagnosis of OFG was usually made later in the course of intestinal Crohn's suggesting it is a later development.

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P288 THE ROLE OF SERUM BETA 2 MICROGLOBULIN IN EVALUATING DISEASE ACTIVITY IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The inflammatory bowel diseases (IBD) are chronic inflammation of the digestive tract. The mucosa of the colon and small intestine of patients are common lymphoplasmacytoid cell infiltration. The inflammatory markers plays role in this inflammatory reaction such as lymphokines, cytokines and leukotriene. Beta 2 microglobulin (β2M) is a low molecular weight protein mainly released from activated lymphocytes. . Erytrocyte sedimantation rate (ESR), white blood cell count (WBC) and C-reactive protein (CRP) are known to be good predictors of disease activity in IBD. Serum β2M levels increase in all chronic inflammatory and autoimmune disease. This increase is linked to the severity and extant of inflammation.

AIMS&METHODS: In the study we examined β2M serum levels in patients suffering from IBD, to assess the extent of the disease and the possible correlation between these serum levels and the activity of IBD. Overall, 78 IBD patients and 30 healthy controls were enrolled. We examined β2M serum levels in 43 ulcerative colitis (UC) patients, 35 with Crohn's disease (CD) and 30 control subjects, using an enzymatic method. UC and CD patients were divided into two groups according to disease activity: Active and remission. Subjects were divided into two groups according to extend of disease: Left and pancolitis for UC ; İleitis and ileocolitis for CD. All groups were compared for the mean serum β2M levels.

RESULTS: Mean β2M values were significantly higher in UC and CD patients than in healthy controls. Mean β2M values were significantly higher in IBD activity than remission. The difference between groups (UC and CD) in terms of serum β2M levels was statistically insignificant

CONCLUSION: Serum β2M levels may be used as indicator to demostrate disease activity in patient with İBH.

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P289 IS THERE A DIURNAL VARIATION IN FAECAL CALPROTECTIN IN INFLAMMATORY BOWEL DISEASE PATIENTS?

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INTRODUCTION: Faecal calprotectin (FC) exhibits day to day variability in healthy subjects [1] and in patients with Crohn's disease [2;3]. However, the diurnal variation of FC in ulcerative colitis (UC), Crohn's Disease (CD) and in healthy controls has not yet been studied.
AIMS&METHODS: To investigate the magnitude of FC diurnal variation in inactive (SCCAI$\leq$2) and active (SCCAI$>$2) UC patients, inactive (HBI$\leq$5) and active (HBI$>$5) CD patients and in healthy controls.
Inflammatory bowel disease (IBD) patients were consecutively recruited from the out-patient clinic at Herlev Hospital during 2012. Controls were healthy healthcare workers and friends. All study subjects were asked to deliver a faecal sample from each stool they had during 3 days. Time and date had to be provided for each sample before sending them by post to the gastroenterology research laboratory for FC analysis by ELISA (CALPRO Inc.). The subject's individual FC diurnal variation was defined as the largest difference between the highest (FC high) and the lowest (FC low) FC values on the same day. Statistical analysis was done by non-parametric Wilcoxon signed-rank and Kruskal-Wallis tests.
RESULTS: A total of 514 FC samples were collected from 51 IBD patients (15 inactive UC (UCI), 14 active UC (UCA), 12 inactive CD (CDI), 10 active CD (CDA); total 55% female) and 30 healthy controls (53% female).

	UCI	UCA	CDI	CDA	Healthy controls
FC diurnal variation, mg/kg (mean ±SD)	229 ±295	581 ±573	137 ±117	289 ±234	18,2 ±20,9
Mean FC, mg/kg (mean ±SD)	237 ±352	752 ±611	371 ±434	232 ±277	20,4 ±24,3
FC high, mg/kg (mean ±SD)	337 ±388	899 ±640	463 ±451	504 ±428	29,8 ±33,0
FC low, mg/kg (mean ±SD)	108 ±135	318 ±332	326 ±399	215 ±317	11,65 ±15,7
Defecations per subject per day (mean ±SD)	2,4 ±0,8	3,3 ±2,7	2,4 ±0,8	3,9 ±2,0	1,8 ±0,5
No. of FC tests	83	106	74	92	159

FC diurnal variation in healthy controls differed significantly from UCI (p=0,001), UCA (p$<$0,0001), CDI (p=0,018) and CDA (p$<$0,0001). Mean FC in healthy controls differed significantly from UCI (p$<$0,0001), UCA (p$<$0,0001), CDI (p$<$0,0001) and CDA (p$<$0,0001). Mean FC in UCA differed significantly from UCI (p$<$0,0001), CDI (p$<$0,032) and CDA (p=0,001).
CONCLUSION: FC diurnal variation in healthy controls is negligible. In both inactive and active CD patients and in inactive UC patients the FC diurnal variation is acceptable when monitoring disease activity by FC in routine clinical practice. In UC patients with active disease, FC diurnal variation is substantial and clinically considerable. We suspect, however, that blood, pus and mucus in the stool could influence FC levels in these patients. Further studies are needed to clarify this issue.
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Keywords: Biological variability, Crohn's disease, Diurnal variation, Faecal Calprotectin (FC), Inflammatory bowel disease (IBD), Ulcerative colitis

P290 ASSESSMENT OF DAILY PHYSICAL ACTIVITY IN PATIENTS WITH CONTROLLED INFLAMMATORY BOWEL DISEASE - RELATIONSHIP WITH DISEASE PHENOTYPE AND OSTEOPOROSIS OR OSTEOPENIA

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INTRODUCTION: Physical activity (PA) has been thought as having beneficial effects in patients with inflammatory bowel disease (IBD), including the

prevention of low bone mineral density [1]. Nevertheless, knowledge concerning the relationships between PA and phenotype and occurrence of bone metabolic disease in IBD is still limited.
AIMS&METHODS: This study aimed at evaluating daily PA in IBD patients and control volunteers using a standard inventory, and at determining differences regarding PA between subgroups of IBD patients stratified according to phenotype and the presence of osteoporosis or osteopenia. Crohn's disease (CD, N=35) and ulcerative colitis (UC, N=25) patients in remission or low disease activity and healthy controls (N=42) answered the long form of the International Physical Activity Questionnaire [2]. Results were expressed as minutes/week in four domains (work, transportation, home and leisure), and classified in three grades (walking, moderate or vigorous). IBD patients also underwent dual X-ray absorptiometry scanning to detect osteoporosis or osteopenia. CD and UC patients were stratified regarding disease extent and the presence or absence of osteopenia or osteoporosis. CD patients were further stratified according to disease behavior.
RESULTS: Total daily PA in CD patients were lower than in the UC group in the four domains assessed, but differences were not statistically significant. PA levels in DC patients in the leisure domain were significantly lower than in controls (164±491 min/week vs. 686±1069 min/week; $p < 0.01$). Also, the proportion of CD patients exerting total daily vigorous activity was lower than in controls (10/35 vs. 20/42), but again statistical significance was not reached (p=0.10). In CD there were no differences concerning PA between patients with and without stenosing or penetrating behavior, as well as between patients with ileal or ileocolonic CD compared to those with exclusive colonic disease. In UC, there was no difference in total daily PA between patients with pancolitis and those with left-side colitis or proctitis. Both CD and UC patients with osteoporosis or osteopenia had lower levels of total daily PA, but statistical significance was not reached ($p > 0.05$).
CONCLUSION: Physical activity in controlled ulcerative colitis seems to be less affected than in Crohn's disease. In controlled IBD patients there seems to be no relationships between physical activity and disease phenotype. Lower levels of daily physical activity in IBD patients seem to be associated with osteopenia and/or osteoporosis, which suggest a role for this factor in the reduction of bone mineral density.
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Keywords: bone metabolic disease, Crohn's disease, Inflammatory bowel disease (IBD), osteoporosis, Physical activity, ulcerative colitis

P291 CLINICAL DECISION MAKING IN CROHN'S DISEASE USING SMALL INTESTINE CONTRAST ULTRASONOGRAPHY

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INTRODUCTION: While there is sufficient data to support the use of small intestine contrast ultrasonography (SICUS) as a valuable and radiation-free tool in the detection of intestinal damage of small bowel Crohn's disease (CD), there is limited data showing its impact on patient management. Our aim was to evaluate whether SICUS has an impact in the clinical management of CD.
AIMS&METHODS: We performed a retrospective analysis of data from patients with CD who underwent SICUS through one year (2011) and were followed up for at least one year. A total of 216 CD pts (121 M; median age 44 yrs; disease duration: median 139 mos; CD site: ileal in 171 pts, ileo-colonic in 45 pts; CD behavior: non-stricturing non-penetrating in 77 pts, penetrating in 44 pts, stricturing in 95 pts; previous ileocolonic resection in 113 pts) were included. CD therapy at the time of the examination included: 49% on mesalamine, 26% on steroids, 1% on antibiotics, 8% on thiopurines, 13% on biological drugs, 2% on SMAD7 antisense oligonucleotide (GED0301), and 1% no therapy. Indications of patient evaluations were assessment of disease activity, obstructive symptoms, pre-surgical evaluation, and monitoring therapy.
RESULTS: After SICUS variation in clinical management was made in 109/216 pts (50.5%). Eighteen pts underwent surgery and 91 pts experienced changes in medical therapy. Twenty-seven out of 91 pts started a steroid course; 14 pts started an antibiotic course; 20 pts were treated with immunosuppressives. Twelve pts started biological treatment. Six pts optimized anti-TNFs maintenance dose. Three pts stopped biological therapy and one pt switched from Adalimumab to Infliximab. Eight pts were enrolled in the clinical trial GED0301. After SICUS median time of follow-up of pts who underwent a change in clinical management was 15.9 mos. One hundred and seven pts continued their treatment after SICUS with a median time of follow up of 16.4 mos. Abnormal sonographic findings (bowel wall thickness, lesion extent, stenosis with or without dilation, fistula, and abscess) yielded significantly more in the group who experienced a change in clinical management compared with pts who continued previous treatment (p=0.001).
CONCLUSION: More than half CD pts had a change in clinical management on the basis of SICUS. SICUS is a non-invasive, radiation-free and easily available imaging modality therefore its use might be implemented as part of a focused diagnostic examination in CD.
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Disclosure of Interest: None Declared
Keywords: CROHŃS DISEASE, Imaging, managment

P292 COLONIC MUCOSAL HEALING IN IBD PATIENTS DURING CLINICAL REMISSION. A PROSPECTIVE STUDY USING COLONOSCOPY, CONFOCAL LASER ENDOMICROSCOPY (CLE) AND HISTOLOGY

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INTRODUCTION: In IBD, mucosal healing seems associated with a lower relapse rate. Very few studies have used confocal laser endomicroscropy (CLE).
AIMS&METHODS: Our aims were: 1) to prospectively assess and characterize the inflammatory pattern of colonic lesions in IBD patients during full clinical remission, 2) to compare results of real-time CLE with classical histology.
73 patients (44 years, 35 males) with ulcerative Colitis (n=41), Crohn's Disease (n=29), or indeterminate (n=3) gave their informed consent. All patients had long duration IBD (18.4 years) and were in clinical remission (Harvey-Bradshaw < 3 or CDAI < 150). Colonoscopy was performed first, followed by CLE (with fluorescein). Colon was divided in 4 segments and systematic optical biopsies were taken. Then, biopsies were obtained at the same spots for histology (30 to 40 in total). Inflammatory lesions were scored according to previously defined grades.
RESULTS: Among 73 patients, 18 were excluded from the analysis for various reasons (2 stenosis, 2 CLE technical failures, 14 others). Out of remaining 55 patients, 16 showed mucosal erosions or ulcerations at colonoscopy. Among the 39 patients completely healed, only 10 had no inflammatory lesions at both CLE and histology. Finally, in 29 patients, despite complete healing at colonoscopy, various degrees of inflammation persisted in at least one segment. Globally the results of CLE and histology were well correlated with only 5 cases of major discrepancy. The procedures were well tolerated.
CONCLUSION: 1) Despite complete healing at endoscopy, the majority of IBD patients in remission still have inflammatory lesions at microscopic examination. The role of this residual inflammation in further relapse of IBD remains to be further elucidated. 2) Since the information obtained by CLE is well correlated with routine histology, CLE may help better characterize the phenotype of patients in remission as well as reduce the need for numerous biopsies.
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Disclosure of Interest: None Declared
Keywords: endomicroscopy, mucosal healing, remission

P293 RESTORATION OF HEALTH RELATED QUALITY OF LIFE IN CROHN'S DISEASE PATIENTS WITH ADALIMUMAB MAINTENANCE THERAPY.

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INTRODUCTION: In Crohn's disease (CD), adalimumab maintenance therapy provides sustained clinical remission and improvement of health related quality of life (HRQOL). However, there is scarce information about its long-term effect on HRQOL and whether it is able to induce a sustained restoration of normal patient's perception of health.
AIMS&METHODS: AIMS: To determine HRQOL and restoration of normal perception of health in patients with adalimumab induced long-term CD clinical remission. METHODS: Observational study in patients with CD in clinical remission (CDAI index < 150) for at least 12 months, treated with long-term adalimumab 40 mg every other week, with or without thiopurines. Patients were followed each year during 4 years or until clinical relapse (CDAI index > 150), intensification or surgery was needed. HRQOL was evaluated with the specific IBDQ-36 items version validated to Spanish. Restoration of health was defined as an overall IBDQ score ≥ 209 [JCC 2010;4:637-41]).
RESULTS: From 63 eligible patients, 43 patients with CD in stable clinical remission sustained over one year were included. During the follow-up, at 12 months 43 patients remained in remission, at 24 months 30 patients, at 36 months 15 and in the last visit at 48 months remained 9 patients in clinical remission. Overall score of IBDQ-36 remained unchanged in patients with stable inactive CD, even with a tendency to score better with time (median global score of 226 at 12 months and 241 at 4 years). Restoration of health increased with time (72 % to 100 % at 1 and 4 years follow-up respectively).
CONCLUSION: Sustained clinical remission of CD achieved with maintenance adalimumab treatment restores HRQOL, which remains stable at long-term follow-up.
Disclosure of Interest: None Declared
Keywords: crohn's disease, quality of life, restoration of health

P294 LONG-TERM PROGRESSION OF BOWEL DAMAGE IN CROHN'S DISEASE PATIENTS TREATED WITH ANTI-TNF THERAPY: A PROSPECTIVE OBSERVATIONAL COHORT STUDY.

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INTRODUCTION: Crohn's disease (CD) leads to complications and consequent bowel damage (BD). Magnetic resonance imaging (MRI) can assess BD and its progression during disease course. There are no data on the role of current medications on CD-related damage progression.
AIMS&METHODS: We aimed to explore the long-term progression of BD in a cohort of CD patients treated with anti TNF. This was a prospective observational cohort study on consecutive CD subjects followed within 3 years. They all underwent an abdominal MRI and colonoscopy, and a pelvic MRI in case of

perianal disease, before starting anti-TNF therapy and then each year. CD-related BD at baseline and at follow-up was graded by a semiquantitative scale from 0 to 3 for strictures, abscesses and penetrating lesions per bowel segment. BD progression and regression were defined as an increase or a reduction in the sum of scores from baseline, respectively. The primary outcome was to assess the progression of BD. Secondary outcomes were to assess the role of MRI findings in detecting and predicting BD progression, and the rate of surgery and its correlation with damage progression. Statistical analysis included χ^2 test, logistic regression and survival analysis by Kaplan-Meyer curves and log-rank test. Any difference was considered statistically significant if $p<0.05$.

RESULTS: Twenty-eight CD patients were enrolled,11 infliximab (IFX), 17 adalimumab (ADA). The mean baseline damage score in the whole study population was 4.19 (range 0.19-32.42). Ten subjects (35%) had perianal disease. Mean follow up was 35 months. At follow-up, 67.9% had BD regression (IFX=9; ADA=6), while 29.6% of had BD progression (IFX=2; ADA=6),. Mean difference in the BD score between baseline and follow-up was -0.30 (range -0.28-1.92). Seven subjects (25%) of the whole population had major bowel surgery due to symptomatic complications (IFX=2; ADA=5), 2 for refractory disease, and 5 for stricturing and penetrating disease. Subjects with BD progression were more likely to undergo major surgery in the following 12 months (HR 0.23, CI 95% 0.02-0.87, p=0.03). MRI findings suggestive for BD alone was significantly predictive of global BD (OR 30.0, CI 95% 2.5-354, p=0.007). No other significant predictive factors of surgery were found. No statistically significant differences were found between IFX and ADA.

CONCLUSION: In the majority of subjects treated by anti-TNF, a reduction of BD can be achieved in the long term. BD progression assessed by MRI is predictive of major surgery within 12 months.

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Keywords: biologics, Bowel damage, CROHŃS DISEASE, magnetic resonance imaging

P295 CORRELATION BETWEEN ADALIMUMAB TROUGH SERUM CONCENTRATION, ANTI-ADALIMUMAB ANTIBODIES AND TNF-A LEVELS WITH CLINICAL OUTCOME IN PATIENTS AFFECTED BY CROHN'S DISEASE

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INTRODUCTION: Few data are available on the role of Adalimumab (ADA) trough serum concentrations and anti-ADA antibodies (AAA) in influencing the therapeutic response of Crohn's Disease (CD), and even less, on the importance of analyzing TNF-α serum levels in ADA-treated patients during long-term follow-up

AIMS&METHODS: To evaluate the course of ADA trough serum concentrations, AAA formation and TNF-α serum levels and their clinical relevance during a long-term follow-up period of patients with CD.

In this prospective study, 21 consecutive CD patients (13M/8F; mean age 41), who achieved remission and in maintenance treatment with ADA, were included in a 2-years follow-up program. Blood samples were drawn at standardized time points (at 6, 12, 18, 24 months and in case of CD relapse) just before ADA injection. Trough ADA serum concentrations and AAA were measured using an enzyme-linked immunosorbent assay (Matriks biotek). Moreover, TNF-α serum levels were measured using a human TNF-α ELISA (DIACLONE). Disease activity was assessed at the same time points by means of the Harvey-Bradshaw Index (HBI; remission <5, mild disease 5-7, moderate disease 8-16, severe disease >16) and CRP blood level (normal if <5 mg/L).

RESULTS: During follow-up, 16 (76%) patients maintained clinical remission and continued ADA therapy until 96 weeks, while 5 (24%) patients withdrew ADA because of perianal abscess development (n=1) and lack of response despite escalation of ADA administration (n=4). At the time of recurrence, patients who relapsed had lower median ADA serum concentrations compared to those in remission [3.7 mcg/ml (range 0.0-6.1) vs. 7.8 mcg/ml (6.8-9.1), (p=0.0001)]. There was a good correlation between ADA serum concentration and disease activity expressed by HBI (r^2=0,6583, $p<0.001$). Values of CRP were higher in patients who relapsed than in those in remission [(3.3 mg/l (0.8-4.8) vs. 8.3 (3.3-36.2)] (p=0.0018). In addition, median TNF-α serum levels were not different between these two groups (51.4 pg/ml [1-143.2] vs. 28.1 [3.3-72.9], p=0.1). No correlation was found between ADA serum concentrations and TNF-α levels (r^2=0,0084, $p<0.692$). AAA were found in only 2 (9%) patients and did not affect ADA serum concentrations (8.8 mcg/ml before and after AAA development) and outcome.

CONCLUSION: Earlier ADA therapy discontinuation and disease relapse correlated well with lower ADA serum concentrations during a 2 year follow-up period. The measurement of TNF-α serum levels seems of limited value in the management of CD patients and ADA efficacy. Development of AAA does to not influence ADA serum concentrations and good outcome.

Disclosure of Interest: None Declared

Keywords: adalimumab, Crohn's disease, IBD

P296 SCREENING FOR DYSPLASIA AND COLORECTAL CANCER IN ULCERATIVE COLITIS

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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

To evaluate the proportion of dysplastic lesions detected from targeted biopsies of macroscopically visible abnormalities, as opposed to non-targeted biopsies of colonic mucosa.

In this prospective study, consecutive patients with clinically inactive, longstanding UC (8 years) were recruted from 3 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 endoscopy were performed by a single endoscopiste, all the biopsies have beneficied of a second lecture by a pathologist experienced in gastroenterology

RESULTS: 177 chromoendoscopy were performed in 100 patients (45 men and 55 women); Median age of patients at inclusion was 50 years (range 22–78); median age at onset of ulcerative colitis was 34,4 years (range 15–66); and the median duration of colitis was 15.70 years ±6.79 .

The proximal extent of macroscopic inflammation at diagnostic of ulcerative colitis was pancolonic in 50 patients (50%), Left-sided colitis in 26 (26%), Proctosigmoiditis 24 (24 %)

Overall, 324 suspicious mucosal areas were biopsied or removed in 76 patients: there were 5 adenocarcinomas,3 high grade dysplasia with 2 DALM , 14 low grade dysplasia, 5 villous adenomas with low grade dysplasia, 7 serrated adenomas, and 289 post-inflammatory polyps.

Non-targeted quadrantic biopsies detected: high grade dysplasia in one patient and low grade dysplasia in 5 patients.

A total of 33 neoplastic lesions were identified in 25 patients (25%): 5 adenocarcinomas and 28 dysplasia. 81.81% of these lesions were macroscopically visible at colonoscopies, whereas18.18% were detected only by random biopsies. All the adenocarcinomas were perfectly visible at endoscopy before coloration

Dysplasia was endoscopically visible in 22 patients, in 2 patients dysplasia was detected both by random biopsies and target biopsies; in 3 patients dysplasia was invisible at endoscopy, detected only by random biopsies.

CONCLUSION: Colonoscopic surveillance is actually the only way to detect colorectal cancer at an early stage in ulcerative colitis

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Disclosure of Interest: None Declared

Keywords: colorectal cancer screening, Dysplasia, ulcerative colitis

P297 EVALUATION OF MUCOSAL INFLAMMATION OF CROHN'S DISEASE OR ULCERATIVE COLITIS BY A QUANTITATIVE FECAL IMMUNOCHEMICAL TEST

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INTRODUCTION: Colonoscopy is gold standard for evaluating colon mucosal inflammation in Crohn's disease (CD) or ulcerative colitis (UC). But it is invasive, time-consuming and expensive test. Quantitative fecal immunochemical tests (FITs), which have been used recently to screen for colorectal neoplasia are rapid, easy and economic method.

AIMS&METHODS: The aim of this study is to determine whether quantitative FIT can reflect the colonic mucosal inflammation in CD or UC patients. Feces collected from CD or UC patients who underwent colonoscopy were examined by FITs, and results were compared with colonoscopic findings. Mucosal inflammation status was assessed using the simple endoscopic score for Crohn's Disease (SES-CD) in CD and the Mayo endoscopic subscore classification in UC.

RESULTS: FIT results were evaluated in conjunction with 70 colonoscopies that were performed in 55 CD patients and 118 colonoscopies in 99 UC patients. When the positive FIT was defined as $\geq$100 ng/ml, the proportion of positive FIT results increased with increased in the SES-CD (SES-CD 0-3: 17.4%, SES-CD 4-10: 54.2%, SES-CD 11-19: 60.0% and SES-CD$\geq$20: 100%, $p<0.001$, Chi Square test for trend) and Mayo endoscopic subscore (Mayo 0: 0%, Mayo 1: 33.3%, Mayo 2: 65.8% and Mayo 3: 88.2%, $p<0.001$, Chi Square test for trend). The mean of SES-CD and Mayo endoscopic subscore were significantly different according to the quantitative levels of FIT (One way ANOVA, $p<0.001$). When mucosal inflammation was defined as SES-CD$\geq$4 and Mayo 2 or 3, the sensitivity, specificity, positive predictive value and negative predictive value of a positive FIT for mucosal inflammation were 63.8%, 82.6%, 88.2% and 52.8% in CD and 76.4%, 71.7%, 80.9% and 66.0% in UC, respectively.

CONCLUSION: The FITs could be a potential alternative method for crude evaluating and monitoring mucosal inflammation.

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Disclosure of Interest: None Declared

Keywords: Crohn's disease, fecal immunochemical test, mucosal inflammation, ulcerative colitis

P298 QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE PATIENTS: CLINICAL, DEMOGRAPHIC AND SOCIAL FACTORS

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INTRODUCTION: Inflammatory Bowel Disease (IBD) causes physical, psychological and social consequences that can affect the Quality of Life (QOL) of patients.
AIMS&METHODS: The aim of our study was to analyze the relationship between clinical, demographic and social factors and the QOL in patients with IBD. A total of 150 patients, 98 with Crohn' disease and 58 with ulcerative colitis, filled in a specific questionnaire to assess QOL in IBD patients (Inflammatory Bowel Disease Questionnaire, IBDQ-32) and a questionnaire to collect demographic and clinical data.The association between categorical variables and IBDQ-32 scores was determined using Student t test. Factors statistically significant in the univariate analysis were included in multiple linear regression model. The statistical level of significance was established at 5%. Statistical analysis was performed with SPSS (version 18.0).
RESULTS: Univariate analysis revealed QOL scores significantly lower in patients with an individual perception of a lack of awareness of co-workers ($p < 0.001$), decreased employment success ($p < 0.001$) and need for psychological support ($p = 0.010$). Female patients ($p < 0.001$), patients requiring pharmacological treatment of anxiety or depression ($p = 0.002$) or that resorted to alternative therapies ($p = 0.027$) also presented with significantly lower QOL scores. A multiple linear regression analysis identified as significant predictors of impaired QOL female gender ($p < 0.001$), individual perception of a lack of awareness of co-workers ($p = 0.037$) and decreased employment success ($p = 0.001$). This model was highly significant ($p < 0.001$) and explained 32.3% of the variation in QOL scores in patients with IBD.
CONCLUSION: The decrease in quality of life was significantly related with female gender and personal perception of disease impact in success and social relations. These factors deserve a special attention, so timely measures can be implemented in other to improve the quality of life of these patients.
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Disclosure of Interest: None Declared
Keywords: Crohn' disease, Inflammatory Bowel Disease, Quality of Life, Ulcerative Colitis

P299 MEASUREMENT OF FECAL CALPROTECTIN IN ULCERATIVE COLITIS: CORRELATION TO ULCERATIVE COLITIS ENDOSCOPIC INDEX OF SEVERITY, MAYO ENDOSCOPIC SCORE AND HISTOLOGICAL INFLAMMATORY ACTIVITY SCORE

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INTRODUCTION: Mucosal healing in ulcerative colitis (UC) has emerged as a treatment goal in international guidelines because mucosal healing implies decreased risk of relapse. Therefore reliable non-invasive methods to assess the grade of inflammation and mucosal healing need to be developed and validated. In this study we evaluate the correlation between fecal calprotectin (FC) and two endoscopic score modalities as well as histological inflammatory activity score.
AIMS&METHODS: In a prospective cross-sectional study, 54 patients including subjects with both clinically active and inactive UC underwent sigmoidoscopy. Mayo Endoscopic Score (MES) and the newly developed Ulcerative Colitis Endoscopic Index of Severity (UCEIS) were used to evaluate the endoscopic inflammation. Rectal biopsies were evaluated for the grade of inflammation using a histological activity score with 4 categories based on the extent of cryptitis, crypt abscesses and the presence of erosions/ulcers. Prior to the sigmoidoscopy stool samples were obtained and FC was determined. We used Kruskal-Wallis test to compare FC with MES and histology and linear regression to compare FC with UCEIS. Wilcoxon Rank Sum Test was used to compare FC between groups.
RESULTS: The median age was 38 years, 32 (59%) were female and the median disease duration was 6 years. 23 (43 %) had endoscopic remission. We found a significant difference in FC between the MES-groups (0-3) (Chi-square=24,4090, p=<0,0001) and in FC between the histological groups (0-3) (Chi-square=19,3668, p=0,0002). We found a significant relationship between FC and UCEIS with an estimate (slope) for UCEIS on 376,18 g/kg (CI95%: 268,13;484,24 g/kg, p=<0.0001). Specifically we found a significant difference in FC between MES=0 and MES=1 (p=0,0088) as well as between UCEIS=3 and UCEIS=4 (p<0,0001)
CONCLUSION: We compared FC with MES, UCEIS and histological inflammatory activity score and in all cases significant correlations was demonstrated. The correlation between FC and MES has been shown in previous studies and confirmed by our data. Especially we found that FC is able to discriminate between MES 0 and 1 as well as between UCEIS 3 and 4, an important message regarding the evaluation of mucosal healing. Studies comparing FC with UCEIS and histological inflammation are lacking but in our study significant correlation between both of them were obtained. With mucosal healing as an important treatment goal in ulcerative colitis FC might have a place in determining the grade of inflammation and achievement of mucosal healing.
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Keywords: calprotectin, endoscopic severity, histologic severity, inflammation, ulcerative colitis

P300 FETAL RISKS IN INFLAMMATORY BOWEL DISEASE PREGNANT PATIENTS. A PROSPECTIVE STUDY

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INTRODUCTION: During pregnancy(P) of inflammatory bowel disease (IBD) patients ,fetal risk is generally considered as low.
AIMS&METHODS: To evaluate influence of IBD on P,we have in a 5-year follow-up prospective study, compared the fetal prognosis in pregnant IBD patients to that of a control group (CG) of 104099 non IBD pregnant women who have had 1 or several pregnancies during the same period.Fetal risk was assessed for the last P by evaluating,in the two groups,the rate of normal childbirth ,abortions,premature births,stillbirths,low birth weight and congenital abnormalities.In IBD patients outcome of P was also evaluated as regards to the evolutive statute of the disease at conception and to their gestational status;Statistical analysis:Student Fisher's test and Mann Whitney's U test.
RESULTS: Regarding the last pregnancy :1/The rate of caesareans was surprisingly lower in UC patients than in the CG (7,1% vs 23,3%; p=0,0001);In return abortions (3,6% vs 3%; p=0,9244),premature births (6,2% vs 4%; p=0,3441), stillbirths (1,8% vs 1,4%; p=0,9663),low birth weight (8% vs 5,2%; p=0,2624) were more frequent in UC patients but they did not reach SSD.2/The same results were found in CD vs CG pregnant patients:caesareans (11,8% vs 23,3%; p=0,045), abortions (7,1% vs 3% ; p=0,0236), stillbirths (1,8% vs 1,4% ;p=0,9147), premature births (6,2% vs 4%; p=0,3441), low birth weight (8,5% vs 5,2%;p=0,1742). 3/Caesareans and abortions rates were higher in CD than in UC ;11,5% vs 7,1% (p=0,3662) and 7,1% vs 3,6% (p=0,3859) respectively but didn't reach SSD.Concerning the whole number of pregnancies after onset of the disease:1/Complications were more frequent in primiparous than in multiparous UC and in CD pregnant patients:caesareans (UC:19,2% vs 2,7%: p<0,0001; CD:35,7% vs 6,7%: p<0,0001), stillbirths (UC=3,8% vs 1%; p<0,2237; CD=3,6% vs 1,7%, p=0,9528), congenital abnormalities (UC = 3,8% vs 0%, p=0,0318; CD=3,6% vs 0,5%, p=0,5947). Those complications seem to be due to the gestational status himself than to IBD as they were found to the same extent in the CG.2/Fetal risk was proportional to the disease activity at conception in UC as well as in CD pregnant patients.
CONCLUSION: During P of IBD patients fetal risk is relatively low as well in UC as in CD.Complications are proportional to the level of disease activity at conception and seems to be higher in primipary pregnant IBD patients.
Disclosure of Interest: None Declared
Keywords: Fetal risk, IBD, Pregnancy

P301 LEVELS OF ANTI-DOUBLE-STRAINED DNA BUT NOT ANTINUCLEAR ANTIBODIES IN PATIENTS WITH IBD TREATED BY ANTI-TNFS ARE ASSOCIATED WITH ADVERSE OUTCOMES

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INTRODUCTION: Treatment of Crohn's disease (CD) by infliximab has been associated with the induction of antinuclear (ANA) and anti-double stranded DNA (dsDNA) autoantibodies and in some studies the formation of dsDNA antibodies was associated with lupus-like syndromes.
AIMS&METHODS: The aim of this study was to analyze the relationship between the development ANA and ds-DNA antibodies during anti TNF therapy and adverse outcome (LOR, allergy, lupus like syndrome, induced autoimmune disorders) in patients with inflammatory bowel diseases (IBD). Data of 105 (96 CD, age at diagnosis: 27.1 SD: 10.05 years, duration: 8.2 SD 6.6 years, males/females 48/57) patients treated with anti-TNFs for at least one-year. Records of a total of 198 one-year treatment cycles were collected and levels of auto antibodies were determined at induction and after the one-year period.
RESULTS: The majority of CD patients had ileocolonic (67.4%) and complicated (B2-B3: 72.6%) with perianal lesions (63.2%). ANA (12.3%) but not dsDNA positivity was frequent already and induction. Any time ANA or dsDNA positivity was 28.6% and 18%. Elevated level of ANA at induction time or during anti-TNF therapy was not associated with the efficacy of the therapy or the development of adverse outcomes. In contrast, treatment efficacy (no/partial response, dsDNA positivity: 31.5% vs. 68.5%, p=0.003) was inferior and adverse outcomes were more frequent (dsDNA positivity: 38.7% vs. 14.6%, p=0.01, OR: 3.71, 95%CI: 1.31-10.5) in patients with dsDNA positivity.
CONCLUSION: Our data suggest that development of ds-DNA during biological therapy is associated with treatment efficacy and adverse outcomes.
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Disclosure of Interest: None Declared
Keywords: autoantibodies, biological therapy, inflammatory bowel disease, therapy monitoring

P302 EFFECTS OF DIET AND PHYSICAL ACTIVITY INTERVENTIONS ON FATIGUE IN PATIENTS WITH QUIESCENT ULCERATIVE COLITIS

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INTRODUCTION: Fatigue in ulcerative colitis (UC) is often to be considered an effect of disease activity. But when the disease is clinically inactive, many patients still suffer from fatigue suggesting that fatigue is related to other factors which could be important to identify to improve UC patients' well-being.
AIMS&METHODS: The aim of our study was to evaluate the effects of diet and physical activity interventions on fatigue in patients with quiescent UC. Seventy patients (M/F=40/30, median age 44 years) with quiescent UC were enrolled in the study. A six-month lifestyle intervention which included diet and physical activity was performed. All participants were prescribed a diet in which the estimated daily caloric needs was carried out according to physical activity and ideal body weight and the daily intake of individual nutrients was carried out according to recommended daily intake of nutrients. Moreover, moderate-intensity physical activity progressed to 60 minutes, 3 days per week was prescribed. Fatigue was assessed by the Multidimensional Fatigue Inventory (MFI), a 20-item, self-report instrument designed to measure five fatigue dimensions: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue.
RESULTS: Fifty-six patients completed the study. Two patients showed a reactivation of UC and were excluded. After six months of diet and physical activity interventions a significant reduction of MFI scores for general fatigue (12.93 ± 2.46 vs 10.4 6 ±2.37; p=0.01), physical fatigue (12.64 ± 3.03 vs 10.17 ± 2.37; p=0.03), reduced activity (13.14 ± 2.63 vs 10.77 ± 2.05; p=0.01), and mental fatigue (12.57 ± 1.99 vs 10.31 ± 1.49; p= 0.002) was seen. On the other hand a not significant reduction of MFI score for reduced motivation (11.79 ± 1.89 vs 10.29 ± 2.37; p=0.07) was seen. Moreover, the percentage of patients with MFI score for general fatigue >12 was significantly reduced (51.8% vs 27.7%; p= 0.01).
CONCLUSION: The high prevalence of significant fatigue in patients with quiescent UC has implications for the clinician. The pathogenesis of fatigue in these patients is almost certainly multifactorial. Our data have shown that diet and physical activity interventions can improve fatigue in quiescent UC. If the improvement was due to psychological or biological factors remains to be elucidated.
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Disclosure of Interest: None Declared
Keywords: Diet, Fatigue, Physical activity, Ulcerative colitis

P303 CLINICAL COMPARISON OF TWO DIFFERENT FECAL CALPROTECTIN IMMUNOASSAYS FOR THE DIAGNOSIS AND FOLLOW-UP OF INFLAMMATORY BOWEL DISEASE.

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INTRODUCTION: Backgrounds: Fecal calprotectin (FC) is a useful marker for diagnosis and follow-up of inflammatory bowel disease (IBD). Recently, a fast and automated test has been introduced for detection of FC. We prospectively evaluated the performance of 2 different calprotectin immunoassays for the diagnosis of IBD and for monitoring disease activity in patients with Crohn's disease (CD).
AIMS&METHODS: Materials and Methods: 183 consecutive patients with suspected IBD were prospectively included over a two- month period. Additionally, 26 patients in follow-up provided consecutive stool samples over a 26-week period for FC measurement. We determined FC by a quantitative immuno-chromatographic point-of-care-test (POCT) Quantum Blue (Bühlmann) and a fully automated immunoassay (Thermo-Fisher). Results were compared with endoscopic and histological findings.
RESULTS: Results: Among the study population, the prevalence of IBD was 27.9% (51/183). After adjusting the optimal cut-off by ROC-curve analysis, sensitivity and specificity for diagnosis of IBD were comparable for both assays. For the Quantum Blue POCT (cut-off 113 µg/g), a sensitivity and specificity of 90.2% and 90.9% were obtained, respectively; for the EliA Calprotectin assay (cut-off 56 µg/g), a sensitivity and specificity of respectively 94.12% and 87.9% were obtained. For the Quantum Blue POCT and the EliA Calprotectin assay, we found an area under the curve of respectively 0.955 and 0.962 (P=0.586). The overall accuracy was 90.2% for the POCT assay and 89.6% for the EliA assay.
When using the manufacturer's cut-offs (both 50 µg/g), the sensitivity of the POCT assay increased up to 100%; although a decrease in specificity was obtained (72.0%). For the EliA assay, the same sensitivity (87.9%) and specificity (94.12%) as for the optimal cut –off were determined.
For the follow-up patients, we noticed a similar pattern throughout the period for both assays, but the results with the EliA calprotectin assay were lower.
CONCLUSION: Conclusions: Both FC assays showed acceptable and comparable clinical performance for diagnosis if IBD. Sensitivity varies with the chosen cut-off. For follow-up of known IBD, performance of both assays was equally. Although a similar pattern was noticed, multiple follow-up samples of one patient must be measured by the same assay. The automated EliA immune-assay is a good alternative to the more labor intensive POCT as the first screening assay in patients with IBD.
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Disclosure of Interest: None Declared
Keywords: Automated Assay, Diagnosis, Fecal calprotectin, Follow-up, Inflammatory Bowel Disease

P304 HOSPITALIZATION RATES BEFORE AND AFTER ANTI-TNF THERAPY, RESULTS FROM A SINGLE CENTER

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INTRODUCTION: Hospitalization is an important outcome measure and a major driver of costs in patients with IBD.
AIMS&METHODS: Our aim was to analyze prospectively the prevalence and predictors of hospitalization and re-hospitalization before and after anti-TNF therapy.
Data of 91 consecutive IBD (77 CD, 14 UC) patients were analyzed (male/female: 45/46, median age at diagnosis: 24.0; SD: 9.8 years) in whom anti-TNF therapy was started after January 1, 2009. Total follow-up was 859 patient-years and 251 patient-years with anti-TNF exposure. Both in- and outpatient records were collected and comprehensively reviewed.
RESULTS: The hospitalization rate in the 2 years preceding anti-TNF therapy was significantly higher compared to the hospitalization rate after the start of continuous anti-TNF therapy (47.2/100 patient-years vs. 19.1/100 anti-TNF exposed patient-years, OR: 0.40, 95%CO 0.27-0.61, $p < 0.001$). The risk for hospitalization before or after the anti TNF-therapy was not associated to any clinical or treatment parameter assessed in this study (e.g. gender, sex, age, disease type, location/extent, phenotype, steroid or immunosuppressive exposure, surgery or anti-TNF type).
CONCLUSION: Hospitalization rates decreased significantly in this referral IBD cohort after the introduction of anti-TNF therapy. We were unable to identify any predictors for hospitalizations preceding or during anti-TNF therapy.
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Disclosure of Interest: None Declared
Keywords: anti-TNF, hospitalization, referral centrum

P305 ABERRANT CRYPT FOCI IN THE RECTUM OF PATIENTS WITH ULCERATIVE COLITIS - ANY ASSOCIATION WITH THE RISK OF NEOPLASIA?

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INTRODUCTION: Ulcerative colitis (UC) is associated with an increased risk of colorectal cancer. Concomitant primary sclerosing cholangitis (PSC) and disease extent are the only factors that influence the start and periodicity of colonoscopy surveillance in these patients. Optimization of this screening strategy requires identification of additional risk factors. Aberrant crypt foci (ACF) have been associated with increased risk of sporadic colorectal cancer. Their correlation with the risk of neoplasia in UC remains controversial.
AIMS&METHODS: Aim: To determine if the existence and number of ACF have any relation with the risk of intraepithelial neoplasia (IEN) in patients with long-standing UC.
Patients and methods: 58 patients with distal/extensive UC with ≥ 8 years of disease and no history of PSC and/or IEN, were prospectively screened by chromoendoscopy-guided endomicroscopy and targeted biopsy/polypectomy of the detected lesions. The existence and number of ACF were evaluated in the distal rectum. Patients were divided into two groups: group I = with IEN, group II = without IEN.
RESULTS: Of the 88 circumscribed lesions identified by screening colonoscopy and biopsied, low-grade IEN was found in 5 (belonging to 4 patients). Distribution of patients: group I = 4 patients, group II = 54 patients. ACF were detected in all patients of group I and in only 28 (51.8%) of group II ($p = 0.085$). ACF performance in predicting the existence of IEN was: sensitivity = 100.0%, specificity = 48.1%, positive predictive value = 12.5% and negative predictive value (NPV) = 100.0%. Regarding the number of ACF, 5.3±2.2 were detected in group I and 2.1±2.9 in group II ($p = 0.037$).
CONCLUSION: In patients with long-standing UC and without history of PSC and/or IEN, there seems to be a significant association between the existence/number of ACF and the risk of IEN. ACF have high sensitivity and high NPV in predicting the existence of IEN.
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Disclosure of Interest: None Declared
Keywords: Aberrant crypt foci, Chromoendoscopy, Colonoscopy surveillance, Colorectal cancer, Endomicroscopy, Ulcerative colitis

P306 FAECAL S100A12 IS NO BETTER THAN FAECAL CALPROTECTIN (F-CP) IN THE NON-INVASIVE ASSESSMENT OF INFLAMMATORY BOWEL DISEASE (IBD).

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INTRODUCTION: Faecal calprotection (F-Cp), is currently in clinical use within the UK for distinguishing between functional (IBS) and organic (IBD) bowel disease. Another neutrophilic protein S100A12 is, like f-Cp, also strongly up-regulated in chronic active IBD. However, unlike f-Cp which is expressed in a variety of different cell types, S100A12 is predominantly expressed in granulocytes thus potentially making it more specific than f-Cp. S100A12 elevation is a highly sensitive and specific discriminator of chronic IBD from functional non-organic disease.
AIMS&METHODS: Patients with ulcerative colitis (UC), Crohns disease or irritable bowel syndrome (IBS) were prospectively evaluated and the following were collected to define clinical activity of IBD: (i) demographic data, (ii) clinical activity indices (Harvey-Bradshaw index or Mayo score), and (iii) serum and whole blood samples for inflammatory markers. F-Cp was measured using a standard commercially available assay. S100A12 was measured according to manufacturer's instructions by ELISA.
RESULTS: 60 patients provided specimens; 28.3 % had IBS (n=17), 25% Crohns (n= 15) and 46.7% had UC (n=28). S100A12 was significantly higher in patients with UC (median = 75.4 ug/g; $p<0.0001$) and patients with Crohns (median = 47.2 ug/g; p=0.0001) compared to those with IBS (0.71 ug/g). The sensitivity and specificity of faecal S100A12 (91.9% and 94.1% respectively) was similar to f-Cp (97.7% and 82.3% respectively) in differentiating disease groups and there was a strong correlation between these results (r=0.808; 95% CI 0.6865 to 0.8856; $p<0.0001$). There was no correlation between S100A12 and disease activity in Crohns disease (Harvey-Bradshaw index). There was a significant difference in faecal S100A12 comparing patients who had severe UC compared to moderate UC disease activity (p=0.0004), but this was equally well identified with f-Cp (p=0.0109).
CONCLUSION: S100A12 demonstrated similar results to f-Cp in discriminating between functional and inflammatory bowel disease. The use of faecal S100A12 did not improve the assessment of disease activity in IBD compared to the use of f-Cp. This study does not support the previously published data suggesting that S100A12 may be more specific for the identification of inflammatory bowel disease.
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Disclosure of Interest: S. Whitehead: None Declared, C. Morgese: None Declared, B. McKaig: None Declared, P. Banerjee: None Declared, A. ali: None Declared, J. Waldron: None Declared, C. Ford: None Declared, R. Gamma: None Declared, M. Brookes Financial support for research from: Vifor International
Keywords: calprotectin, disease monitoring, inflammatory bowel disease

P307 THE EFFECT IMMUNOSUPPRESSIVE DRUGS ON PERFORMANCE OF INTERFERON-GAMMA RELEASE ASSAY FOR TUBERCULOSIS SCREENING IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: It is mandatory that patients with inflammatory bowel disease (IBD) receive tuberculosis screening prior to anti-tumour necrosis factor therapy. Interferon Gamma Release Assay (IGRA) has higher sensitivity and specificity than Tuberculin skin test (TST) but it is not clear whether immunosuppressive (IS) therapy can affect the sensitivity of IGRA.
AIMS&METHODS: This prospective study aims to evaluate the effect of IS therapy on Quantiferon TB Gold (QFT-G) results in IBD subjects in a TB endemic region. QFT-G was performed on 426 consecutive subjects (111 Crohn's disease, 134 ulcerative colitis, 5 indeterminate colitis, and 176 controls). IBD subjects on IS drugs (corticosteroids, azathioprine, mercaptopurine or methotrexate) had both TST and QFT-G performed.
RESULTS: 89.5% of all subjects have been vaccinated with Bacille-Calmette-Guérin (BCG); 21.2% IBD subjects and 19.9% of controls tested positive for QFT-G. There were no significant differences between IBD subjects and controls for history of or contact with TB. 44.4% of IBD subjects were receiving at least one IS therapy. Significantly fewer patients on IS therapy tested positive for QFT-G than did patients not receiving IS therapy (15.3% vs. 25.9%; p=0.044). Further stratification suggested that individuals receiving more IS drugs were less likely positive for QFT-G (p=0.0097), and had lower interferon gamma responses to TB antigens (p=0.043). Female gender and older age were associated with higher rate of QFT-G positivity in IBD ($p=2.35x10^{-5}$and p=0.0134, respectively). The mean age for QFT-G-positive IBD patients was 54.0 years and that for QFT-G negative patients was 42.7 years. Smoking, appendectomy and previous BCG did not affect QFT-G results. There were 5 indeterminate QFT-G results among BCG vaccinated individuals, but none among non-vaccinated individuals. Comparison of QFT-G with TST showed a concordance rate of 85% (kappa=0.23).
CONCLUSION: In a TB-endemic area, QFT-G test results are negatively impacted by IS therapy. Current guidelines suggesting TB screening before anti-TNF therapy may be inadequate in patients already on IS drugs. Latent TB testing appears best performed prior to the initiation of IS or corticosteroid therapies in IBD patients.
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Disclosure of Interest: None Declared
Keywords: anti-TNF, biologics, corticosteroids, crohn's disease, inflammatory bowel disease, ulcerative colitis

P308 FAECAL CALPROTECTION AND LACTOFERRIN ARE RELEVANT MARKERS FOR MONITORING DISEASE ACTIVITY AND PREDICTING RECURRENCE IN PATIENTS WITH QUIESCENT CROHN'S DISEASE FOLLOWING ILEOCOLONIC RESECTION

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INTRODUCTION: The assessment of intestinal inflammation in patients with inflammatory bowel disease remains a challenge. Endoscopy is the most reliable and the gold standard method for assessing intestinal inflammation, but it is invasive, and time-consuming. To overcome these limitations, a non-invasive marker to monitor inflammatory activity would be desirable. The clinical significance of faecal calprotectin or lactoferrin in postoperative Crohn's disease (CD) is not evaluated.
AIMS&METHODS: This prospective study was to investigate the relationship between endoscopic activity, and faecal calprotectin and lactoferrin, and assess the predictive value of these markers for future recurrence. Twenty patients who remained in remission during 6-12 months after ileocolonic resection for CD were included. All patients underwent ileocolonoscopy for assessing endoscopic activity (Rutgeerts score) in the neo-terminal ileum. A stool sample was collected for measurement of calprotectin and lactoferrin. All patients were then following for 12 months, and clinical recurrence was defined as CD activity index (CDAI) $\geq$150.
RESULTS: The endoscopic scores were i0 or i1 in 10 patients, i2 in 6 patients, i3 in 3 patients, and i4 in 1 patient. Both calprotectin and lactoferrin positively correlated with the endoscopic scores (P=0.0001 and P=0.038, respectively). Six patients developed clinical recurrence during the 12-month follow-up. Both calprotectin and lactoferrin levels were significantly higher in patients with clinical recurrence than those in remission (P=0.0007 and P=0.025, respectively). A cutoff value of 170 μg/g for calprotectin had a sensitivity of 83% and a specificity of 93% to predict a risk of clinical recurrence, while a cutoff value of 140 μg/g for lactoferrin had a sensitivity of 67% and a specificity of 71%.
CONCLUSION: This study showed that both calprotectin and lactoferrin levels correlate well with endoscopic activity after ileocolonic resection for CD. Assays of faecal calprotectin and lactoferrin should serve as low cost, and non-invasive biomarkers to monitor disease activity and predict recurrence after surgery for CD.
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Disclosure of Interest: None Declared
Keywords: Calprotectin, Crohn's disease, Faecal marker, Lactoferrin, Postoperative recurrence

P309 THE IMPACT OF EARLY ENDOSCOPIC LESIONS ON THE CLINICAL COURSE OF PATIENTS AFTER ILEOCOLONIC RESECTION FOR CROHN'S DISEASE: A FIVE-YEAR PROSPECTIVE COHORT STUDY

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INTRODUCTION: Early endoscopic lesions following resection for Crohn's disease (CD) are often observed. The severity of the endoscopic inflammation at the proximal site of the anastomosis during the first year after resection is considered to be a reliable predictive risk factor for future clinical recurrence. Currently, the relationship between this endoscopic observation and subsequent occurrence of CD lesions or recurrence is not understood well, but should be valuable in the context of predicting CD course.
AIMS&METHODS: This prospective study was to investigate the impact of early endoscopic lesions on future clinical recurrence rates following ileocolonic resection for CD. Forty patients who had maintained clinical remission, CD activity index (CDAI) $<$150 with mesalazine during 6 months after ileocolonic resection for CD were included. At 6 months after surgery, ileocolonoscopy was performed, and the endoscopic activity score at the proximal site of the anastomosis was determined according to Rutgeerts. All patients were regularly monitored for 5 years, and clinical recurrence was defined as CDAI $\geq$150. Corticosteroids, immunosuppressants or biologic agents were not given unless there was clinical recurrence.
RESULTS: At 6 months after surgery, the endoscopic scores were i0 or i1 in 27 patients, i2 in 7 patients, i3 in 4 patients, and i4 in 2 patients. During the following 5 years, the clinical recurrence occurred in 3 (11%) of the 27 patients with endoscopic score of i0 or i1, 4 (57%) of the 7 patients with i2 score, 3 (75%) of the 4 patients with i3 score, and 2 (100%) of the 2 patients with i4 score, showing a significant positive correlation (P=0.001) between the endoscopic severity of the proximal site of the anastomosis at 6 months after surgery and the clinical recurrence rate during the following 5 years.
CONCLUSION: The assessment of endoscopic lesions at the proximal site of the anastomosis appeared to be valuable for predicting subsequent clinical recurrence after ileocolonic resection for CD. The results in the present study are valuable not only for identifying patients with a high risk of recurrence after surgery for CD but also for creating an integrated management strategy for prevention of postoperative recurrence. Further studies in larger cohorts of patients are warranted to strengthen our findings.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, Endoscopic lesions, Postoperative recurrence, Prophylactic medications, Resection

P310 MR ENTEROCOLONOGRAPHY IS USEFUL TO PREDICT CLINICAL RECURRENCE OF CROHN'S DISEASE AND IDENTIFY PATIENTS WHO NEED MORE AGGRESSIVE TREATMENT.

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INTRODUCTION: Assessing the extension and severity of the disease is critical to determine appropriate therapeutic strategies in patients with Crohn's disease (CD). MR enteroclysis or enterography(MRE) can assess both intestinal walls and and extraintestinal structures without radiation exposure and anesthesia, which makes it appropriate for repeated evaluation in CD patients. We developed novel magnetic resonance enterocolonography (MREC) for simultaneously evaluating both small and large bowel lesions in patients with CD and reported its excellent correlation with endoscopy. However, there is few report about predictability of CD recurrence by MRE. The aim of this study was to evaluate the capability of MREC for prediction of clinical recurrence in CD.
AIMS&METHODS: One hundred and thirty-three patients with established CD were prospectively examined by MREC between July 2009 and February 2013. Patients underwent ileocolonoscopy (ICS) or double-balloon endoscopy (DBE) after MREC on the same day. MREC score (0-60) was defined by modifying SES-CD. Presence and size of ulcers, extent of ulcerated surface, extent of affected surface and presence of narrowings were scored (0-3) in each segment of small and large intestine. MREC score, simplified endoscopic activity score for Crohn's disease (SES-CD), Chrohn's Dease Activity Index (CDAI) and CRP was evaluated. Patients were followed up for a maximum of 4 years unless clinical recurrence occurred earlier.
RESULTS: The median follow up time was 15.8 months (±1.2(se)), 76 patients recurred, 31 needed hospitalization and 24 had operation. Patients who recurred more often had higher MREC score (≧2; reflected active disease), higher SES-CD, higher CDAI and higher CRP, at baseline than those who didn't. But only higher MREC score was predictor for both hospitalization and operation (27.3% vs 0%, $p < 0.001$). Especially, in patients with remission (CDAI < 150), higher MREC score group had more recurrence (43/56, 76.8% vs 2.4%, $p < 0.001$) and operation (16.0% vs 0%, p=0.06). Even in 73 patients in remission with negative CRP, higher MREC score group had recurrence significantly more often (24/36, 66.7% vs 0%, $p < 0.001$) and had operation (6/36, 16.7% vs 0%, $p < 0.001$).
CONCLUSION: This data suggest that MR enterocolonography is useful for prediction for recurrence of Crohn's disease.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, IBD, monitoring, MR enterography

P311 THERAPEUTIC DRUG MONITORING OF INFLIXIMAB AND MUCOSAL HEALING IN INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE STUDY

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INTRODUCTION: Whether therapeutic drug monitoring of infliximab (IFX) trough levels and antibodies to infliximab (ATI) concentrations) could be useful in predicting mucosal healing (MH) in inflammatory bowel diseases (IBD) after infliximab optimization is unknown.
AIMS&METHODS: All consecutive IBD patients receiving ongoing IFX 5 mg/kg treatment and developing secondary failure to IFX were enrolled in a prospective observational study between June 2010 and May 2011. Dose was increased to 10 mg/kg in all patients. A clinical relapse was defined by a CDAI > 220, a fecal calprotectin > 400 μg/g and a C-reactive protein (CRP) level > 10 mg/L for Crohn's disease. In UC, clinical relapse was defined by a Mayo score > 7 with a Mayo endoscopic subscore > 1. IFX trough levels, antibodies to IFX concentrations (ATI), CRP levels, and fecal calprotectin were measured before infliximab optimization and at week 8. A proctosigmoidoscopy was performed the day of first infliximab optimization and at week 8 in all UC patients.
RESULTS: We included 52 IBD patients: 34 had CD (mean CDAI: 280; C-reactive protein: 28+/- 10 mg/L; fecal calprotectin : 705 +/- 300 μg/g) and 18 UC patients. Following IFX dose intensification, half of IBD patients achieved mucosal healing. Increase in infliximab trough levels (called "delta infliximab", μg/mL) was associated with mucosal healing (MH) (irrespective of IBD type) (P;001). A parallel increase in MH rates was observed according to the four quartiles (0%, 7%, 30%, and 70%, respectively; P=0.001). A "delta infliximab" > 0.5μg/mL was associated with HM (sensitivity (se): 0.88, specificity (sp): 0.77, positive predictive value (PPV): 0.79, negative predicitve value (NPV): 0.87; p = 0.0001, AUROC: 0.89). An IFX trough level < 2μg/l before drug optimization without ATI beyond 200 nanog/mL had a strong predictive value for achieving MH. On multivariate analysis, the only factor associated with HM after iIFX optimization was a delta infliximab IFX > 0.5 µg/mL (Likelihood ratio (LHR), =2.02, 95% CI,: 1.01-4.08; p=0.048). There was a strong tendency between IFX trough level IFX < 2 before drug optimization and MH : LHR=5.3, 95%: 0.82-34.2; p=0.08). The type of IBD was not associated with HM (p=0.26).
CONCLUSION: Therapeutic drug monitoring of IFX strongly predicts the likelihood of achieving mucosal healing following IFX dose intensification in both CD and UC. Measurement of IFX trough levels and ATI may be useful to guide decisions in IBD patients with secondary failure to IFX.
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Keywords: IBD, infliximab, trough levels

P312 MULTIVARIATE ANALYSIS REVEALS DISCERNIBLY DIFFERENT CYTOKINE PATTERNS BETWEEN INFLAMED MUCOSA OF ULCERATIVE COLITIS AND CROHN'S DISEASE

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INTRODUCTION: Many previous studies have shown that various pro-inflammatory cytokines are upregulated in affected mucosa of patients with inflammatory bowel disease (IBD). But in most of these studies, expressions of each cytokine in relation to disease phenotypes were individually analyzed, not yielding phenotype-specific cytokine expression patterns in diseased tissues. To take into account the correlations and interactions of multiple targets, we conducted multivariate analysis on the gene expression data after analysing mucosal biopsy samples from patients with ulcerative colitis (UC) and Crohn's disease (CD) for helper T cell-related cytokines and transcription factors by quantitative real-time PCR (qRT-PCR).
AIMS&METHODS: Total of 154 biopsy samples (87 from UC, 42 from CD and 25 from control) were obtained by endoscopy from inflamed and non-inflamed mucosa of 47 UC, 20 CD patients and 14 control subjects. Total RNA was extracted from the specimens and mRNA expressions of Th1-related (IFNG, IL12A, IL12B, TBX21 and TNFA), Th2-related (IL13, IL33 and GATA3), Th17-related (IL17A, IL17F, IL21, IL22, IL6, IL23A and RORC) and Treg-related (TGFB and FOXP3) cytokines and transcription factors were evaluated by qRT-PCR using TaqMan probes. Linear discriminant analysis was applied to the observed data for the differentiation of IBD phenotypes.
RESULTS: Marked gene expression differences, especially of pro-inflammatory cytokines like IL6, IFNG and IL17A, were observed between inflamed and non-inflamed mucosa, particularly in UC. IL6 alone, for example, was able to discriminate inflamed from non-inflamed mucosa with an AUC value of 0.90. In contrast, gene expression profiles of inflamed mucosa of UC (UCI, n=40) and CD (CDI, n=20) seemed almost comparable and only expressions of IL13 and IL21 were significantly different with AUC values of 0.66 and 0.70 respectively. Stepwise linear discriminant analysis yielded a set of 5 genes (IFNG, IL12A, TBX21, GATA3, IL21), which discriminated UCI from CDI with an AUC value of 0.95 and an accuracy of 91.7% on the training data, which remained 86.7% after internal leave-one-out cross validation.
CONCLUSION: Multigene analysis discriminated between inflamed mucosa of UC and CD, which were similar in single-gene analysis, with high accuracy, reflecting possible differences in pathogenesis. This method might be useful for evaluation of cases initially diagnosed with indeterminate colitis.
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Disclosure of Interest: None Declared
Keywords: cytokine profile, Diagnosis, discriminant analysis, inflammatory bowel disease, qRT-PCR

P313 IBD PATIENTS' PARTNER- HOW IMPORTANT IS THEIR SUPPORT?

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INTRODUCTION: Chronic inflammatory disease of the bowel causes significant distress to the patients and his family. Data assessing the need of these patients for support and sharing with their partners is scarce.
AIMS&METHODS: Our aim was to assess patients' view regarding information sharing with their partners.
All IBD patients treated at the Sheba Medical center between 1.2011-1.2013 were asked to fill an anonymous questionnaire. Only patients that had a stable partner and that completed more than 95% of the questionnaire were included.
RESULTS: One hundred thirty four patient filled the questionnaire, of them 101 were included.53 were men. Mean age:45±15. 50% had academic education. Only 42% of patients reported that their partner accompanies them to the doctor. 93% of patients share health problems with their partner. 64% would like their partner to receive more medical information, and 70% would like their partner to be more involved. 88% of patients believe that more partners' involvement can help them deal better with the disease. 70% think that support group for partners should be established. No association was found between patients' demographic data to their answers. Patients that felt that their partner's involvement can help them dealing with the disease tended to share with them medical information and wanted them to be more involved in health decisions ($p < 0.001$)
CONCLUSION: Most IBD patients want their partner to be more involved with their health problems, and believe that greater involvement can help them deal better with their disease. Therefore, more attention should be attributed towards better cooperation with patients' families.
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Disclosure of Interest: None Declared
Keywords: IBD, information sharing, partner

P314 A SYSTEMATIC REVIEW: THIOPURINE MONITORING IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Thiopurines are widely used for maintenance of remission in children with inflammatory bowel disease (IBD). Current evidence on importance of thiopurine metabolite and peripheral blood count monitoring for assessment of therapeutic response and thiopurine toxicity is controversial.
AIMS&METHODS: To systematically review the evidence on the utility of thiopurine metabolite and peripheral blood count monitoring in assessing therapeutic response and thiopurine induced haematologic and hepatic toxicity in children with IBD.
Medline, Embase, Cochrane Central Register of Controlled trials and www.clinicaltrials.gov. were searched. Randomised controlled trials (RCTs), cohort studies and large case series were eligible. Primary outcome was the clinical usefulness of routine thiopurine metabolite and peripheral blood count monitoring in assessing therapeutic response and toxicity in children with IBD. Secondary outcome was to investigate a possible correlation between these markers.
RESULTS: Sixteen studies of variable quality were included (n=1093). None of the studies were RCTs. While high 6TGN levels were not consistently associated with leucopenia, a positive correlation between 6TGN levels and optimal clinical outcome was frequently reported. Several studies supported the use of high 6MMP levels as an indicator of hepatotoxicity.
CONCLUSION: Thiopurine metabolite testing does not safely represent therapeutic response or thiopurine toxicity. Current evidence does not support routine metabolite monitoring, however favours a combination of metabolite and white blood count testing for safe dose escalation in cases of suboptimal response. Leucopenia is not necessary for achievement of optimal therapeutic response. Well designed RCTs and identification of additional surrogate markers of thiopurine efficacy and toxicity are required.
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Disclosure of Interest: None Declared
Keywords: 6 mercaptopurine, azathioprine, children, inflammatory bowel disease, thiopurine

P315 RISK ASSESSMENT AND MINIMIZATION FOR PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML) (RAMP): A PROGRAM TO ASSESS FOR POTENTIAL EARLY SIGNS AND SYMPTOMS OF PML DURING CLINICAL DEVELOPMENT OF VEDOLIZUMAB

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INTRODUCTION: Since 2007, the RAMP program, involving education and a stepwise screening algorithm, has been used to monitor all patients treated with vedolizumab (VDZ), a gut-selective $\alpha_4\beta_7$ integrin antagonist, for potential early PML signs/symptoms in ulcerative colitis (UC) and Crohn's disease (CD) clinical studies.
AIMS&METHODS: All patients completed a subjective checklist on recent changes in vision, speech, gait, sensation, comprehension, coordination, and personality at screening, at each study visit, and whenever new neurologic symptoms presented. Positive findings led to VDZ cessation and a site investigator–administered neurologic evaluation, followed by referral to a neurologist familiar with the study for patients in whom objective findings confirmed symptoms. In some cases, patients without objective findings were also referred. If PML remained in the differential, an independent adjudication committee (IAC) of PML experts expedited a centralized real-time review of results from the neurologic evaluation, brain MRI, and lumbar puncture with PCR analysis of cerebrospinal fluid (CSF) for JC virus (JCV) DNA to determine PML likelihood. Site investigators received IAC guidance on further management of patient safety.
RESULTS: As of March 2013, 2913 patients (UC, 1142; CD, 1771) completed 57,986 subjective checklists (UC, 24,919; CD, 33,067). Positive subjective findings led to completion of 165 and 341 objective checklists in 95 UC and 189 CD patients, respectively. Results from 83 patients (UC, 24; CD, 59) were evaluated by the IAC, including 62 patients with abnormal objective checklist results (UC, 17; CD, 45) and 21 (UC, 7; CD, 14) referred without objective findings. Among these, 56 patients underwent brain MRI (UC, 15; CD, 41) and 5 underwent lumbar puncture with PCR analysis of CSF for JCV (UC, 2; CD, 3). MRI results were inconsistent with PML, and no JCV was detected in CSF. No PML cases have been identified by the IAC to date.
CONCLUSION: No PML cases have been reported to date in VDZ trials. The RAMP program is an important, practical monitoring tool for early PML detection and elimination of false positives, which can be applied on a global scale.
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Disclosure of Interest: A. Parikh Shareholder of: Takeda Pharmaceuticals International, Inc, Other: Employee of Takeda Pharmaceuticals International, Inc, M. McAuliffe Shareholder of: Millennium Pharmaceuticals, Inc, Other: Employee of Millennium Pharmaceuticals, Inc, K. Stephens Shareholder of: Millennium Pharmaceuticals, Inc, Other: Employee of Millennium Pharmaceuticals, Inc, E. Major: None Declared, I. Fox Shareholder of: Millennium Pharmaceuticals, Inc, Other: Employee of Millennium Pharmaceuticals, Inc, C. Milch Shareholder of: Millennium Pharmaceuticals, Inc, Other: Employee of Millennium Pharmaceuticals, Inc, S. Sankoh Other: Employee of Millennium Pharmaceuticals, Inc, J. Provenzale Financial support for research from: GE Healthcare, Bayer Pharmaceuticals, Consultancy for: Bayer Pharmaceuticals, SHIRE, Amgen, Shareholder of: Amirsys Publishing, Other: Royalties from Amirsys Publishing, M. Lev Financial support for research from: GE Healthcare, Consultancy for: Millennium Pharmaceuticals, Inc, Shareholder of: GE Healthcare, E. Freedland Shareholder of: Millennium Pharmaceuticals, Inc, Other: Employee of Millennium Pharmaceuticals, Inc, J. Berger Financial support for research from: PML Consortium, Lecture fee(s) from: Bayer Schering Pharma, Biogen Idec, Genzyme, Consultancy for: Bayer Schering Pharma, Biogen Idec, Eisai, Genentech, Millennium, Novartis, Pfizer, Sanofi, D. Clifford Financial support for research from: Bavarian Nordic, Lilly, Roche, Biogen Idec, Cytheris, Lecture fee(s) from: Biogen Idec, Canada – Speaking fee, American Academy of Neurology, University of Kentucky, ACTRIMS, ECTRIMS, IAS-USA, Consultancy for: Pfizer – DMC Consultant, Genzyme – DMC Consultant, Millennium – DMC Consultant and Consultant at FDA Hearing, Drinker, Biddle, Reath – Consultant for PML Consortium Expert Advisory Panel, Amgen – Consultant, Quintiles – DMSB Consultant, Arnold Todara & Welch – legal consultation, W. Holt Smith Attorney, legal consultation, Biogen Idec – Consultant, Cytheris – clinical trial development, FDA hearing
Keywords: Crohn's disease, inflammatory bowel disease, progressive multifocal leukoencephalopathy, risk assessment, ulcerative colitis, vedolizumab

P316 THE TEMPORAL EVOLUTION OF ANTI-DRUG ANTIBODIES IN INFLAMMATORY BOWEL DISEASE PATIENTS TREATED WITH INFLIXIMAB

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INTRODUCTION: Despite ample research on the prevalence of antibodies to infliximab (ATI), their incidence during therapy is poorly defined. This knowledge gap may hamper the understanding of the clinical impact of anti-TNFs immunogenicity. We aimed to characterize the temporal evolution of ATI.
AIMS&METHODS: This was a tertiary-center prospective observational study of all infliximab-treated IBD patients between 2009-2012. Trough levels of infliximab were determined and ATI were measured before each infusion by anti-lambda ELISA. Patients were monitored for disease activity by clinical activity indexes and for dose-intensification or infliximab cessation. The occurrence of transient ATI disappearing spontaneously without any intervention was recorded separately.
RESULTS: 125 patients were included (98 CD, 27 UC, Median follow 11.5±22 months) and 1119 sera were analyzed for infliximab and ATI levels during the 4-year study. Kaplan-Meyer analysis showed that 42% of patients remained ATI-free by 4 years of treatment. Most (90%) of the patients who developed ATI did so within the first 12 months of therapy, whereas transient ATIs were detected throughout the duration of infliximab therapy ($P<0.001$). ATI incidence was similar between patients who received infliximab previously (episodic patients, n=14) and scheduled therapy patients (n=111). In the scheduled therapy group, combination immunomodulator+infliximab resulted in longer ATI-free survival compared to monotherapy (p=0.003, log rank test). Survival free of clinical loss of response was enjoyed by 51% of patients, and serial measurements showed that ATI development often preceded the onset of clinical flare.
CONCLUSION: When followed prospectively, most patients who develop ATI do so within the first 12 months of therapy, and this incidence is reduced by combination immunomodulator even in scheduled therapy patients. In contrast, transient ATIs, which are of little clinical significance, can appear haphazardly at any time during treatment. The onset of clinical loss of response may lag behind the appearance of anti-infliximab antibodies.
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Keywords: anti-TNF, IBD, immunology, infliximab, response to treatment

P317 BENEFIT OF INFLIXIMAB RE-INTRODUCTION AFTER SUCCESSIVE FAILURE OF INFLIXIMAB AND ADALIMUMAB IN INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Infliximab (IFX) and adalimumab (ADA) are effective in inflammatory bowel disease (IBD) for induction and maintenance therapy. However, high annual rate of discontinuation for loss of response or intolerance may lead to a switch for another anti-TNF agent. In clinical practice, patients with successive failure to IFX and ADA are more and more frequent. The aim of this study was to assess whether re-treatment with IFX in patients who successively failed to IFX and ADA is feasible.
AIMS&METHODS: Sixty nine IBD patients (21 males, 65 Crohn's disease, 1 ulcerative colitis, 3 IBD unclassified, 14 L1, 22 L2, 30 L3, 12 L4, 20 p, 1 E3) who received and discontinued successively IFX and ADA, and who were re-exposed to IFX were indentified in 4 French tertiary centres and retrospectively analyzed. Clinical data, response to IFX, follow-up and outcome were abstracted from electronic database or medical records. For statistical analysis, Mann Whitney test, Chi2 test, logrank test or Cox regression model were used when appropriate.
RESULTS: Median age at second IFX treatment start was 29.1 years (15.9-84.3), and 22% had prior surgery. Median duration of the first IFX treatment was 14

months (0-127), and reasons for discontinuation were loss of response (38), intolerance (16), primary non response (4) and other (11). Median duration between the two IFX treatment periods was 37.6 months (3.2-144.3). Concomitant-immunosuppression (co-IS) with thiopurine or methotrexate was given in 61% and 49% of cases during first and second IFX treatments respectively. Remission (Harvey-Bradshaw Index <5) was achieved in 46% of cases at week 6-8 after IFX re-induction. 64% and 52% of patients were still under IFX therapy 12 and 24 months after IFX re-induction, respectively. Twenty nine patients had to discontinue the second IFX treatment due to intolerance (14), primary non response (11), loss of response (3) and other (1). In multivariate analysis, receiving co-IS in both first and second IFX treatment (p=0.006) and shorter interval between first and second IFX treatment (p=0.0006) were independently associated with longer duration of second IFX treatment.

CONCLUSION: For IBD patients who successively failed IFX and ADA, re-introducing IFX is feasible and often clinically efficient. More than half patients are still under treatment at 12 months. This strategy is particularly interesting in patients who received co-IS during both first and second IFX treatment.

Disclosure of Interest: None Declared

Keywords: adalimumab, IBD, infliximab

P318 GRANULO-MONOCYTOAPHERESIS IS MORE EFFECTIVE IN INDUCING AND MAINTAINING CLINICAL RESPONSE AT 24 WEEKS IN MILD ULCERATIVE COLITIS THAN IN MODERATE TO SEVERE DISEASE

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INTRODUCTION: Granulo-monocytoapheresis (GMA) consists on extracorporeal removal of granulocytes and monocytes from the peripheral blood. It has been used in patients with mild to severe disease active ulcerative colitis (UC) in order to modulate intestinal inflammation with conflicting results.

AIMS&METHODS: To evaluate whether GMA effectiveness varies according to severity of UC. This study is designed as a retrospective review of prospectively collected medical records of patients undergoing GMA at our center, with a median follow-up period of 6 months. Demographics, clinical and laboratory data were extracted from the patients' charts and electronic records. Severity of UC was measured according to Modified Truelove Witts Severity Index (MTWSI). Clinical response was defined as a decrease from baseline in MTWSI of $\geq$2 points or a value of MTWSI $\leq$2 points .

RESULTS: A total of 35 [21M/14F; mean age 48(19-82)] patients were included (table 1). At 1-month follow-up period after GMA, 75% (n=18/24) of mild UC underwent clinical response compared to 54% (n=6/11) of patients with moderate to severe disease (p=0.26). At 6-months, 55% (n= 13/24) of mild UC maintained clinical response compared to 18% (n=2/11) of patients with moderate to severe disease(p=0.06).

	Mild (n=24)		**Moderate to severe** (n=11)		*p value*
	n	%	n	%	
Disease Duration (range)	11 (1-31)		4 (0-11)		0,02
Disease Localisation:					
Proctitis	1	4	0	0	
Left sided UC	7	29	1	9	0,3
Extensive UC	16	67	10	91	
Mean MTWSI (range)	6 (4-8)		11 (9-15)		
Reasons For GMA:					
CS res/dep	19	79	10	91	0,63
CS intol	0	0	2	18	0,17
IS res	6	25	1	9	0,5
IS intol	4	17	2	18	0,9
IS CI	1	4	1	9	0,56
BIO res	1	4	0	0	0,49
BIO intol	2	8	2	18	0,78
BIO CI	2	8	1	9	0,94
Concomitant treatments:					
CS	9	38	5	45	0,94
IS	4	17	3	27	0,78
BIO	0	0	0	0	n.a
Mean **CRP** (range) at study entry (mg/dl)	13,4 (1-73)		15 (1,22-61)		0,85
Mean **lactoferrin** (range) at study entry (mg/dl)	83,8 (13-100)		85,9 (28-100)		0,87

CS: corticosteroids; IS: immunosuppressors; BIO: biologics; Res: resistance; Dep: dependence; CI: contraindications; CRP: C-reactive protein; n.a: not applicable.

CONCLUSION: Our data show that patients with mild disease could benefit of GMA more than patients with moderate to severe disease. Thus, in patients with mild disease, GMA can be considered as a valid and alternative therapeutic approach, particularly in case of contraindications to immunosuppressors/ corticosteroids.

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Disclosure of Interest: None Declared

Keywords: Granulocytoapheresis, Ulcerative Colitis

P319 MALIGNANCIES WITH ANTI-TUMOR NECROSIS FACTOR-ALPHA THERAPY IN INFLAMMATORY BOWEL DISEASE: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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INTRODUCTION: Several anti-tumour necrosis factor-α (TNFα) antibodies have demonstrated efficacy in Crohn's disease (CD) and ulcerative colitis (UC). These drugs carry a theoretical risk of malignancy, particularly lymphoma, but no systematic review and meta-analysis has examined this issue specifically.

AIMS&METHODS: We pooled data from all available placebo-controlled studies to estimate the risk of malignancy with anti-TNFα therapy. MEDLINE, EMBASE and the Cochrane central register of controlled trials were searched to November 2012. Randomized controlled trials (RCTs) comparing anti-TNFα therapy with placebo in adults with CD or UC were eligible. Data were pooled to obtain a relative risk (RR) of malignancy with a 95% confidence interval (CI).

RESULTS: The search strategy identified 20,563 citations, of which 22 RCTs were eligible (11 infliximab, six adalimumab, four certolizumab and one golimumab) involving 7,054 patients (4,566 CD and 2,488 UC). In total, there were 16 (0.4%) malignancies in 4,135 patients allocated to anti-TNFα therapy, compared with 13 (0.45%) in 2,919 assigned to placebo. Among patients receiving anti-TNFα therapy these included two basal cell carcinomas, two rectal adenocarcinomas, one hypernephroma, one breast cancer, one bladder carcinoma, one prostate adenocarcinoma, one lung cancer, one gastric cancer, one cutaneous squamous cell carcinoma, one adenocarcinoma of unknown origin, and four cancers of unspecified type. There were no cases of lymphoma in the active treatment group compared with three (0.1%) in the control group. The RR of malignancy for patients receiving anti-TNFα therapy was 0.77 (95% CI 0.37 to 1.59). There was no statistically significant heterogeneity detected between studies ($I^2 = 0\%$, $P = 0.82$) and no evidence of funnel plot asymmetry (Egger test, $P = 0.37$). We performed sensitivity analyses excluding trials where placebo patients were exposed to anti-TNFα during induction of remission, and trials of eight weeks duration or less. The RR of malignancy with anti-TNFα compared with placebo, excluding trials where placebo patients were exposed to anti-TNFα, was 0.81 (95% CI 0.30 to 2.16). The RR of malignancy with anti-TNFα compared with placebo, excluding trials of eight weeks duration or less, was 0.80 (95% CI 0.37 to 1.73).

CONCLUSION: Anti-TNFα therapy was not associated with an increased risk of malignancy in patients with inflammatory bowel disease. No trials provided data for risk of malignancy beyond one year of treatment meaning that the long-term effect of anti-TNFα therapy could not be addressed by the current study.

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Keywords: ANTI-TNF-ALPHA THERAPY, inflammatory bowel disease, MALIGNANCY, Meta-analysis

P320 CLINICAL RESPONSE, QUALITY OF LIFE AND WORK ACTIVITY IN PATIENTS WITH CROHN'S DISEASE TREATED WITH ADALIMUMAB IN ROUTINE CLINICAL PRACTICE.

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INTRODUCTION: Several clinical trials have demonstrated the efficacy of adalimumab (ADA) for inducing and maintaining clinical response in patients with Crohn's disease (CD).

AIMS&METHODS: The aim of the study was to determine the effectiveness, measured as clinical response, quality of life (QoL) and work activity, of ADA in CD patients in routine clinical practice.

Methodology: Multicentre prospective observational cohort study with follow up of 12 months. Inclusion criteria: Patients with CD naïve to biologics, in which the doctor prescribes ADA according to routine clinical practice. In the medical visit at the beginning of the biologic treatment (V0), sociodemographic variables, Crohn's Disease Activity Index (CDAI), Perianal Disease Activity Index (PDAI), quality of life (QoL) indices (Inflammatory Bowel Disease Questionnaire (IBDQ-9) and EuroQol five dimensions (EQ-5D)) and Work Productivity Activity Index (WPAI) were collected. Such data were again recorded 12 months later (V12). When the data distribution was normal, the mean ($\pm$SD) were used as statistics. When the data distribution was not normal, the median (Percentil25-percentil75) were used. For hypothesis testing, parametric or nonparametric tests were used according to the data distribution. Differences were considered significant at $p < 0.05$.

RESULTS: 126 patients (50.8% men; age 39.1$\pm$13.8 years; 60.3% active workers) from 33 centres were included. The proportion of patients in remission (CDAI$<$150) increased from 34.1% in V0 to 83.0% in V12. The CDAI decreased from 194 (21-269) to 48 (10-122) ($p<0.001$). The PDAI decreased from 4.0 (0.0-4.0) to 0.0 (0.0-4.0) ($p<0.001$). The quality of life measured by

the EQ-5D improved from 0.735 (0.633-0.790) to 0.797 (0.726-1.000) ($p<0.001$). The IBDQ-9 score increased ($p<0.001$) from 56.7 (51.6-61.5) to 66.5 (60.1-73.6) ($p<0.001$). The work hours lost by the EC in the previous week decreased from 2.0 (0.0-27.0) at V0 to 0.0 (0.0-1.0) at V12 ($p=0.004$) and the work productivity (0-10 scale) decreased from 3.0 (0.3-5.8) to 1.0 (0.0 to 2.0) ($p=0.006$).

CONCLUSION: In clinical practice, ADA has proven to be effective with a statistically significant improvement in clinical variables, quality of life, and work productivity.

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Disclosure of Interest: None Declared

Keywords: adalimumab, Crohn's disease, Effectiveness, IBD

P321 CHANGES IN RESOURCE UTILISATION IN PATIENTS WITH CROHN'S DISEASE TREATED WITH ADALIMUMAB IN ROUTINE CLINICAL PRACTICE

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INTRODUCTION: Crohn's disease (CD) is a chronic and recurrent disease with numerous complications, producing a high consumption of health and social resources. It could be suggested that because of the efficacy of biologic treatments, their use could reduce the resource utilisation.

AIMS&METHODS: The aim of the study is to compare the resource utilisation during the 12 months prior to treatment with adalimumab (ADA) in the EC with respect to the following 12 months in routine clinical practice.

Methodology: Multicentre prospective observational cohort study with follow up of 12 months. Inclusion criteria: Patients with CD naïve to biologics, in which the doctor prescribes ADA according to routine clinical practice. In the medical visit at the beginning of the biologic treatment, direct (hospitalisations, medical visits, surgeries, diagnostic tests and medications) and indirect resource (Work Productivity and Activity Impairment (WPAI)) consumption during year previous (Y-1) to the ADA treatment were retrospectively collected. Such data were again recorded prospectively in 5 visits during the following year (Y-2). Y-1 and Y-2 data were compared. For hypothesis testing, parametric or nonparametric tests were used according to the data distribution.

RESULTS: 126 patients (50.8% men; age 39.1±13.8 years; 60.3% active workers) from 33 centres were included. The respective means for Y-1 vs. Y-2 of the following resources per patient were: 12.4 vs. 7.4 ($p<0.001$) medical visits, 1.2 vs. 0.7 ($p<0.001$) emergency room visits, 4.4 vs. 3.7 (NS) hospitalisation days, 0.0 vs. 0.1 (NS) days in intensive care units, 0.9 vs. 1.5 (NS) days in day hospital, 5.3 vs. 2.4 ($p<0.001$) diagnostic tests. The number of surgeries decreased from 33 during Y-1 to 29 during Y-2. The consumption of non-biologic drugs during Y-2 decreased with respect Y-1 ($p<0.001$). The mean of work hours lost by the EC decreased from 12.9 to 4.0 ($p=0.004$) and lost by other causes from 3.7 to 0.9 (NS). The work productivity impact (scale 0-10) decreased from 3.3 to 1.6 ($p=0.006$) and the impact in non-work activities (scale 0-10) decreased from 5.0 to 2.3 ($p<0.001$).

CONCLUSION: In clinical practice, the treatment with ADA decreases the direct and indirect resources utilisation comparing the 12 months before the treatment with the following 12 months.

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Disclosure of Interest: None Declared

Keywords: adalimumab, Crohn's disease, IBD, Resources utilisation

P322 FREQUENCY, TYPE AND OUTCOME OF REPORTED SIDE EFFECTS AND ADVERSE EVENTS OF NON-BIOLOGIC DRUGS USED IN INFLAMMATORY BOWEL DISEASE: A NATIONWIDE COHORT STUDY USING THE GERMAN FEDERAL INSTITUTE FOR DRUGS AND MEDICAL DEVICES (BFARM) PHARMACOVIGILANCE DATABASE

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INTRODUCTION: Inflammatory bowel disease (IBD) patients are treated with a variety of conventional and biologic medications with a diverse safety profile. Comprehensive, real world safety data, particularly of non-biologic agents are sparse.

AIMS&METHODS: We systematically searched all cases (n=233.000) reported to the German Federal Institute for Drugs and Medical Devices (BfArM) - the independent higher federal authority for risk monitoring of medicinal products, medical devices and the legal traffic of controlled substances - from 1993 to 2009. We extracted all reports involving Crohn's disease (CD) and ulcerative colitis (UC) and analyzed the results using the Medical Dictionary for Regulatory Activities (MedDRA) terminology grouped by system organ class (SOC), high level group term (HLGT), high level term (HLT), preferred term (PT), lowest level term (LLT).

RESULTS: We identified 1102 reports concerning IBD and focused on the established cases (CD=461, 44.4% male, age 40.8 ± 17.7 SD, BMI 23 ± 5.8 SD; UC=470, 49.6% male, 45.7 ± 20 SD, BMI 23.3 ± 6 SD). Event severity (CD vs. UC serious 86 / 85.5%, life threatening 10.4 / 11%, deadly 5.2 / 5.7% and disabling 2 /1.7% and hospitalization rates (49.2 /52.3%) were comparable among both conditions. The five most common SOC in CD vs. UC were: gastrointestinal disorders 36.7 / 30.2%, general disorders and administration side conditions 21 / 23.2%, investigations 17.4 / 17.7%, nervous system disorders 15.8 / 15.5% and blood lymphatic disorders 15.2 / 15.5%, respectively. The top five most frequently suspected or interacting drugs (percent of affected patients, median dose, median duration of administration) were in CD azathioprine (27.3%, 113 mg, 36 days), mesalamine (11.1%, 3000 mg, 60 days), sulphasalazine (3.7%, 3000 mg, 26 days), mercaptopurine (3.5%, 75 mg, 21 days) and prednisolone (2.8%, 25 mg, 7 days) and in UC mesalazine (18.5%, 2700 mg, 86 days), azathioprine (14.0%, 100 mg, 39 days), prednisolone (5.1%, 30 mg, 49 days), sulfasalazine (3.8%, 1500 mg, N/A), and mercaptopurine (3.6%, 87.5 mg, 45 days).

CONCLUSION: The overall low fraction (0.47% of all reported cases) of suspected medication related complications in this 16 year national cohort is likely owed to the relatively low prevalence of IBD in the population. However, the majority of reported cases classified in the serious or life threatening categories and half of them requiring hospitalization emphasize the importance of pharmacovigilance among clinicians caring and prescribing medicines for IBD patients.

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Disclosure of Interest: None Declared

Keywords: adverse events, Crohn's disease, IBD, pharmacovigilance, safety, ulcerative colitis

P323 THERAPEUTIC ESCALATION IN PATIENTS WITH ULCERATIVE COLITIS: SYSTEMATIC ANALYSIS OF THE PREVALENCE AND RISK FACTORS IN THE SWISS IBD COHORT

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INTRODUCTION: There is a paucity of large cohort studies having systematically assessed the need for therapeutic escalation in patients with ulcerative colitis (UC).

AIMS&METHODS: We aimed to assess in what percentage of UC patients a therapeutic escalation is needed over time and to identify escalation-associated risk factors. Data from the Swiss IBD Cohort Study (SIBDCS) were analyzed. The frequencies of patients under the following medications were assessed according to disease duration: 5-aminosalicylates (5-ASA), steroids, immunomodulators (IM, azathioprine and 6-mercaptopurine), anti-TNF drugs (infliximab, adalimumab), and calcineurin-inhibitors (cyclosporine, tacrolimus). Patients without any therapy and UC related surgery were also evaluated.

RESULTS: A total of 901 UC patients were included (45.3% females), median age 41 [32-52] years. Median age at diagnosis was 31 [24-40] years, disease duration was 6 [2-14] years. Forty two percent presented with pancolitis, 42% with left-sided colitis, and 16% with proctitis. A progressive decrease of patients treated solely with 5-ASA and an increase of patients needing immunomodulators and/or steroids as well as surgery was noted over time. The following treatments regimens were observed: for a disease duration of 0 to 2 years: 5-ASA 28%, steroids and/or IM 51%, anti-TNF and/or calcineurin inhibitors 18.3%, surgery 2.3%, no therapy 0.4%; disease duration of 3-6 years: 5-ASA 18.9%, steroids and/or IM 49.5%, anti-TNF and/or calcineurin inhibitors 28.6%, surgery 2%, no therapy 1%; disease 7-14 years: 5-ASA 16.3%, steroids and/or IM 57.5%, anti-TNF and/or calcineurin inhibitors 20.4%, surgery 5%, no therapy 0.8%; disease duration ≥15 years: 5-ASA 15%, steroids and/or IM 60.9%, anti-TNF and/or calcineurin inhibitors 9.7%, surgery 14%, no therapy 1.4%. Young age at UC diagnosis (OR 0.955, 95% CI 0.929-0.981, $p = 0.001$) as well as pancolitis (OR 2.404, 95% CI 1.261-4.584, $p = 0.007$) were the main risk factors for a rapid therapeutic stepup with need for treatment by anti-TNF drugs and/or calcineurin inhibitors within the first two years after UC diagnosis.

CONCLUSION: A relatively small proportion of our UC patients could be treated in the long-term run by 5-ASA only, which may be related to the fact that 80% of patients were recruited by hospitals and only 20% by gastroenterologists in private practice. Young age at disease onset and pancolitis are the major risk factor for a need for a rapid stepup within the first two years of disease course.

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Disclosure of Interest: None Declared

Keywords: treatment escalation, ulcerative colitis

P324 IMPACT OF TREATMENT OF INTESTINAL PARASITES ON THE ACTIVITY OF ULCERATIVE COLITIS

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INTRODUCTION: Ulcerative colitis (UC) is most common in Western industrialized countries, while it is uncommon in developing countries where helminthes are frequent. People with helminthic infection have an altered immunological response to antigens.

AIMS&METHODS: We aimed to study the impact of treatment of intestinal parasites on the activity of ulcerative colitis. Twenty patients with ulcerative colitis and intestinal parasite infection were selected out of 57 patients with UC, after 3 successive days stool analysis and anal swab. They were randomized into two groups: group I was treated for intestinal parasites while group II was not. Patients were evaluated using simple clinical colitis activity (SCCA) index, laboratory investigations and colonoscopy, before and one month after

treatment of intestinal parasites in group I, one month from the first visit in group II to evaluate the activity of the disease.
RESULTS: Patients who were treated for intestinal parasites had statistical significant deterioration in bowel frequency/day (p=0.04), and bowel frequency/night (p=0.038) .On the other side, the untreated group showed non significant change in all parameters of SCCA index after one month, but, their bowel frequency/day, bowel frequency/night and the general condition were significantly ameliorated in comparison with the treated group. There was statistically significant deterioration in hemoglobin (p=0.049), WBC's (p=0.01) in the treated group, while the platelets count, ESR and CRP which remained unchanged in treated group showed significant improvement in the untreated group in addition to improved hemoglobin levels after one month, finally, WBC's and CRP were significantly lower in the untreated group in comparison with the treated group after one month. There was statistically significant increased friability, exudation and spontaneous hemorrhage among the treated group without significant change in colonoscopic finding among the untreated group, the treated group had more severe colonoscopic finding in comparison with the untreated group after one month (p=0.02).
CONCLUSION: Treatment of intestinal parasites in ulcerative colitis patients deteriorates the clinical activity of the ulcerative colitis.
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Disclosure of Interest: E. Saad : none, A. Mourad : none, A. Mahmoud : none, H. Hussien : none, S. Ahmed : none, S. Elhawari : none, M. Emara : none
Keywords: immune modulation, intestinal parasite, Ulcerative colitis

P325 EFFICACY AND SAFETY OF IBD98E, A SODIUM HYALURONATE TOPICAL PREPARATION, IN THE INDUCTION OF CLINICAL AND ENDOSCOPIC REMISSION IN PATIENTS WITH DISTAL ULCERATIVE COLITIS: AN OPEN LABEL PILOT STUDY

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INTRODUCTION: Ulcerative colitis (UC) is characterized by inflammation and ulcers in the rectum and colon. Sodium hyaluronate (Na-HA) can contribute significantly to the hydration and maintenance of the integrity of the intestinal mucosa. Altered mucosal layer found in UC is associated to the inflammation. Enhancement of the mucosal repair mechanisms may provide a new potential way of treating UC. Restoration of the protective layer with Na-HA may contribute to the induction of remission of UC.
AIMS&METHODS: We aimed to investigate whether supplementation of the mucosal lining of the rectum with sodium hyaluronate might be a potential alternative treatment in distal active UC. This was a prospective uncontrolled open-label trial. Adult patients with defined active distal UC (UCDAI $\geq$ 4 and sigmoidoscopy score $\geq$ 1) were included and evaluated for clinical and endoscopic activity at day 0 and day 28. All subjects received IBD98E enema once a day (containing Na-HA 60 ml with xantham gum) during the study period. The primary endpoint was clinical response rate, defined as a decrease in UCDAI of at least 2 points, and/or at least 30% reduction from baseline, with a decrease in the sub-score for rectal bleeding of at least 1 point. Secondary endpoints included clinical remission (total UCDAI score $\leq$3), with no individual sub-score $>$1. Endoscopic remission was defined as a sub-score for sigmoidoscopy $\leq$1. A descriptive evaluation was performed, and a paired Student's t test was performed to assess statistically significant differences in subjects between baseline and D28.
RESULTS: From June to December 2012, 21 subjects (10 males) completed the study and were included in the final analysis. Average time of entry to the study from first UC diagnosis was 77.9 months (3.7-204). At D28, 9 subjects (42.9%) were clinical responders, 10 subjects (47.6%) had endoscopic response, defined as a reduction of endoscopic subscore from baseline. Eight patients (38.1%) achieved clinical remission, and ten subjects (47.6%) achieved endoscopic remission. Average UCDAI score decreased on average from 6.10 to 3.81 at D28 (p=0.001), and average endoscopic score decreased from 1.57 to 1.10 (p=0.004). A decrease in the mean PGA e PGS scores was also observed (p=0.02 and 0.04). Safety profile was generally good, no serious adverse events were recorded.
CONCLUSION: IBD98E was effective and safe to induce clinical and endoscopic remission in about half of subjects with active distal UC. Sodium hyaluronate might be a potential new treatment due to its mucosal healing properties. Placebo-controlled studies are warranted.
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Keywords: sodium hyaluronate, treatment, ulcerative colitis

P326 TIME TO REMISSION AND RESPONSE IN ADALIMUMAB-TREATED PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS FROM ULTRA 2

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INTRODUCTION: Objective: To determine the time to achieve remission and response per partial Mayo score (PMS) in patients (pts) with moderately to severely active ulcerative colitis (UC) treated with adalimumab (ADA) enrolled in ULTRA 2[1].
AIMS&METHODS: In the 52-week (wk) trial ULTRA 2, pts with moderately to severely active UC (Mayo score 6-12; endoscopy subscore 2-3) received double blind (DB) ADA 160/80mg at wks 0/2, followed by ADA 40mg every other week (eow) or placebo (PBO). Pts with inadequate response could receive open-label (OL) ADA 40mg eow beginning at wk 12 followed by 40mg weekly. Prior anti-TNF use was allowed. Remission (PMS $\leq$2 with no subscore $>$1) and response (decrease in PMS $\geq$2 points and decrease $\geq$30% from baseline plus a decrease in rectal bleeding subscore [RBS] $\geq$1 or an absolute RBS of 0 or 1) up to wk 52 were analyzed for the ITT population. Subgroup analyses by prior anti-TNF use were also performed. The time to remission or response (number of days from study day 1 to the date of the first occurrence of remission or response, respectively) was determined using Kaplan-Meier curves and tested between treatment groups using weighted log-rank test. Pts were analysed "as randomized" and were not censored at time of moving to OL ADA.
RESULTS: The median time to remission was significantly shorter for ADA-treated than PBO-treated pts (20 wks vs 29 wks, respectively, p=0.015). Similar results were observed for median time to response (4 wks ADA-treated vs 10 wks PBO-treated, p$<$0.001). In subgroup analyses, ADA-treated pts, naïve to prior anti-TNF therapy, achieved remission and response significantly faster than PBO pts (Table). In anti-TNF-experienced pts, median time to response was similar for both treatment groups (8 wks ADA-treated vs 12 wks PBO-treated).
Table. Median wks to clinical remission and response per PMS in ULTRA 2

	All Patients - ITT		Anti-TNF-naive		Anti-TNF-experienced	
	PBO N=246	ADA N=248	PBO N=145	ADA N=150	PBO N=101	ADA N=98
Time to remission (wks)	29	20*	20	12*	44	NR
Time to response (wks)	10	4†	8	4†	12	8

NR: not reached; *p$<$0.05, †p$<$0.001 vs PBO, weighted log-rank test
CONCLUSION: In ULTRA 2, pts with moderately to severely active UC randomized to ADA had shorter times to remission and response than pts randomized to PBO, even though the latter included pts that moved from PBO to OL ADA. Pts naïve to anti-TNF therapy derived the greatest treatment benefit.
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1. Sandborn WJ, et al. Gastroenterology. 2012:142:257
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Keywords: adalimumab, ulcerative colitis

P327 HOSPITALIZATION RATES IN PATIENTS WITH CROHN'S DISEASE AND DEEP REMISSION: DATA FROM THE 56-WEEK CHARM TRIAL

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INTRODUCTION: Deep remission (DR), an emerging treatment goal in Crohn's disease (CD), may be associated with improved patient outcomes.
AIMS&METHODS: We assessed all-cause and CD-related hospitalization rates among patients (both ADA- and PBO- treated) in the 56-week CHARM trial (NCT00077779) who achieved predicted DR vs. those who did not. Predicted DR was defined as having both predicted mucosal healing (using an index comprised of non-invasive biomarkers and symptomatology[1]) and clinical remission (Crohn's Disease Activity Index [CDAI] total score <150) at Week 12 in CHARM. Hospitalization rates were compared in predicted DR achievers vs. non-achievers from Week 12 to Week 56 using chi-square tests. Logistic regression was used to compare the odds of being hospitalized from Week 12 to Week 56, adjusting for adalimumab treatment and CD disease duration at Week 12. Analyses were performed as observed and with non-responder imputation (NRI) for patients with missing predicted DR data.
RESULTS: At Week 12 in CHARM, 193 of 686 patients achieved predicted DR at Week 12 in CHARM. From Week 12 to Week 56, hospitalizations for any reason (11% vs. 18%; OR=0.59, 95% CI: 0.36, 0.98; *P*=.04) as well as those specifically related to CD (6% vs. 13%; OR=0.43, 95% CI: 0.23, 0.83; *P*=.01) were significantly less among predicted DR achievers vs. non-achievers (**table**; as observed). In the NRI analysis, CD-related hospitalizations were significantly less in DR achievers vs. non-achievers (6% vs. 12%; OR=0.68, 95% CI: 0.25, 0.93; *P*=.03).

Hospitalization Rates in predicted DR Achievers vs. Non-achievers

	As-Observed			NRI		
	Achievers	Non-achievers	*P*-Value	Achievers	Non-achievers	*P*-Value
Week 12 to Week 56	N=193	N=493		N=193	N=585	
All-cause, n (%)	22 (11)	91 (18)	<.05	22 (11)	96 (16)	.12
CD-related, n (%)	12 (6)	66 (13)	<.05	12 (6)	70 (12)	<.05

CONCLUSION: Hospitalizations for any reason or specifically related to CD were fewer in patients with CD who achieved predicted DR compared with those who did not.
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Keywords: Crohn's disease, deep remission, hospitalization rate

P328 INTRAVENOUS CORTICOSTEROIDS IN MODERATE ACTIVE ULCERATIVE COLITIS NOT RESPONDING TO ORAL CORTICOSTEROIDS

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INTRODUCTION: Oral corticosteroids remain the mainstay of conventional therapy for moderate flares of ulcerative colitis. In patients who fail to respond to oral CS, it is recommended to attempt the intravenous route before starting rescue therapies, although no evidence supports this strategy.
AIMS&METHODS: To evaluate the efficacy of i.v. CS in moderate attacks of UC according to previous failure to oral CS or not, and to identify differences in long-term outcomes. All UC patients admitted to three University hospitals between 2005 and 2011 were identified. Disease severity was defined according to the Montreal classification, and only patients with moderate active UC treated with i.v. CS were included. Patients were grouped depending on previous treatment with oral CS for the index flare. Main end-points were: *initial efficacy* (defined as mild severity or inactive disease according to Montreal classification at day 7 after starting i.v. CS without a rescue therapy) and the long term clinical outcome.
RESULTS: A total of 110 attacks were included (89 patients),45% of the attacks were initially treated with oral CS without response, with a median dose of 60mg/d and during a median time of 10 days. No differences in clinical features and biological parameters between both groups, except for a younger age and lower C-reactive protein levels at the beginning of i.v. CS in the group of patients initially treated with oral CS. The i.v. CS dose was 60mg/d and the median concentration of C-reactive protein at the beginning of i.v. treatment was 44mg/L. Initial response was achieved in 75%, without differences between the both study groups (78% vs. 75%). Rescue therapy during the admission was required in 26% of cases, with a colectomy rate of 3%. No predictive factors to initial response to i.v. CS were found. After a median follow-up of 12 months (IQR, 4-24), 35% of initial responders developed steroid-dependency and up to 13% required colectomy. The unsuccessful response to oral CS was the only factor associated to steroid-dependence in the long-term (54% vs. 18%, P=0.001).
CONCLUSION: Intravenous CS are efficient for inducing remission in moderately active UC not responding to oral CS, but almost half of the patients develop steroid-dependency later on. Alternative therapeutic strategies should be assessed in this clinical setting.
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Disclosure of Interest: None Declared
Keywords: efficacy intravenous corticosteroids therapy, moderate flare ulcerative colitis, previous failure oral steroids

P329 MANAGEMENT AND OUTCOME OF SEVERE ATTACKS OF ULCERATIVE COLITIS IN THE ERA OF BIOLOGICALS

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INTRODUCTION: The availability of predictors of response to corticosteroids (CS) and the use of cyclosporine and infliximab as rescue therapies should have modified the management and outcome of severe ulcerative colitis (SUC).
AIMS&METHODS: To describe the current need of rescue therapies and colectomy in CS-treated SUC.All UC patients admitted to three University hospitals between January 2005 and December 2011 were identified from electronic databases. Disease severity was defined according to the Montreal classification, and only patients with SUC treated with intravenous CS were included. Main endpoints were: initial CS efficacy (defined as mild or inactive UC activity assessed by Montreal Classification at day 7 after starting intravenous CS without a rescue therapy), medical rescue therapy requirements, colectomy rate, and long-term clinical outcome (steroid dependency, colectomy).
RESULTS: A total of 62 flares were included (57 patients), 18% in active smokers, 70% extensive disease, 33% while on azathioprine maintenance therapy, and 22% previously treated for the same flare with oral GCS. Median C-reactive protein concentration at the beginning of intravenous CS was 99.5 mg/L (IQR, 55.5-163). Initial response of CS was achieved in 50% and 43% of flares required medical rescue therapies (12 cyclosporine, 15 infliximab) and one patient needed colectomy. Median time between the beginning of intravenous CS and rescue therapy was 7 days (IQR, 4-9), without differences between cyclosporine and infliximab-treated patients. The initial treatment with oral CS was the only risk factor (P= 0.017) and to be a former smoker the only protective factor (P= 0.003) for needing rescue therapies. During follow-up, 38% of those patients responding to CS developed steroid-dependency and 4 patients who needed a rescue treatment during admission underwent colectomy. The initial treatment with oral GCS for the index flare, the failure of intravenous CS and the need of rescue therapy were associated with colectomy, but the initial treatment with oral CS was the only independent predictive factor of colectomy in the multivariate analysis (P<0.0001).
CONCLUSION: The efficacy of intravenous CS in SUC is 50%, but the colectomy rate is <10% in the short and long-term. Patients worsening after oral CS are at a higher risk for needing rescue therapies and colectomy.
Disclosure of Interest: None Declared
Keywords: biological era, management and outcome of severe ulcerative colitis

P330 EFFECTS OF AZATHIOPRINE ON OUTCOME OF PREGNANCY IN INFLAMMATORY BOWEL DISEASE PATIENTS . A PROSPECTIVE STUDY

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INTRODUCTION: It is generally believed that Azathioprine (AZT) is harmless in pregnancy(P)of inflammatory Bowel Disease patients(IBD) both for the pregnant women and fetus .Nevertheless studies are rare,frequently retrospective and concern generally small cohorts .
AIMS&METHODS: To assess in a prospective study influence of AZT on fetal prognosis and natural history of the disease in IBD pregnant patients,we have enrolled 261 consecutive IBD patients in a prospective long term follow-up study from 1/1/2005 to 31/12/2009 of whom 244 (Group I;GI) were pregnant during the study or have had pregnancies;37 had no P (Group II;GII). 37 patients (19 Ulcerative colitis :UC and 18 Crohn's disease :CD) received AZT (2,5 mg/kg/day),(GI:n=30;GII:n=7) during 29 to 36 months.Evaluation was based on

characteristics of the last P with AZT and its outcome. Statistical analysis : Student Fisher's t test and Mann Withney's U test.
RESULTS: Comparison of IBD GI patients who received AZT (IBD/GI/AZT+) and GI patients who did not received AZT (IBD/GI/AZT-) did not show any significant statistical difference (SSD) as regards to demographic and anatomoclinical characteristics,gestational statute and outcome of disease.The same results were found when comparing UC/GI/AZT+ patients and UC/GI/AZT- patients. In return,CD/GI/AZT+ patients differ from CD/GI/AZT– patients by a greater number of anoperineal(27,7% vs 17,5%;p<0,4818) and proximal (11,1% Vs 0%;p=0,0109) locations.Caesareans (13,3% Vs 8,7%;p<0,629),stillbirths (3,3% Vs 1,5%;p=0,9613) and congenital abnormalities (3,3% Vs 0,5%;p=0,6318) were more frequent in IBD /GI /AZT+ than in IBD/GI/AZT- but didn't reach SSD whereas abortions (6,6% Vs 5,2%),premature births (6,6% Vs 5,2%),low weight birth (10% Vs 8,2%) where found at the same rates UC/GI/AZT+ patients didn't differ from UC/GI/AZT-patients as regards to gestational complications.Caesareans(21,4% Vs 10,2%;p=0,4366),low weight births (14,2% Vs 8,2%;p=0,814) and congenital abnormalities (7,1% Vs 0%;p=0,26) were more frequent in CD/GI/AZT+ than in CD/GI/AZT- patients .Long term outcome of the disease,was evaluated according to 4 heading: unchanged, improved,worsened, need for surgery.We found no SSD between IBD/GI/AZT+ and IBD/GI/AZT-patients and between IBD/GI/AZT+ and IBD/ GII/AZT+ patients.
CONCLUSION: Use of AZT in IBD pregnant women is associated with a slight increase in fetal risk mainly in CD.This pejorative effect cannot be entirely imputable to AZT as this drug is prescribed in severe IBD;in this instance, fetal outcome may be due at least in part to the disease activity.
Disclosure of Interest: None Declared
Keywords: azathioprine, IBD, Pregnancy

P331 HYPOGONADAL MEN WITH INFLAMMATORY BOWEL DISEASES (M. CROHN AND COLITIS ULCEROSA) BENEFIT FROM LONG-TERM TREATMENT WITH INJECTABLE TESTOSTERONE UNDECANOATE

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INTRODUCTION: Testosterone (T) has anti-inflammatory effects. T treatment has been found to be beneficial in rheumatoid arthritis and chronic obstructive pulmonary disease. We had reported effects of two years of T treatment in a small group of hypogonadal men with Crohn's disease (Haider A et al., Horm Mol Biol Clin Invest 2010; 2(3): 287–292).
AIMS&METHODS: In a prospective, cumulative, observational registry study, 71 hypogonadal men with Crohn's disease and 2 men with Colitis ulcerosa with T ≤ 12 nmol/L from 2 centers in Bremerhaven, Germany and Aleppo, Syria received treatment with parenteral testosterone undecanoate on day 1, after 6 weeks and thereafter every 12 weeks for up to 75 months. 12 hypogonadal men of similar age with Crohn's disease who did not receive T served as an untreated control group. In total, 73 men received T and 12 hypogonadal men remained untreated. The Crohn's Disease Activity Index (CADI) was assessed as an indicator of the severity of the disease every 3 months. In addition, highly sensitive C-reactive protein (hsCRP) and leukocyte count as markers of inflammatory activity were measured. The Aging Males' Symptoms Scale (AMS) was used as a self-administered quality of life (QoL) questionnaire.
RESULTS: T levels at baseline were 9.37 ± 1.08 nmol/l in the T group and 10.75 ± 0.36 in the control group. During treatment, T increased to 15. 72 ± 0.53 and slightly declined in the control group. The CADI decreased from 231.3 ± 35.96 to 75.0 in the treated group and increased from 196.25 ± 7.11 to 210.0 in the control group. hsCRP (mg/dL) levels at baseline were 14.13 ± 9.18 in the T group vs 7. 3 ± 0.98 in the control group. They decreased to 2.63 ± 1.91 after 72 months in the T group and increased to 13.7 in the control group. Leukocyte count decreased from 12.52 ± 2.76 to 5.97 ± 0.51 in the treated group and remained unchanged in the control group (from 11.38 ± 1.29 to 12.7). The AMS improved from 49.74 ± 8.37 in the T group to 17.33 ± 0.58. In the control group, AMS remained unchanged from 47.17 ± 1.03 at baseline to 48 at the end of the observation period.
CONCLUSION: Normalization of T in hypogonadal men with Crohn's disease led to improvements of the CADI, hsCRP, a reduction of leukocytes and an improvement of QoL. The mechanism of this improvement may be through anti-inflammatory and immunosuppressive effects of testosterone, reducing chronic inflammation of the intestinal wall in Crohn's disease.
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Keywords: C-reactive protein, Crohn's disease, hypogonadism, long-term follow up, testosterone

P332 EFFICACY AND SAFETY OF ADALIMUMAB IN CHILDREN WITH CROHN'S DISEASE PREVIOUSLY TREATED WITH INFLIXIMAB.

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INTRODUCTION: Adalimumab (ADA) is effective in the treatment of Crohn's disease (CD) in children naive to infliximab (IFX) (1)
AIMS&METHODS: The objective of this study was to evaluate the effectiveness and safety of ADA in children with CD refractory or intolerant to IFX.This retrospective study included all children with CD from a paediatric-onset population-based cohort who received ADA before the age of 18 years because of failure or intolerance to IFX. Response to ADA was evaluated with the Physical Global Assessment (PGA). The effectiveness of ADA was defined as clinical remission (PGA=1) or clinical response defined by a decrease of at least 2 points of PGA 6 mos after the ADA induction.The following parameters were recorded from ADA initiation to maximal follow-up: growth (height/age Z-score); nutritional status (BMI/age Z-score);and inflammatory biomarkers (CRP, orosomucoid). Adverse effects due to ADA were detailed.
RESULTS: 27 CD patients diagnosed from 2001 to 2010 were included.Median age at diagnosis and at ADA initiation were 11 yrs [Q1=10-Q3=12] and 15 yrs [13-15], respectively.Indication of ADA was primary failure to IFX in 4 patients (14%), loss of response to IFX in 16 (60%) and intolerance to IFX in 7 (26%).At ADA induction 5 patients received systemic steroids and 2 azathioprine. Median duration of ADA treatment was 10 months [6-18]. After a follow-up of 9 months, ADA was effective in 19 patients (70%).13 patients had ADA failure including: 8 primary; (30%) and 5 secondary. Optimizing therapy (increase of ADA dose and/or decrease of intervals between ADA injections) was required in 14 patients. Eleven patients (40%) had a total of 19 adverse effects. The main adverse events were: 1) cutaneous (xerosis; n=6, depigmentation; n=3, acne; n-2 and psoriasis: n=1); 2) local reactions (pain, inflammatory reaction) at the injection site (n=3); and 3) transient arthralgia and/or myalgia (n=4). None adverse effects resulted in ADA discontinuation. There was no significant change in growth and nutritional status over the study period but there was a significant decrease of median CRP from ADA initiation to maximal follow-up (18 mg/L [5-39] *vs* 7 [3-19]; p=0.026) and median orosomucoid (1.64 g/L [1.50- 2.56] *vs.* 1.17 [0.88-1.89]; p<0.001).
CONCLUSION: In this cohort of paediatric-onset CD patients previously treated with IFX, treatment with ADA was safe and effective in 70% after a median follow-up of 9 months. Controlled trials are needed.
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Disclosure of Interest: None Declared
Keywords: adalimumab, biological therapy, CROHŃS DISEASE, paediatrics

P333 EXPOSURE-EFFICACY RELATIONSHIP (ER) FOR ADALIMUMAB DURING INDUCTION PHASE OF TREATMENT OF ADULT PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS (UC)

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INTRODUCTION: The efficacy and pharmacokinetics (PK) of adalimumab in patients (pts) with moderate to severe UC was studied in a Phase 3 trial (ULTRA 2). The purpose of this exposure-response (ER) analysis was to characterize the relationship between serum adalimumab trough concentration (C_{trough}) and clinical remission and response per Mayo Score.
AIMS&METHODS: Adult pts with moderate to severe UC (N=518) were enrolled, where 260 pts received placebo and 258 received adalimumab (160/80 mg at Wks 0/2, and 40 mg every other wk). C_{trough} was measured immediately prior to dosing at Wk 0, 2, 4 and 8 and remission/response was assessed at Wk 8. The relationship between Wk 8 remission/response and C_{trough} was explored by grouping pts C_{trough} into quartiles and plotting C_{trough} vs remission/response rates. Only pts with available C_{trough} at Wk 8 were included in the analysis. The ER was also assessed using logistic regression. Models (linear and E_{max}) were fit to the individual ER data for remission/response at Wk 8. In the E_{max} model, the upper 95% limit of the observed remission/response was used for E_{max}.
RESULTS: The ranges of adalimumab C_{trough} quartiles were <5, 5-8.7, 8.7-11.7 and >11.7 μg/mL. C_{trough} vs remission quartile plots showed a clear ER at Wk 8. Higher C_{trough} values were associated with higher rates of remission. Quartile plots for response showed that the % of pts with Wk 8 response was higher for the 2nd and 3rd C_{trough} quartiles compared with the 1st quartile. The % of pts with Wk 8 response did not increase beyond the 3rd quartile. Logistic regression ER models for remission showed a statistically significant relationship between the % of pts with remission at Wk 8 and C_{trough} (p<0.001 for linear and p=0.011 for E_{max}). Goodness-of-fit plots showed that both models describe the data adequately. For response, the logistic regression models also showed a statistically significant relationship (p<0.001 for for linear and p=0.032 for E_{max}), but the ER observed with response was flatter compared to remission.

CONCLUSION: A statistically significant ER was identified between C_{trough} and remission during the induction phase. The ER for response appeared to be shallower compared to that for remission. This indicates that dosing regimens that result in higher exposures could provide greater efficacy in some pts.
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Keywords: adalimumab, IBD, pharmacokinetics/Pharmacodynamic relationship, ulcerative colitis

P334 EFFICACY OF CONCOMITANT ENTERAL NUTRITION DURING ADALIMUMAB MAINTENANCE THERAPY IN CROHN'S DISEASE

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INTRODUCTION: Adalimumab (ADA), a fully human anti-tumour necrosis factor (TNF) monoclonal antibody, is effective for inducing and maintaining remission in patients with active Crohn's disease (CD). Currently, loss of response to ADA during maintenance therapy in the clinical management of CD is a major therapeutic challenge. In Japan, until now, enteral nutrition (EN) has been associated with efficacy for inducing and maintaining remission in patients with CD. However, no study has investigated the efficacy of concomitant EN for sustaining response to ADA in patients with quiescent CD during maintenance therapy.
AIMS&METHODS: The aim of this study was to assess the efficacy of concomitant EN in patients with CD during ADA remission induction and maintenance therapy. In this endeavour, a cohort of 78 consecutive patients with moderate to severe CD; CD activity index (CDAI) ≥150 who had received subcutaneous ADA, 160mg, 80mg at weeks 0, 2 as remission induction therapy were retrospectively evaluated. Of 78 patients, 44 had received concomitant EN (≥300kcal/day, EN group) and 34 had received ADA without EN (control group). At week 4, clinical remission (CDAI < 150) rates were compared between the two arms. Patients who had successful ADA induction therapy received ADA maintenance therapy at 40mg, every two weeks. Loss of response to ADA was defined as CDAI≥150 and an increase of >70 points in the CDAI score. All patients were followed for at least 24 weeks. Long-term outcomes in both arms were evaluated by the Kaplan-Meier survival analysis.
RESULTS: Of 78 patients, 44 were in the EN arm (522±260kcal/day), and 34 were in the control arm. In the EN arm, 26 of 44 patients (59.1%) achieved remission vs 24 of 34 (70.6%) in the control arm. There was no significant difference in remission rates between the two arms. Fifty patients who achieved remission during ADA induction therapy received maintenance ADA. Three of 26 patients (11.5%) in the EN arm showed loss of response to ADA vs 8 of 24 (33.3%) in the control arm ($P < 0.01$). The Kaplan-Meier survival analysis showed significantly lower loss of response in favour of the EN arm ($P < 0.05$).
CONCLUSION: This is the first study which has investigated the clinical efficacy of concomitant EN therapy in patients with the loss of response to ADA. Based on the outcomes of the present investigation, concomitant EN should be considered in the management of CD during ADA maintenance therapy.
Disclosure of Interest: None Declared
Keywords: Crohn's disease, Enteral nutrition, Adalimumab, Maintenance treatment

P335 THE COMBINATION OF MESENCHYMAL STROMAL CELLS AND INFLIXIMAB INCREASES THE ANTI-INFLAMMATORY EFFECT OF THE TREATMENT OF ULCERATIVE COLITIS

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INTRODUCTION: Mesenchymal stromal cells (MSCs) have a high potential for differentiation and immunosuppressive properties. Concentration of azathioprine, methotrexate, 6-mercaptopurine, infliximab no effect on the viability, differentiation, phenotype MSC and ability to suppress proliferation of peripheral blood mononuclear cells [1].
AIMS&METHODS: Assess the clinical and endoscopic efficacy of combination therapy with concurrent use of UC MSC and infliximab (IFX). According to the method of therapy 3 groups of patients with UC with chronic continuous and chronic relapsing severe and moderate severity: 1 group patients (n=28) who were administered MSCs, 2 group patients with UC (n=26) received IFN, the introduction of which was carried out according to the standard treatment regimen of patients with UC. 3-d group of patients with UC (n=10) received MSC and IFX. Duration of disease from 3 to 15 years (Me-8 years), follow-up was 24 months. According to the results of clinical and endoscopic studies of the colonic mucosa we conducted a comparative analysis of the effectiveness of different biologic therapy of patients with UC after 2, 6 and 12 months of therapy. Initial level clinical activity index before treatment was in 1-st group - 8,98±0,38 points, 2-nd - 9,1±0,4, and 3-rd - 9,1±0,6. The level of endoscopic activity index was in the 1-st group 7,46±0,2 points, 2-nd - 7,62±0,16, 3-rd - 7,6±0,4. Statistical difference in groups according to the initial indexes was not ($p > 0,05$).
RESULTS: After 2 months of clinical activity index decreased significantly from baseline in group 1 - 1,53±0,24 points, in the 2nd - to 1,27±0,12, in the 3-rd to 1,1±0.17 points ($p > 0,05$). After 6 months of clinical activity index was in 1-st group 1,64±0,24 points in the 2-nd - 1,35±0,14 points, 3-rd - 0,7±0,15 points, which was significantly lower than in the 1-st and 2-nd groups ($p < 0,05$). After 12 months of clinical activity index was in 1-st group - 1,68±0,8 points in the 2-nd - 1,62±0,16 points, 3-rd - 0,5±0,16 points, which was significantly lower than in the 1st and 2nd groups ($p < 0.05$). Endoscopic activity index Mayo 2 months decreased significantly from baseline in the 1-st, 2-nd and 3-rd groups of up to 1,57±0,24, 1,65±0,25, 1,22±0,2 scores ($p < 0,05$). After 6 months the index Mayo; 1-st - 1,6±0,24 points, 2-nd - 1,65±0,19, 3-rd - 1,1±0,2. After 12 months, the index of Mayo 3-rd group was 0,8±0,2 points, which was significantly lower ($p < 0,05$) than in 1-st group - 1,46±0,22 points and 2-nd - 1,43±0,1 groups.
CONCLUSION: Combined biological therapy of inflammatory bowel disease contributes to more stable clinical and endoscopic remission compared to monotherapy with biological agents.
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Keywords: ulcerative colitis, infliximab, mesenchymal stromal cells

P336 PREDICTING THE OUTCOME AFTER DISCONTINUATION OF TNFA –BLOCKING AGENTS IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH DEEP REMISSION

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INTRODUCTION: Only few data exist of prognosis of patients with inflammatory bowel disease (IBD) after stopping TNFα- blocking therapy in deep remission. In this prospective multicenter study we evaluated the risk of relapse, predicting factors and the response to re-treatment after discontinuation of TNFα- blocking therapy.
AIMS&METHODS: We prospectively recruited fifty-two patients (18 Crohn's disease [CD], 30 ulcerative colitis [UC] and 4 inflammatory bowel disease type unclassified [IBDU]) in clinical, endoscopic and faecal calprotectin-based ($< 100\mu g/g$) remission after at minimum one year of TNFα- blocking therapy. Patients had been in corticosteroid free remission for at least six months. They were followed up to approximately one year after the discontinuation of TNFα-blocking therapy. Endoscopy was performed at 4 and 12 months after stopping therapy. Clinical relapse in CD was defined as Harvey Bradshaw Index (HBI) ≥8 or an increase of HBI >3 points from baseline to at least 5 points. Clinical relapse in UC or IBDU was defined as partial Mayo score ≥3. Severe endoscopic relapse was defined as the simple endoscopic score for Crohn's disease (SES-CD) ≥16 or Mayo endoscopic subscore ≥2 in UC/IBDU. In case of a clinical relapse or severe endoscopic relapse, TNFα- blocking therapy was restarted.
RESULTS: 16 (31%) patients relapsed after a median follow-up time of 24 months (range 10-37). 5/18 (28%) CD, 10/30 (30%) UC, and 1/4 (25%) IBDU patients relapsed. Re-treatment of TNFα-blocking agents was effective in 94% (15/16) of patients with relapse. No specific factor such as age, gender, disease duration, localization, or behavior, smoking, previous surgery, the TNFα-blocking therapy used, concomitant medications, or duration of the medication based on univariate analysis was associated with the relapse.
CONCLUSION: Of IBD patients in deep remission at the time of cessation of TNFα-blocking therapy, up to 70% sustained their remission during 10 months follow-up. The response to re-induction of TNFα antagonists seems to be effective and well tolerated.
Disclosure of Interest: None Declared
Keywords: Crohn's disease, relapse, remission, stopping treatment, ulcerative colitis

P337 DISEASE CONTROL AMONG ULCERATIVE COLITIS PATIENTS TREATED WITH CONVENTIONAL THERAPIES AND BIOLOGICS NAÏVE IN EUROPE: ULCERATIVE COLITIS CONDITION, ATTITUDE, RESOURCES AND EDUCATIONAL STUDY (UC CARES)-AN INTERIM ANALYSIS

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INTRODUCTION: Thiopurine immunomodulators are recommended for moderate to severe ulcerative colitis (UC) patients. However, use of UC therapies among bio-naïve patients varies considerably in clinical practice, and it is unknown whether disease is well controlled.
AIMS&METHODS: The aim is to describe disease control and treatment satisfaction of biologics-naïve UC patients receiving conventional treatment (5-ASA, steroids and/or thiopurine).
Patients with moderate to severe active UC (Mayo score ≥ 6), aged 18 years or older who received thiopurines during the 12 months prior to the index date were recruited from 46 hospitals across the following 11 European countries: Belgium,

France, Germany, Greece, Italy, The Netherlands, Spain, Sweden, Switzerland, Turkey, and The United Kingdom. Patients who had received biologic therapies, colectomy procedure or ileo-anal J-pouch reconstruction were excluded. Disease control was defined as 1) maintaining remission status, 2) partial Mayo score ≤2 and 3) no corticosteroid use in the past 2 months. Patient surveys and medical charts were reviewed to provide data for analysis. Since November 2012, inclusion criteria were amended by removing the requirements of thiopurines to facilitate more rapid patient enrollment.

RESULTS: By March 20th, 2013, 90 patients were enrolled for an interim analysis. Patients' mean age was 43 (SD =15) and 62% were male. The median duration of UC was 5 years (IQR 2-13). Extent of UC included 20% proctitis, 13% left-sided, and 67% extensive. At the index date, 75 (83%) patients were treated with thiopurines, 65 (72%) were treated with aminosalicylates, 25 (28%) were on corticosteroids, and 3 patients were treated with other types of immunosuppressants. 82% of patients did not have controlled disease. Mean full Mayo score was 4.5 (SD=2.9). In addition, 21% of patients were in remission while 28% of patients received corticosteroids in the past 2 months. Specifically, 27% of patients had Mayo score ≤2, 36% had Mayo score 3-5 and 38% had Mayo score ≥6. Based on a patient satisfaction survey, 57% of patients were satisfied with current UC therapies.

CONCLUSION: The vast majority of biologics naïve UC patients treated with conventional therapies (majority on 5-ASA and thiopurines) were not well controlled and half of patients were unsatisfied with their UC treatment.

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Keywords: disease control, remission, thiopurines, ulcerative colitis

P338 SAFETY AND EFFICACY OF HIGH DOSE INTRAVENOUS CORTICOSTEROIDS IN ACUTE ULCERATIVE COLITIS

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INTRODUCTION: Acute severe ulcerative colitis in children is associated with a high morbidity and it has a colectomy rate of 61% before and 19% even after introduction of biologics. Due to reported steroid unresponsiveness in up to 46% of children treated with a dose of 1.0-1.5 mg/kg/d methylprednisolone, salvage therapy is recommended by ECCO and ESPGHAN. Although the short-time response with CsA (80%), tacrolimus (68%) or infliximab (75%) is limited, there is profound lack of data to define the efficacy and safety of high dose intravenous methylprednisolone.

AIMS&METHODS: To evaluate the efficacy and safety of high dose Methylprednisolone in Acute severe Ulcerative Colitis

Methods:We compared two dosage regimens for the treatment of acute severe and moderate-severe UC using either low dose (LDMP) intravenous Methylprednisolone(< or = 2mg/kg/d) or high dose (>15mg/kg/d, max. 1g) IV Methylprednisolone(HDMP) without randomisation in comparable cohorts. We did a Retrospective case note review on children (n=34) admitted for moderate- or acute-severe UC requiring ivMP over 8 years, by analysis of the one year follow-up data. Disease activity was correlated using actual or retrospective PUCAI score, applying two-tailed student's t-test.

RESULTS: Patient Characteristics

The baseline characteristics of patients in the high dose and low dose MP group were similar with 75-80% of patients in each of the groups having pancolitis. The steroid, azathioprine and salicylate use in the 2 groups was also comparable($p > 0.05$).

Response to treatment

Median PUCAI score	High dose MP	Low dose MP	p-value
Day 1 of iv MP	60	55	p=0.58
Day 3 of iv MP	25	20	p=0.85
Day of Discharge (5-8 days)	6	7	p=0.85
Median Length of Stay in Hospital	7 days	6days	p=0.87

Salvage therapy-

4 out of 14 patients from the LDMP group required Colectomy and none from the HDMP group. The number of patients requiring Inflixmab and ciclosporin in the 2 groups were similar.

Side effects-

Side effects of iv MP were only minor, temporary and comparable in both groups.

CONCLUSION: Our results demonstrate a very low overall colectomy rate (11.7%), and high remission rate (85.2%) for children with acute or moderate severe UC treated with ivMP. Notably, patients with high dose steroids required no colectomy, and their requirement for salvage therapy was not more frequent than in those with low dose steroids. With a median stay of 6.5 days, patients treated with ivMP had no persistent or severe side effects from this medication.

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Disclosure of Interest: None Declared

Keywords: Colectomy, High Dose Methylprednisolone, Severe Ulcerative Colitis

P339 IMPROVEMENT IN PATIENT QUALITY OF LIFE DURING TREATMENT WITH INFLIXIMAB, AZATHIOPRINE, OR COMBINATION INFLIXIMAB+AZATHIOPRINE FOR MODERATE TO SEVERE ULCERATIVE COLITIS

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INTRODUCTION: Improvement in quality of life (QoL) is an important treatment goal for patients with ulcerative colitis (UC). We evaluated QoL in patients with UC who were treated with azathioprine (AZA), infliximab (IFX), or a combination of the 2 therapies.

AIMS&METHODS: UC SUCCESS was a 16-week, double-blind, controlled trial of patients with moderate to severe UC (baseline total Mayo score 6–12). All patients had failed corticosteroids, were biologic-naïve, and were AZA/6-mercaptopurine-naïve or had stopped AZA ≥3 months prior. Patients were randomised to treatment for 16 weeks: AZA 2.5 mg/kg + placebo; IFX 5 mg/kg + placebo; or IFX 5 mg/kg + AZA 2.5 mg/kg. Week 8 nonresponders in the AZA group were eligible for IFX rescue added to AZA. QoL was assessed with the Inflammatory Bowel Disease Questionnaire (IBDQ) and 36-item Short Form Health Survey (SF-36). Treatment group differences were analysed with Mann-Whitney U tests.

RESULTS: 239 patients were enrolled. Of 231 patients eligible for efficacy analyses, 75–80% completed the QoL assessments. Improvements in all IBDQ scores were greater in the combination group than either monotherapy group ($P < .05$, all comparisons; Table). SF-36 physical and mental summary scores (Table) and all 8 component scores showed the same pattern of greater improvement in the combination group than either monotherapy group, although not all of these comparisons were statistically significant. Overall, adverse events were similar across treatment arms.

Table. Mean Change in IBDQ and SF-36 Scores from Baseline to Week 16

		IFX+AZA n=57	IFX n=58	AZA[a] n=53
IBDQ	**Total score**	57.70[bc]	38.55	32.51
	Bowel symptoms	19.40[bc]	12.78	11.30
	Emotional health	18.56[bc]	13.33	10.79
	Systemic function	8.81[bc]	5.14	4.09
	Social function	10.93[bc]	7.31	6.32
		n=59	n=59	n=54
SF-36	**Physical summary**	7.95[b]	4.18	5.28
	Mental summary	11.57	7.55	6.6

[a]26 were week-8 nonresponders and received rescue IFX; their data were imputed by last observation carried forward from week 8; [b]$P < .05$ versus IFX; [c]$P < .05$ versus AZA.

CONCLUSION: Combination treatment with IFX+AZA resulted in greater improvement in QoL than monotherapy with either IFX or AZA. These data are consistent with previous UC SUCCESS reports indicating that clinical responses (steroid-free remission, mucosal healing, and Mayo scores) were better with combination IFX+AZA treatment.

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Keywords: azathioprine, biologic, infliximab, quality of life, ulcerative colitis

P340 EFFICACY OF INFLIXIMAB AND ADALIMUMAB FOR THE TREATMENT OF ULCERATIVE COLITIS – AN INDIRECT COMPARISON OF RCT EVIDENCE.

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INTRODUCTION: Biologics have been demonstrated to be effective in the treatment of patients with moderate to severe ulcerative colitis (UC).
AIMS&METHODS: The objective of this study was to compare the efficacy of adalimumab (ADA) and infliximab (IFX) for the treatment of moderate to severe UC through a network meta-analysis of randomized controlled trials. A systematic literature review identified 5 randomized controlled trials (RCTs) assessing the efficacy of IFX and ADA as induction and/or maintenance treatment for moderate to severe UC. Clinical response was defined as a decrease in Mayo score of ≥30% and ≥3 points, accompanied by a decrease in rectal bleeding score of ≥1 point or a rectal bleeding score of 0 or 1. Clinical remission was defined as a total Mayo score of 2 points or lower, with no individual subscore exceeding 1 point. Mucosal healing was defined as absolute subscore for endoscopy of 0 or 1. Results regarding response, remission, and mucosal healing following induction and maintenance up to 1 year as reported in the individual RCTs were synthesized with network meta-analyses within the Bayesian framework to allow for indirect comparisons.
RESULTS: As induction treatment, IFX 5mg showed greater response (odds ratio= 2.13; 95% Credible Interval, 1.26, 3.61) and remission (OR =2.28; 95%CrI, 1.12, 4.67) than ADA160/80/40mg. This also holds for IFX 10mg (response: OR, 1.98; 95% CrI, 1.17, 3.34; remission: OR=1.76; 95% CI, 0.85, 3.64). Sustained response (OR=1.75; 95%Crl 0.80, 3.93; P(better)=92%) and remission (OR=1.68; 95%CrI 0.53, 5.49, P(better)=81%) at 52 weeks follow-up was more likely with IFX 5mg than with ADA. IFX 10mg showed similar results. IFX 5mg and 10mg showed greater improvement in mucosal healing after induction than adalimumab. (5mg OR=2.20, 95% Crl 1.30, 3.71, P(better)>99%; 10mg OR= 2.12, 95%Crl 1.26, 3.57, P(better)>99%). This remained the case for sustained mucosal healing at week 52 (5mg OR=1.51, 95% Crl 0.69, 3.31, P(better)=85%; 10mg OR= 1.54, 95%Crl 0.70, 3.35, P(better)=86%).
CONCLUSION: Based on indirect comparison of RCT evidence, IFX seems more efficacious to induce and maintain long term response than ADA among moderate to severe UC patients.
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Disclosure of Interest: None Declared
Keywords: ANTI-TNF-ALPHA THERAPY, indirect comparison, ulcerative colitis

P341 REPEATED TREATMENT WITH THE TOLL-LIKE RECEPTOR 9 AGONIST DIMS0150 REINDUCES REMISSION AND LOW LONG TERM COLECTOMY RATES IN TREATMENT REFRACTORY ULCERATIVE COLITIS PATIENTS

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INTRODUCTION: DIMS0150 is a DNA based immunomodulatory oligonucleotide that targets the Toll-like receptor 9 (TLR9) and has shown positive effects in patients with treatment refractory, chronic active ulcerative colitis. The aim of this open label program was to determine the long term colectomy rate and potential treatment regimens after repeated DIMS0150 therapy in treatment refractory ulcerative colitis patients.
AIMS&METHODS: We treated a total of 14 ulcerative colitis patients classed as treatment failures who were elected for colectomy with DIMS0150 as add on to their current therapies. Within the first three months 11 patients received a single topical dose of 30 mg/50mL via endoscopy to or proximal to the inflamed area. Three patients received three doses with four weeks between dosing within the initial 12 week period. 6/14 patients received additional doses beyond the 12 week period. Patients were followed up in average for approximately 27 months and colectomy rates were monitored.
RESULTS: Following an intracolonic dose of DIMS0150 the clinical remission rates at week 12 were 73% for single treatments (8/11) and 100% in the multidose group (3/3) illustrating that DIMS0150 was a very effective short term treatment. Beyond 3 months 6/14 patients were treated with an additional dose of DIMS0150 due to a flare or upcoming relapse of the disease. Interestingly all 6 patients responded to this additional treatment either with a clear response or with an induction of remission.
The follow-up period of 27 months in average indicated that 71% (10/14) of the overall treated patients had avoided colectomy with the longest patient being in symptom free remission for over 48 months. The first year colectomy rate was determined to be 8%, the total cumulative colectomy rate over 2.25 patient years in average was 28% and the annual average colectomy rate was calculated to be 12 %.
Based on the data of 11 patients with longer term follow up data the dosing regimen ranged from a single DIMS0150 application resulting in years in remission up to biannual dosing in some patients. In the repeated dose group (6 patients) an additional dose was given in average at 18 months after initial dosing.
CONCLUSION: DIMS0150 has the potential to be an effective agent for treatment refractory, chronic active ulcerative colitis patients with the prospect to avoid colectomy on a long term basis. A repeated dosing due to relapse resulted in induction of remission and was performed in average 18 months after the initial treatment course.
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Keywords: therapeutic development, therapy, ulcerative colitis,

P342 DETAILED ANALYSIS OF FACTORS DETERMINING PATIENTS ADHERENCE TO THERAPY IN ULCERATIVE COLITIS

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INTRODUCTION: Improvement of patients' adherence to therapy in IBD is challenging. Detailed knowledge of determining factors may help to improve compliance and lead to lower flare rates.
AIMS&METHODS: 343 patients with ulcerative colitis (UC) were included into a non-interventional prospective study which was conducted in 113 IBD-focused gastroenterology practices in Germany. Oral mesalazine was prescribed either as granules or tablets using doses at the discretion of the physician. Compliance with mesalazine therapy as part of adherence was rated by patients using questionnaires. Severity of UC was rated according to UCDAI. Patients are followed up to 12 months. Interim results on compliance rating at inclusion visit are presented. Results are given as mean±SD and differences were calculated using chi^2-testing.
RESULTS: At inclusion patients preferred granules (77 %) to tablets (13 %) or had no preference (10 %). The prescription was driven by physicians' decision in 76 %, by patients' preference in 24 % only. Patients rated their general compliance on a scale from 1 (very good) to 10 (very bad) as 1.95±2.62. General compliance did not differ significantly between females (1.88±2.45) and males (2.02±2.77), between initial therapy (1.82±2.51) and re-therapy (2.17±2.69) or between high doses (1.91±2.63) and low doses (2.19±2.75). There was a significant difference ($p<0.05$) in compliance in favour of granules (1.77±2.51) vs. tablets (2.68±2.97). In general, compliance was better when the prescribed formulation was based on patients' preference (1.64±2.13) vs. physicians' decision (2.01±2.75). This effect was more pronounced in patients initially treated (1.07±1.87 vs1.89±2.55) than in patients with mesalazine re-therapy (2.08±2.35 vs. 2.21±2.85).
Patients with a short disease course (≤ 2 years) rated their compliance better than those with longstanding disease (> 2 years), irrespective of severity of the disease or mesalazine dosage (1.78±2.54 vs. 2.08±2.69).
CONCLUSION: Detailed analyses of factors determining compliance revealed significant effects of patients' preference and participation in decision making while disease characteristics showed no or less influence on compliance.
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Keywords: adherence, compliance, Mesalamine, Mesalazine, preference, ulcerative colitis

P343 HEPATITIS B VIRUS INFECTION IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Hepatitis B virus (HBV) infection and inflammatory bowel disease (IBD) can exist in the same patients. Considering the pathogenesis of both diseases belongs to T lymphocyte immune anomaly, we proposed that there might be interaction between HBV infection and IBD in IBD patients infected with HBV.
AIMS&METHODS: Retrospective study was performed on 675 consecutive IBD patients (449 CD and 226 UC). Clinical features, therapeutic approaches and laboratory results were collected from the database established by IBD center in the First Affiliated Hospital of Sun Yat- Sen University.
RESULTS: The prevalence rates of HBV infection were 13.6%,16.8% and 13.8% in CD,UC patients and general population,respectively (P=0.418). No significant difference in clinical characters was found between HBsAg-positve and –negative IBD patients. Liver function was not affected by the use of immunosuppressants in HBV infected IBD patients. Inflammatory parameters, ESR(P=0.026), HsCRP(P=0.026) and platelet count(P=0.000) were significantly lower in HBsAg-positive CD patients compared to HBsAg-negative CD patients. Infliximab was used less often in HBsAg-positive than -negative CD patients (P=0.010). Further multivariate analysis showed that only lower platelet count (OR 0.992,*P*=0.000) and less common use of infliximab therapy (OR 0.1271,*P*=0.127) were independent related factors for CD patients infected with HBV.
CONCLUSION: The prevalence of HBV infection in IBD patients was similar to that in general population in South China. HBV infection didn't affect the clinical characters and medicine choices in either CD or UC. HBV-postive CD patients have lower PLT count and less common use of infliximab compared with HBV-negative CD patients.

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Disclosure of Interest: None Declared
Keywords: Crohn's Disease, Hepatitis B virus infection, Inflammatory bowel disease, Ulcerative Colitis

P344 PREVENTION OF POSTOPERATIVE RECURRENCE OF CROHN'S DISEASE BY INFLIXIMAB: A META-ANALYSIS OF PROSPECTIVE STUDIES

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INTRODUCTION: Although promising, the evidence supporting the use of infliximab (IFX) in the post-operative (PO) setting of Crohn's disease (CD) is still based on limited experience.
AIMS&METHODS: To conduct a meta-analysis of prospective studies evaluating the efficacy of IFX for prevention of PO recurrence of CD.
Selection of studies: Evaluating infliximab for prevention of PO recurrence of CD. **Study quality**: Independently assessed by two reviewers. **Data synthesis**: by "intention-to-treat".
RESULTS: Four prospective clinical trials met criteria were included.
(ii) **Clinical remission: short-term (1 yr PO)** was observed in 90% (18/20) of the IFX group vs. 38% (8/21) in the placebo group (OR 9.32; 95% CI 2.14∼40.59; RD 0.53; 95% CI 0.29∼0.78; NNT=2, $P<0.0001$). **Long-term (≥2 yr PO)** was observed in 100% (20/20) of the IFX group vs. 48%(13/27) in the placebo group (OR 18.51; 95% CI 2.18∼156.87; RD 0.44; 95% CI 0.24∼0. 64; NNT=2, $P<0.0001$), the overall clinical remission was achieved in 95% (38/40) of the IFX group vs. 44%(21/48) in the placebo group (OR 12.05; 95% CI 3.60∼40.37; RD 0.48; 95% CI 0.33∼0. 64; NNT=2, $P<0.0001$)
(ii) Post-operative clinical recurrence **(PO-CR)** was observed in 5% (2/38) of patients in the IFX group vs. 40% (20/50) in the placebo group (OR 0.13; 95%CI 0.04 to 0.47; RD 0.34; 95%CI 0.18∼0.51; NNT=3, $P<0.0001$).
(iii) Post-operative endoscopic recurrence **(PO-ER)** was observed in 31% (12/39) of the IFX group vs. 88% (44/50) of the placebo group (OR 0.03; 95%CI 0.01∼0.14; RD 0.61; 95% CI 0.46∼0.77; NNT=2, $P<0.0001$).
CONCLUSION: IFX may be effective for maintaining both short-term and long-term **clinical remission** in PO CD, reducing both PO-CR and PO-ER with no serious adverse events reported.

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P345 EFFICACY OF ADIPOSE-DERIVED STEM CELLS FOR THE TREATMENT OF COMPLEX PERIANAL FISTULAS

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INTRODUCTION: To conduct a meta-analysis of randomized clinical trials (RCTs) evaluating the efficacy of Adipose-Derived Stem Cells (ASCs) for the induction complex perianal fistula healing.
AIMS&METHODS: Search strategy: MEDLINE (PubMmed), The Cochrane Central Register of Controlled Trials, the IBD/FBD review group specialized register and the ISI-Research Institute were searched (1997∼2013) to identify relevant studies all randomized trials. **Selection of studies:** Evaluating ASCs for induction clinical fistula closure. Randomized-controlled-trials comparing ASC with placebo were included in the meta-analysis. **Study quality:** Independently assessed by two reviewers. **Data synthesis:** By "intention-to-treat".
RESULTS: Two RCT studies were included in the meta-analysis.
Induction of fistula healing (Healing was predefined as the absence of drainage through the external openings (whether occurring spontaneously or under externally applied pressure) and complete reepithelialization of external openings, assessed by a blinded evaluation committee.):
two studies (148 ASC-treated patients) showed mean efficacy of 39% vs. 15% in controls (OR =3.87; 95% CI=1.95∼7.71, RD 0.14; 95% CI 0.05∼0.24; NNT = 7, P=0.0003). We further analysis if more dosages will achieve better efficacy, three studies were included, showing no significant difference between more than one dose vs. single dose in introducing complete closure of fistula closure, with the rate of 38% and 44%, respectively (OR =0.74; 95% CI 0.33∼1.67).
CONCLUSION: ASCs are more effective than placebo for the the induction fistula healing, with an odds ratio 3.87 (95% CI=1.95∼7.71) with an NNT of 7 and an absolute risk reduction of 24%.

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Disclosure of Interest: None Declared
Keywords: Efficacy, Perianal Fistulas, Stem Cells

P346 TACROLIMUS (FK506) FOR INDUCTION OF REMISSION IN REFRACTORY ULCERATIVE COLITIS: A META-ANALYSIS

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INTRODUCTION: To conduct a meta-analysis of randomized controlled trials (RCTs) evaluating the efficacy and safety of tacrolimus (FK506) for corticosteroid refractory ulcerative colitis (UC).
AIMS&METHODS: Selection of studies: Evaluating FK506 for induction of remission in refractory UC. **Study quality**: Independently assessed by two reviewers. **Data synthesis**: by "intention-to-treat".
RESULTS: Two RCTs met criteria were included.
Efficacy
(i) **Clinical remission** was observed in 19% (9/11) of patients in the FK506 group and in 5% (1/47) in the placebo group (OR 4.13; 95% CI 0.71∼24.01, P=0.11).
(ii) **Clinical response** was observed in 51% (37/72) of patients in the FK506 group,

and in 12% (6/50) in the placebo group (OR 7.81; 95%CI 2.92∼30.89; RD 0.23; 95%CI 0.11∼0.35; NNT=4, $P<0.0001$). (iii) **Mucosal healing** was achieved in 54% (37/69) of patients in the FK506 group, and 13% (6/46) of the placebo group (OR 7.07; 95%CI 2.64∼18.95; RD 0.23; 95% CI 0.11∼0.36; NNT=4, $P=0.0001$).

Safety

Patients in the FK506 group (45%, 34/75) were significantly more likely than placebo patients (26%, 13/50) to experience adverse events related to treatment (OR 2.97; 95%CI 1.29∼ 6.80, $P=0.01$). Moreover, there were 2 cases of serious adverse events happened in the FK506 group while none in the placebo patients. However, when taking account all the adverse events, there were no significantly difference between two groups (OR 2.0; 95% CI 0.9∼4.47, $P=0.09$).

CONCLUSION: FK506 may be effective for both clinical improvement and mucosal healing in patients with refractory UC. The use of tacrolimus in the clinical setting requires careful consideration of risks versus benefits and close monitoring for adverse events.

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Disclosure of Interest: None Declared

Keywords: Efficacy, Safety, Tacrolimus (FK506), Ulcerative Colitis

P347 SURGERY AT PRESENTATION OF ILEAL CROHN'S DISEASE: WHAT IS THE PROGNOSIS?

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INTRODUCTION: Crohn's disease (CD) is a heterogeneous entity with unpredictable behavior. Bowel resection is common during the course of the disease, and although it is not often curative, it induces prolonged remission.

AIMS&METHODS: The aim of this work is to compare the clinical course of patients with CD who underwent ileocecal resection at diagnosis with the others who were not.

Retrospective study of patients diagnosed with ileal CD (L1 of Montreal Classification) in the period of 2000-2007, with a minimal follow-up of 5 years. They were divided into two groups: Group A - Diagnosis in the surgical specimen after resection for acute abdomen and Group B - Diagnosis by conventional clinical and laboratory tests. Were assessed personal history, clinical parameters and medical/surgical treatment during the follow-up.

RESULTS: We included 139 patients (Group A-20, Group B-119) over a mean follow-up of 8 years. There was no statistical difference ($p>0.05$) between the two groups in sex (female: A-70,0%, B-58,8%), family history of inflammatory bowl disease, smoking or extra intestinal manifestations. According to the Montreal classification, the category *Behavior* was predominantly penetrating in group A (60%) and non-penetrating non-stricturing in B (49,6%) ($p<0.05$), but no statistical difference was seen in *Age* category (Group A-A2 55,0%, Group B-A2 74,8%) or perianal disease (A-0%, B-13,4%). Group A required less corticosteroids (A-30,0%; B-86,6%; OR 0,067: 0,02-0,19), less immunosuppressive drugs (A-25,0%; B-73,9%; OR 0,117: 0,04-0,35) and less biologic therapy (A-5,0%; B-28,6%; OR 0,132: 0,02-1,02) - $p<0.05$. In group B, 37% of patients required surgery, and the average time between diagnosis and surgery was 26 months. There was no difference ($p>0.05$) in the rate of re-intervention (A-5%, B-10%) or the time until the same (A-5,0 and B-6,1 years).

CONCLUSION: Patients with the diagnosis of Crohn's disease established after intestinal resection for acute abdomen have less need for medical therapy.

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Disclosure of Interest: None Declared

Keywords: Crohn's disease, Surgery

P348 TERMINAL ILEITIS IN ADULT PATIENTS WITH CROHN'S DISEASE: IS SURGERY POSSIBLE AS FIRST-LINE THERAPY?

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INTRODUCTION: Although uncomplicated terminal ileitis is usually managed medically, limited resection could represent a relevant alternative. It was demonstrated in a pediatric population that early surgery was associated with a reduced need of immunosupressors (IS) and biologics (1). The aim of this case-control retrospective study was to compare the course of the disease according to the carried treatment (medical or surgical) in adult patients

AIMS&METHODS: Each patient with an uncomplicated and limited terminal ileitis treated by intestinal resection was matched with two controls treated medically. Matching was performed according to three major criteria i.e. length of ileitis, disease duration, history of intestinal resection and three minor criteria (smoking status, sex and age). The need for IS, biologics, steroids, hospitalization, surgery and the rate of relapses or recurrences were assessed and compared during a two years follow-up. Univariate analyses (Student t-test or Mann-Whitney and Fischer or Mantel-Haenszel test) were performed and the most informative variables ($P < 0.2$) were introduced in a logistic regression model to assess the OR [CI95]

RESULTS: Fifty one patients were identified (17 cases and 34 controls). The clinical, demographic and radiological characteristics were similar between cases and controls excepted the B3 phenotype more frequent in the cases (P=0.01). During the follow-up, the patients treated surgically received less corticosteroids, IS and biologics as compared to the controls (P= 0.03, P= 0.05 and P=0.003 respectively). The number of hospitalization days was similar in the two groups (23 vs 15 dys; $P = 0.1$). Fourty two % of the patients initially treated medically needed a surgery during the two years of follow-up and 13 % of the cases were re-operated

CONCLUSION: In selected patients, surgery appears to be an attractive alternative to the medical management leading to a diminished use of steroids, IS and biologics but prospective studies are needed to define more precisely the best candidates to this strategy

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Disclosure of Interest: None Declared

Keywords: Crohn's disease, ileitis

P349 THE CUMULATIVE 30-YEAR BURDEN OF ABDOMINAL AND PERIANAL SURGERIES IN A MEDITERRANEAN IBD REFERRAL CENTER.

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INTRODUCTION: The surgical burden of inflammatory bowel disease (IBD) represents a major determinant of IBD related quality of life, disease severity and health care costs. The aim of the study was to assess the cumulative burden of surgical therapies in patients with ulcerative colitis (UC) and Crohn's disease (CD) in a well-defined geographically Mediterranean area.

AIMS&METHODS: Tertiary referral center 30-year (1981-2010) retrospective study. All serial general records for abdominal and perianal surgeries were reviewed and all operated patients with IBD (UC, CD) were recorded on a separate file including demographics, IBD characteristics as well as indication, type and number of surgeries. In parallel, our 652 IBD patient database was reviewed for abdominal and perianal surgical events.

RESULTS: 1469 abdominal and perianal surgeries were reviewed and 71 surgeries (71/1469, 4.8%) in 69 (47 males) IBD patients (38 UC, 31 CD, aged 39.1 ± 7.2) were recorded. Two patients were operated twice for perianal fistula. The indications for IBD abdominal surgeries included acute bowel obstruction or sub-obstruction in 15 patients (7 UC, 8CD), refractory disease (10UC, 3CD), bleeding (2UC, 2CD), perforation (2UC, 6CD), intussusceptions (1CD, 1UC) and internal fistula (4CD).The indications for perianal surgeries in 23/71 (31%) IBD (16UC, 7CD) patients included perianal fistulas (7CD, 4UC) perianal abscesses (8CD, 3UC) and Fournier's gangrene (1UC).

CONCLUSION: In this 30-year retrospective study the cumulative burden of abdominal and perianal surgeries affects 10.5% (69/652) of our IBD patients reflecting also a corresponding 4.8% in the general abdominal and perianal surgery population. One third of IBD surgeries were performed for perianal disease and equally affected CD and UC patients.

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Disclosure of Interest: None Declared

Keywords: inflammatory bowel disease, surgery

P350 POST-OPERATIVE COMPLICATIONS ARE NOT DECREASED BY A PROLONGED NUTRITIONAL SUPPORT IN PATIENTS WITH IBD OPERATED FOR A PERFORATING DISEASE

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INTRODUCTION: Perforating CD are often treated by resection with a high rate of morbidity and fecal diversion. Recently, it was suggested that a pre-operative nutritional therapy could decreased the occurrence of post-operative complications (1). However, the benefit was demonstrated in a cohort mixing patients with a perforating and/or a fibrostenotic disease. The aims of our study were 1) to evaluate the benefit of a pre-operative nutritional therapy, and 2) to determine the risk factors of post-operative complications in a cohort of patients operated for an abcess and/or a fistula excluding stenosis.

AIMS&METHODS: All the medical charts of the patients with a CD operated for an abcess or a fistula between 2000 and 2010 were retrospectively reviewed. The pre-operative nutritional therapy was defined by a bowel rest and an enteral or parenteral feeding during more than 2 weeks. The post-operative complications were defined according to the classification of Dindo. Quantitative data were expressed as mean ± SD and compared by a student t test ; the relative risk (RR) and the confidence interval [CI95] were calculated by the Fischer exact test

RESULTS: 72 patients (41 females), mean age 38yrs were operated for an abcess in 47 cases (65 %) and a fistula in 25 cases (35 %). 33 patients (46 %) had a pre-operative nutritional support ;they were not statistically different from the others. A complication occurred in 19 patients (26 %), classified as minor in 10 and major in 9 patients. A diverting stoma was performed in 32 patients (44 %). The pre-operative nutritional support did not decreased the rate of post-op complications (RR 0.3 [0.3 – 1.6]). The delay between the diagnosis and the surgery was not significantly increased by the nutrition: 47 ± 11 vs 34 ± 8 days. Among all the clinical and

demographic factors tested i.e. sex, age, BMI, tobacco, IS, anti-TNF, location and size of the abcess, only steroids and a past history of abcess increased the rate of post-op complications with a RR of 2.0 [1.0 – 3.9] and 3.2 [1.5 – 6.8] respectively

CONCLUSION: Our results confirm the deleterious effect of corticosteroids on the risk of post-op complications; the benefit of pre-op nutritional therapy was not confirmed in this cohort of patients with a perforating disease. Interestingly, IS and anti-TNF had no impact on the risk of complications

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Disclosure of Interest: None Declared

Keywords: Crohn's disease, Crohn's disease, Enteral nutrition, fistula, surgery

P351 EFFECT OF INFLIXIMAB ON SHORT - TERM SURGICAL COMPLICATIONS IN PATIENTS UNDERGOING PROCTOCOLECTOMY WITH ILEAL - POUCH ANAL ANASTOMOSIS

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INTRODUCTION: Infliximab treatment may increase the risk of subsequent postoperative complications of patiens with chronic ulcerative colitis (CUC). Patiens who are on combination immunosuppressive therapy that includes Infliximab may benefit from a three stage ileal-pouch anal anastomosis (IPAA).

AIMS&METHODS: The aim of this study was to asses the association between preoperative IFX use and short-term surgical complications in a refractory CUC in a single-surgeon cohort at The Centre of colorectal surgery.

A prospectively collected database of pts with a diagnosis of CUC was retrospectively reviuwed for short - term surgical complications after IPAA between January 2006 and December 2012. Of the 112 pts, 51 were treated by IFX until less than 12 weeks of the first stage of their surgery. 61 of pts remained as IFX naive controls, they were indentified from the same database.

Short-term complications were defined as these between the first stage IPAA surgery until up to within 30 days after the last stage IPAA. These complications between the two groups were compared. The pts in both groups were similar with respect to distribution on gender, age and concomitant medication with Azathioprine and corticosteroids. Median time between last infusion and the first operation was 56 (days) IQR 38 (32-70). IPAA was stapled. All pts were operated by one surgeon.

RESULTS: 108 out of all 112 pts a restorative proctocolectomies were perfomed. 12.8% of pts IFX group vs control 24.6% ($p = 0.13$) the procedure was perfomed under urgent conditions.

Overall short-term surgical complications statistically were similar in the IFX and control group 7/47 vs 13/61 (14.9 % vs 21.3 %,Odds ratio /OR/ 0.65, 95 % Confidence Interval /CI/ 0.24 - 1.77 $p = 0.397$).

There was no difference in the rate of infectious complications (10.6 % vs 16.4%, 0R:0.61, $p = 0.394$). In the case of pelvic sepsis there were no differences between groups 2/47 vs 3/61 (4.3 % vs 4.9 %, p=0.79). The occurrence of the wound infection have been the same in both groups (6.4% vs 11.5%, p=0.37) although a trend towards lover rate of overall infectious complications in the IFX group was observed 5/47 vs 10/61. Except slightly more pouch bleeding (6,4% vs 4.9%, OR 1.32 p =0.74),pouch anastomotic leak 2/47 vs 1/61 (4.2% vs 1.6%). Finally, adjusted Odds ratios with respect to age and duration of disease no revealed significant differences between treatment groups for overall (OR 0.72 $p = 0.529$, for infectious OR = 0.63, $p = 0.44$, hemorragic complications 0R 1.83,$p = 0.497$).

CONCLUSION: Preoperative use IFX was not associated with an increased risk of short-term complications after a three stage IPAA.

Disclosure of Interest: None Declared

Keywords: ileal anal pouch anastomosis, IPAA, infliximab,pelvic sepsis,ulcerative colitis,complications

P352 SURGICAL RATES AND CHARACTERISTICS OF THE FIRST INTESTINAL RESECTION IN CROHN'S DISEASE – A LONG TERM PROSPECTIVE STUDY-

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INTRODUCTION: Surgical resection rates in Crohn's disease (CD) are high ranging from 25 to 61% at 5 years .Need for surgery remains impredictable.Identifying of predictors for surgery may be of interest for medical therapeutic strategies.

AIMS&METHODS: To determine surgical rates,characteristics and predictive factors of the first intestinal resection in CD,we have studied the outcome of 226 CD patients (103 males:M ;123 females:F),included in a prospective follow-up from 1/1/2005 for at least 5 years or until surgical resection.Mean age at inclusion was 30,6 ± 6,5 y .41 patients (18,1%) were smokers.Disease was located in both colon and small intestine (CSI; n=116;51,4%),small intestine alone (SI;n= 67;29,6%) or colon alone (C;n=43;19%).Lesions were of inflammatory (I),stricturing (S) or penetrating (P) type in 92 (40,7%),76 (33,6%),58(25,7%) cases respectively .Medical treatment of flares was a conventional one;relapses were prevented by 5ASA (n=125;65,3%) or immunosuppressive drugs(n=32 ;14,1%);69 patients (30,5%) received no maintenance treatment .All patients underwent at least 2 annual clinical controls and complete investigation including endoscopy when necessary.Statistical analysis :Student Fisher's t test and Mann Whitney's U test.

RESULTS: The 5-year intestinal resection rate was 29,6%(n=67/226). Annual rate of surgery increased according to duration of disease and varied from 4% between the first and second year to 7% between the forth and the fifth year of follow-up.Emergent surgery was needed in 24 patients (10,6%) and elective one in 19%(n=43) of all the cases.During the follow-up surgical resection was more frequent:1/when disease begun before 20 y (13/29 ;44,8%) comparatively to patients aged between 20 and 40 y (46/160 ;28,7%; $p < 0,001$) or over 40 y (8/ 37;21,6%):$p < 0,1103.2$/ in patients with SI (35/116;37,5%) or CSI (25/67; 30,4%) location compared to patients with C disease (7/43;16,3%) :p=0,06 ;3/in patients with S(38/76 ;50%) or P disease (23/53 ;43,4%)comparatively to I type lesions at inclusion (6/92;6,5%):p=0,0019. In return, rate of surgical resection was not influenced by :1/Gender (F:37/123=30%,M:30/103 =29,1%; $p > 0,05$);2/ Smoking statute of patients :smokers (10/33;30,3%), previous smokers (5/ 15;33,3%) and non smokers (52/170; 30,5%);$p > 0,05$.

CONCLUSION: In this prospective study, the 5-year surgical rate of the first intestinal resection in Crohn's disease was 29,6%. The need for surgery was more frequent when disease begun before 20 years in stenosing and penetrating disease and in SI or CSI location.

Disclosure of Interest: None Declared

Keywords: Crohn's disease, Resection

P353 EXPERIMENTAL MODEL REPRODUCING PERIANAL CD FISTULAS AND EXPERIMENTAL VERIFYING OF THE TREATMENT BY AUTOLOGOUS ADIPOSE TISSUE DERIVED STEM CELLS

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INTRODUCTION: Conservative and surgical treatment of perianal fistulas in patients with Crohn's disease (CD) is effective in about 40-60% (1). Local administration of Adipose Tissue Derived Stem Cells (ADSCs) represents new approach in human fistula treatment with mixed results (2). Clinical relevant experimental model of intestinal fistula is essential for preclinical evaluation of this promising method. Creation of caecostomy was presented previously as a possible technique of fistula simulation in small animal (3).

AIMS&METHODS: The aim of the study was to evaluate experimental model reproducing fistulazing perianal CD suitable for investigation of treatment methods and performation of ADSCs application by various techniques.

Model: Caecostomy with 2-3 cm long subcutaneous canal was used as a model of intestinal fistula in 23 Whistar rats. Attempts to close fistula after its maturation were performed 4 weeks after index surgery by suture of the external opening (4 animals) or ligation of the fistula track (4 animals).

ADSCs therapy: The adipose tissue from inguinal region was harvested and ADSCs were isolated using collagenase technique and cultured in H-MEM medium. Acellular xenodermis (Xe-Derma) as a layer was settled by ADSCs. The Xe-Derma plug was applied into the fistula followed by injection with ADSCs in the peri-fistular tissue (group A). ADSC mixed with fibrin glue (Tissucol) was injected into the fistula (group B). Suspension of pure ADSCs was injected into the fistula tract and peri-fistular region and the external opening was sutured (group C). The fistula tract was evaluated on the 7th, 14th and 30th postoperative day.

RESULTS: All fistulas remained open 4 weeks after caecostomy creation confirmed by fistulography. Suture of the external opening did not lead to permanent fistula closure. After ligation only 1/4 fistula was closed. Application of ADSCs was technically successful without morbidity and mortality. The healing rate was 0/9 in group A and 0/2 in group B and 3/4 in group C within 30 days follow-up.

CONCLUSION: The model of intestinal fistula which persisted despite the surgical treatment was introduced. Simple application of ADSCs using acellular xenodermis did not lead to fistula closure. Combination of external opening closure and ADSCc application could be more effective. Further investigation will be performed.

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Disclosure of Interest: None Declared

Keywords: Experimental animal models, mesenchymal stem cells, Perianal Fistulas

P354 APPENDICECTOMY AND CLINICAL COURSE OF PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: In the pathogenesis of ulcerative colitis (UC) the appendix is thought to be a risk factor for onset and severity of disease. Recent studies even show a prognostic benefit of appendicectomy (AE) in chronic active UC. The objective of this study was to evaluate the rate of AE in patients with UC

compared to controls as well as a potential influence of AE on the course of an existing UC.
AIMS&METHODS: 322 patients with UC (mean age 45±15) out of the IBD clinics of the university hospital in Graz, Austria, were compared in respect to AE with 277 controls (mean age 53±15) out of the clinics for liver diseases. Various therapy regimens since onset of disease served as a surrogate marker of the clinical course of UC. The acquisition of data was performed via questionnaire and retrospective out of the patients' files.
RESULTS: The rate of AE performed before the onset of ulcerative colitis in patients with this IBD was significantly lower compared to controls. [9% (22/237) vs. 42% (115/277) $p < 0{,}001$]. In regard to the demand of medical therapy (5-ASA, corticosteroids, immunosuppressants, biologics) since onset of disease, there was no significant difference in UC patients with and without AE (Tab.1).
Tab.1: percentage of medical therapy according since onset of disease in UC patients with and without appendicectomy (AE)

	5-ASA	Steroids	Immunosuppressants	Biologicals
UC − AE (n=205)	**99%** (n=202)	**72%** (n=171)	**46%** (n=94)	**18%** (n=36)
UC + AE (n=22)	**100%** (n=22)	**82%** (n=18)	**36%** (n=8)	**14%** (n=3)

CONCLUSION: In this study patients with UC presented with significant lower AE rates than controls. However, there was no significant difference of medical therapies in patients with or without AE before disease onset, suggesting a minor role of the appendix in the course of UC. Surprisingly, both, the rate of AE in our patients (9%) and controls (42%), were far higher compared to literature (1% > 8% for patients; 10% > 24% for controls).
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Disclosure of Interest: None Declared
Keywords: Appendicectomy, appendix, ulcerative colitis

P355 MANAGEMENT OF POUCH STRICTURES AFTER TOTAL COLECTOMY WITH ILEO-ANAL POUCH ANASTOMOSIS (IPAA)

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INTRODUCTION: Strictures are one of the most common complications after IPAA (3-17%). There may be at the site of ileo-anal anastomosis or at the pouch inlet due to fibrosis or local ischemia. They may result in evacuation problems, pouch dilatation and bacterial overgrowth. Most of them are webs that can be treated by finger dilation or the use of dilators.
AIMS&METHODS: We present clinical outcome and treatment strategy of patients with IPAA who developed post surgery pouch strictures of variable severity. In a total series of 670 patients with IPAA we investigated 65 patients with anastomotic strictures (9, 7%) and 6 patients with pouch inlet strictures (1,08%). Based on patients symptoms and digital examination we ordered pouchography, pouchoscopy and in selected cases CT/MRI enterography. Finally, different treatment modalities were applied.
RESULTS: 65 patients with anastomotic strictures presented with symptoms like increased frequency (95%), incontinence (84%), urgency (73%) and perianal irritation (58%). 55 were treated with digital dilatation under endoscopic view (mean 2,1 times). In 10 patients hegar/savary dilators were applied (mean 3,2 times) to achieve satisfactory dilatation. In 2 tight stricture cases corticoid injection and kneedle knife cutting of circular fibrotic tissue was used and in 2 other cases endoscopic dilatation was possible after intubation of the efferent loop (rendez-vous). In most cases there was no need of hospitalization or systemic use of major analgesics. 6 patients with pouch inlet stricture presented mainly with abdominal pain (80%) and increased frequency (22%). All were treated surgically by local excision and anastomosis or by stricture by-pass. Crohn 's disease was diagnosed in 2 patients.
CONCLUSION: Anastomotic strictures after IPAA are relatively common but usually can be treated safely by digital dilatation on ambulatory basis. In difficult cases endoscopic methods are valuable. Pouch inlet strictures are rare and surgical treatment is needed.
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Disclosure of Interest: None Declared
Keywords: IPAA, POUCH STRICTURES

MONDAY, OCTOBER 14, 2013 9:00–17:00
OTHER LOWER GI DISORDERS I – Poster Area

P356 THE ROLE OF SERUM INTERLEUKIN 17 LEVELS IN EVALUATING DISEASE ACTIVITY AND GASTROINTESTINAL INVOLVEMENT IN BEHÇET'S DISEASE

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INTRODUCTION: Behçet's disease (BD) is a systemic inflammatory vasculitis of unknown etiology, characterized by relapsing episodes of oral aphthous ulcers, genital ulcers, cutaneous and ocular lesions and other manifestations, including vascular, neurological and gastrointestinal involvements.
AIMS&METHODS: The aim of this study was to evaluate the potential role of serum interleukin 17 (IL-17) in the pathogenesis and GIS manifestations of BD and to compare their value in determining the disease activity with the conventional markers like, erythrocyte sedimentation rate (ESR) and C- Reactive protein (CRP).
RESULTS: Thirty-five adult patients with a confirmed diagnosis of BD and 25 age and sex matched healthy individuals were approached for inclusion in this study. Participants with an acute/chronic infection or inflammatory bowel disease, other systemic disorders, transplant recipients and those with a suspicion of pregnancy were excluded. After a detailed history and physical examination, the patients' laboratory findings and endoscopic procedures, performed within 3 months, were noted. Comparisons were made between both groups with regards to demographic, clinical and laboratory (complete blood count, liver enzymes, ESR, CRP and serum IL-17) findings. The mean hemoglobin and mean corpuscular volume values were significantly lower while RDW values was significantly higher in BD group ($p=0{,}039$, $p=0{,}048$ and $p= 0{,}001$, respectively). Among the markers evaluated, mean ESR levels were significantly higher in BD group than in control group ($p=0{,}000$). But, the difference between groups, regarding CRP and serum IL-17 levels, were not statistically significant. When a subgroup analysis on BD patients was performed only CRP levels were significantly higher in active BD group ($p=0{,}012$). When the endoscopic examinations evaluated, it is found that 28 of 35 patients had an upper GIS endoscopy and 30 of 35 patients had a colonoscopic examination. Colonoscopies performed were normal in 24 patients while one patient had ileitis and 5 patients had ileal ulcers larger than 1 cm, in diameter. Regarding endoscopic findings, serum IL-17 levels were not significantly higher in the group with positive colonoscopic findings ($p=0{,}05$).
CONCLUSION: Even studies with more patients are needed, we concluded that serum IL-17 levels are not a good marker for disease activity and probable gastrointestinal involvement.
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Disclosure of Interest: None Declared
Keywords: behçet's disease, serum interleukin 17

P357 ACTIVATION OF HUMAN VISCERAL AFFERENTS BY BRADYKININ VIA B2 RECEPTORS, BUT NOT B1 RECEPTORS

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INTRODUCTION: We have recently developed *in vitro* electrophysiological recordings of human visceral afferent (HVA) fibre activity from isolated human intestine as a translational model of visceral pain. These HVAs respond to chemical mediators, including bradykinin (BK), known to be involved in pain signalling in the viscera. The aim of the present study was to examine the receptor pharmacology underlying BK activation of HVAs.
AIMS&METHODS: All experiments were performed in accordance with UK human ethics regulations [NREC 09/H0704/2]. Surgically resected human colon, ileum and appendix were obtained from consenting patients undergoing bowel resections. Tissue was pinned in a tissue bath, or cannulated (appendix), and superfused with carbogenated Krebs buffer (7ml/min, 32-34°C), containing nifedipine and atropine (10 μM). Mesenteric nerve bundles were carefully dissected and few fibre activity were recorded using suction electrodes. To test the reproducibility of BK responses, three individual applications of BK (20ml, 10μM) were superfused into the bath, each separated by a 60 minute washout period (n=4). To evaluate the contribution of B1 and B2 receptors to the BK response, the preparation was pre-treated with either the B1 antagonist, R715 or the B2 antagonist, HOE140 (100ml, 300nM) before the second application of BK. In addition, to examine the functional presence of B1 receptors on HVAs, the B1 agonist, Sar [D-phe^8]-des-Arg^9-BK (20ml, 1μM) was applied to the tissue (n=2)
RESULTS: Few fibre recordings were made from 15 tissues (8 colon, 2 ileum, 1 rectum, 4 appendix). Responses to repeat applications of BK were reproducible, especially the second and third applications: Application 1, 26.5±20.2 to peak 57.8±36.0 spikes/20s; Application 2 baseline 28.3±23.7 to peak 50.75±32.5 spikes/20s; Application 3 baseline 28.5±18.8 to peak 45±25.9 spikes/20s. B2 antagonism reduced the HVA peak firing rate to BK application: Pretreated baseline 60.6±29.1 to peak 100.0±42.1 spikes/20s vs. Control: baseline 63.0±31.6 to peak 141.0±56.7 spikes/20s (n=6). In contrast, B1 antagonism had no effect on HVA response to BK: Pre-treated baseline 71.6±18.6 to peak 102.5±12.5 spikes/20s vs. Control: baseline 54.0±21.8 to peak 78.5±23.5 spikes/20s (n=2). Furthermore, the application of the B1 agonist had no effect on HVA firing rate baseline 54.0±21.8 to peak 78.5±23.5 spikes/20s ($p > 0.05$).
CONCLUSION: Reproducible HVA responses to BK can be attained, allowing for pharmacological manipulation studies. HVA responses to BK are predominantly through the B2 receptor. This has relevance in intestinal sensory physiology and future strategies for therapeutic intervention.
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Disclosure of Interest: None Declared
Keywords: B1 Receptors, B2 Receptors, Bradykinin, Electrophysiology, Human

P358 ASSESSMENT AND TOPOGRAPHICAL ANALYSIS OF THE TOTAL HISTAMINE DEGRADATION CAPACITY (THDC) AT THE LOWER GI-TRACT

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INTRODUCTION: Irritable bowel syndrome (IBS) may cause various symptoms including abdominal pain, diarrhoea, constipation and is often associated with food intolerances.
AIMS&METHODS: To further evaluate the biological capacity of the GI-mucosa to degradate histamine 96 samples from the lower GI tract were homogenized and quantitative histamine degradation followed at different time points (0,8,12,20 min). Samples were taken from 24 patients with either IBS symptoms or known food allergy from ileum, cecum, colon ascendens and sigmoid. Histamine was measured by ELISA, THDC given as median (25-75%) ng histamine/mg protein x ml x min or % degradation.
RESULTS: Endogenous histamine released from homogenized tissue was quantitatively catabolized within 20 min. The degradation kinetics showed a 50 + 10% degradation rate already after 8 min and was two-staged. Interestingly, repeated experiments showed the THDC for terminal ileum 47,95 (22,07-74,70), followed by cecum 24,67 (16,63-37,70)) and colon ascendens median 23,73 (14,47-45,17)) respectively), while sigmoid had always the lowest histamine catabolization median 24,92 (13,71-35,40)). THDC was positively correlated to the number of lymphoid follicles at the lower gi tract.
CONCLUSION: Measurement of the biological histamine degradation along the lower GI tract exhibited a topographical gradient for histamine catabolization with higher levels at the terminal ileum and cecum, followed by, to distal parts, decreasing values. Future studies will clarify whether disturbances of the histamine degradation in ileum or cecum may be associated with intestinal swelling, induction of inflammation or IBS symptoms.
Supported by AiF Berlin
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Disclosure of Interest: None Declared
Keywords: histamine degradation capacity, Irritable bowel syndrome

P359 IMMUNE COMPARTMENTALIZATION IN THE GASTROINTESTINAL TRACT: DIFFERENCES BETWEEN ASCENDING AND DESCENDING HUMAN COLON.

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INTRODUCTION: The gastrointestinal tract is in contact with a wide variety of commensal microbiota and diverse pathogens so a balance between immunity and tolerance is required. Dendritic cells (DC), the most potent antigen presenting cells, determine the type and location of immune responses. Most studies of gut immunity are performed in mouse which may not constitute appropriate models for human immunity. Ascending and descending colon have different embryological origins, blood supply, enzymatic activities and gene expression profiles which may affect local DC. We hypothesise that human ascending and descending colon are independent immunological entities.
AIMS&METHODS: Paired colonic samples from ascending and descending colon were obtained from healthy controls and cells characterized by flow cytometry and electron microscopy.
RESULTS: The human ascending colon had higher numbers of total intraepithelial lymphocytes ($CD45^+CD3^+CD103^+$) than the descending colon, most of them with a cytotoxic ($CD8^+$) profile. Electron microscopy revealed higher densities of plasma cells and DC in the ascending colon. The latter was also confirmed by flow cytometry and DC identified as $HLA\text{-}DR^+CD3^-CD14^-CD16^-CD19^-CD34^-$. No difference was found in the type of DC between compartments when determined as myeloid DC ($CD11c^+$) or as CD1c (BDCA1) or CD141 (BDCA3) within $CD11c^+$ DC. However, DC from the ascending colon had significantly decreased expression of innate immunity receptors TLR2 and TLR4. Gut-homing markers $\beta7$, CCR9 and CD103 (restricted to $\beta7^+$ DC) were also decreased on DC from the ascending colon. Finally, ascending colon DC were more mature as determined by increased CD40, CD80 and CD86 expression, increased ongoing production of IL-12 (but not IL-10), decreased phagocytic capacity and ILT3 expression, and increased stimulatory capacity for allogeneic T-cells.
CONCLUSION: The human ascending colon appeared more immunologically active than the descending colon which was also indicated in the different phenotype and function of the DC. Therefore ascending and descending colon should not be considered as a single immune entity but, on the contrary, the human immune system is compartmentalized in different areas of the gastrointestinal tract.
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Disclosure of Interest: None Declared
Keywords: colon, compartmentalization, dendritic cells, Human, immunology

P360 INTESTINAL MICROBIOME AND THE RISK OF CHEMOTHERAPY-INDUCED DIARRHEA IN CANCER PATIENTS

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INTRODUCTION: A common side effect of chemotherapy treatment is diarrhea. The underlying mechanisms of chemotherapy-induced diarrhea (CID) are poorly understood and it is unclear whether changes in the intestinal microbiota during chemotherapy contribute to the development of CID. We aim to determine if intestinal microbiota changes precede and predispose to CID.
AIMS&METHODS: 36 patients with Non-Hodgkin lymphoma were included. All of them underwent the same chemotherapy regimen, from Day 1 to Day 6, conditioning for Hematopoietic Stem Cell Transplantation (HSCT). Fecal samples were collected on Day 7 and analyzed using 454 high throughput pyrosequencing spanning the V5-V6 hypervariable regions of the 16S rRNA gene.
RESULTS: 8 patients (22.2%) developed a severe CID (median delay: 13 days [11-15]). By studying fecal metagenomes, principal component analysis and heatmap with hierarchical clustering identified 2 robust clusters, differencing patients who will develop CID and patients who will not develop CID. The main contributors of the clusters were *Bacteroides* for patients who will develop CID and *Escherichia* for patients who will not develop CID. Co-occurrence network demonstrated that the 2 clusters are in fact driven by a group of species contributing to the two different community compositions.
CONCLUSION: Our study demonstrates that intestinal microbiota changes precede CID by a median of 6 days and that the determination of the fecal microbiota composition can identify patients at high risk for severe CID. We demonstrate how high-throughput sequencing technologies can have relevance in clinical disease and can guide the treatment of pertinent populations such as HSCT recipients.
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Disclosure of Interest: None Declared
Keywords: chemotherapy-induced diarrhea, intestinal microbiota, mucositis, risk factor

P361 EXPRESSION OF MUCOSAL TOLL-LIKE RECEPTORS AND GRANINS IN IRRITABLE BOWEL SYNDROME

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INTRODUCTION: The pathogenesis of irritable bowel syndrome (IBS) is not completely understood. Recent studies suggest that low-grade mucosal immune activation may contribute to the pathogenesis of IBS. Toll-like receptors (TLR), recognising danger signals, play a key role in the innate immune system. Chromogranins (Cg) and secretogranins (Sg) are secretory proteins ubiquitous in cells of the endocrine, enteric and immune systems.
AIMS&METHODS: The aim of this study was to evaluate the mucosal expression of TLRs, Cg and Sg in IBS patients. Thirty-four patients with IBS (IBS-A=8, IBS-C=10, IBS-D=11, IBS-U=5)(19 females, median age 35 (26-47) years, BMI 22.8 (20.9-24.4)), defined according to Rome III Criteria were included. Ten patients reported a post-infectious onset of IBS. Also, 17 healthy controls (12 females, age 27 (24.3-38.3) years, BMI 23 (20.5-24.5)) were included in the study. Total RNA was prepared from biopsies obtained from the sigmoid colon during unprepared sigmoidoscopy. The levels of mRNA for TLR2, TLR6, TLR9, CgA, CgB, SgIII and the house-keeping gene HPRT were assessed by quantitative real-time PCR. Results were normalized to the expression level of HPRT and expressed as $2^{-\hat{}\ \text{target-HPRT}}$.
RESULTS: The mucosal expression of CgA was lower in IBS patients compared to healthy controls (19.8 (14.5-29.8) vs. 25.6 (17.8-37.9) (median (25-75) percentile); p=0.03). The expression of CgB (0.4 (0.2-0.7) vs. 0.5(0.3-0.7); n.s.) and SgIII (0.07 (0.06-0.1) vs. 0.09(0.07-0.1); n.s.) was comparable in patients and controls. Moreover, the mucosal expression of TLR9 tended to be lower in patients relative to controls (0.06 (0.05-0.2) vs. 0.1(0.1-0.2) p=0.1), whereas the expression of TLR2 (0.13 (0.09-0.16) vs. 0.12(0.08-0.14) n.s.) and TLR6 (0.14 (0.1-0.17) vs. 0.13(0.1-0.16) n.s.) was similar in patients and controls.
CONCLUSION: The reduced mucosal CgA levels might reflect an increased release of the protein from CgA expressing cells in IBS patients. The tendency of reduced TLR9 levels indicates that IBS patients have an altered innate immune response to TLR9 ligands, i.e. unmethylated CpG oligonucleotides. Thus, we conclude that an altered expression pattern or activity of CgA and TLR9 expressing cells may be of importance for the pathogenesis of IBS
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Disclosure of Interest: None Declared
Keywords: Chromogranin, Irritable bowel syndrome, Secretogranin, Toll like receptor

P362 MYOPENIA AND THE SYSTEMIC INFLAMMATORY RESPONSE IN PATIENTS WITH OPERABLE COLORECTAL CANCER

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INTRODUCTION: Neutrophil to lymphocyte ratio (NLR) reflects a systemic inflammatory response, suggesting that elevation preoperatively is associated with poorer survival in colorectal cancer patients. Body composition may be influenced by the host inflammatory response and alterations in muscle mass have been linked to poorer outcomes in cancer patients. The aim of the present study was to examine the relationship between myopenia (clinically relevant muscle wasting) and the systemic inflammatory response expressed as NLR in patients with primary operable colorectal cancer [1].
AIMS&METHODS: Data from 306 consecutive patients diagnosed with colorectal adenocarcinoma undergoing elective curative surgical resection between 2006 and 2011 were included. Cut-offs for low muscularity normalised for stature were based on a CT-based sarcopenic obesity study of cancer patients by Prado et al (L3 skeletal muscle index (cm^2/m^2): ≤38.5 for women and ≤52.4 for men) [2]. Patients were stratified into two groups: low NLR (≦3), high NLR (>3). The relationship between myopenia, NLR and other clinicopathological parameters was assessed using non-parametric statistics for the univariate and binary logistic regression for the multivariate analysis. Analysis considered predictive factors of "association" with myopenia, including age, sex, preoperative albumin levels, BMI, stage and site of the tumour, Charlson comorbidity index and deprivation score (IMD).
RESULTS: 306 patients included in the analysis with median age of 69 years [IQR, 61-75]. 187 patients (61%) were males, 76 (24.9%) and 135 (43.5%) were obese or overweight respectively. The majority of the study's population had reduced muscle mass (n=191, 62.4%). Multivariate regression analysis identified age >75 years (OR 3.736, (95% CI 1.873-7.453) P<0.001), male gender (OR 2.850(1.629-4.988) P<0.001), BMI<25 kg/m^2 (OR 6.907 (3.447-13.839) P<0.001) and NLR>3 (OR 1.812 (95% CI 1.063-3.091) P=0.029) as an independent prognostic factors for being myopenic.
CONCLUSION: The present study highlights a direct and independent relationship between myopenia in patients with primary operable colorectal cancer and age, sex, BMI, and altered systemic inflammatory response. Understanding what factors contribute to these body composition changes may lead to novel and more effective interventions that support optimal body composition and metabolism, ultimately improving clinical and metabolic outcomes in cancer patients both in the perioperative period and in the long term. Whether attempts to reverse myopenia can alter the host immune response remain to be established.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, Myopenia, Systemic inflammatory response

P363 THE EFFECT OF INOS INHIBITORS AND HYPERBARIC OXYGEN TREATMENT IN AN EXPERIMENTAL MODEL FOR RADIATION COLITIS IN RATS

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INTRODUCTION: Radiation-induced enterocolitis comprises an important concern in patients treated with radiotherapy for abdominal or pelvic malignancies. Exposure of normal tissues in the radiotherapeutic management of these malignancies is almost inevitable, and consequent deleterious effects of therapeutic radiation on small intestine and colon may be observed as acute or chronic complications in the form of radiation enteritis or radiation colitis.
AIMS&METHODS: We aimed to investigate the effect of S-Methlyisothiourea (SMT), hyperbaric oxygen (HBO), and the combination of both in an experimental acute radiation-induced enterocolitis model. Sixty Sprague-Dawley rats were randomly divided into 5 groups (12 animals per group) of sham group, control group, HBO-only group, SMT-only group and SMT + HBO group. Anesthetized rats were delivered a single dose of gamma irradiation (25 Gy) through the colorectal region. After irradiation, each animal was monitored daily for changes in weight and in the appearance of the anal region. In the control group, we applied 2 ml saline solution intraperitoneally for 5 days. In the HBO group, 100% oxygen at 2.5 atm pressure was applied for 5 days. In the SMT group, 10 mg/kg/day SMT was applied intraperitoneally for 5 days. In the HBO + SMT group, HBO and SMT were applied, respectively. At the end of 5 days, rats were sacrificed and colon samples were collected for histological grading. Blood samples were collected for tumor necrosis factor (TNF)-α, interleukin (IL)-10, IL-1β, transforming growth factor (TGF)-β, intercellular adhesion molecule (ICAM)-1 mRNA assays.
RESULTS: TNF-α, IL-1β, IL-10, TGF-β, ICAM-1 mRNA levels were reduced by SMT, HBO, and HBO + SMT application ($p<0.05$). The microscopic scores differed significantly between SMT, HBO, HBO + SMT groups and control group. There was histologically significant improvement, especially in the HBO + SMT group. When we compared the weight of the rats before and after the study, weight loss was significantly lower in the SMT, HBO and HBO + SMT groups compared with the control group ($p<0.05$).
CONCLUSION: Both HBO and SMT were significantly effective in preventing weight loss and in reducing the inflammatory activities and severity of colitis histology, when comparing with HBO and SMT separately.
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Disclosure of Interest: None Declared
Keywords: Hyperbaric Oxygen, iNOS Inhibitors, Radiation Colitis

P364 INTRAPERITONEALLY INJECTED MESENCHYMAL STROMAL CELLS IN EXPERIMENTAL COLITIS HOME AS STRUCTURED SPHERES IN THE SEROSAL FAT SURROUNDING THE INTESTINES.

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INTRODUCTION: Mesenchymal stromal cells (MSCs) are multipotent cells with immunomodulatory and tissue regenerative properties. Therefore, they may be useful in the treatment of inflammatory bowel disease (IBD). Whether or not MSCs need to home to and engraft at the site of inflammation to exert their beneficial effect in colitis needs to be elucidated. We compared the homing and engraftment capacity of MSCs and prestimulated MSCs in experimental colitis.
AIMS&METHODS: MSCs were isolated from bone marrow of wild type BALB/c mice and transduced with a firefly-luciferase and GFP construct. The week before infusion, some MSCs were prestimulated with interferon-gamma to give iMSCs. TNBS-colitis was induced in BALB/c mice and 2x10^6 transduced (i)MSCs were injected intraperitoneally. (i)MSCs were visualized in vivo by bioluminescence imaging (BLI). At sacrifice, 3 days after injection of the cells, inguinal lymph nodes (ILNs), mesenteric lymph nodes (MLNs), spleen, small intestine (SI) and colon were also imaged by BLI. Organs were imbedded in paraffin for immunohistochemistry.
RESULTS: A 5,5 fold higher amount of injected MSCs and 4,9 fold higher amount of injected iMSCs was traceable by BLI in the abdomen of mice with colitis compared to control mice without colitis 2 days after infusion of the cells (P<0,0001 and P=0,0029). A similar difference was observed a day later (P=0,0005 (MSCs); p=0,0048 (iMSCs)). BLI at sacrifice 3 days after (i)MSC injection showed the same trend in colon, SI and MLN. Nineteen days after infusion of the (i)MSCs BLI-signal was completely disappeared in the mice that were not sacrificed at day 3. Colons and SI stained for GFP showed spherical (i)MSC formations situated in the fat surrounding the serosal site of the intestines. In these spheres macrophage were found close to (i)MSCs. No (regulatory) lymphocytes were observed inside the spheres, whereas in the surrounding area some CD3 and FoxP3 positivity was found. Furthermore, collagen deposition and some proliferation was observed in these (i)MSC-spheres.
CONCLUSION: The amount of traceable injected (i)MSCs in the abdomen was significantly higher in mice with colitis compared to healthy controls. (i)MSCs were more likely to cluster around the intestines when colitis was present. No difference in homing or engraftment was observed between MSCs and iMSCs.
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Disclosure of Interest: None Declared
Keywords: bioluminescence imaging, experimental colitis, homing, mesenchymal stromal cells

P365 GENOMIC DNA FROM HEALTHY AND TUMOROUS COLONIC EPITHELIAL CELLS HAS AUTOCRINE AND PARACRINE ACTIVATING EFFECT ON HT-29 COLON CARCINOMA CELLS, HDF-ALPHA FIBROBLASTS AND PERIPHERAL MONONUCLEAR BLOOD CELLS

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INTRODUCTION: The methylation pattern of genomic DNA fragments may represent its organ origin. In case of tumorous and inflammatory conditions, the amount of self-DNA is elevated in the serum. The Toll-like receptor 9(TLR9)-mediated immunobiologic effect of self-DNA of normal and tumorous origin may be different.
AIMS&METHODS: We aimed to compare the TLR9- and pro-inflammatory cytokine-associated effects of self-DNA originated from normal and colorectal cancer on different cell types and ex vivo peripheral mononuclear cells (PBMCs). $5x10^5$ HT-29 colon cancer cells, $2x10^5$ HDF-alpha fibroblasts, and $2x10^6$ PBMCs were incubated with 15-15μg of normal or tumorous epithelial genomic self-DNA for 6 hours. Expression levels of TLR9-signaling and pro-inflammatory cytokine related genes were measured by qPCR. Activation of 84 genes in PBMCs was determined by qPCR-based Qiagen T and B cell activation arrays.
RESULTS: Regarding TLR9 pathway, IL-1β expression altered after incubation with both DNA types (dct in control vs. tumorous vs. normal DNA treated samples were: 25.87 ± 0.1627 vs. 23.54 ± 0.2613 vs. 24.28 ± 0.2253). In case of HDF-alpha cells, only normal self-DNA activated the elements of TLR9-signaling pathway (IRAK2: average dct at the treatment with normal DNA was 18.73 vs. 21.31 in control samples; MYD88A dct was: 17.18 vs. 19.16; MYD88B dct was: 16.75 vs. 19.32; NFκB dct was: 17.55 vs. 19.76; IL-8 dct was: 14.22 vs. 18.14; IL-1β dct was: 23.1 vs. 27.24; $p<0.05$ in all cases). PBMCs showed higher IL-2 mRNA expression after the incubation with

normal self-DNA (dct of control sample: 11.74 ± 0.1650; dct of tumorous self-DNA treated sample: 10.18, ± 0.1900; dct of normal self-DNA treated sample: 9.45 ± 0.2900).
CONCLUSION: DNA from tumorous colonic epithelium could act as an endogenous pro-inflammatory ligand in HT29 cells. DNA from normal colonic epithelium may promote fibrogenesis through TLR9 activation. In normal PBMCs normal and tumorous DNA induced IL-2 mRNA overexpression, which was higher in the sample treated with normal DNA. Genomial DNA can act on the different cell types as a paracrine and autocrine regulatory signal factor depending on its methylation grade.
Disclosure of Interest: None Declared
Keywords: colon cancer, fibrogenesis, PBMC, TLR signalling, TLR9

P366 MELATONIN EXHIBITS ANTI-INFLAMMATORY EFFECT IN LPS-INDUCED MURINE MACROPHAGES VIA NFKB SUPPRESSION AND NRF-2 AND HO-1 INDUCTION.

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INTRODUCTION: Melatonin is an indolamine involved in the regulation of multiple functions, including the control of the gastrointestinal system under physiological and pathophysiological conditions. Melatonin exerts its physiological effects through specific membrane receptors which can be found in the gut, regulating gastrointestinal motility, inflammation and pain. Nevertheless, the immunomodulatory molecular mechanisms of melatonin under inflammatory conditions still remain unclear. Since macrophages play a key role in the immunopathogenesis of inflammatory based diseases, the current study was designed to investigate the cellular mechanisms underlying the redox modulation in lipopolysaccharide (LPS)-stimulated inflammatory response by melatonin (12.5, 25, 50 and 100 μM), in murine peritoneal macrophages and deep insight into the action mechanisms involved in its anti-inflammatory effect.
AIMS&METHODS: Cell viability was determined using sulforhodamine B (SRB) assay and nitric oxide (NO) production was measured using the Griess reaction. Changes in the protein expression of the proinflammatory enzymes cyclooxygenase (COX)-2, inducible nitric oxide synthase (iNOS), microsomal prostaglandin E synthase-1 (mPGES-1), heme oxygenase 1 (HO-1) and p38 phosphorylation were determined by western blot. Finally, the role of the nuclear transcription factor kappa B (NFκB) and nuclear factor-E2-related factor-2 (Nrf2) signalling pathways were also analyzed by immunoblotting.
RESULTS: LPS-induced inflammatory response in peritoneal macrophages characterized by an increase in NO production, an upregulation of COX-2, iNOS and mPGES-1 protein expressions and p38 MAPK phosphorylation, a decrease in HO-1 protein expression as well as Nrf2 activation, followed by an increase in nuclear p65 protein expression, as a parameter for NFκB activation.On the contrary, melatonin treatment was found to reduce significantly the levels of nitrites without affecting cell viability. Similarly, melatonin induced a significant decrease in COX-2, iNOS and mPGES-1 protein expressions, an important decrease of p38 phosphorylation and a remarkable increase in antioxidant enzymes(HO-1 and Nrf2) expression levels, which were accompanied by an IκBα protein degradation prevention and a reduced nuclear p65 protein expression.
CONCLUSION: Melatonin reduces inflammatory mediators and enhances the expression of HO-1 via NFκB, p38 MAPK and Nrf2 cascade signalling pathways in LPS-induced macrophages. Thus, melatonin might be a promising target for diseases associated with overactivation of macrophages.
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Disclosure of Interest: None Declared
Keywords: inflammation, macrophage, melatonin

P367 MILK FAT GLOBULE-EPIDERMAL GROWTH FACTOR 8 ACCELERATES ANGIOGENESIS-RELATED GENE EXPRESSION IN COLONIC MUCOSA DURING REGENERATING PHASE OF COLITIS

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INTRODUCTION: Milk fat globule-epidermal growth factor 8 (MFG-E8), a glycoprotein secreted from different cell types, promotes phagocytic clearance of apoptotic cells to maintain normal tissue homeostasis. In addition to this scavenging function under physiological conditions, we recently found that MFG-E8 ameliorates intestinal inflammation due to its anti-inflammatory function by regulating NF-kB-dependent cellular signaling (J Immunol 2009). However, little is known regarding the role of MFG-E8 in angiogenesis during intestinal inflammation.
AIMS&METHODS: In the present study, we investigated the effects of MFG-E8 on expressions of angiogenesis-related genes in colonic mucosa of MFG-E8 knockout (KO) mice during both active and recovery phases of colitis, and compared those results with the same in wild-type (WT) mice. Experimental colitis was induced in 8-week-old male C57BL/6N WT and MFG-E8 KO mice by administration of dextran sodium sulfate (DSS) for 7 days. To determine the colonic mucosal condition during the recovery phase of colitis, time-course changes of histological score and pro-inflammatory cytokine expression were evaluated for 50 days after stopping DSS administration. Furthermore, to confirm the effects of MFG-E8 on angiogenesis, expressions of 84 angiogenesis-related genes in colonic mucosa of WT and MFG-E8 KO mice during the recovery phase were analyzed using a PCR array profiling system.
RESULTS: The severity of colonic inflammation in the KO mice during the recovery phase was significantly greater, while the regenerating potential of colonic epithelial cells was lower as compared with the WT mice. PCR array results showed that the gene expression profiles of angiogenesis-related genes differed between the WT and KO mice. We also observed markedly decreased expression levels of angiogenesis-accelerating genes including VEGF-A, angiopoietin-2 (ANGPT2), and the endothelial-specific receptor tyrosine kinase (TEK), and increased expression of the anti-angiogenic gene thrombospondin 1 (THBS1) in colonic mucosa of KO mice as compared to WT mice, which was confirmed by real-time PCR findings.
CONCLUSION: MFG-E8 accelerates the expressions of various angiogenesis-related genes in colonic mucosa during the recovery phase of colitis, suggesting its contribution to mucosal repair in the colon when damaged by inflammatory disease.
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Disclosure of Interest: None Declared
Keywords: angiogenesis, Milk fat globule-epidermal growth factor 8 (MFG-E8)

P368 CIRCULATING TUMOUR CELLS (CTC) IN COLORECTAL CANCER - MESENTERIC VS PERIPHERAL CIRCULATION CELL COUNTS

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INTRODUCTION: Histopathological examination of colorectal cancer allows an estimate of any occult hepatic metastases at the time of resection, the chance increasing with depth of primary tumour penetration, grade and lymph node status. However in 30% of cases, nodal involvement can skip a tier of glands. In addition, a percentage of patients with node negative disease will develop liver metastasis. Blood borne metastasis is initiated by circulating tumour cells (CTC) that are transported through the circulation from the primary tumour to vital distant organs and is directly responsible for most cancer related deaths. The portal circulation provides a unique method of sampling blood directly from the vein between the primary colorectal tumour and the liver.
AIMS&METHODS: This study aims to compare the number of circulating tumour cells in the mesenteric and peripheral circulation and assess whether the volume of CTCs predict the development of liver metastasis.
Patients presenting to Ninewells Hospital, Dundee for curative resection of a colorectal cancer were considered for the study. Patients with transverse colon and low rectal tumours were excluded from our analysis due to variable venous drainage. Operations were performed by laparoscopic or open technique. 10 ml of blood were collected from the draining mesenteric vein of the resected specimen and from the peripheral circulation intra-operatively into Cyto-Chex cell preservative tubes. Samples were then assessed using Rarecyte, an EpCAM independent CTC isolation technique and number of CTCs quantified. Patients then entered routine intensive folow-up with clinic review, blood check and 6 monthly CT imaging.
RESULTS: Mesenteric and peripheral blood samples were obtained from 27 patients during the study period. 12 patients underwent right hemicolectomy, 4 patients had a left hemicolectomy and 11 patients had an anterior resection. 15 patients underwent laparoscopic resection with the others performed by open technique. The CTC count was higher in mesenteric blood samples compared to peripheral, (6 CTC/ml vs. 0.2CTC/ml respectively; $p=<0.05$). The average number of CTC per ml increased with increasing tumour depth (T1 2CTC/ml; T4 10 CTC/ml; $p<0.05$). There was no correlation between nodal stage and average number of CTC (N0 7 CTC/ml; N2 10 CTC/ml; p=ns). At a median follow-up of 9 months (range 3-13), 3 patients have developed liver metastasis. All three patients had higher CTC counts (range 10-14 CTC/ml).
CONCLUSION: CTC counts are higher in the mesenteric circulation compared to peripheral circulation in patients with colorectal cancer. CTC counts correlate with advanced T-stage and may predict hepatic metastasis.
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Disclosure of Interest: None Declared
Keywords: Circulating tumour cells, Colorectal cancer

P369 CONNEXIN 43 EXPRESSION IN PATIENTS WITH COLORECTAL ADENOMATOUS POLYPS

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INTRODUCTION: Connexins are family of transmembrane proteins that build channels in gap junctions. Gradual loss of functional gap junctions and membranous connexin expression during colorectal carcinogenesis has been shown. The aim of this study was to assess the expression of connexin 43 (CX43) in colorectal adenomas and surrounding mucosas, as well as to analyse CX43 correlation with patients' characteristics and pathological features of polyps.
AIMS&METHODS: Forty patients with endoscopically proven colorectal adenomatous polyps were included in the study. Polypectomy was performed in all the patients, and two biopsies from surrounding mucosa were taken. CX43 expression was determined by immunohystochemical staining, both in polyp dysplastic mucosa and surrounding mucosa. The expression of CX43 was analysed in 10 different fields by two independent experienced pathologist, and was assessed according to a 2-point scale : negative, <10% CX43 positive cells; positive, >10% CX43 positive cells. CX43 expression was correlated with patients' clinical data, size and pathohystological characteristics of polyps according to the WHO 2010 classification.

RESULTS: Expression of CX43 was found in mucosa surrounding polyps in 50% of patients (10/20) with low grade adenomatous polyps, and in 85% of patients (17/20) with high grade adenomatous polyps (p=0.009). Statistical analysis showed no significant difference in CX43 expression among low and high grade dysplastic adenomatous polyps. Significant correlation of CX43 expression was neither found with patients' clinical characteristics nor with polyps' characteristics.
CONCLUSION: To our knowledge, this is the first description of CX43 expression characteristics in surrounding mucosa of colorectal adenomatous polyps. We have found no significant difference of CX43 expression in epithelium of low and high grade adenomatous polyps. Despite this fact, frequent CX43 expression in observed surrounding mucosa of adenomatous polyps with high grade dysplasia and frequent lack of CX43 expression in surrounding mucosa of adenomatous polyps with low grade dysplasia, suggests there is a the role of CX43 in the progression of dysplasia in adenomatous polyps as well as in colorectal carcinogenesis.
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Disclosure of Interest: None Declared
Keywords: Colorectal adenoma, colorectal carcinogenesis, connexin 43

P370 SERRATED ADENOMAS OF THE COLON. NEW ENTITY OR UNDERDIAGNOSED?

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INTRODUCTION: There is recently a great interest for serrated polyps (S.P), mainly due to the identification of the "serrated pathway of carcinogenesis".
AIMS&METHODS: The aim of this retrospective study was to compare the rates of histological diagnosis of S.P with those of "hyperplastic" (H.P) and "mixed polyps" (M.P) over a thirty months period form January 2010 to June 2012. Additionally, demographic characteristics of S.P (age, sex), as well as localization and grade of dysplasia, were also compared to conventional adenomatous polyps (A.P).
From 1100 polypectomies of 643 patients, all S.P, H.P and M.P were recorded and alterations in histology were estimated between the first and the last year of study (x^2 Yates correction). Additionally, the 76 S.P (6.9%) were compared to the 769 A.P (69,9%) with logistic regression analysis regarding age, sex, localization and grade of dysplasia.
RESULTS: The number per year and the percentage of the histological diagnosis of polyps are presented in the Table. A significant increase in the identification of S.P with a parallel decrease of H.P (p=0,001) and M.P (p=0,001) was observed. Additionally, 257 A.P and 39 S.P were recorded in women and 509 and 37 in men respectively. The mean age of patients was 66.2 and 62.8 years for patients with A.P and S.P respectively. 106 A.P but only 1 S.P had high grade dysplasia. 20 S.P were detected in right colon and 56 in left, while 265 and 451 A.P were respectively detected (n.s). An increase of age by 10 years decreased the probability of presence of S.P in comparison to A.P by 22% (p=0.014). S.P showed 52% less probability of occurrence in men in comparison to A.P (p=0.002). Finally S.P showed 91% less probability of expressing high grade dysplasia in comparison to A.P (p=0,013).

Polyps/Year	H.P.	S.P.	M.P.
398 / 2010	82 (20.6%)	9 (2.26%)	47 (11.8%)
394 / 2011	47 (11.9%)	10 (2.5%)	34 (8.6%)
308 / 2012	34 (11%)	57 (18.5%)	11 (3.6%)

CONCLUSION: There is an increase in the histological diagnosis of S.P with a parallel decrease of HP and MP in the last years. This probably correlated to the publication of the WHO classification in 2010 and emphasizes the importance of familiarization with the new classification. In comparison to A.P, S.P seem to have decreased presence probability by age, to be less common in men and to show low probability for high grade dysplasia.
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Disclosure of Interest: None Declared
Keywords: adenomatous polyps, serrated adenoma/polyp

P371 WIF1 METHYLATED GENE TEST AND MICROBIAL CHANGES AS COLORECTAL CANCER (CRC) DIAGNOSIS MARKER.

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INTRODUCTION: Faecal occult blood test (FOBT) is recommended for CRC screening. However, FOBT had fair sensitivity and specificity as compared to Colonoscopy. Sporadic CRCs result from the environment. Colon microbiota dysbiosis, consequence of environment, is associated with CRC; this may induce mutation(s) and/or hypermethylation in anti oncogenes. The aim was to evaluate FOBT, dysbiosis, mutated and methylated genes in reference to colonoscopy.
AIMS&METHODS: A cross-sectional study included consecutive subjects referred (2003 up to 2007) for colonoscopy screening to endosocpy units. Those with germline mutation, IBD and previous colon or rectal surgery have been excluded. Clinical factors (age, gender, personal and familial history of cancer, BMI, diabetes, and treatments, nutrition behaviours) were recorded. Prior to colonoscopy, effluents (fresh stools, sera-S and urines-U) were harvested and FOBT performed. Seven dominant and subdominant bacterial populations in stools and genes (Wif1, ALX4, and vimentin) methylation levels in stools, S and U were quantified. Mutation gene markers (Kras s, Bat25, Bat 26) have been detected in tissues and stools. Bacteria were quantified (qPCR). Calibration was assessed by Hosmer-Lemeshow chisquare and discrimination by Area Under ROC curve (AUC)
RESULTS: 247 patients were included (mean age 60.8 yrs, extremes 50-75, 52% men). Colonoscopy and pathology identified 90 pts with CRC (n=66) or large adenomas (>10 cm) and remaining cases with normal colonoscopy or adenomatous less than 10 min in diameter. A multivariate model adjusted for age, male gender, and previous personal history of polyps and familial history of cancer leaded to AUC of 81.5% (95%CI: 75.7-87.4). After supplementary adjustment in different models, for dysbiosis, AUC increased to 83.4% (77.9-88.9 with bacteroides and leptum levels being border line; p= 0.08), to 84.9% (79.6-90.3; p=0.02) after adjustment for FOBT, to 90.1% (85.8; 94.4; p<0.001) after adjustment for Wif1 (S or U). When adjusted jointly for clinical parameters, FOBT, dysbiosis and wif1, only FOBT and wif1 remained independently associated with CRC. However, the AUC of the full-adjusted multivariate model did not increase significantly (91.7; 87.8; 95.6; p=0.075).
CONCLUSION: A single qPCR of methylated gene marker in S or U improved diagnosis accuracy compared to FOBT while microbial changes in dominant or subdominant bacteria populations did not improve it. Blood methylated testing can be used in those individuals reluctant to stool testing.
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Disclosure of Interest: None Declared
Keywords: COLONIC CANCER, Diagnosis, DNA methylation, DNA mutation, Microbiota, Screening

P372 FACTORS INFLUENCING LYMPH NODE HARVEST IN SURGICAL TREATED STAGE I-III RECTAL CANCER.

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INTRODUCTION: According to American Joint Committee on Cancer a lymph node (LN) harvest (LNH) of a minimum of 12 LNs is required to ensure LN negative disease in rectal cancer (RC).
Correlations between age, BMI, pT/ypT stage and preoperative chemoradiotherapy (pCRT) and LNH in RC have been proposed. Overall survival (OS) has been related to LNH.
AIMS&METHODS: The aims of this study were in a large nationwide cohort of patients with radical treated RC to evaluate:
LNH in relation to age, BMI, pT/ypT stage and pCRT
OS according to LNH
All patients in The Danish Colorectal Cancer Group's database who had a curative resection of a stage I-III adenocarcinoma (1 Jan 2001 to 31 Dec. 2012) were included. Univariate and multivariate tests were used.
RESULTS: A total of 7950 patients (4832 males and 3118 females) were included. The median LNH was 13 (interquartile range (iqr) 8-19). No difference

between sex was observed. A number of 2302 ptt. had pCRT and a number of 5655 ptt. had surgery alone. A total of 3447 (43.4%) had a LNH < 12 and 4503 (56.6%) had a LNH > =12.
Age: The median LNH according to age (< 60 years; 61-75 years and > 75 years) were: 13 (iqr 9-20); 13 (iqr 8-19) and 12 (iqr 8-18), p < .0001.
BMI: The median LNH according to BMI (BMI < 25; 25 to 29 and ≥30) were: 13(iqr 8-20); 13(8-19) & 13(8-19), N.S.
T-stage: The median LNH according to the T stages were: ypT0: 9(iqr 6-14), p/ypT1: 10(iqr 6-15), p/ypT2: 12(iqr 7-17), p/ypT3: 14(iqr 10-21), & p/ypT4: 16(iqr 10-26), p < .0001.
Preoperative CRT: The median LNH according to +/- pCRT were: 10(iqr 6-14) and 14(iqr 9-20), p < .0001. The percentage of patients having LNH < 12 according to +/- pCRT were 58.7% and 37.1%, p < .0001.
OS: The median OS for LNH < 12/ > =12 were 93/117 months (-pCRT), p < .0001, and 118/114 months (+pCRT), N.S.
In a multivariate analyse with age and year of operation as covariates, T-stage and pCRT had a significant impact on mean LNH with a distribution as follows: ypT0: 6.2, pT1/ypT1: 12.4/9.0, pT2/ypT2: 14.7/10.0, pT3/ypT3: 18.3/12.1 and pT4/ypT4: 21.8/12.9, p < .0001.
CONCLUSION: No relation between sex, BMI and LNH was found.
A minor reduction of LNH with increasing age was observed, p < .0001.
We found a significant relation between T stage and LNH, why T-stage has to be taken into account, when LNH is evaluated.
We also found a significant relation between +/- pCRT and LNH, but no difference in OS for < 12/ > = 12 LN was found in the +pCRT group opposite to the –pCRT group. Therefore, our results do not support a LNH of 12 as a surrogate marker for oncological sufficiency in RC patients treated with pCRT.
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Disclosure of Interest: None Declared
Keywords: Rectal cancer, staging

P373 FECAL IMMUNOCHEMICAL TEST (FIT) AND SIMULATED SIGMOIDOSCOPY DIAGNOSTIC ACCURACY FOR PROXIMAL ADVANCED COLORECTAL NEOPLASIA

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INTRODUCTION: Colorectal cancer (CRC) screening programs effect on proximal colorectal neoplasia is limited.
AIMS&METHODS: To compare FIT diagnostic accuracy (one determination, 100ng/ml threshold) and simulated sigmoidoscopy according to UK, SCORE and NORCCAP criteria for proximal advanced colorectal neoplasia (CRC, advanced adenoma) in a cohort of asymptomatic individuals undergoing screening colonoscopy.1292 individuals (mean age 56.4 ± 7.9 years, 53% women, at least one first-degree relative with CRC 45.1%) with complete colonoscopy included in two prospective multicenter, blind diagnostic tests studies to determine FIT (OC-sensor ^{TM}) diagnostic accuracy were analyzed. Sigmoidoscopy diagnostic yield was simulated according to UK, SCORE and NORCCAP criteria to complete colonic examination. We compared diagnostic accuracy with ROC curves, area under the curve and the homogeneity area test. Sensitivity, specificity, positive and negative predictive value and the number needed to scope (NNS) were also determined and sensitivity and specificity were compared with McNemar test.
RESULTS: Distal and proximal advanced neoplasms were detected in 115 (8.9%) and 47 (3.6%) individuals, respectively. FIT ≥ 100ng/ml was determined in 6.6% of the subjects included and 10.1, 12.7 and 23.5% met UK, SCORE and NORCCAP criteria to complete colonoscopy respectively. No statistically significant differences in AUC for proximal advanced neoplasia detection between FIT(0.56, 95% CI 0.5 to 0.61) and UK (0.56, 95% CI 0, 5 to 0.62, P = 0.88), SCORE (0.56, 95% CI 0.49 to 0.62, P = 0.88) and NORCCAP criteria (0.6, 95% CI 0.53 - 0.68, p = 0.21). In the table below data regarding sensitivity, specificity, predictive values and NNS are shown. FIT was significantly more specific than sigmoidoscopy (p < 0.001) but significantly less sensitive than NORCCAP criteria (P = 0.004).

Diagnostic test	FIT ≥100ng/ml	UK criteria	SCORE criteria	NORCCAP criteria
Sensitivity (%)	17	21,3	23,4	42,6
Specificity (%)	93,8	90,4	87,7	77,2
Positive predictive value (%)	9,4	7,7	6,7	6,6
Negative predictive value (%)	96,8	96,8	96,8	97,3
Number needed to scope	10,62	13	14,9	15,2

CONCLUSION: FIT and sigmoidoscopy diagnostic yield for proximal advanced colorectal neoplasia is low. FIT is more specific than sigmoidoscopy but less sensitive than sigmoidoscopy according to NORCCAP criteria.
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Disclosure of Interest: None Declared
Keywords: colorectal cancer screening, fecal immunochemical test, proximal colorectal advanced neoplasia, Sigmoidoscopy

P374 DIAGNOSIS OF COLORECTAL POLYPS USING OPTICAL PROJECTION TOMOGRAPHY– HOW WELL DO PATHOLOGISTS AGREE?

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INTRODUCTION: Optical Projection Tomography (OPT) is a non-destructive, in vitro 2D and 3D imaging technology, which is being evaluated as a diagnostic tool for colorectal polyps. Colonic polypoid cancers are the earliest detectable form of colorectal cancer (CRC) and if completely excised, can offer a potential cure. However, their diagnosis using conventional 2D histopathology gives rise to marked inter-observer variation due to features such as epithelial misplacement but also due to the lack of clarity in differentiating between areas of dysplastic change.
AIMS&METHODS: Our aim was to identify how well OPT compares to conventional methods and to evaluate agreement among specialist pathologists. Polyps from the UK screening population were scanned using OPT and their corresponding H&E glass and digital slides reviewed. Images were analysed by 5 gastrointestinal pathologists blinded to the specimen diagnosis in each of the three imaging modalities. Observers classified each specimen as low grade dysplasia (LGD), high grade dysplasia (HGD) or invasive cancer (ICA)and the surface morphology as tubular, tubulovillous or villous. Inter and intra observer variation analyses were made and the glass slide diagnosis taken as the current gold standard (GS).
RESULTS: 59 (39 LGD; 8 HGD; 12 ICA) specimens were reviewed. Inter-observer analysis showed that no pathologist agreed with the GS for all specimens when reviewing glass slides alone. Intra-observer analysis of dysplasia diagnoses showed substantial agreement when comparing glass and digital slides (k 0.68-0.74; specificity 93.6-100%) and fair to moderate agreement between glass and OPT images (k0.27-0.47; specificity 86.3-97.6%). Evaluation of surface morphology demonstrated a similar pattern of agreement between glass and digital slides (k0.31-0.71 specificity 50-73.7%) and OPT images (k0.23-0.45; specificity 21.1-72.7%) but a much lower specificity. The pathologist with the most OPT experience had the best agreement. Inter-observer analysis of ICA polyps showed that all 5 pathologists gave this same diagnosis on glass slides in 66.7%, digital slides in 58.3% but 0% on OPT images.
CONCLUSION: Inter-observer variation remains a significant problem when making a qualitative pathological assessment of colorectal polyps. Introducing a new technology, such as OPT, creates more variation in those with limited experience and highlights the growing need for a robust semi-automated or quantitative diagnostic tool to aid pathologists in making an accurate diagnosis.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, colorectal polyps, Diagnosis, Imaging, Pathology

P375 IS ECTOPIC CRYPT FORMATION SPECIFIC FOR TRADITIONAL SERRATED ADENOMAS?

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INTRODUCTION: Ectopic crypts, defined as abnormally positioned crypts that have lost orientation toward the muscularis mucosae, are suggested to be a pathognomonic finding of traditional serrated adenomas (TSAs). However, the significance of the ectopic crypt formation (ECF) in the distinction between TSAs and conventional adenomas (CAs) has rarely been studied.
AIMS&METHODS: We designed this study to determine whether ECF can be found in CAs and its presence is pathognomonic of TSAs. We studied 107 TSAs and 191 CAs including 106 tubular adenomas (TAs), 66 tubulovillous adenomas (TVAs), and 19 villous adenomas (VAs).
RESULTS: ECF was identified in most (79.4%) but not all TSAs. ECF was not infrequent in CAs (62 of 191, 32.5%) and its presence correlated with the presence of a villous component and larger tumor size ($P < .001$, each). Focal serration of crypts was noted in 20 (10.5%) cases of CAs. Abundant eosinophilic cytoplasm was noted in 10 (5.2%) of CAs and its presence was significantly associated with the presence of ECF ($P < .001$).
CONCLUSION: Based on its strong association with the presence of a villous component and larger tumor size, ECF appears to be involved in the villous or protuberant growth of colorectal adenomas. The identification of ECF is very helpful in the diagnosis of TSAs, however, ECF can be found in CAs, particularly in cases with a villous component. Therefore, a possibility of CA should be considered before making a diagnosis of TSA if we encounter colorectal adenomas with ECF because ECF is not uncommon in CAs.
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Disclosure of Interest: None Declared
Keywords: Conventional adenoma, Ectopic crypt formation, Traditional serrated adenoma

P376 THE YIELD OF FECAL IMMUNOCHEMICAL TEST IN SCREENING INDIVIDUALS WITH A FAMILY HISTORY OF COLORECTAL CANCER

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INTRODUCTION: The role of fecal immunochemical test (FIT) in screening individuals with a positive family history of colorectal cancer (CRC) is not clear.
AIMS&METHODS: We assessed the diagnostic accuracy of FIT using colonoscopy findings as gold standard in identifying colorectal neoplasms. We analyzed data from 4,539 asymptomatic subjects aged 50-70 years who had both colonoscopy and FIT at our bowel cancer screening center between 2008 and 2012. We assessed sensitivity of FIT in detecting advanced neoplasms and cancers in subjects with a family history of CRC. Advanced neoplasm was defined as lesions with one of the following: size $\geq$10 mm, have villous or tubulovillous component, high-grade dysplasia or carcinoma-in-situ
RESULTS: Advanced neoplasms and cancers were found at screening colonoscopy in 219 (4.8%) and 22 (0.5%) individuals, respectively. The mean age was 57.68 $\pm$ standard deviation (SD) 4.86 and 44% were male. 572 subjects (12.6%) had a family history of CRC. FIT was positive in 59 (10.3%) subjects. The sensitivity of FIT in detecting adenoma, advanced neoplasm, and cancer in subjects with a family history of CRC was 9.5% (95% confidence interval [CI], 5.7%>15.3%), 35.1% (95% CI, 20.7%>52.6%), and 25.0% (95% CI, 1.3%>78.1%), respectively. Among FIT negative subjects, adenoma was found in 152 (29.6%), advanced neoplasm in 24 (4.7%) and invasive cancer in 3 (0.6%) individuals who have a family history of CRC.
Table 1: Diagnostic performance of FIT in subjects with a family history of CRC

Colonoscopy findings	FIT positive (N=59)	FIT negative (N=513)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
All neoplasms	28 (8%)	302 (92%)	8.5 (5.8-12.2)	87.2 (82.2-91.0)	47.5 (34.5-60.8)	41.1 (36.9-45.5)
Hyperplastic polyps	1 (3%)	32 (97%)	3.0 (0.2-17.5)	89.2 (86.2-91.7)	1.7 (0.1-10.3)	93.8 (91.2-95.6)
Adenomas	16 (10%)	152 (90%)	9.5 (5.7-15.3)	89.4 (85.8-92.1)	27.1 (16.7-40.5)	70.4 (66.2-74.3)
Advanced neoplasms	13 (35%)	24 (65%)	35.1 (20.7-52.6)	91.4 (88.6-93.6)	22.0 (12.7-35.1)	95.3 (93.0-96.9)
Invasive cancers	1 (25%)	3 (75%)	25.0 (1.3-78.1)	89.8 (86.9-92.1)	1.7 (0.1-10.3)	99.4 (98.2-99.8)

CONCLUSION: Compared with colonoscopy, FIT is more likely to miss advanced neoplasms or cancer in individuals with a family history of CRC.
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Disclosure of Interest: None Declared
Keywords: colorectal cancer screening, Family history, Fecal immunochemical test

P377 A COMPUTATIONAL MODEL FOR EARLY DETECTION OF COLORECTAL CANCER BASED ON COMPLETE BLOOD COUNTS, DERIVED FROM AN ISRAELI POPULATION, PERFORMS EQUALLY WELL ON A UK POPULATION

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INTRODUCTION: Compliance with colorectal cancer
(CRC) screening programs is sub-optimal. Recently, we developed an automated model that analyzes existing clinical data (complete blood counts- CBCs, age and gender) and produces a personal score for stratifying the probability of having CRC. Our model was developed and validated on an Israeli population of 860,000 individuals, and is able to accurately identify (specificity 90%) more than half of the CRC patients (sensitivity 50.4%). Notably, our model can potentially double the number of CRC cases detected by current Israeli screening program. Although externally validated, our model was not validated in non-Israeli populations.
AIMS&METHODS: Here we aim to validate our model on a UK population to determine its applicability to other populations. To achieve this we applied our model to 77,550 primary care UK patients (age 40+) using the health information network (THIN) database, including 5,977 CRC cases. The CBCs were analyzed at different points in time prior to cancer diagnosis date. The model performance was evaluated by standard area under the receiver operating curve (AUC) (with value approaching 1 for perfect identification and 0.5 for random scoring) and the portion of CRC cases detected (sensitivity) at a given accuracy (specificity).
RESULTS: Compared to the Israeli population, the UK population has fewer CBC records (average of 4 CBCs during 8 years, vs 8 in Israelis), and these CBCs were lacking information, such as RDW. In spite of these differences, the model performed very well, achieving similar performance for both populations. When considering CBCs 3-6 months prior to the CRC diagnosis date, the AUC is 0.81 and the model detected 55.6% of the UK CRC cases at 90% specificity. When considering CBCs taken up to one month before the diagnosis date, performance is even more impressive (AUC 0.84, 60.4% of UK CRC cases at 90% specificity).
CONCLUSION: We developed a computational method based on age, gender and CBCs that efficiently detects CRC. Importantly, compared to the existing screening program, the wide availability of CBCs allows us to cover a much larger proportion of the population and to greatly increase the number of CRC cases detected potentially at an earlier stage. Here we applied our model on a UK population, which is very different from our original dataset in terms of ethnicity, age composition, health care practices, and more. Remarkably, we were able to achieve similar performances in both populations, suggesting that our model is applicable to other populations.
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Keywords: Colorectal cancer, compliance, Early Detection, prevention, Screenig

P378 EICOSAPENTAENOIC ACID-FREE FATTY ACID PREVENTS AND SUPPRESSES COLONIC TUMOURS IN COLITIS-ASSOCIATED COLORECTAL CANCER.

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INTRODUCTION: Inflammation plays a critical role on colorectal cancer (CRC) development. The consumption of n-3 polyunsaturated fatty acids (n-3 PUFAs) reduces the risk of sporadic CRC but its effect on colitis-associated cancer (CAC) has yielded conflicting results. The Notch pathway is critical for colon carcinogenesis, with opposite activity between sporadic CRC and CAC.
AIMS&METHODS: We evaluated the effectiveness of eicosapentaenoic acid as free fatty acid (EPA-FFA; SLA Pharma UK) in preventing tumours in murine models of CAC. C57BL/6 mice treated with AOM-DSS were randomized into three groups (n=20 each) to be fed either standard (Ctrl) or EPA-FFA 1%>containing diets and the effects were evaluated on both initiation (Init) and promotion (Prom) of carcinogenesis. Blood was collected for cytokine levels, lipid peroxidation and antioxidant activity. Urine was obtained for PGE2 levels, and tissues were collected for macroscopic and microscopic analysis and mucosal fatty acids composition. Expression of Notch1 targets (Nrarp, Hath1 and Hes1) and ligands, were tested by Real time PCR.
RESULTS: EPA-FFA strongly decreased tumour multiplicity in the Prom (76.4%) and Init (67.2%; $p<0.01$ for each group vs. Ctrl). EPA-FFA reduced the incidence in the Prom (70.5%) and Init (50.8%; $p<0.01$ for each group vs. Ctrl), and reduced max tumour size in the Prom (72.7%) and Init (60.9%; $p<0.05$ for each group vs. Ctrl). The combined content of mucosal arachidonic and linoleic acids decreased with EPA-FFA ($p<0.001$ for each group vs. Ctrl) while combination of EPA, DPA, DHA increased ($p<0.001$ for each group vs. Ctrl). EPA-FFA reduced interleukin-1β by 49.2% (Prom), and interferon-γ by 40.7% (Init) ($p<0.05$). EPA-FFA decreased PGE2 excretion, parcicularly in the Init (Init vs. Ctrl $p<0.05$). No changes in lipid peroxidation and antioxidant activity were observed. Concordant with previous reports, the Ctrl arm showed low Notch1 activity. A trend toward increased Hes1 and downregulated Hath1 was found in treated arms, while a significant increase of Nrarp was observed in the Init arm ($p<0.001$).
CONCLUSION: Our data suggest that EPA-FFA could be an excellent candidate for chemoprevention in colitis-associated colorectal cancer.
Disclosure of Interest: G. Piazzi: None Declared, A. Prossomariti: None Declared, G. D'Argenio: None Declared, V. Lembo: None Declared, G. Mazzone: None Declared, P. Vitaglione: None Declared, V. Fogliano: None Declared, A. Munarini: None Declared, C. Ceccarelli: None Declared, C. Fazio: None Declared, L. D'Angelo: None Declared, A. Belluzzi: None Declared, P. Chieco: None Declared, M. Hull: None Declared, M. Romano: None Declared, F. Bazzoli: None Declared, L. Ricciardiello Financial support for research from: SLA Pharma
Keywords: chemoprevention, colon cancer, Omega-3 fatty acid, ulcerative colitis

P379 PREOPERATIVE NEUTROPHIL TO LYMPHOCYTE RATIO >3 AS A PREDICTOR FOR DISEASE-FREE SURVIVAL AFTER CURATIVE COLORECTAL CANCER SURGERY.

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INTRODUCTION: Neutrophil to lymphocyte ratio (NLR) reflects a systematic inflammatory response, with some evidence suggesting that an elevated preoperative NLR >5.0 is associated with poorer survival in colorectal cancer patients [1-4]. This study aims to determine the role of the NLR as a prognostic marker for colorectal cancer patients with non-metastatic disease undergoing curative resections.

AIMS&METHODS: Data from 506 consecutive patients diagnosed with non-metastatic colorectal adenocarcinoma undergoing surgical resection between 2006 and 2011 were included. Receiver Operating Characteristics (ROC) curve analysis was used to identify the optimal value for NLR in relation to disease-free and overall survival. Univariate and multivariate Cox regression models were used to determine the role of NLR after stratification by several clinicopathological factors. Patients were followed by a standardised protocol until February 2013.

RESULTS: Median follow-up was 44.57 months [IQR, 20.97-65.16]. Multivariate Cox regression analysis identified NLR > 3 as an independent prognostic factor for disease free survival (OR 2.41, (95% CI 1.12-5.15) P= 0.024,) but not for overall survival (OR 1.23, (95% CI 0.80-1.90) P=0.347). A high NLR was significantly associated with older age, higher T and N stage, presence of micro vascular invasion, low pre-operative albumin levels and ASA status of the patients.

CONCLUSION: For patients diagnosed with CRC, a pre-operative NLR > 3 is an independent prognostic factor for disease free survival. Considering this in addition to well-established prognostic variables may improve the processes of identifying patients at higher risk of recurrence who would benefit from adjuvant therapies, thereby providing more personalised care.

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Disclosure of Interest: None Declared

Keywords: colorectal cancer, Neutrophil to lymphocyte ratio, survival outcomes

P380 PROTON PUMP INHIBITOR CAN INDUCE APOPTOSIS IN CACO2 CANCER CELL LINES

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INTRODUCTION: Recent studies suggested that proton pump inhibitors induced selective apoptosis of cancer cell and concept for anti-tumor effect due to changes of intracellular acidity in tumor cells was emerged. Until now, whether proton pump inhibitors induce apoptosis of CaCO2 (human intestinal cancer cell line) is not known, where as the effects of proton pump inhibitor on gastric cancer, pancreatic cancer, B-cell lymphoma were studied before. The aim of this study is to evaluate the effect of proton pump inhibitor (omeprazole) on apoptosis of human CaCO2 cells.

AIMS&METHODS: For MTT assay, human intestinal CaCO2 cells were incubated with each concentrations of omeprazole for 24 hours in 37°C incubator and concentrations showed 25% and 50% of cell viability were selected. Apoptosis of human CaCO2 cells were measured by performing TUNEL assay with the concentrations decided by MTT assay. We measured apoptosis related signals such as caspase-3, caspase-8, Bcl-2, Bax, PARP using western blot analysis.

RESULTS: TUNEL assay showed that omeprazole induced the apoptosis of human CaCO2. The expression of major signals related apoptosis such as caspase-3, caspase-8, Bax, PARP were significantly increased and anti-apoptosis signal, Bcl-2 was decreased.

CONCLUSION: Proton pump inhibitor induces apoptosis of human CaCO2 cells and expression of important signals related to apoptosis. Further studies about anti-tumor effect of proton pump inhibitors are needed.

Disclosure of Interest: None Declared

Keywords: Apoptosis, human CaCO2 cells, MTT assay, proton pump inhibitor

P381 ACID PUMP ANTAGONIST; APOPTOTIC EFFECT AGAINST HUMAN CACO2 CANCER CELL LINES

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INTRODUCTION: Tumor environment contributes to tumor progression, chemoresistnance and metastatic feature. It is well known that medium surrounding tumor is acidic and cytosolic pH is alkaline. Acid pump antagonist is the reversible inhibitor of gastric H^+/K^+-ATPase by competing with K^+ onthe surface of the enzyme so that is independent of secretory status and results rapid onset. Recent studies suggested that proton pump inhibitors induced selective apoptosis of cancer cells due to changes of intracellular and extracellular acidity in tumor cells. However, effect of acid pump antagonist to tumor cells has not been studied. The aim of this study is to evaluate the effect of acid pump antagonist (YH-1885) on apoptosis of human colorectal adenocarcinoma cell lines (CaCO2).

AIMS&METHODS: For MTT assay, human CaCO2 cell lines were incubated with each concentrations of YH 1885 for 24 hours in 37°C incubator and concentrations showed 25% and 50% of cell viability were selected. Apoptosis of human CaCO2 cell lines was measured by performing TUNEL assay with the concentrations decided by MTT assay. We measured apoptosis related signals such as Bax, Bcl-2, cleaved PARP, caspase-3, caspase-8 using western blot analysis.

RESULTS: TUNEL assay showed that YH-1885 induced the apoptosis of human CaCO2 cells. The expression of major signals related apoptosis such as Bax, cleaved PARP, caspase-3, caspase-8 were significantly increased and anti-apoptosis signal, Bcl-2 was decreased.

CONCLUSION: Acid pump antagonist may have an effect to microenvironment of tumor cells and induces apoptosis of human CaCO2 cell lines. Further studies are needed to evaluate the apoptotic effect of acid pump antagonist for tumor cells.

Disclosure of Interest: None Declared

Keywords: Acid pump antagonist, Apoptosis, Human CaCO2 cell lines, MTT assay

P382 AGE AND FIVE-YEAR SURVIVAL IN OPERATED PATIENTS FOR COLORECTAL CANCER

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INTRODUCTION: Colorectal carcinoma in elderly patients is increasing. There is a tendency to offer a sub-standard treatment for these patients because of their chronologic age.

AIMS&METHODS: To analyse the influence of patients age in the survival for colorectal cancer**.** Cohort of 1779 patients diagnosed of colorectal cancer in a 21 years period (1985- 2006), divided in four groups of age: < 65 years (482 cases), 65-74 years (553 cases), 76-84 years (547 cases) and ≥ 85years (193 cases). Measurements: demographic data, peri-anaesthetic risk (American Society of Anaesthesiologists (ASA) grade), character (elective or non-elective) and curability of surgery, pathological data, mortality, and survival. The cancer was staged using the TNM cancer staging system. Statistics: The chi-squared test was performed to determine significance in nonparametric variables. Kaplan-Meier curves were used in survival and comparisons made with Log-rank test. Logistic regression was used to estimate crude and specific survival risk including the follow variables: sex age, ASA grade, curative or palliative surgery, tumour differentiation, starved nodes, invaded nodes, venous invasion, and TNM stage. For all tests is has been considered a level of signification P ≤ 0,01.

RESULTS: Perioperative risk increases with age increase (P=0.0001). Rate of curative surgery decreases from 73% in the group under 65 years of age to 48% in patients aged 85 years of age and older (p=0.0001). Non-elective surgery and postoperative mortality have increased with the age (p=0.0001). No differences have been observed in pathological data between groups. Crude five-years survival in operated patients with curative intent has been 72% for those under 65 years of age, 68% for the group 65-74 years, 57% for the group 75-84 years and 33% for those aged ≥ 85 years (p=0.0001). Nonetheless, cancer specific five-years survival has been 74%, 73%, 66% y 59%, respectively. By logistic regression analyses, crude five-year survival of operated patients is related to age (p=0.0001), ASA grade (p=0.0001), curative surgery (p=0.0001), starved nodes (p=0.004), tumour differentiation (p=0.001) and tumour stage (p=0.0001). By regression analyses of specific five-year survival in operated patients, age disappear as a related factor. Only curative surgery (p=0.0001), starved nodes (p=0.007), tumour differentiation (p=0.002), and tumour stage (p=0.0001) are related factors to specific five-year survival in operated patients.

CONCLUSION: The age of operated patients for colorectal cancer is not a factor related to specific five-year survival

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Keywords: Age, Colorectal cancer, Survival Rate

P383 A NATIONAL SURVEY OF HEREDITARY COLORECTAL CANCER SERVICES IN THE UNITED KINGDOM

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INTRODUCTION: The appropriate management of genetic susceptability is an essential tool for the prevention of colorectal cancer. Heritable factors contribute about 35% of all colorectal cancer risk which has a significant impact on clinical activity in centres managing colorectal cancer. The British Society of Gastroenterology (BSG) and Association of Coloproctologists of Great Britain and Ireland (ACPGBI), released updated guidelines in 2010 for the management of patients with a family history of colorectal cancer in the United Kingdom(1). There is evidence that adherence to these guidelines is highly variable both for endoscopic screening and testing individuals for inherited conditions such as Lynch Syndrome and the Polyposis Syndromes.

AIMS&METHODS: The aim of this survey was therefore to facilitate understanding of how services for patients with inherited colorectal cancer risk can be improved, and to raise awareness of this issue amongst clinicians. This survey was designed by members of the BSG Cancer Group. Gastroenterologists, Colorectal Surgeons, and Oncologists were invited to complete a short 10 point questionnaire. This was cascaded by email to 1,793 members of the Royal College of Radiologists (RCR), Association of Cancer Physicians (ACP), the BSG and ACPGBI. We sought their opinion and perception of local hereditary colorectal cancer services, also their adherence to and understanding of current national guidelines.

RESULTS: Three hundred and eighty-two members responded to the survey, an overall response rate of 21.3%. Although 69% of respondents felt there was an adequate service for these patients, 64% also believed that another clinician was undertaking this work. There was no apparent patient pathway in 52% of centres, and only 33% maintain a register of these patients. Patients rarely receive initial tumour block testing for Lynch Syndrome. When asked what they would like to augment the service they receive many respondents requested 'clear guidelines', 'pathways' and dedicated support networks. Many appeared to be unaware of the BSG/ACPGBI guidelines for the management of these patients.

CONCLUSION: There is wide variability in local management and in subsequent clinical pathways for hereditary colorectal cancer patients. There is a perception that they should be managed by 'another' unspecified clinician. National guidelines are not adhered to, therefore we recommend improved education, well defined pathways and audit in order to improve care of patients with hereditary colorectal cancer risk.

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Disclosure of Interest: None Declared

Keywords: Colorectal cancer, Genetics, SURVEY

P384 DOWNREGULATION OF MTOR SIGNALLING IN COLORECTAL CANCER CELLS BY A COMBINATION OF EICOSAPENTAENOIC ACID-FREE FATTY ACID, EPIGALLOCATECHIN-3-GALLATE AND PROANTHOCYANIDINS.

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INTRODUCTION: The low incidence rates of colorectal cancer (CRC) in Mediterranean countries has been mainly attributed to their dietary habits. In preclinical settings, many natural compounds display potent chemopreventive activities but at high doses. mTOR (mammalian target of rapamycin) signaling is a key regulator of translation initiation and plays a critical role in CRC.

AIMS&METHODS: The aim of the study was to explore the effect of a combination of three natural compounds, eicosapentaenoic acid-free fatty acid (EPA-FFA, SLA Pharma UK), epigallocatechin-3-gallate (EGCG) and proanthocyanidins (grape seeds extract, GS) at low concentrations on HCT116 CRC cells and test their activity on mTOR pathway and on translational regulation through analysis of polysome profiles. MTT assay was employed to evaluate cell viability. Fatty acid incorporation was analyzed by GC-MS. Protein analysis was performed to evaluate the effect on downstream effectors of mTOR. Polysomal RNA was isolated from polyribosomal fractions after treatment. Gene expression analysis was performed by Real-Time PCR.

RESULTS: After establishing their $IC_{50,}$ EPA-FFA, EGCG and GS were employed either as single agents, or in combination at concentrations that at 24h showed: 1) No cell death (comb. #1, EPA-FFA 100μM+EGCG 125μM+GS 5μM); 2) 10% cell death (comb. #2, EPA-FFA125μM+EGCG 150μM+GS 10μM); 3) 30% cell death (comb #3, EPA-FFA150μM+EGCG 175μM+GS 15μM). We found that each single compound differently affected the downstream mTOR targets, pS6K and p4EBP1. The highest effects were found with 4h treatments. Importantly, the combination of three compounds at concentrations lower than IC_{50} resulted in the strongest inhibition, up to 98% for pS6K/S6K (#3), and to 78% for p4EBP1/4EBP1 (#3). The combination #3 led to an inhibition comparable with that obtained using the mTOR inhibitor rapamycin at 20nM for 48h. Importantly, the combination #3 reduced the translation of mRNAs encoding for ribosomal protein (L5, L11, L13), cell cycle regulators (C-Myc, Cyclin D1).

CONCLUSION: The treatment with EPA-FFA, EGCG and GS on HCT116 cells decreased mTOR activity and the translation of its targets when used in triple combination and at concentrations much lower than their IC_{50}. Our results indicate that these natural compounds, when used at non-cytotoxic concentrations, could be very effective chemopreventive agents.

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Keywords: chemoprevention, colon cancer, Colorectal cancer, Diet, epigallocatechin gallate, Omega-3 fatty acid

P385 THE RISK OF ADENOMAS AND CARCINOMAS IN THE ILEAL POUCH AND RECTUM AFTER SURGICAL TREATMENT IN PATIENTS WITH FAMILIAL ADENOMATOUS POLYPOSIS

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INTRODUCTION: Restorative proctocolectomy has become the most common surgical procedure for patients with familial adenomatous polyposis (FAP). However, over time adenomas and even carcinoma may develop in the ileal pouch.

AIMS&METHODS: We evaluated the incidence and nature of rectal adenomas, and also ileal pouch and non-pouch adenomas and carcinomas in patients with familial adenomatous polyposis. Endoscopic and medical records of all patients with FAP (n=75) treated in Aichi cancer center hospital, Nagoya, between January 1965 and December 2010 were reviewed. Forty patients from 28 families (23 women; median age: 51.7 years; range: 28 to 75 years) were enrolled in endoscopic surveillance, and are the subjects of this retrospective study. These patients had undergone Kock's continent ileostomy (Kock) (n=8), ileorectal anastomosis (IRA) (n=8), and ileal pouch-anal anastomosis (IPAA) (n=24). All patients were followed with a standardized protocol including chromoendoscopy and biopsies of visible polyps in the ileal pouch, non-pouch mucosa, and the rectum.

RESULTS: Median follow-up period was 17.4 years (2.3 to 36.1 years). Twenty of 32 pouch patients (Kock and IPAA) developed adenomas in the ileal pouch mucosa, and all 8 patients with IRA developed adenomas in the rectal mucosa, none in the ileal mucosa. The prevalence of ileal adenomas was significantly higher in pouch patients than in IRA patients ($P<0.01$). Three cases of adenocarcinomas developed in the ileal pouch mucosa. One of them died of ileal cancer. The risk of adenoma development in the ileal pouch was 10%, 45%, and 90% at 5, 10, and 20 years of follow-up, respectively after proctocolectomy with Kock and IPAA. The risk of rectal adenomas after colectomy with IRA was 50%, 75%, and 100% at 5, 10, and 20 years of follow-up, respectively. The overall risk of adenoma development was significantly higher in IRA patients compered to pouch patients ($P<0.05$).

CONCLUSION: Although the overall risk of adenoma development was significantly higher in IRA patients, we also found a high frequency of adenomas in the ileal pouch mucosa, with evolution into carcinoma. Regular endoscopic surveillance of the ileal pouch is recommended in these patients.

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Disclosure of Interest: None Declared

Keywords: Familial adenomatous polyposis, ileo-anal pouch anastomosis, J-pouch, restorative proctocolectomy

P386 IMPACT OF 5-FU ENZYME ON CHEMOTHERAPY FOR PATIENTS WITH RESECTABLE COLORECTAL CANCER

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INTRODUCTION: Recently, there is a useful biomarker for molecularly targeted drug. However, there has been no useful biomarker yet for 5-FU in spite of being the key drug for colorectal cancer (CRC). 5-FU based chemotherapy has been the key regimen for CRC. Orotate Phosphoribosyl Transferase (OPRT) converted into mostly 5-FU active form in the first step. Dihydropyrimidine dehydrogenase (DPD) is the initial enzyme of 5-FU catabolism. Also Prodrugs of 5FU (ex. TS-1, capecitabine) were initially converted into active or inactive forms by these enzymes. Accordingly, it was important for antitumor activity of 5-FU that these enzymes were evaluated. The correlation between these enzymes and the response of 5FU was suggested. However, the correlation was not yet investigated prospectively.

AIMS&METHODS: The aim of this prospective cohort study is to evaluate these enzymes as a predictive factor of 5-FU for patients with resectable CRC. This study was a multicenter prospective cohort study. 14 centers collaborated in this study. OPRT and DPD activities were assessed in surgical biopsies obtained from patients with resectable CRC. These enzyme activities were assayed for actual kinetic enzyme activity in vivo. We calculated the value of OPRT and DPD activity followed by OPRT, and the DPD activity ratio (OPRT/DPD) and the cut off value of OPRT/DPD were calculated for 5 years disease free survival (DFS) and overall survival (OS). Patients were treated with 5-FU/Leucovorin (LV) regimens (bolus 5-FU on day1 and LV in 2-hour infusion on day1 weekly for 6 consecutive weeks postoperatively). This study's endpoint was the correlation between OPRT/DPD ratio and 5 years DFS and OS. The cut off value of OPRT/DPD ratio was determined by the maximum χ^2 statistic method against 5 years DFS and OS.

RESULTS: 68 patients were eligible (median age 66, male 42pts, female 26pts) from July 2003 to May 2005. Median follow up was 1925 days. Mean OPRT activity was 0.270 nmol/min/mg protein and DPD was 36.5 pmol/min/mg protein. Mean OPRT/DPD ratio was 0.01360. Cut off value of OPRT/DPD ratio for 5 years DFS and OS was 0.01467, 0.01254, respectively. In 5 years DFS, patients with higher cut off had better prognosis than lower (p=0.0280). In 5 years OS, patients with higher cut off had better prognosis than lower (p=0.0208).

CONCLUSION: This result suggested that OPRT/DPD ratio could be a predictive factor for 5-FU /LV adjuvant chemotherapy and FOLFOX therapy was need for the poor responder.

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Disclosure of Interest: None Declared
Keywords: Dihydropyrimidine dehydrogenase, 5-FU, biomarkers, Orotate Phosphoribosyl Transferase

P387 LACK OF EFFECT OF SACRAL NERVE STIMULATION FOR SCLERODERMA FAECAL INCONTINENCE

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INTRODUCTION: Scleroderma is a multi-system disorder of unknown aetiology leading to the deposition of excessive connective tissue in the skin, blood vessels and internal organs. GI involvement is present in 90% of cases and the prevalence of faecal incontinence is 38%. The predominant type of faecal incontinence is passive faecal soiling, related to connective tissue deposition and internal anal sphincter (IAS) dysfunction. The only published study of sacral nerve stimulation (SNS) in scleroderma enrolled five patients and reported that temporary SNS was successful in four, all of whom had complete resolution of their incontinence episodes following a permanent implant. The mechanism of SNS in this indication, and others, remains unclear.
AIMS&METHODS: To assess the outcome of SNS in patients with scleroderma faecal incontinence.
This was a retrospective analysis on prospectively collected data performed on all scleroderma patients from our two centres who had undergone SNS for faecal incontinence.
RESULTS: A total of 10 female patients with a mean age of 54 (37-72) had temporary SNS performed. Faecal incontinence symptom duration ranged from 2 to 25 years (mean 13 years, median 12). All had passive faecal incontinence symptoms. Each patient had pre-procedure ano-rectal physiology and endoanal ultrasound documenting internal sphincter atrophy/fragmentation, or reduced anal resting pressure. Overall, there was no statistically significant difference (p=0.567) in the total Wexner incontinence scores obtained before and (mean 15.1 range 11-19) and during temporary SNS procedures (mean 13.1 range 13-18) . Two patients with a significant improvement went on to have permanent SNS with only one patient achieving a favourable outcome at one year.
CONCLUSION: This study shows that SNS in scleroderma passive faecal incontinence did not achieve favourable results in 9 of 10 patients.
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Disclosure of Interest: None Declared
Keywords: fecal incontinence, Sacral nerve stimulation, scleroderma

P388 PREDICTION PATHWAYS FOR INNATE IMMUNE PATHOLOGY, IBS, ANXIETY AND DEPRESSION IN A GENERAL POPULATION (THE POPCOL STUDY)

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INTRODUCTION: Irritable bowel syndrome (IBS) is a common diagnosis known to be associated with anxiety and depression. Interaction between innate inflammatory mediators and immune cells may disturb neural pathways in IBS causing dysmotility and pain which could lead to anxiety and depression.
AIMS&METHODS: The aim of this study was to ascertain whether low grade innate inflammation contributes to a pathway of depression and anxiety via IBS. We evaluated immune cell counts in colonic mucosa in normal subjects and those with IBS (Rome III) from a population based study in which 745 randomly selected subjects had a colonoscopy (mean age 51 years;57% women). Intraepithelial lymphocytes (IELs) per 100 enterocytes and eosinophils (eos) per five non-overlapping high power fields (HPF) were counted by light microscopy in 90 controls and 100 cases; immunocytochemistry (CD117) was performed for mast cells per 5HPF in 80 controls and 81 cases. IELs, mast cells and eos were individually summed over 5 sites (terminal ileum, caecum, transverse colon, sigmoid colon and rectum) to give a total cell load. Anxiety and depression scores were calculated from HADS. A causal model path model which hypothesises immune cells being associated with IBS which, in turn, is associated with elevated anxiety and depression was tested using path analysis implemented in the MPlus software. Standardized path coefficients are reported along with two-tailed p-values. The model's fit to the observed variance-covariance structure was assessed in several ways, viz the residual Chi-Square test which is ideally non-significant ($p > 0.05$), the ratio of Chi-Square to degrees of freedom (ideally < 5.0) the comparative fit index (CFI, ideally > 0.95) and the Tucker-Lewis index (TLI, ideally > 0.95).
RESULTS: All hypothesised paths reached statistical significance supporting the individual hypothesized pathways, see table. The overall model fit was not ideal in all respects but also was not indicative of a poorly-fitting model (X^2_4=10.46, p=.03, X^2/df=2.6, CFI=.91, TLI=.83).

		Unstandardized		Standardized	
Predictor	**Outcome**	**b**	**SE**	**b**	**p-value**
MC	IBS	-0.001	<0.0010	-0.277	0.006
IEL	IBS	0.016	0.006	0.295	0.004
EOS	IBS	0.005	0.002	0.185	0.040
IBS	Anxiety	1.734	0.342	0.471	<0.001
IBS	Depression	1.181	0.251	0.390	<0.001

CONCLUSION: In this model there is a significant contribution of innate immune inflammatory load leading to anxiety and depression via IBS. Whether therapy directed to decreasing this inflammatory load also lifts depression and anxiety is an interesting concept which should be further explored.
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Disclosure of Interest: None Declared
Keywords: anxiety, depression, Innate Immunity, Irritable bowel syndrome, psychoneuroimmunology

P389 FEMALE GENDER FAVORS GUT PROINFLAMMATORY RESPONSES TO STRESS

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INTRODUCTION: Irritable bowel syndrome (IBS) is a highly prevalent disorder, linked to intestinal epithelial dysfunction and mucosal microinflammation, with unexplained increased women susceptibility. We have demonstrated that female gender *per se* determines intestinal barrier dysfunction in response to acute experimental stress. This response could represent, in susceptible individuals, an early stage towards the onset of functional digestive diseases.
AIMS&METHODS: We aim to identify gender-dependent molecular biomarkers of intestinal barrier dysfunction in response to acute stress in healthy individuals to understand the mechanistic origin of increased female prevalence in IBS.
METHODS:Twelve men (M) and 12 age-matched females (F) were recruited. In each participant, two consecutive jejunal biopsies were obtained by Watson's capsule: one at baseline and another 90 min after 15 min of intermittent cold pain stress (CPS). Throughout the study, autonomic (blood pressure and heart rate), hormonal (plasma cortisol) and psychological responses (Subjective Stress Rating Scale) to CPS were monitored. Mucosal RNA was isolated and submitted to microarray analysis followed by differential gene expression and biological pathways identification.
RESULTS: CPS induced a significant autonomic response identified by increased heart rate, blood pressure and plasma cortisol, in association with elevated stress perception in all participants. Interestingly, gene expression studies uncovered differential responses to stress between M and F. Particularly, in the female group, CPS induced circadian rhythm regulation ($P < 0.00001$), along with NK and T cell activation (NFIL3: 1.8; MAL: 1.8 fold change vs basal), and changes in epithelial integrity proteins (KRT13: 1.9 fold change vs basal). In the male group, the stress response was associated with urea cycle and aminoacid metabolism activation ($P < 0.005$), and upregulation of antioxidant genes (SOD1: 1.9 fold change vs basal).
CONCLUSION: Acute experimental stress highlights gender-specific molecular responses involving immune activity and regulation of epithelial integrity in healthy gut, responses that may be linked to female predominance in IBS.
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Disclosure of Interest: None Declared
Keywords: Gender, IBS, stress

P390 MUCOSAL IMMUNE BIOMARKERS IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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INTRODUCTION: At present, a useful biomarker of irritable bowel syndrome (IBS) does not exist. In mechanistic pharmacological studies, immune cells has been proposed as biomarkers both for entry into the study and as an end-point.
AIMS&METHODS: We assessed mucosal biopsies of patients with IBS, ulcerative colitis (UC) and healthy controls (HC) to evaluate if total immune cells, mast cells or immune gene expression may be useful IBS biomarkers. We included in our study a total of 144 patients with IBS, 32 patients with UC, and 68 HC. All subjects underwent colonoscopy and histological examination. Colonic immunocytes were identified with quantitative immunohistochemistry. The expression of toll-like receptor (TLR)-4, pre-haptoglobin-2, nerve growth factor and interferon (INF)-gamma was evaluated in a total of 37 formalin-fixed, paraffin-embedded colonic biopsy samples (10 HC, 20 IBS and 7 CU). Total RNA was extracted, reverse transcribed to cDNA and analyzed using quantitative real-time RT-PCR assays. Sensitivity, specificity, positive and negative predictive value, and diagnostic accuracy (DA) were analyzed.
RESULTS: Total immune cells, mast cells, TLR-4 and INF-gamma expression were significantly increased in patients with IBS compared to HC ($P<0.01$). As expected, the magnitude of this immune activation in IBS was significantly lower than that of UC ($P<0.01$), with the exception of mast cells which were similar in patients with IBS and UC. The best cut-off range between IBS and HC was: 20.2% to 20.3% for total immune cell count (sensitivity: 77.1%; specificity: 87.5%; DA: 80.6%); 4.3% to 4.7% for mast cell count (sensitivity: 93.8%; specificity: 73.5%; DA: 87.3%); 1.063-1.149 2^-DDCt for TLR-4 expression (sensitivity: 80.0%; specificity: 90.0%; DA: 83.3%); and 0.001 to 0.257 2^-DDCt for INF-gamma expression (sensitivity: 85.0%; specificity: 90.0%; DA: 86.7%). The best cut-off range between IBS and UC was: 33.8% to 34.0% for total immune cell count (sensitivity: 87.5%; specificity: 91.7%; DA: 90.0%); 1.536-1.653 2^-DDCt for TLR-4 expression (sensitivity: 85.7%; specificity: 90.0%; DA: 88.9%); and 6.764 to 8.674 2^-DDCt for INF-gamma expression (sensitivity: 100.0%; specificity: 95.0%; DA: 96.3%).
CONCLUSION: Our data suggest that mucosal total immune cells, mast cells and immune gene expression have good sensitivity and specificity in distinguishing patients with IBS not only from HC but also from patients with UC.
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Disclosure of Interest: None Declared
Keywords: Biomarkers, immune activation, Irritable bowel syndrome, MAST CELL, ulcerative colitis

P391 DETERMINANTS OF HEALTH RELATED QUALITY OF LIFE IN IRRITABLE BOWEL SYNDROME PATIENTS

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INTRODUCTION: Irritable bowel syndrome (IBS) is a disorder of the lower gastrointestinal tract, characterized by abdominal pain and discomfort as well as changes in stool frequency and stool consistency. The main psychological characteristics are higher scores on trait neuroticism and trait anxiety. IBS, like other chronic diseases, has a negative impact on the patients' quality of life and affective state.
AIMS&METHODS: The aim of this study was to examine which factors contribute to the patients' health related quality of life (HRQoL). The data was obtained from 31 IBS patients (26 F and 5 M; age range 18 to 69). The patients first completed a set of questionnaires, including Big Five Inventory (BFI), State-Trait Anxiety Inventory (STAI-T), Beck Depression Inventory (BDI) and Short Form-36 Health Survey (SF-36). Following that, the patients filled out a symptom severity scale for 14 days. The symptom severity score was calculated as the average intensity of present symptoms over the period of 14 days. The patients' faecal calprotectin levels were also obtained.
RESULTS: In order to determine which factors contribute to the patients' quality of life, we performed two regression analyses. The dependent variables used were the two composite scores of SF-36 – physical and mental component, while the predictors were neuroticism, anxiety, depression, symptom severity and calprotectin. The results of the analyses showed depression was the only significant predictor of the mental component of HRQoL (β=-,47; p<,05), while the physical component of HRQoL was predicted by anxiety (β=-,49; p<,05), depression (β=-,45; p<,05) and calprotectin (β=-,61; p<,01).
CONCLUSION: We can conclude that higher levels of anxiety and depression are indicative of lower HRQoL in IBS patients. This implies that lowering anxiety and depression through psychological treatment could increase the patients' HRQoL. Also, calprotectin seems to be a good indicator of the physical component of HRQoL, supporting it as an important marker of disease severity in IBS patients.
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Disclosure of Interest: None Declared
Keywords: Fecal calprotectin, IBS, quality of life

P392 THE TRANSCRIPTIONAL REGULATION OF SERT BY EGF VIA EGFR CONTRIBUTES TO THE EFFECTS OF EGF ON THE FORMATION OF VISCERAL HYPERSENSITIVITY

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INTRODUCTION: Serotonin transporter (SERT) in the colon tissues of the patients with diarrhea-predominant irritable bowel syndrome (D-IBS) was down-regulated. The mechanisms underlying are not fully understood. It was reported that epidermal growth factor(EGF) via EGF receptor(EGFR) regulated the expression of SERT in gut.
AIMS&METHODS: The present study was designed to investigate the role of the modulation of SERT gene expression by EGF in visceral hypersensitivity, and to delineate the mechanisms. Rat models of visceral hypersensitivity were established by intra-colonic infusion of acetic acid in 10-day-old Sprague-Dawley rats. Abdominal withdrawal reflex (AWR) and electromyography (EMG) were used for assessing visceral sensitivity. The levels of EGF in plasma and intestinal tissues were measured by enzyme-linked immunosorbent assay (ELISA). The study was performed to examine the regulation of SERT by EGF using rat intestinal epithelial cell -6(IEC-6) cells. EGFR kinase inhibitor PD153035 was used in this study. The expression of SERT was detected by Real-time PCR and western blot. EGFR
involved.
RESULTS: The EGF levels in colon tissue and plasma are significantly decreased and the EGF levels are positive correlated with SERT expression in the model rats with chronic visceral hypersensitivity. The expression of SERT in IEC-6 cells treated with EGF was significantly increased in dose-dependent and time–dependent manner, compared with control. Inhibition of EGFR tyrosine kinase activity by PD153035 blocked the stimulatory effects of EGF on SERT expression. These results suggest EGF via EGFR can up-regulate the SERT expression.
CONCLUSION: These findings suggest that transcriptional regulation of SERT by EGF via EGFR may contribute to the formation of visceral hypersensitivity.
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Disclosure of Interest: None Declared
Keywords: visceral hypersensitivity, epidermal growth factor, Serotonin transporter

P393 A POTENT AND SELECTIVE 5-HT4 RECEPTOR AGONIST, YH12852 EXHIBITS ROBUST IN VIVO EFFICACY FOR STIMULATING GASTROINTESTINAL MOTILITY WITH EFFECTIVE SUPPRESSION OF VISCERAL HYPERSENSITIVITY

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INTRODUCTION: YH12852, a novel 5-hydroxytryptamine 4 (5-HT_4) receptor agonist, is being investigated for the next generation therapeutics of functional gastrointestinal (GI) disorders.
AIMS&METHODS: The pharmacological properties of YH12852 were examined in a variety of *in vitro* and *in vivo* experiments. *In vitro* profile of YH12852 was evaluated with binding affinity, agonistic activity, and selectivity for 5-HT_4 receptor. *Ex vivo* contractile activity was studied in isolated guinea pig colon. *In vivo* GI motility activities were evaluated by measuring fecal pellet output in guinea pigs, colonic motility in dogs, and gastric emptying rate in rats. The antinociceptive property of YH12852 was tested in an acute acetic acid-induced visceral hypersensitivity rat models.
RESULTS: In *in vitro* assays, YH12852 had high affinity (pKi=10.3) and selectivity for human recombinant $5\text{-HT}_{4(a)}$ receptor over other 5-HT family subtypes and other non-related receptors. In addition, YH12852 (pEC_{50}=11.3) showed 3.4 times more potent agonistic activity than tegaserod (pEC_{50}=10.8). YH12852 (pEC_{50}=9.1) had 17 times more potent intrinsic contractile activity than 5-HT (pEC_{50}=7.9) using the isolated guinea pig colon. Moreover, intraluminal administration of YH12852 increased the rate of propulsive motility by 43 ± 14% at 1 nM from the baseline. Oral administration of YH12852 at 0.1-10 mg/kg significantly increased the fecal pellet output (FPO) in guinea pigs. In this test, YH12852 induced 90% increase in FPO at 0.3 mg/kg while prucalopride induced 71% increase in FPO at the maximum response dose, 3 mg/kg. The maximum response of YH12852 was shown at 10 mg/kg where it increased the fecal pellet output (FPO) by 149%. In conscious beagle dogs, intravenous administration of YH12852 at 10 μg/kg increased the colonic motility. In gastric emptying study in rats, YH12852 at 3 mg/kg significantly increased gastric emptying rate which is comparable to mosapride. Following oral administration of YH12852 at 10 mg/kg, visceromotor response was significantly suppressed, inhibiting visceral hyprsensitivity induced by acetic acid in rats.
CONCLUSION: The strong *in vitro* potency and high selectivity for 5-HT_4 receptor of YH12852 were well translated into robust *in vivo* activity. YH12852 significantly increased GI motility and effectively inhibited visceral hypersensitivity in animal models indicating that YH12852 would be the next generation therapeutics to fulfill the unmet needs in patients with IBS-C and other GI motility disorders.
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Disclosure of Interest: None Declared
Keywords: 5-HT4 agonist, animal models, GI motility, IBS-C, Visceral hypersensitivity

P394 MECHANOTRANSDUCTION IN MOUSE VISCERAL AFFERENT FIBRES IS MODULATED BY VOLTAGE-GATED SODIUM CHANNEL SUBTYPE 1.9 (NAV1.9)

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INTRODUCTION: Mechanical stimulation of the bowel either by obstruction or distension is a principle cause of pain in functional and inflammatory bowel conditions, particularly in combination with visceral hypersensitivity. The voltage gated sodium channel subtype 1.9 (Nav1.9) has been implicated in the generation of mechanical hyperalgesia in models of inflammatory pain;

however the role of Nav1.9 in visceral afferent sensitivity to mechanical distension in the gut has not been studied in great detail. Using Nav1.9 -/- mice we show that Nav1.9 has an important role in determining afferent activity to distension *ex vivo*.

AIMS&METHODS: The distal colon and mesentery from C57BL6, Nav1.9 +/+ or Nav1.9 -/- mice were removed from mice euthanized by rising concentration of CO_2, and placed in a recording chamber superfused with carbogenated Krebs buffer at 32-34°C supplemented with nifedipine (10μM), atropine (10μM) and indomethacin (3μM). The lumbar splanchnic nerve bundles were dissected free and nerve activity was recorded using a suction electrode. The tissue was luminally perfused (0.1mL/min) and the afferent response to ramp distensions (0-80mmHg or 0-145mmHg) determined. In separate preparations the afferent response to repeated (10min interval) phasic 80mmHg distensions (60secs duration) were examined. Data is expressed as mean ± S.E.M. and statistically compared using a 2-way ANOVA or t-test, where appropriate.

RESULTS: In Nav1.9 +/+ mice ramp distensions of 80mmHg evoked pressure-dependent increases in colonic afferent firing producing a maximum response of 13.3 ± 3.7Hz (n=6) at 80mmHg which was greatly attenuated in recordings from Nav1.9 -/- mice (1.4 ± 0.6Hz n=6; $P<0.05$). By contrast no significant difference was seen in the maximum response to ramp distensions of 145mmHg between tissue from Nav1.9 +/+ mice (34.6 ± 7.3Hz n=6) compared with Nav1.9 -/- mice (25.4 ± 7.8Hz n=5). Similarly afferent responses to the first 80mmHg phasic distension were comparable in tissue from Nav1.9 +/+ and Nav1.9 -/- (n=6) mice. In Nav1.9 +/+ mice, further phasic distensions (2^{nd} – 3^{rd}), led to a decrease in magnitude of the afferent response, reaching a stable response during the 4^{th} - 6^{th} distensions (6^{th}, 36.3 ± 5.0Hz). The decrease in afferent response to repeat distensions was more rapid in Nav1.9 -/- mice (6^{th}; 8.0 ± 1.3Hz; $P<0.05$) and failed to reach a stable response.

CONCLUSION: Together these data demonstrate that Nav1.9 significantly contributes to colonic afferent mechanosensitivity dependent on the magnitude, frequency and dynamics of the stimulus.

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Keywords: Afferent nerve, mechanotransduction, sodium channel, visceral pain

P395 LIFE STRESS DETERMINES DIFFERENTIAL CELLULAR AND MOLECULAR PROFILES IN HEALTHY GUT IN RESPONSE TO ACUTE STRESS

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INTRODUCTION: The body response against stressful events is an essential physiologic mechanism to ensure energy input and to guarantee survival. Functional gastrointestinal disorders (FGID) are associated with chronic psychosocial stress, although the stress-derived mechanisms leading to gut dysfunction remain unsettled.

AIMS&METHODS: To determine whether grade of life stress *per se* leads to altered systemic and local response to incoming acute experimental stimuli.

METHODS: Twenty four healthy volunteers were recruited and stratified by levels of psychosocial stress (Holmes-Rahe questionnaire) in 2 groups: low stress (LS, n=18; 9 men) and moderate-high stress (MS, n=6; 3 men). In each participant, two consecutive jejunal biopsies were obtained by Watson's capsule: one at baseline (pre-CP) and another 90 min after (post-CP) 15 min of intermittent cold pain stress (CP). Throughout the study, autonomic (blood pressure and heart rate), hormonal (plasma cortisol) and psychological responses (Subjective Stress Rating Scale) to CP were monitored. Mucosal eosinophils, mast cells, and intraepitheal lymphocytes were quantified. RNA from pre-CP and post-CP biopsies was isolated and submitted to microarray analysis followed by differential gene expression and biological pathways identification.

RESULTS: CP induced a strong and reproducible clinical and biological response in all participants, but MS subjects showed higher stress perception (MS: 6.2 (5.0-8.5); LS: 4.4 (2.9-5.5); $P<0.05$) and increased eosinophilic infiltrate (pre-CP: 1.2 vs. post-CP: 3.7 cells/HPF; $P<0.05$), respect to LS participants. Gene expression analysis revealed distinctive biological functions in response to acute stress: LS group displayed altered migration of antigen presenting cells, lipid oxidation and circadian rhythm ($P<0.0001$) associated with CCL20 and HSP71 up-regulation (1.9; 2.2 fold-change; $P<0.0001$); and MS group showed cytokines expression, apoptosis, inflammatory response, and chemotactic activity ($P<0.001$), associated with HSP71 and Aldolase-B up-regulation (1.9; 1.8 fold-change; $P<0.001$) and IL-18 and SLC26A3 down-regulation (-1.7; -1.6 fold-change; $P<0.001$).

CONCLUSION: Life stress acts as a relevant factor determining intestinal responses to acute experimental challenge in healthy subjects. Whether this altered response represents a step of progression between healthy gut and disordered "functional gut" remains to be explored.

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Disclosure of Interest: None Declared

Keywords: Irritable bowel syndrome, stress

P396 ASSOCIATION BETWEEN ABDOMINAL PAIN AND EATING IN PATIENTS WITH IRRITABLE BOWEL SYNDROME. ROLE OF SOMATISATION

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INTRODUCTION: It has been reported that abdominal pain worsens after eating in about half of the patients with irritable bowel syndrome (IBS), but it has not yet been established whether this is due to chance. Somatisation might increase the strength of the association as it enhances the intensity of symptoms after a meal, but an opposite effect might be expected from an unspecific increase in the frequency of reported symptoms.

AIMS&METHODS: To assess the strength of the association between meals and abdominal pain in IBS patients using a validated statistical method, and whether it is influenced by somatisation. Sixty-two IBS patients according to Rome III criteria (age 37±12 years; 61% female) recorded meal times (MTs) and the occurrence and intensity (0-10) of abdominal pain (AP) on a 10-day diary card divided into 30-minute intervals, and completed the IBS Symptom Severity Scale (IBS-SS), the SCL90-R for psychological symptoms and the SF36 for the quality of life. Fisher's exact test was used to calculate the probability (P) that MT and AP were unrelated in a time window of 90 minutes; the symptom-association probability (SAP) was calculated as (1-P) x 100%, and the discordance of the association between AP and MT was calculated using the frequency of false positives (AP+,MT-) - false negatives (AP-,MT+)/$\sqrt{}$(AP+,MT-) + (AP-,MT+). Normalized SCL90-R values were calculated for the somatisation, anxiety and depression scores, with a t score of ≥63 indicating a positive case. The Mann-Whitney U test was used to make the statistical comparisons. The data are given as mean values±SD.

RESULTS: A SAP of ≥95% ($P \leq 0.05$) was observed in 27 patients (44%) and ≥99% ($P \leq 0.01$) in 20 patients (32%). Age, gender, bowel habit, the frequency and intensity of pain, the scores of somatisation and the quality of life were not significantly different between the patients with and without a significant SAP (data not reported). The somatisation score was ≥63 in 30 patients (48%), who were younger (32±9 *vs* 40±12 years; $P=0.006$), more anxious (61±8 *vs* 54±9; $P=0.004$), and had more severe IBS (327±73 *vs* 262±80; $P=0.003$) and a poorer quality of life (physical 41±8 *vs* 46±9, $P=0.016$; mental 35±11 *vs* 47±11, $P=0.0007$). SAP was not significantly different between patients with somatisation scores of ≥63 or <63 (64%±38% *vs* 53% ±39%; $P=0.49$) nor was the discordance of the association (-0.30±4.13 *vs* 0.17±4.35; $P=0.80$).

CONCLUSION: Meals and abdominal pain are significantly associated in more than one-third of patients with IBS. Somatisation significantly influences the severity of IBS and the patients' quality of life, but does not seem to affect the strength of this association.

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Disclosure of Interest: None Declared

Keywords: Irritable bowel syndrome, somatisation

P397 MOLECULAR MIMICRY AND AUTOIMMUNITY TO VINCULIN IN HUMANS: THE MISSING LINK IN THE PATHOPHYSIOLOGY OF IBS

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INTRODUCTION: In a *C. jejuni* rat model of post-infectious IBS, rats develop altered bowel habits, small intestinal bacterial overgrowth (SIBO) and reduction of interstitial cells of Cajal (ICC). After infection with mutant *C. jejuni* lacking cytolethal distending toxin B (CdtB), rat sequelae were mitigated. Later experiments determined that antibodies to CdtB predict SIBO and through molecular mimicry have affinity for ICC and enteric ganglia. In this translational study, we investigate the human antigen to which anti-CdtB binds.

AIMS&METHODS: First, non-IBS human full thickness ileal tissue (from right hemicolectomy) was obtained. Ileal sections were incubated with purified rabbit antibodies to CdtB, washed and incubated with fluorescent secondary antibodies. Colocalization studies were performed with anti-c-kit (specific for ICC), S-100 (specific for neurons) and PGP 9.5 (specific for ganglia). Next, immunoprecipitation was performed by generating a column with anti-CdtB through which a lysate of human enteric neuronal cells (Emory University) was passed. Anti-CdtB adherent protein was eluted and western blots performed with anti-CdtB and the other with anti-CdtB pre-incubated with CdtB protein (blocking peptide). A band was identified at 117kDa, purified and identified by mass spectroscopy as human vinculin. An aliquot of 0.4 ug of commercial vinculin was coated per well in 96 well plates. Anti-CdtB was added to one series of wells, and anti-CdtB mixed with whole CdtB protein (blocking peptide) to another.

RESULTS: Using full-thickness human ileal tissue, anti-CdtB was specific for ICC and ganglia. This was based on colocalization of anti-CdtB with anti-c-kit, PGP 9.5 and S-100 (see figure). Thus anti-CdtB appeared to be interacting with a human protein on ICCs and ganglia. Based on immunoprecipitation, a protein band was identified at 117kDa. Using mass spectroscopy this protein was identified as human vinculin. Subsequently, human vinculin was obtained commercially and by ELISA, anti-CdtB had a high affinity for human vinculin but not the control peptide. Binding to vinculin was blocked by the CdtB peptide.

CONCLUSION: In the pathophysiology of post-infectious IBS, subjects develop antibodies to CdtB which cross react through molecular mimicry to vinculin, a cell membrane cytoskeletal protein important in neural migration and adherence. Given emerging data of reduced vinculin levels in post-infectious rats, molecular

mimicry to vinculin may be important to the cause of SIBO and IBS through effects on ICC and ganglia.
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Disclosure of Interest: None Declared
Keywords: autoimmune disease, IBS

P398 DENDRITIC CELLS IN THE COLON OF RATS WITH VISCERAL HYPERSENSITIVITY EXPRESS HIGH LEVEL OF PROTEIN DISULFIDE ISOMERASE A3

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INTRODUCTION: Although visceral hypersensitivity is a major pathophysiological feature of irritable bowel syndrome (IBS), its molecular mechanisms 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 processe of antigen presentation. Therefore, in the present study, we established a rat 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 IBS model by using colorectal distention and restraint stress, later 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, and DCs were numbered by double labeling immunofluorescent staining of either CD11c (marker of dendritic cells) and PDIA3 .
RESULTS: In comparison to controls, All rats in the IBS 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 ($P<0.05$). The number of CD11c/PDIA3-positive cells in the IBS group was statistically more than in the control group ($P<0.05$).
CONCLUSION: High level of protein disulfide isomerase A3 observed in dendritic cells could enhance the antigen presentation, which may lead to the dendritic cells mediated abnormal immune response, and contribute to the generation of visceral hypersensitivity in IBS rats.
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Disclosure of Interest: None Declared
Keywords: dendritic cell, protein disulfide isomerase A3, visceral hypersensitivity

P399 ANTIBIOTIC-INDUCED INTESTINAL DYSBIOSIS ATTENUATED VISCERAL PAIN-RELATED RESPONSES IN MICE

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INTRODUCTION: Visceral pain and intestinal dysmotility are common symptoms of functional gastrointestinal disorders (FGDs). It has been suggested that dysbiotic states of the gut commensal microbiota (GCM) might contribute to the pathophysiology of FGDs.
AIMS&METHODS: To determine if a dysbiosis of the GCM results in changes in visceral pain-related responses and colonic contractility. CD1 mice were treated with non-absorbable/broad spectrum antibiotics (bacitracin/neomycin, 0.4 mg/mouse/day, 14 days, PO). Visceral pain-related responses were assessed *in vivo* after intraperitoneal acetic acid (0.6%, 10 ml/kg; Writhing test) or intracolonic capsaicin (50 μg/mouse, 0.05 ml). Colonic contractility was assessed *in vitro* (organ bath). Luminal microbiota was characterized using fluorescence *in* situ hybridization. Colonic gene expression of pain-related markers [cannabinoid receptors (CB1/CB2), μ-opioid receptor (MOR), vanilloid receptors (TRPV1/3), tryptophan hydroxylase (TPH1/2) and serotonin transporter (SERT)] and anti- (IL10) and pro-inflammatory cytokines (IL6, IL12p40 and TNFα) were assessed by RT-qPCR.
RESULTS: Antibiotics reduced by 2.5-fold total bacterial counts ($x10^8$ cells/ml; vehicle: 434±28; antibiotic: 174±11; $P<0.05$, n=6 each) and induced a specific dysbiosis, lowering Clostridia and increasing *Lactobacillus* spp./Enterobacteria counts. Abdominal contractions in response to acetic acid were reduced by 33% in antibiotic-treated mice (contractions/30 min: 40.9±7.6, $P<0.001$ vs. vehicle: 61.4±4.0; n=6 each). Similarly, capsaicin-induced pain-related behaviors were reduced by 48% in antibiotic-treated mice (behaviors/30 min: 12.9±4.2, $P<0.05$ vs. vehicle: 25.1±2.3; n=6 each). Spontaneous colonic contractility was similar in both groups. However, contractile responses to carbachol were higher in antibiotic-treated animals (2-fold reduction in the EC_{50}: $5.2x10^{-7}$ M vs. vehicle: $1.0x10^{-6}$ M, n=6 each). Response to the NO-synthase inhibitor L-NNA were higher in antibiotic-treated mice (56±8 g vs. vehicle: 28±17 g; P=0.07, n=6 each). In dysbiotic mice, expression of CB2 was up-regulated, while CB1 and MOR were down-regulated. Neither histological nor molecular signs of colitis were observed.
CONCLUSION: Intestinal dysbiosis was associated to a reduction in visceral pain-related responses and a selective modulation of pain-related markers. Altered colonic contractility to cholinergic stimulation or NO inhibition was also noted. These data indicate that GCM is able to modulate gut sensory and motor systems, leading to functional changes. Similar mechanisms might explain the beneficial effects of antibiotics in the treatment of FGDs.
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Disclosure of Interest: None Declared
Keywords: endocannabinoid system, microbiota, motility, visceral pain

P400 SPINAL CORD STIMULATION IN THE IRRITABLE BOWEL SYNDROME – A RANDOMIZED CROSS-OVER TRIAL

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INTRODUCTION: Irritable bowel syndrome (IBS) is a common disorder of multifactorial origin. Presently existing therapies are often ineffective. Spinal cord stimulation (SCS) has long been used for treatment of certain forms of chronic pain. In animal studies, SCS has been shown to reduce the reaction to colonic balloon dilatation, known to be increased also in IBS patients. Beneficial results of SCS in a single IBS patient have been reported as well as for other forms of abdominal pain.
AIMS&METHODS: To elucidate the potential for SCS as a treatment for IBS a limited clinical trial has been performed. Ten patients with IBS, mean age 39 (26-56) were recruited. A SCS system with a 4-polar electrode at the T5-8 level was implanted. In a randomized, cross-over study, stimulation was tested and compared to a period without stimulation, with an ensuing stimulation period, twice as long. At the end of the study patients could choose to retain their stimulating system or have it removed. Patients recorded average pain level, pain attacks and diarrheas as well as global quality of life evaluations in a diary.
RESULTS: A total of 18 IBS patients were selected by the gastroenterologist according to the Rome II criteria and referred to the neurosurgical team. Ten patients were successfully implanted, 9 of which completed the whole trial period. Implantation was made percutaneously at T11/12 and advanced to a position yielding adequate paresthesias. During the stimulation periods median pain scores were significantly lower as compared to non-stimulating periods (6.3±1.1 vs 4.7±1.3, $p<0.05$). The number of pain attacks was also reduced (4.5±1.5 vs 2.5±1.3).
Individual patients also reported diminished number of diarrheas. After study termination six patients chose to retain their stimulating system.
CONCLUSION: The outcome of the present trial suggests that SCS may be a useful treatment IBS as a majority of patients submitted to neurostimulation responded favorable. To further evaluate the clinical usefulness of SCS on this indication larger, multi-centre, studies are warranted.
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Disclosure of Interest: None Declared
Keywords: abdominal pain, diarrhea, irritable bowel syndrome, Spinal cord stimulation

P401 ALTERED RECTAL STRUCTURE AND SENSITIVITY IN THE GENESIS OF FAECAL INCONTINENCE AFTER DIFFERENT ANORECTAL SURGERY PROCEDURES

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INTRODUCTION: To investigate the anal sphincter and rectal factors that determines faecal incontinence after anorectal surgery (FIAS).
AIMS&METHODS: Twenty-seven patients with faecal incontinence after different anorectal surgery procedures were studied [rectosigmoidoscopy, manometry and barostat (sensitivity, tone, compliance and capacity) and compared with asymptomatic healthy subjects (HS). Time since surgery was at least two years. All patients suffered from 10±15 incontinence episodes per week. The postoperative continence score was 13.6±2 (St Mark's faecal incontinence grading system).
RESULTS: (Table: All data represent the mean (95% CI). *$p<0.05$ Vs. HS) Rectal structure: Vs. HS, rectal tone was increased in patients who had undergone sphincterotomy or fistulotomy (p=0.005). Rectal compliance decreased after fistulotomy (p=0.021) and rectal capacity lessened after rectal prolapsed procedures (p=0.037). Rectal sensitivity: FIAS patients at similar pressures as HS reported the noxious stimulus of pain. In sphincterotomy patients, the thresholds for non-noxious stimuli of the sensations of gas (p=0.016) and urge to-defecate (p=0.043) were reported at higher pressures compared with HS. Internal anal sphincter function: Only patients with sphincterotomy showed greater anal resting and squeeze pressures (p=0.014) and a higher amplitude of relaxation in their rectoanal Inhibitory reflex (p=0.0006) than HS.

	Sphincterotomy (n=8)	Fistulotomy (n=8)	Rectal prolapse (n=6)	Healthy subjects (n=10)
Tone (ml)	50.7 (16-85)*	37.8 (16-59.5)*	53 (15.8-90.5)	103.5 (71.8-135)
Compliance (v/p)	6 (1.8-10.7)	4.7 (2-7.5)*	6.7 (1.9-11)	11.7 (7-16)
Rectal capacity (ml)	342.6 (304-380.7)	347.5 (306-388)	207 (145.6-268.9)*	302.8 (251.8-353.9)
First sensation (mmHg)	18 (15.8-20.9)	15 (13-17.6)	15 (11.7-19)	14 (10.9-17)
Gas sensation (mmHg)	24.9 (21.7-28)*	21.6 (19-24)	21 (14-28)	17.9 (14-21.6)
Urge defecate (mmHg)	31 (24-38)*	28.7 (23-34)	24 (12-35.9)	22 (17.9-26.9)
Pain sensation (mmHg)	35.8 (32-39)	39 (36-42)	26 (15.7-36.9)	35.9 (30-41)
Anal resting pressure (mmHg)	62 (48.8-75)*	43 (26.5-61)	22 (7-38)	34 (21-48)
Anal squeeze pressure (mmHg)	113 (67.5-158)*	69 (19.8-118.6)	66 (24.6-108)	43 (28.4-57.9)

CONCLUSION: Most FIAS patients preserve internal anal sphincter function but present with impaired rectal tone, compliance, capacity and rectal hyposensitivity for non-noxious stimuli. It seems that an impaired afferent nerve pathway and abnormal rectal structure and function are involved in the genesis of FIAS. The rectum seems to be more involved than the internal anal sphincter in the genesis of FIAS; therefore, surgeons should preserve the rectal anatomy and neural networks as much as possible.

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Disclosure of Interest: None Declared

Keywords: anorectal surgery, barostat, Faecal incontinence, manometry, visceral sensitivity

P402 COLONOSCOPIC FEATURE OF 293 IRRITABLE BOWEL SYNDROME (IBS) PATIENTS IN JAPAN

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INTRODUCTION: As there is no pathognomonic diagnostic measurement for IBS, the diagnosis relies on the clinical symptoms, and is only made after exclusion of organic diseases.

We have reported a non-sedative painless colonoscopy, "WATER NAVIGATION COLONOSCOPY (Mizukami T. Dig Endosc 2007 19: 43-48.)". When colonoscopies are done only with spasmolytic, persistent colonic movements are observed in approximately 10% of the patients, and most of them have IBS symptom (Mizukami T. Gastroenterology 2010; 138: S-233.).

On the other hand, there are some IBS patients without persistent colon movement and most of them have abnormal colon morphology, these are difficult cases for cecal intubation.

AIMS&METHODS: The present study was designed to evaluate colon motility and morphology of IBS by colonoscopy, and assess its pathophysiology. 293 IBS patients and 50 asymptomatic subjects were recruited. Diagnosis of IBS was based on ROME III. Colonoscopy was performed according to "WATER NAVIGATION COLONOSCOPY" only with 20 mg scopolamine butylbromide IM and cecal intubation time was recorded. Duration time and the patterns of colon movement persisting after spasmolytic IM were recorded.

RESULTS: Persistent colon movement after scopolamine butylbromide IM was significantly frequently observed in IBS (24.9% vs 2.0%, $p<0.001$). It was significantly frequently observed in IBS-D more than IBS-C and IBS-M group (IBS-C 23.1% vs IBS-D 52% vs IBS-M 6.2%, $p<0.001$). Peristalsis was frequently observed in IBS-D, which causes incontinent passing of gas during colonoscopy and probably causes diarrhea. Segmental movement was observed in IBS-C, which makes it difficult to intubate colonoscope and probably causes constipation. IBS patients with persistent colon motility had experienced stress related to the symptoms.

Abnormal colon morphology such as mesocolon descendens and sigmoidcolon malrotation was frequently observed in IBS group (82.5% vs 24.0%, $p<0.001$). This was more frequently observed in IBS- M and IBS- C more than IBS- D (IBS-C 81.8% vs IBS-D 61.3% vs IBS-M 100%, $p<0.001$). IBS patients only with persistent abnormal colon morphology had not experienced stress related to the symptoms.

Cecal intubation time was significantly longer in IBS group (12.1+6.9min vs 4.6+1.9min, $p<0.001$). There were no significant difference in cecal intubation time among IBS subgroups (IBS-C 12.2+7.2 vs IBS-D 9.5+5.4 vs IBS-M 11.7+5.4, ns).

CONCLUSION: Non-sedative colonoscopy reveals that there are 2 types of IBS "Abnormal colon motility type" and "Abnormal colon morphology type". "Abnormal colon morphology type" is very common in Japan, and is very difficult for cecal intubation. Classification based on non-sedative colonoscopy will improve understanding of the pathophysiology in IBS.

Disclosure of Interest: None Declared

Keywords: abnormal colon morphology, abnormal colon motility, colonoscopy, IBS, water immersion method

P403 ADVANCED AGE LEADS TO REDUCED SENSITIVITY OF MOUSE INTESTINAL AFFERENT NEURONS TO BRADYKININ

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INTRODUCTION: The ability to sense visceral pain or respond to acute GI inflammation during peritonitis is often impaired in the elderly, leading to difficulties in diagnosis (*Hall 2002, Am J Physiol 283 G827-32*).

AIMS&METHODS: To explore the possibility that the sensitivities of visceral nociceptors and myenteric neurons to inflammatory stimuli are reduced with age we examined the effects of noxious inflammatory mediators on intestinal mesenteric nerves and neuromuscular functions in adult and aged C57B6 mice. (1) Nerve recordings: Intestine with attached mesentery were removed, cannulated and perfused externally (7ml/min) and internally (0.1ml/min) with carbogenated Krebs' supplemented with nifedipine, atropine (10μM each) and indomethacin (3μM). A mesenteric nerve bundle was isolated and on-going nerve discharge recorded using suction electrodes. Changes in nerve discharge were determined following bath perfusion with 20ml bradykinin (BK; 1μM) or adenosine (1mM); a maximum of 2 stimuli separated by at least 60 min were studied in each preparation and peak changes in nerve discharge from baseline determined. (2) Neuromuscular experiments: Mucosa-intact loops, cut parallel to the circular muscle of the colon from 3 month mice, were suspended in Krebs solution in tissue baths for electrical field stimulation (EFS; 5 Hz, 0.5ms, 50V for 30s every 120s) and isometric recording of muscle tension. Data are expressed as means ± sem and compared between ages using a one way ANOVA vs. the 3 month group.

RESULTS: Robust afferent responses were observed with each stimulus in tissue from 3 month mice (BK: 54.6±8.3 Hz; Adenosine: 14.3±3.5 Hz, n=4 each). In aged mice the response to BK was greatly reduced (18.9±5.9 and 18.3±2.2 Hz, respectively, for the 18 and 24 month mice; $P<0.01$ each; n=5 and 10). In contrast the response to adenosine remained unchanged (9.9±2.7 and 18.0±4.5 Hz, respectively; n=5 and 6). In the muscle loops, EFS evoked relaxations followed by after-contractions (abolished by TTX 1μM; n=5); the relaxations and after-contraction were separately abolished by L-NAME 300μM and atropine 1μM (n=3, 4). BK 1μM reduced the amplitude of the after-contractions by 28.7±8.0% and decreased baseline muscle tension (by 2.8±1.0% of the maximum contraction to carbachol; $P<0.05$ each; one sample t test; n=5).

CONCLUSION: Afferent responses to the algogenic inflammatory mediator BK were impaired in aged mice. By contrast the response to adenosine was unchanged, suggesting some specificity in age-related changes of afferent sensitivity to inflammatory mediators. Studies into age-related changes in neuromuscular functions of BK are on-going.

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Disclosure of Interest: None Declared

Keywords: Afferent nerve, Aging, Bradykinin, Enteric nervous system, Intestine, Mouse

P404 INCIDENCE OF NEW ORGANIC GASTROINTESTINAL DISEASE IN IRRITABLE BOWEL SYNDROME (IBS) REMAINS HIGH EVEN 10 YEARS FOLLOWING IBS DIAGNOSIS

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INTRODUCTION: Symptoms of Irritable bowel syndrome (IBS) are common and are also seen in coeliac disease, colorectal cancer (CRC) and inflammatory bowel disease (IBD). Clinicians are often keen to exclude these diseases before diagnosing IBS. In those diagnosed with IBS there is little evidence about rates of these other diseases, changes over time, or if years after a diagnosis of IBS they still require consideration.

AIMS&METHODS: A cohort of 189826 incident IBS patients was constructed from the Clinical Practice Research Dataset. All prevalent coeliac disease (398), CRC (142) and IBD (1536) was excluded. A Poisson model determined incidence of each disease at different intervals following IBS diagnosis, stratified by age at IBS diagnosis. Rate ratios (IRR) were derived, with 5 years after IBS diagnosis as baseline.

RESULTS: Initially high rates of IBD and coeliac disease fall over the first 5 years then plateaux. For IBD in particular, they remain higher than might be expected in the general population, especially in the young. Rates of CRC in patients diagnosed with IBS are high in all ages groups at all time periods. Rates of new diagnosis significantly increase after 5 years following IBS diagnosis.

CONCLUSION: It is currently unclear if the rates seen are due to initial misdiagnosis or to associations between IBS and the other conditions, nor whether increasing CRC rates after 5 years can be fully explained by advancing age. It is important to remain mindful of these organic conditions when treating patients with existing IBS diagnoses.

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Keywords: Coeliac disease, Colorectal cancer, epidemiology, IBD, IBS, misdiagnosis

Table: P404

Age at diagnosis of IBS		Overall rate in IBS patients/10000 person years	IRR: Within 6 months of IBS diagnosis	IRR: 6 months to 1 year after IBS diagnosis	IRR: 1 to 5 years after IBS diagnosis (baseline)	IRR: 5 to 10 years after IBS diagnosis	IRR: 10 to 15 years after IBS diagnosis
18-29 *(n=45679)*	**Coeliac** (n=77)	**3.78** *(3.08-4.63)*	2.41 (1.14-5.10)	1.20 (0.66-2.18)	1.00	0.50 (0.15-1.72)	0.50 (0.07-3.92)
	CRC (n=22)	**0.89** *(0.59-1.35)*	5.37 (1.28-22.46)	0.58 (0.11-2.88)	1.00	6.22 (1.61-24.07)	5.53 (0.34-11.79)
	IBD (n=526)	**21.61** *(19.84-23.53)*	3.96 (2.85-5.49)	1.83 (1.39-2.42)	1.00	1.02 (0.77-1.85)	0.90 (0.41-1.96))
30-49 *(n=82848)*	**Coeliac** (n=241)	**4.64** *(4.11-5.23)*	1.64 (1.00-2.67)	1.21 (0.88-1.66)	1.00	0.54 (0.31-0.98)	0.96 (0.46-2.01)
	CRC (n=309)	**5.33** *(4.77-5.96)*	1.19 (0.73-1.95)	0.87 (0.64-1.18)	1.00	1.40 (0.97-2.03)	3.83 (1.46-3.18)
	IBD (n=791)	**13.87** *(12.93-14.87)*	3.81 (2.97-1.93)	1.57 (1.28-1.93)	1.00	0.75 (0.53-1.06)	0.86 (0.51-1.45)
50-75 *(n=61299)*	**Coeliac** (n=172)	**4.39** *(3.80-5.07)*	2.33 (1.37-3.95)	1.21 (0.82-1.79)	1.00	1.2 (0.70-2.09)	0.9 (0.33-2.55)
	CRC (n=1401)	**33.33** *(31.63-35.12)*	1.83 (1.49-2.24)	1.02 (0.89-1.18)	1.00	1.55 (1.29-1.85)	2.94 (2.36-2.79)
	IBD (n=590)	**14.21** *(13.11-15.40)*	1.89 (1.37-2.61)	1.32 (1.06-1.64)	1.00	0.88 (0.62-1.25)	0.88 (0.49-1.60)

P405 A PROSPECTIVE SURVEY OF FUNCTIONAL GASTROINTESTINAL DISORDERS IN U.K. GASTROENTEROLOGY CLINICS: WORKLOAD AND ITS MANAGEMENT

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INTRODUCTION: Functional gastrointestinal disorders (FGIDs) are extremely common constituting up to 5% of all and 50% of GI primary care patient visits, and up to 50% of secondary care visits[1]. Diagnosis however, can sometimes be challenging leading to testing, despite well established guidelines encouraging a positive diagnosis based on the Rome III criteria in the absence of alarm features alone[2].

AIMS&METHODS: To determine the work load that FGIDs present to UK secondary care, reasons for referral from primary care, and whether clinicians embrace a positive diagnosis rather than one by exclusion.

Prospective data was collected from 45 general gastroenterology out-patient clinics in 28 hospitals between 2010 and 2011. For every new and follow-up patient a questionnaire was completed by the clinician or trainee gastroenterologist.

RESULTS: Of a total of 439 patients seen, 81(18.5%) were diagnosed with a FGID of which 20%(16/81) were male and 80%(65/81) female. 62%(50/81) had symptoms consistent with a FGID for less than 2 years. 50%(40/81) had received a diagnosis of FGID by the primary care physician at the time of referral, with 9% (7/81) been referred because of associated alarm symptoms and 41%(33/81) because of uncontrolled symptoms. Despite hospital clinicians reporting reasonable confidence in their FGID diagnosis in 86%(70/81) patients, 73%(59/81) of patients were still scheduled for endoscopy and 43%(35/81) for ultrasound or CT scanning. Only 37%(30/81) of hospital clinicians used formal diagnostic criteria (eg Manning, Rome etc) with even less using the current Rome III criteria (6%(5/81)).

CONCLUSION: Secondary care FGID workload was lower than expected maybe because of increased awareness (NICE and BSG guidelines)[3] and confidence in diagnosing FGIDs in primary care. Positive FGID diagnosis however remains low with little use, in particular, of the Rome III criteria. Thus there is a need for better implementation of these and forthcoming guidelines to improve the cost-effectiveness of care.

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Keywords: functional gastrointestinal disorders, gastroenterology outpatient, IBS

P406 PREDICTIVE FACTORS FOR A CLINICAL DIAGNOSIS OF IRRITABLE BOWEL SYNDROME IN A COHORT OF 440,822 YOUNG ADULTS.

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INTRODUCTION: The prevalence of irritable bowel syndrome (IBS) in the community has been reported in numerous cross-sectional surveys. However, less is known about the incidence and predictive factors for the clinical diagnosis of IBS.

AIMS&METHODS: We examined the association of socioeconomic, anthropometric and occupational factors with the incidence of IBS in a cohort of 440,822 young Israeli adults aged 18-39 who served in active military service during the years 2005-2011.

RESULTS: During follow-up of 1,925,003 person years, IBS was diagnosed de novo in 926 and worsened in 50, giving an incidence rate of 0.2% (221:100,000) for the diagnosis or worsening of IBS. On multivariable Cox analysis, higher socioeconomic state (HR 1.629 95%CI 1.328-1.999, $p<0.0001$), Israeli birth (HR 1.362, 95%CI 1.084-1.712, p=0.008), Jewish ethnicity (HR = 2.089, 95%CI 1.344-3.248, p=0.001), education of more than 11 years (HR 1.674, 95%CI 1.019-2.751,p=0.042) and a non-combative military position (HR 1.196, 95%CI 1.024-1.397, p=0.024) were found to be risk factors for the diagnosis or for the worsening of IBS. Overweight (HR 0. 0.744, 95%CI 0.589-0.941, p=0.014), obesity (HR 0.698, 95% CI 0.510-0.95, p=0.025), living in a rural settlement (HR 0.705, 95%CI 0.561-0.886, p=0.003), and Asian (HR 0.739, 95%CI 0.617-0.884, p=0.001,) or African origin (HR 0.702, 95%CI 0585-0.842, $p<0.001$) were found to be protective for the diagnosis or the worsening of IBS.

CONCLUSION: The incidence of IBS in our cohort was similar to that reported in the western countries. Specific socioeconomic, anthropometric and occupational factors were associated with the occurrence of IBS.

Disclosure of Interest: None Declared

Keywords: epidemiology, ibs, incidence, risk factors

P407 DIENTAMOEBA FRAGILIS AND BLASTOCYSTIS: TWO PARASITES THE IRRITABLE BOWEL MIGHT BE MISSING. A POPULATION-BASED CASE-CONTROL STUDY OF SUBJECTS WITH AND WITHOUT GASTROINTESTINAL (GI) SYMPTOMS

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INTRODUCTION: Several studies have demonstrated that the parasites *D. fragilis* and *Blastocystis* are frequently found in patients with irritable bowel syndrome (IBS) and suggest that these may be involved in the pathogenesis of IBS. However, previous studies have all lacked a well-defined asymptomatic control group. We hypothesised that intestinal parasites may be associated with symptoms of IBS.

AIMS&METHODS: In 2010, members of a web-panel (n=19.567), representative of the Danish population aged 18-49 years (females 50%), were invited by e-mail to fill out a questionnaire. 6.112 responded to screening questions on age, sex and GI symptoms. Those reporting of GI symptoms were linked to a questionnaire based on the Rome III criteria for IBS. Stool samples were requested from 200 subjects with IBS symptoms and 300 asymptomatic controls. Two consecutive stool samples were tested for parasites (microscopy, culture for *Blastocystis* and real-time PCR for *D. fragilis, Cryptosporidium spp., Entamoeba histolytica and dispar* and *G. intestinalis*). The questionnaire and stool sampling was repeated after 1 year in responders from the first survey.

RESULTS: In 2010, stool samples were analyzed from 328 subjects (124 had IBS symptoms; 204 controls). Intestinal parasites were found in 44.5% (n=146) of all. Subjects with IBS were significantly *less* likely to harbor parasites than the asymptomatic background population (35.5% *vs.* 50%, p=0.01). Harboring parasites was not associated with gender. *D. fragilis* was found in 30.1% of all subjects; significantly more prevalent in controls compared to IBS subjects (34.8% *vs.* 23.4%, p=0.03). *Blastocystis* was found in 18.9% of all subjects and more often in controls (22% *vs.* 14.5%, p=0.09).

In 2011, follow-up was completed in 275/328 (83.8%) subjects, who gave stool samples in 2010 (106 IBS subjects and 169 controls). In both IBS subjects and controls there were no significant differences in development of GI symptoms over 1 year between those with and without parasites ($p>0.1$), nor when analyzed for *D. fragilis* or *Blastocystis* separately.

CONCLUSION: In an asymptomatic adult background population 50% harbor intestinal parasites, this is significantly more compared to subjects with IBS symptoms. Harboring intestinal parasites does not influence the development or disappearance of IBS symptoms over 1 year.

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Disclosure of Interest: None Declared

Keywords: Blastocystis, Dientamoeba fragilis, Irritable bowel syndrome, Microbiota, Parasites

P408 EPIDEMIOLOGY OF IRRITABLE BOWEL SYNDROME (IBS) A POPULATION- BASED SURVEY IN DENMARK.

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INTRODUCTION: IBS is a common gastrointestinal GI disorder, varying in prevalence between countries and according to diagnostic criteria. Patients with IBS pose a significant health burden partly because IBS is often considered a diagnosis of exclusion.
AIMS&METHODS: We aimed to investigate the epidemiology of IBS in the Danish adult population according to Rome III criteria. An internet-based survey was conducted in 2010 with a 1 year follow-up in 2011. In 2010, members of a web-panel (n=19.567) representative of the Danish adult population aged 18-49 years (mean age 35,3 yr, females 49,5%) were invited by email to fill out a questionnaire. Responders (n=7.827, 40%) were linked to screening questions on sex, age and GI symptoms. 6.112 subjects completed the screening, and those reporting of GI symptoms within the past 3 months (n=2.928, 48%) were linked to the Rome III questionnaire for IBS. Responders were further asked about healthcare seeking and details of diagnosis likely to explain their symptoms. In 2011, 6.112 initial responders were invited to fill out the same questionnaire. A total of 3.784 (62%) (mean age 36,8 yr, females 60%) completed screening. 2.026 reported GI symptoms within the past 3 months and were linked to the Rome III questionnaire.
RESULTS: In 2010, a total 979/6.112 (16%; 95% CI: 15.1-16.9%) had symptoms compatible with IBS and no organic diagnosis (72% women, mean age 34.9 yr). The prevalence of IBS in 2011 was 672/3.784 (17.6%).
The incidence of IBS was 9% (95 % CI: 8.1-9.9%) (339/3.784) of these 128 were asymptomatic in 2010 and 211 had GI symptoms not fulfilling criteria for IBS (non-IBS) in 2010.
Table 1 shows transition in symptom-status from 2010 to 2011, n (%).

Table 1	IBS	Asymptomatic	Non-IBS	Missing
IBS (n=979)	319 (32,6)	114 (11,6)	198 (20,2)	348 (35,5)
Aymptomatic (n=3184)	128 (4)	1255 (39,4)	558 (17,5)	1243 (39)
Non-IBS (n=1800)	211 (11,7)	364 (20,2)	533 (30,7)	692 (38,4)

In 2010, 18.4% (180/979) had consulted a doctor for their symptoms within the past 3 months but only 7.9% (77/979) were diagnosed with IBS. Of the incident IBS-cases, 14.7% (50/339) had consulted a doctor within the past three months for their symptoms and 4.4% (15/339) had the diagnosis.
CONCLUSION: IBS defined by the Rome III criteria is very prevalent in the Danish adult population and furthermore there is a high incidence of 9%. The high prevalence and high consultation-rate emphasizes that IBS is associated with significant healthcare cost. At the 1 year follow up most IBS subjects continuously reported of GI symptoms with a minority becoming asymptomatic.
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Disclosure of Interest: None Declared
Keywords: epidemiology, HEALTH CARE SEEKING, Irritable bowel syndrome

P409 FREQUENCY AND EPIDEMIOLOGICAL PROFILE OF FUNCTIONAL BOWEL DISORDERS: AMONG 4850 ILEOCOLONOSCOPY

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INTRODUCTION: Clinical manifestations of functional bowel disorders (FBD) are not specific. Diagnosis is assessed after elimination of organic causes by ileocolonoscopy.
AIMS&METHODS: The aim is to study the frequency and the epidemiological characteristics of these disorders in a Hepato-gastroenterology Unit in Morocco. Patients were selected from subjects with present or past symptoms of FBD (abdominal pain, transit disorders and abdominal bloating) who underwent ileocolonoscopy in our Unit during 4 years. Patients with alarm signs (rectal bleeding, melena, anemia, and weight loss) or with incomplete ileocolonoscopy were excluded. Therefore, the diagnosis of FBD is based on criteria of Rome III (characteristic symptoms for at least 12 weeks during the last 12 months) and in the absence of endoscopic or biochemical abnormalities.
RESULTS: Out of 4850 ileocolonoscopies performed during this period, 1218 (25%) are indicated for symptoms of FBD without alarm signs. Mean age is 47 years (16-89 years) with a female predominance (67%). Frequency of symptoms is as follows: abdominal pain in 64.3% of cases, chronic diarrhea in 33%, chronic constipation in 30.8%, alternating diarrhea-constipation in 18% and abdominal bloating in 10.7%. 611 patients (50.1%) have a normal ileocolonoscopy while it is abnormal in 607 patients (49.9%) of cases. The endoscopic lesions are colonic polyps in 47 %, diverticula in 19 %, congestive or ulcerated aspect of ileal and/or colonic mucosa in 18.8% related to Inflammatory Bowel Disease (IBD), colorectal tumor in 7%, colonic lipoma in 4.7% and melanosis coli in 3.5%.
CONCLUSION: Ileocolonoscopy is mandatory to exclude organic causes of functional bowel disorders. Indeed, half of our patients with these symptoms have organic lesion dominated by colonic polyps, diverticula and IBD.
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Disclosure of Interest: None Declared
Keywords: functional bowel disorders, ileocolonoscopy

P410 PATIENTS' EXPERIENCE OF LIVING WITH IRRITABLE BOWEL SYNDROME (IBS) FROM A GENDER PERSPECTIVE- AN INTERVIEW STUDY

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INTRODUCTION: There is limited knowledge of how patients experience living with IBS, particularly from the male perspective. In general, a sex rather than a gender perspective has been used in research on men, women and IBS. Such a perspective refers to the biological maleness or femaleness of an individual as opposed to a gender perspective that investigates cultural and social constructs associated with biological sex. Such cultural constructs are likely to influence experience of ill-health so to truly understand patient experience of IBS means being sensitive to gender issues.
AIMS&METHODS: Aim: The aim of the study was to explore the impact of IBS on daily life from a gender perspective.
Methods: A qualitative, hermeneutic method was applied (Gadamer 1989). Interviews were conducted with 19 (10 men) patients in 2011. Interviews were analysed within a constructionist gender framework based on the work of Butler (2006).
RESULTS: The main theme to emerge from the interviews was: *A normative framework of femaleness and maleness leads to suffering for persons with IBS*. This consists of three interwoven themes: *Being forced to abandon gender illusions; Being forced to transcend taboos and Reinforced suffering in healthcare encounters*. Both men and women suffer from that IBS is invisible to others and how this negatively affects that amount of support one receives. They also feel that the unpredictability of symptoms restricts life. Men demonstrated masculinity in their narratives by stressing the importance of being solid family providers and felt that IBS made them feel weak and not in control. Women demonstrated femininity through speaking of their nurturing and relational responsibilities and also stated that IBS severely impaired their performance at work.
CONCLUSION: The experience of living with IBS differs between men and women due to differing societal expectations, their life situation and the everyday construction of gender identities. Gender stereotyping by healthcare professionals perpetuates rather than alleviates the suffering experienced by men and women with IBS. In healthcare encounters, women risk being trivialised and men risk being overlooked due to the 'female health concern' label applied to IBS.
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Disclosure of Interest: None Declared
Keywords: Gender, Irritable bowel syndrome, patient beliefs, patient's perception

P411 IS LYMPHOCYTIC DUODENOSIS A MARKER FOR IRRITABLE BOWEL SYNDROME?

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INTRODUCTION: Lymphocytic duodenosis (LD) is defined by normal villous architecture and intraepithelial lymphocytes (IELs) >25 per 100 enterocytes. Such patients should not be diagnosed with coeliac disease (CD), solely by histology, as recent studies have suggested other associations with LD. Despite a paucity of data, previous investigators have suggested that LD may also be associated with irritable bowel syndrome (IBS).
AIMS&METHODS: We aimed to prospectively assess the associations between LD and IBS.
Two hundred patients with LD were investigated for associated LD conditions, by means of revisiting the patient's history and recent investigations including the initial coeliac serology, followed by a combination of gluten challenge, HLA typing, repeat duodenal biopsies, and exclusion of infection/inflammatory bowel disease.
A diagnosis of CD was based on the persistence or progression of LD on a gluten-containing diet, the presence of HLA DQ2 or DQ8, and a clinical response to a gluten free diet.
In the absence of an alternative cause, a diagnosis of IBS was made on the presence of the ROME III criteria.
RESULTS: 150 female, 50 male, mean age 49, SD 16, age range 17-83
An identifiable association was found in 70% of patients with CD (20%), NSAIDs (17%) and H,pylori (16%) accounting for the majority. Other causes included gastrointestinal infections (7%), autoimmune disorders (6%), inflammatory bowel disease (2%), TB or HIV (1.5%), and IgA deficiency (1%).
In 60 cases (30%) no cause was found, although reassuringly two-thirds normalised their histology. In just over half of those without an identifiable cause, symptoms were consistent with IBS (35/60). IBS, therefore, accounted for 17% of all LD cases.
Whereas all patients with CD were HLA positive, only 55% of those with alternative causes or IBS were HLA positive ($p < 0.0001$).
CONCLUSION: 17% of LD is associated with the Rome III criteria for IBS. LD may, therefore, be a disease marker for IBS and a reflection of low grade inflammatory response although no clues to the triggering mechanism were elucidated.

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Disclosure of Interest: None Declared
Keywords: Irritable bowel syndrome, Lymphocytic duodenosis

P412 GASTROINTESTINAL MANIFESTATIONS OF EHLERS-DANLOS SYNDROMES: RESULTS OF A NATIONAL COHORT STUDY ON 134 PATIENTS

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INTRODUCTION: Ehlers-Danlos syndromes (EDS) are a heterogeneous group of connective tissue disorders. Gastrointestinal manifestations in EDS have been described but their frequency, typology and impact are poorly known.
AIMS&METHODS: We aimed to assess digestive features in a national cohort of EDS patients. A questionnaire has been sent to 212 EDS patients through the French patient support group, all of which had been formally diagnosed according to the Villefranche criteria. The questionnaire included questions about digestive symptoms, the GIQLI (Gastrointestinal Quality of Life Index), KESS scoring system and the Rome III criteria.
RESULTS: Overall, 135 patients (64% response rate) have sent the questionnaire and 134 were analyzable (123 women; 91%). Mean age and Body Mass Index were respectively 35±14.7 and 24.3±6.1 kg/m^2. The most common subtype was hypermobility form (n=108; 80.6%). GIQLI and KESS median values were respectively 63.5 (27-117) and 19 [13.5-22] and 84% of patients had functional bowel disorders (FBD) according to the Rome III criteria. An irritable bowel syndrome according to the same criteria was observed in 64 patients (48%) and 48 patients (36%) reported functional constipation. A gastro-esophageal reflux disease (GERD) was reported in 90 patients (68.7%), significantly associated with a poorer GIQLI (60.5±16.8 *versus* 75.9±20.3; $p<0.0001$). There was a significant correlation between FBD and GERD.
CONCLUSION: Natural frequency of gastrointestinal manifestations in EDS seems higher than previously assessed. FBD and GERD are very common in our study population, the largest ever published until now. Their impact is herein shown to be important. A systematic clinical assessment of digestive features should be recommended in EDS.
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Disclosure of Interest: None Declared
Keywords: Ehlers-Danlos syndromes, functional bowel disorders, gastro-esophageal reflux disease

P413 A POSSIBLE ASSOCIATION BETWEEN IRRITABLE BOWEL SYNDROME AND SEPARATION ANXIETY DISORDER

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INTRODUCTION: Irritable bowel syndrome (IBS) in adults, as well as early separation anxiety disorder (SAD) and recurrent abdominal pain (RAP) in childhood are associated with anxiety and somatization.
AIMS&METHODS: The aim of this study was to examine possible associations between IBS in adulthood and SAD in childhood.
Forty adults with IBS and 40 healthy controls completed a demographic questionnaire, the Separation Anxiety Symptom Inventory (SASI), the somatization subscale of SCL-90-R, the Attachment Style Questionnaire (ASQ), and a retrospective self-report questionnaire regarding RAP. A regression model was constructed for the prediction of IBS in adulthood by retrospective SAD symptoms, somatization score, and attachment style.
RESULTS: Groups were similar for mean age and gender distribution. Compared to controls, IBS patients scored higher on the SCL-90-R scale of somatization (25.35 ± 7.47 vs.16.50 ± 4.40, $p<0.001$), and more IBS patients (25% vs.7.5%) reported RAP in childhood. The multiple logistic regression model for predicting the presence of IBS in adulthood was statistically significant with a total (omnibus) significance: chi-square (df=10, n=80) = 80.568, $p<0.0001$. The accuracy of the prediction was 63.5% (Cox and Snell's $R^2 = 0.635$). However, retrospective recall of SAD symptoms in childhood was lower in IBS patients than in controls (20.98 ± 5.07 vs. 25.33 ± 6.80, $p<0.005$).
CONCLUSION: The results of this study suggests that children with a tendency for somatization, SAD and with an avoidant attachment style are more likely to develop IBS in adulthood but less likely to retrospectively report symptoms of SAD in childhood.
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Disclosure of Interest: None Declared
Keywords: Irritable bowel syndrome , separation anxiety disorder

P414 PREVALENCE OF ORGANIC DISORDERS IN CONSECUTIVE NEW PATIENTS MEETING CRITERIA FOR IBS IN A GASTROENTEROLOGY CLINIC

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INTRODUCTION: A positive diagnosis of irritable bowel syndrome (IBS), without the need for recourse to investigation, is encouraged. Patients meeting symptom-based diagnostic criteria for IBS are often given reassurance that there is no serious underlying pathology, and treated symptomatically. However, some studies have suggested that an organic diagnosis, such as coeliac disease or pancreatic insufficiency, may be missed if this approach is adopted. We aimed to examine the yield of investigation in patients meeting criteria for IBS in real-life clinical practice.
AIMS&METHODS: Review of consecutive unselected new patient referrals to a single Gastroenterologist's outpatient clinic during a 3-year period, from January 2010 to December 2012. All clinic letters were reviewed retrospectively, and symptoms reported by the patient at the initial consultation were recorded. Those who described lower abdominal pain associated with a change in bowel habit, in the absence of alarm features such as rectal bleeding, anaemia, or weight loss, were classified as meeting criteria for IBS at presentation. IBS subtype was classified as diarrhoea-predominant (IBS-D), constipation-predominant (IBS-C), or mixed (IBS-M), according to stool pattern. Radiology, endoscopy, chemical pathology, and histopathology databases were then cross-examined in order to ascertain the final diagnosis following full investigation, to the level deemed appropriate by the consulting physician.
RESULTS: There were 613 consecutive unselected new patient referrals to a single Gastroenterologist between January 2010 and December 2012. Of these, 49 (8.0%) (mean age 42.8 years, 31 (63.3%) female) reported symptoms compatible with IBS, (31 (63.2%) IBS-D, 11 (22.4%) IBS-C, and 7 (14.3%) IBS-M). In total, 10 (20.4%) patients were found to have an organic explanation for their symptoms after investigation. The commonest organic diagnosis among patients meeting criteria for IBS was bile acid malabsorption, occurring in 5 (10.2%). Other organic diagnoses detected included coeliac disease (2 patients), Crohn's disease (1 patient), inflammatory bowel disease-unclassified (1 patient), and pancreatic insufficiency (1 patient). Organic diagnoses were commonest among those meeting criteria for IBS-D, occurring in 9 (29.0%) patients.
CONCLUSION: Our data suggest that organic diagnoses may occur in up to one in five patients meeting criteria for IBS without alarm features. Bile acid malabsorption occurred in more than 10%. The yield of investigations in IBS-C was low, suggesting these individuals can be labelled confidently as having IBS without the need for further investigation.
Disclosure of Interest: None Declared
Keywords: Bile acid malabsorption, Coeliac disease, IBS, Irritable bowel syndrome, Organic disease

P415 DIAGNOSTIC APPROACHES TO INFLAMMATORY BOWEL DISEASE, IRRITABLE BOWEL SYNDROME AND CHRONIC CONSTIPATION: A SURVEY AMONG GENERAL PRACTITIONERS, GASTROENTEROLOGISTS AND EXPERTS IN FIVE EUROPEAN COUNTRIES

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INTRODUCTION: The confident diagnosis of chronic abdominal conditions can often be challenging and this study aimed to assess the diagnostic process in irritable bowel syndrome with constipation (IBS-C), irritable bowel syndrome with diarrhoea (IBS-D), inflammatory bowel disease (IBD) and chronic constipation (CC).
AIMS&METHODS: 25 experts, 100 gastroenterologists (GEs) and 104 general practitioners (GPs) from Germany, Spain, France, Italy and the United Kingdom were interviewed online. Following an exploration of their perception, attitude and diagnostic approach to IBS, participants were shown a patient vignette demonstrating a typical case of IBS-C, IBS-D, IBD and CC. For each vignette they were asked to make a diagnosis and answer questions on the investigation and further management of each case.
RESULTS: Ability to make a diagnosis for each patient vignette

	IBS-C			**IBS-D**		
Type of physician	**Experts**	**GEs**	**GPs**	**Experts**	**GEs**	**GPs**
Correct diagnosis	**88%**	**56%**	**31%**	**92%**	**72%**	**64%**
Incorrect diagnosis	4%	4%	5%	8%	12%	14%
Don't know	8%	40%	64%	-	16%	22%
	IBD			**CC**		
Type of physician	**Experts**	**GEs**	**GPs**	**Experts**	**GEs**	**GPs**
Correct diagnosis	**92%**	**87%**	**85%**	**60%**	**60%**	**67%**
Incorrect diagnosis	4%	13%	14%	40%	40%	32%
Don't know	4%	-	1%	-	-	1%

CC and IBS-C caused the greatest diagnostic difficulty. For the IBS-C patient, the majority of GEs and GPs who did not make a correct diagnosis said they did not know what the diagnosis should be. In contrast, an incorrect diagnosis in the CC patient was because they considered the patient to have IBS-C.

The physicians' level of confidence in making the diagnosis was 7.0/9 for IBS-D, 6.8/9 for IBS-C, 6.7/9 for CC and 6.3/9 for IBD. The low score for IBD was because most physicians said they would wait for the result of investigation before making a diagnosis.
Experts were more likely than GEs and GPs to endorse a positive approach to the diagnosis of IBS, IBD or CC, whereas GEs and GPs would rather adopt a diagnosis by exclusion approach. For IBS and CC patients, the physicians' next action would be to prescribe a treatment, whereas for the IBD patient, the next action would be to conduct tests. A good knowledge of the Rome III diagnostic criteria was claimed by 96% of experts and 73% of GEs but only 15% of GPs.
CONCLUSION: The study highlights the difficulty experienced by GPs, GEs and experts in confidently diagnosing conditions such as IBS. Differentiating between IBS-C and CC is particularly challenging and diagnostic criteria designed for research purposes may not necessarily be applicable in the normal clinical setting.
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Keywords: chronic constipation, diagnostic approach, guidelines, IBS-C

P416 APREPITANT USE IN CHILDREN WITH CYCLICAL VOMITING SYNDROME

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INTRODUCTION: Cyclic vomiting syndrome (CVS) is a chronic disorder characterized by recurrent, stereotypical episodes of nausea and vomiting interspersed with symptom-free periods. In a subgroup of children, both acute and prophylactic standard treatments remain unsatisfactory. Aprepitant, a neurokinin-1 receptor antagonist, is efficacious in preventing chemotherapy-induced nausea and vomiting in adults and older children; its role in other disorders remains to be defined. In this study we assessed the efficacy of aprepitant as a prophylactic/acute treatment in CVS children refractory to standard therapies.
AIMS&METHODS: Thirty-eight children (16 males; median age 11 years) fulfilling Rome III criteria for CVS and treated acutely or prophylactically with aprepitant were identified through retrospective chart review. The prophylactic schedule (Regimen A, RA) was: 40 mg twice/week in children <40 kg, 80 mg in children $>40<60$ kg, 125 mg in children >60 kg. The acute schedule (Regimen B, RB) was: 125 mg at day 1 (prodromic phase), followed by 80 mg at day 2 and 3 in children >20 kg, 80 mg for 3 consecutive days for those <20 kg, 80 mg at day 1, 40 mg at day 2 and 3 for those <15 kg. Primary outcome was defined as: 1. complete response, no attacks; 2. partial response, $\geq 50\%$ decrease in attack frequency and intensity; 3. no response, $<50\%$ decrease. Secondary outcomes were: no. of episodes/year, episode length (days), symptom-free interval length (days), and % of school attendance.
RESULTS: During a follow-up period ranging between 12 and 58 months, 37 children were still on treatment. One child discontinued the treatment due to headache. Thirteen children were on RA, while 24 on RB. 30 children (81%) had response to the treatment. Among them, 6 (16%) showed a complete response, while 24 (65%) a partial response. At follow-up there was a significant decrease in no. of episodes/year [6 (2.8-12) vs 12.9 (10-20), $p<0.001$] and in episode length (days) [2.5 (0.5-4) vs 5 (4-5), $p<0.001$], as well as a significant increase in symptom-free interval length (days), [60 (30-127.5) vs 28 (18.5-36.2), $p<0.001$] and % of school attendance [80 (80-100) vs 63 (50-67.5), $p<0.001$]. In the subgroup analysis, no difference was found between RA and RB in the proportion of children showing either complete response (3/13 vs 3/24 respectively, NS) and partial response (8/13 vs 16/24 respectively, NS) as well as for all secondary outcomes. No other side effects were recorded.
CONCLUSION: Aprepitant is effective and well tolerated for acute and prophylactic management of CVS refractory to standard therapies. However, larger randomized studies are needed to confirm our findings.
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Disclosure of Interest: None Declared
Keywords: aprepitant, cyclical vomiting syndrome, EMEND, functional bowel disorders, paediatric

P417 THE FREQUENCY AND THE RISK FACTORS OF FUNCTIONAL CONSTIPATION IN XI'AN CHILDREN OF SCHOOLAGE

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INTRODUCTION: Data regarding the prevalence of constipation in Xi'an children of schoolage using internationally standardized definitions are scarce.
AIMS&METHODS: The aim of this study was to investigate the prevalence rate of FC in Xi'an children of schoolage using pediatric Rome III criteria, and to find out the factors surrounding their daily life which will encourage postponement of defecation and hinder the development of regular bowel habits.
A cross-sectional questionnaire survey with stratified cluster and random sampling was performed in December, 2012.2846 children from 5 primary schools was invited to participate in the survey. The questionnaire is made up of two parts, Part1 is the Questionnaire on pediatric Gastrointestinal Symptoms; Part2 is about risk fators. Functional constipation was defined by pediatric Rome III criteria. A small number of children who met the criteria were further selected to undergo a detailed physical examination to exclude organic disease .
RESULTS: 1. 2846 children was invited to participate in the survey,2131 questionnaires were returned , the response rate is 74.88%. 1997 (70.17% effective response rate)were qualified for analysis.
2. The range of age is 6-12 years , mean age was 8.99 ± 1.80 years, 55.3% (1105/1997)were girls. eighty-four children (4.21%, 95% confidence interval [CI] 3.33%–5.09%) were found to have functional constipation. The prevalence rates of the age groups 6y∼, 7y∼, 8y∼, 9y∼, 10y∼, 11y∼, 12y∼were 8.4%(16/191), 5.6%(17/301), 2.9%(10/341), 2.9%10/342), 3.1% (10/326, 4.1%(13/319), 4.5%(8/177), respectively. A higher prevalence rate of FC was seen in the 6y∼group than in other groups ($P < 0.008$) . There was no difference in prevalence between boys(4.15%,37/892) and girls(4.25%,47/1105) ($P > 0.05$).
3. In this survey, Logisit regression analysis shows that functional constipation was found to be significantly more prevalent among those children who had at least 3 times fast food one week, formula-fed during infant period, lived with niether parent or only father $>50\%$ of time, never been taught by parent about how to defecate correctly, slept less than 7 hours, done exercise less than half an hour, static activities in addition to school hours more than 3 hours, refused to pass bowel movements in school($P<0.05$, $OR>1$).
CONCLUSION: Children functional constipation is a common problem, the highest prevalence of constipation was in age of 6 years. The factors surrounding their daily life have an influence on constipation, paying attention to these risk factors may help prevent or stop the progression of childhood constipation at its early stages.
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Disclosure of Interest: None Declared
Keywords: Functional constipation, Prevalence, Risk factors, Schoolage children

P418 CLINICAL BENEFIT AND PROTECTIVE ROLE AGAINST ACUTE DIVERTICULITIS OF NON-ABSORBABLE ANTIBIOTICS WITH CYCLIC ADMINISTRATION IN DIVERTICULAR COLONIC DISEASE

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INTRODUCTION: Colonic diverticular disease is a relatively frequent disease, with wide clinical spectrum: lack of symptomatology/transit troubles, meteorism, abdominal disconfort or pain/complications as acute diverticulitis.
AIMS&METHODS: AIM: to evaluate the clinical benefit and the protective effect against acute diverticulitis of non-absorbable antibiotics, in cyclic long-term administration, in patients with colonic diverticular disease. PATIENTS AND METHODS: we prospectively studied all patients diagnosed during one year in the Center of Gastroenterology and Hepatology with colonic diverticular disease, by colonoscopy or barium enema, with lower intestinal tract symptoms and to whom major colonic lesions were excluded. All patients received specific medication for irritable bowel syndrome and different supplementary treatment: group A-fiber-rich diet, B-fiber-rich diet and rifaximin 7 days/month, 400 mgx2/day, for 1 year. We analyzed after one year of treatment the clinical benefit on the lower intestinal tract symptoms (by questionning the patients) and the percent of patients which developped acute diverticulitis.
RESULTS: 84 patients diagnosed with colonic diverticular disease were followed. In the group A (42 patients), clinical benefit was obtained in 29 patients (69%) and 1 case of acute diverticulitis (2.3%) was noted. In the group B (42 patients), clinical benefit was obtained in 32 patients (76%) and 1 case of acute diverticulitis (2.3%) was noted.
CONCLUSION: Non-absorbable antibiotics with cyclic administration could bring clinical benefit to symptomatic patients with colonic diverticular disease, but not in a significant manner, while prevention of acute diverticulitis was not demonstrated. More studies with longer follow-up and with cost-efficiency analysis would be useful.
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Disclosure of Interest: None Declared
Keywords: colon diverticulitis, non-absorbable antibiotics, prophylactic treatment

P419 UNDERWEIGHT IS A RISK FACTOR FOR COMPLICATED DIVERTICULITIS IN MALE: MULTICENTER STUDY IN JAPAN

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INTRODUCTION: With the westernization of diets, incidence of acute colonic diverticulitis has been increasing in Japan. Recently, several studies have shown a

relationship between obesity and complication of diverticulitis such as abscess or perforation. However, the relationship between obesity and complicated diverticulitis: (CD) remains a matter of debate.

AIMS&METHODS: The aim of this retrospective study was to assess the relationship between obesity and CD in large retrospective multicenter Study in Japan. This retrospective study included 1110 patients (654 males, 456 females, mean age 51.8 ±16.6 years) diagnosed with acute colonic diverticulitis between May 2006 and January 2011 at 20 flagship hospitals with diverticular disease study groups in Japan. Complication case was defined as abscess or perforation case. We divided the patient into four groups based on WHO criteria of obesity. The four groups were Underweight group (BMI < 18.5kg/m^2), Normal group (18.5kg/m^2≦BMI < 25 kg/m^2), Overweight group (25 kg/m^2≦BMI < 30kg/m^2) and Obesity group (30kg/m^2≦BMI). Then, we compared normal group and other groups with respect to complication rate.

RESULTS: In male patient, complication rate in each group was below, Underweight group (36.0%: 10/29), Normal group (15.2%: 62/411), Overweight group (12.7%: 24/189) and Obesity group (8.0%: 2/25). In female patient, complication rate in each group was below, Underweight group (7.1%: 4/56), Normal group (10.9%: 35/321), Overweight group (11.1%: 7/63) and Obesity group (6.3%: 1/16). Complication rate revealed no significant differences between Normal group and Obesity group both male (15.2% *vs.* 8.0%: P=0.3317) and female (10.9% *vs.* 6.3%: P=0.8422). On the other hand, in male patient, complication rate was significantly higher in Underweight group compared to Normal group (36.0% *vs.* 15.2%: P=0.0064). However, this trend was not seen in female patient (7.1% *vs.* 10.9%: P=0.3945).

CONCLUSION: Obesity wasn't a risk factor for CD both male and female in Japan. On the other hand, underweight was a risk factor for CD in male. We need to pay attention to underweight male patients to prevent complicated diverticulitis.

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Disclosure of Interest: None Declared

Keywords: Complicated diverticulitis, Obesity , Underweight

P420 IMMUNE AND EXTRACELLULAR MATRIX REMODELLING ALTERATIONS IN PERIDIVERTICULAR INFLAMED MUCOSA OF PATIENTS WITH DIVERTICULITIS

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INTRODUCTION: Increased mucosal expression of pro-fibrogenic mediators such as collagen has been reported in diverticulitis and, to a lesser extent, in diverticulosis. While tumor necrosis factor (TNF)-α is overexpressed in diverticulitis, no information exists on other innate and adaptive pro-inflammatory cytokines in diverticulitis and diverticulosis. We therefore investigated the mucosal immunologic changes and the pro-fibrogenic response occurring next to inflamed diverticula.

AIMS&METHODS: Intestinal biopsies were collected from peridiverticular areas of 15 patients with diverticulitis and 15 with diverticulosis, from inflamed areas of 14 inflammatory bowel disease (IBD) patients, from strictured areas of 10 Crohn's disease (CD) patients and from normal mucosa of 15 control subjects. After isolation, lamina propria mononuclear cells (LPMCs) were stimulated with pokeweed mitogen (PWM) or with anti-CD3/CD28 antibodies, whereas myofibroblasts were cultured with medium alone. Interleukin (IL)-1β, IL-6, IL-12, TNF-α, IL-17A, interferon (IFN)-γ and collagen were measured in culture supernatants. Mucosal transforming growth factor (TGF)-β1 transcripts were measured by quantitative RT-PCR and immunohistochemistry for smooth muscle actin (SMA) was performed on biopsy sections.

RESULTS: PWM- and anti-CD3/CD28-stimulated LPMCs from diverticulitis and IBD patients produced significantly higher concentrations of IL-1β, IL-6, IL-12 and TNF-α, and IFN-γ and IL-17A, respectively, than uninflamed diverticula and control mucosa, with no difference between control and diverticulosis patients. Myofibroblasts from diverticulitis and strictured CD patients released significantly higher amounts of collagen than diverticulosis patients and controls. Raised transcripts of mucosal TGF-β1 were found in diverticulitis and strictured CD patients. SMA was overexpressed in the mucosa of diverticulitis compared to diverticulosis patients and controls.

CONCLUSION: Mucosa from peridiverticular inflamed areas is characterized by a marked pro-inflammatory immune activation and by an enhanced pro-fibrogenic response. The abnormal innate and adaptive immune response observed in diverticulitis is likely to amplify the aberrant process of fibrogenesis intrinsically associated to diverticulum formation.

Disclosure of Interest: None Declared

Keywords: collagen, cytokine, diverticulitis, diverticulosis, TGF-beta1

P421 CHALLENGING A DOGMA - NECESSITY OF ROUTINE COLONOSCOPY AFTER COMPUTED TOMOGRAPHY-DIAGNOSED ACUTE DIVERTICULITIS

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INTRODUCTION: Current guidelines recommend computed tomography (CT) to diagnose acute diverticulitis, and a colonoscopy after 6 weeks to confirm the diagnosis and rule out cancer mimicking diverticulitis (1-2). Coloscopy is an invasive method assosiated with 0.04 - 0.07% risk of bowel perforation (3-4). On the other hand only 0.5 - 2 % of CT-diagnosed acute diverticulitis turn out to be colon cancers instead (5-8). Based on recent meta-analysis, scientific data to support routine colonoscopy after CT-diagnosed acute diverticulitis is limited (9).

AIMS&METHODS: The aim of the study was to evalute the risk of colon cancer mimicking diverticulitis, and the need of colonoscopy after CT-diagnosed acute diverticulitis.

This was a retrospective cohort study. Patients treated during 2006-2010 were identified based on ICD-10 code K57. Data was manually obtained from electronic patient records and analyzed for age, sex, laboratory parameters, prior diverticulitis, surgical operations, pathology reports, CT reports and images, and colonoscopy charts. CT-diagnosis of acute diverticulitis was defined as primary diagnosis given by an expert consultant radiologist. All patient records were manually searched for colorectal cancer diagnosis in patients that had not been evaluated by colonoscopy or the colonoscopy had been incomplete. As it is mandotory by law to report all cancer cases to national registry, similar search was performed for Finnish Cancer Registry. Minimum interval between the searches for cancer and index diverticulitis was two years.

RESULTS: Six-hundred and thirty-three patients with CT-diagnosed acute colonic diverticulitis were included. Ninety-seven underwent emergency resection during index hospital admission, whereas 536 were treated conservatively. Three-hundred and ninety-four conservatively treated patients underwent colonoscopy in the follow-up. Seventeen cancers (2.7%) were identified in patients initially treated as having an acute diverticulitis. Sixteen cases (94%) had abscess in the CT-scan, whereas one case had pericolic extraluminal air, but no abscess. 11.4% of patients treated as having a diverticular abscess had cancer instead. No cancer were found in patients treated for uncomplicated acute diverticulitis. In addition to absess, independent risk factors for cancer mimicking diverticulitis included suspicion of cancer by radiologist, thickness of bowel wall over 15 mm, no diverticula seen on CT-scan, and previously undiagnosed metastases in CT-scan.

CONCLUSION: Routine colonoscopy after uncomplicated acute diverticulitis does not seem necessary, while colonoscopy should be performed in all patients treated for diverticular abscess.

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Keywords: colon cancer, Complicated diverticulitis, diverticular absess, uncomplicated diverticulitis

P422 COULD UPPER GI CANCER EXPLAIN 'FALSE POSITIVE' FAECAL OCCULT BLOOD TEST (FOBT) RESULTS IN THE BOWEL CANCER SCREENING PROGRAMME?

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INTRODUCTION: The Bowel Cancer Screening Programme (BCSP) commenced in England in 2006 using the Hemoccult guaiac faecal occult blood test (FOBt). The study aimed to evaluate if significant numbers of upper GI cancers were being diagnosed in patients with a positive FOBt in the absence of colonic pathology.

AIMS&METHODS: A quantitative data analysis of all BCSP patients with a negative colonoscopy cross referenced with all patients within screening age (60yrs>) diagnosed with upper GI cancer in the North East of England, comprising of South of Tyne, North of Tyne, Teesside, Durham and Darlington.

RESULTS: Collectively the North East Bowel Cancer Screening centres carried out 5176 colonoscopies from 2008-2011, resulting in 1108 (21.4%) normal investigations.

In the same time period 589 patients were diagnosed with upper GI cancer. 243 were invited to participate in BCSP and 109 (45%) took part. 33/109 (30%) patients were diagnosed with upper GI cancer prior to submitting FOBt, leaving 76 (70%) presumably undiagnosed.
72/76 (94.8%) returned a negative FOBt, 2 (2.6%) returned an unclear subsequently followed by 2 negative FOBt kits according to BCSP practice, leaving 2 (2.6%) patients with a positive FOBt who subsequently had a normal colonoscopy. At the time of screening both patients were symptomatic with upper GI symptoms, and diagnosed with upper GI cancer within 3 months of screening.
CONCLUSION: These data suggest that carrying out an upper GI investigation in FOBt positive and colonoscopy negative patients is not justified. Consideration to investigate maybe given in the presence of upper GI symptoms; however, further work is needed to evaluate the prevalence of upper GI symptoms in this population.
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Disclosure of Interest: None Declared
Keywords: Bowel Cancer Screening Programme, False positive faecal occult blood test, Missed upper GI cancer

P423 RESULTS AND RISK FACTORS OF COLORECTAL NEOPLASMS IN SCREENING COLONOSCOPY IN PERSONS 40 TO 49 YEARS OF AGE

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INTRODUCTION: Screening guidelines for colorectal cancer include colonoscopy starting at age 50 years based on the prevalence of adenomas and the incidence of colon cancer at that age. However, there is a paucity of data on colonoscopic screening in asymptomatic individuals aged 40 – 49 years. The aim of this study is to investigate the prevalence and risk factors for colorectal neoplasms in persons 40 to 49 years of age.
AIMS&METHODS: Of 4,783 individuals aged 40-49 who underwent colonoscopy for health check up, 2,531 adults received screening colonoscopy for the first time. We analyzed questionnaire information, anthropometric, laboratory and radiologic measurements, and colonoscopic findings for 2,531 adults, based on prospectively collected data.
RESULTS: The prevalence of overall adenoma, high-risk adenoma, and advanced adenoma was 27.2%, 4.4%, 2.1% respectively in 40-49 years aged subjects. Five patients (0.2%) had an adenocarcinoma detected. About half of overall colorectal neoplasms as well as advanced adenoma were showed proximal location. Older age (≥ 45 years), male sex, current smoking, heavy alcohol drinking were associated with an increased risk of overall colorectal adenoma. Metabolic syndrome was also associated with an increased risk of overall adenoma (OR=1.29, 95% CI=1.03-1.63) and high-risk adenoma (OR=1.99, 95% CI=1.30-3.04). Among the individual components of metabolic syndrome, high TG levels and low HDL levels were associated with an increased risk of high-risk adenoma (OR=1.61, 95% CI=1.06-2.45; OR=1.63, 95% CI=1.01-2.64, respectively).
CONCLUSION: We found that metabolic syndrome increased the risk of colorectal adenoma and adenomas were equally distributed proximally and distally in 40-49 aged adults.. Five colorectal cancer were also found. Thus, consideration should be given for age based colonoscopic screening beginning at age 40, especially for individuals with metabolic syndrome.
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Disclosure of Interest: None Declared
Keywords: Colorectal adenoma, Metabolic syndrome, risk factors, Screening, young adults

P424 GECCO 2012: EPIDEMIOLOGY OF CHRONIC CONSTIPATION IN GERMANY

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INTRODUCTION: Prevalence of chronic constipation in Germany has been reported to be 5%. This number is substantially lower than in other European countries and worldwide, but reliable data are unavailable.
AIMS&METHODS: We ran a data-sampling frame using a RDD approach (Random Digit Dialing), and conducted a telephone interview (CATI; Computer assisted telephone interview) with individuals who acknowledged the presence of constipation symptoms during the preceding 12 months. Constipation symptoms for more than 6 months were regarded as chronic. Individuals willing to provide their postal address were sent a questionnaire asking about the presence of other diagnoses, and current regular medication for constipation and co-morbid conditions.
RESULTS: Based on response rates during a test trial with 1005 individuals, we interviewed 15 002 individuals age 18 or older (mean age: 49.5 yrs; 51.4% females) who agreed to participate in CATI. Of these, 2193 (14.6%) acknowledged having experienced constipation during the last 12 months, 864 (5.8%) reported constipation during the last 4 weeks, and 380 (2.5%) having current constipation symptoms. Of the latter, 307 (80.8%) had constipation for more than 6 months. A total of 1037 individuals (46.3% of all constipated participants) agreed to be sent the questionnaire, and 642 questionnaires (61.9%) were returned. More than one third (38%) of all constipated respondents reported 1 or more chronic medical conditions that could account for the constipation (e.g. hypothyroidism, neurological diseases). This was further supported by the fact that many of the constipated respondents regularly took medication that may have induced or exacerbated constipation (e.g. calcium antagonists, L-Thyroxin, pain medication). Sixty-two percent of the 642 respondents had constipation of putative functional origin. Medication use for constipation was different between functional and secondary constipation: Patients with secondary constipation more often used conventional laxatives (bisacodyl, senna, lactulose, macrogol) while patients with functional constipation more often used either nutrition-based measures (psyllium) or novel drugs (prucalopride).
CONCLUSION: Up to 15% of the general German population may report symptoms of constipation. More than 1/3 of them may have constipation secondary to another clinical condition while 2/3 may have functional constipation.
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Keywords: constipation, epidemiology

P425 AN INEQUALITIES ANALYSIS OF INDIVIDUALS INVITED FOR COLORECTAL CANCER SCREENING

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INTRODUCTION: The Scottish Colorectal Cancer Screening Programme commenced a phased roll out in June 2007 (1) with all NHS Boards participating in the Programme by December 2009. By December 2011 everyone within the eligible age range (50-74 years) had been invited to participate in at least one round of screening. Screening uptake is an important performance indicator for population screening, and has been shown to be affected by deprivation and gender, although not in a fully rolled-out national programme.
AIMS&METHODS: In this study we have examined uptake, positive predictive value (PPV) and stage distribution by deprivation and gender in the National Screening Programme. Data on all eligible individuals during the first five years of the Programme were analysed by gender and deprivation quintile. Comparative information was obtained from the National Cancer Registry. The main outcome measures were uptake, cancer and adenoma detection and Dukes' stage.
RESULTS: The expected gradient in uptake was seen with lower uptake in disadvantaged groups and males. Uptake in males ranged from 38% in the most deprived quintile to 58% in the least deprived quintile; for females from 44% to 66%. 80% of those screening once did so again on next invitation and here the deprivation gradient was very small. PPV for both cancers and adenomas was worse in the disadvantaged and women; the PPV for cancer ranged from 3.5% in the most deprived quintile to 6% in the least deprived quintile for females and from 5% to 8% in males. Screen detected cancers are generally diagnosed at an earlier stage. The proportion of cancers which were screen detected increased steadily to round 25% in 2011 and have increased within each deprivation quintile.

CONCLUSION: The recognised differentials by sex and social group are seen. However once engaged in screening the vast majority of individuals in all social groups continue participating. Thus, there are implications for encouraging uptake and targeting funding and resources to traditionally disengaged groups. However, improving screening uptake in disadvantaged groups increases the proportion of false positive investigations.

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Keywords: Colorectal cancer, Screening

P426 THE EFFECT OF A MULTISPECIES PROBIOTIC ON THE INTESTINAL MICROBIOTA DURING ANTIBIOTIC THERAPY

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INTRODUCTION: Antibiotic intake causes a marked and sustained disturbance of the intestinal microbiota resulting in long-term health consequences. Probiotics have shown to be able to prevent these disturbances. However, different probiotics (both mono- and multispecies) and treatment strategies (during or after antibiotic therapy (ABT)) are used. The aim of this study was to investigate the efficacy and safety of a multispecies probiotic "Rioflora®Balance" during and directly after ABT.

AIMS&METHODS: Patients treated with ABT for focal pneumonia were randomized into three groups. Group 1 received 2 capsules Rioflora®Balance twice daily (10^{10}cfu/day) for 14 days in parallel with ABT; group 2 received 2 capsules Rioflora®Balance twice daily (10^{10}cfu/day) for 14 days directly after cessation of ABT; group 3 received ABT only. At the start and end of ABT/multispecies probiotic supplementation complaints were assed by the treating physician. Moreover, gas chromatography was applied to investigate the dynamics of the small intestinal microbiota and quantitative PCR was used to determine changes in the colonic microbiota (*Bacteriodes fragilis, Bacteriodes thetaiataomicron,* lactobacilli, bifidobacteria, *Clostridium difficile, Eschericia coli* and *Faecalibacterium prausnizii*).

RESULTS: 120 patients completed the study (40 in each group, mean age 33.7±9.4 years; 47 men, 73 women). ABT had a profound influence on the small and large microbiota (increase in small intestinal *C. difficile* and Candida, decrease in both small intestinal and colonic bifidobacteria and lactobacilli, decrease in small intestinal *B. fragilis* and an increase in colonic *E.coli*). Multispecies probiotic supplementation was able to completely counteract these antibiotic induced disturbances of the microbiota. Moreover, an increase of both small intestinal and colonic bifidobacteria and lactobacilli was observed. Supplementation of the multispecies probiotic in parallel with ABT was characterized by a more pronounced effect than supplementation after cessation of ABT. No adverse events were reported. No antibiotic associated diarrhea was observed in any of the patients.

CONCLUSION: The intestinal microbiota was markedly affected by ABT. Although the exact long-term consequences of this disturbance need to be fully elucidated it is strongly associated with a negative impact on health. Supplementation with the multispecies probiotic Rioflora®Balance is safe and effective in preventing antibiotic induced disturbances of the intestinal microbiota. Moreover, multispecies probiotic supplementation appears to be more effective if started at the start of ABT than after cessation.

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Disclosure of Interest: None Declared

Keywords: antibacterial therapy, intestinal microbiota, multispecies probiotics

MONDAY, OCTOBER 14, 2013 9:00–17:00

OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS I – Poster Area

P427 PREVALENCE OF SEVERE ATROPHIC BODY GASTRITIS IN DYSPEPTIC PATIENTS SEEN AT THE ENDOSCOPY UNIT OF A BRAZILIAN GENERAL HOSPITAL

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INTRODUCTION: For many dyspeptic patients the diagnosis of atrophic body gastritis (ABG) is the first step indicating the presence of autoimmune gastritis, associated or not with pernicious anemia.

AIMS&METHODS: The aim of this study was to investigate the prevalence of cases of severe ABG among dyspeptic patients undergoing endoscopy in a Brazilian general hospital. We surveyed all cases of upper gastrointestinal endoscopy with biopsy sampling of gastric antropyloric region and gastric body performed from 2007 to 2009 at a general hospital in the city of Belo Horizonte. A total of 6,005 consecutive gastroesophageal endoscopies with gastric biopsies of the antropyloric and body mucosa were reviewed. Among these cases 2,564 (42.7%) had the diagnosis of chronic gastritis as the main pathological condition of the gastric mucosa. Among them, all the cases of gastritis reporting glandular atrophy or intestinal metaplasia were reassessed by an expert GI pathologist (AJAB). When necessary the paraffin blocks of these patients were retrieved for obtaining new histological sections. Immunohistochemical staining of ghrelin-producing cells was used to differentiate atrophic body mucosa with pseudopyloric metaplasia from true antropyloric mucosa. Ghrelin-producing cells are usually numerous in pseudopyloric metaplasia of the corpus and rare in mucous glands of the antropyloric region [1, 2].

RESULTS: Among the 2,564 cases of chronic gastritis 141 (5.5%) patients had the diagnosis of severe atrophic body gastritis in the original reports. After reviewing all the cases other 55 patients were added, making up 196 (7.6%) patients with severe ABG. The 196 patients ranged in age from 11 to 94 years, with a significant predominance of females (76.0%) over males (24.0%). Fifty patients were in relatively young age range (31 to 50 years) with an even more significant predominance of females, i. e., 83.3% *vs.* 16.7%.

CONCLUSION: The present results show that severe ABG seems to be a common pathological condition among Brazilian dyspeptic patients equivalent to 7.6% of patients with chronic gastritis seen at a general hospital. Furthermore, it appears that about 24% of these patients leave the hospital without receiving the correct diagnosis of gastric disease which may delay the final diagnosis of autoimmune gastritis.

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Disclosure of Interest: None Declared

Keywords: Atrophic body gastritis, Prevalence of atrophic body gastritis in Brazil, Severe atrophic body gastritis, Type A gastritis

P428 REGULATION OF OESOPHAGEAL KERATINOCYTE PROGENITOR CELLS FUNCTION BY THE COX2/ PROSTAGLANDIN E/C-AMP/PKA PATHWAY AND BY KGF. IMPLICATIONS FOR OESOPHAGEAL EPITHELIAL RENEWAL, HEALING AND THE THERAPEUTIC ACTIONS OF HYDROTALCITE

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INTRODUCTION: Oesophageal progenitor cells (OPC) are critical for maintenance, renewal and healing of oesophageal epithelium. The mechanisms regulating OPC function, survival and proliferation remain unknown.

AIMS&METHODS: We tested hypotheses that: 1) Prostaglandin E (PGE) EP receptors, cycloogygenase2 (Cox2) and keratinocyte growth factor (KGF) receptors (KGFR) are expressed in OPC and regulate their survival and proliferation; 2) upregulation of Cox2 (generating PGE) and KGFR by hydrotalcite (HTL, a newest generation antacid) is the basis for protective and healing actions of this drug. METHODS: We used: 1) normal rat oesophageal tissues, 2) organ cultures of rat oesophageal explants, and 3) human oesophageal epithelial HET-1A cell line, which has many features of OPC. Organ cultures and HET-1A cells were treated with placebo or HTL (1-5 mg/ml) for 1-4 hrs; HET-1A cells were also treated with: 1 μg/ml misoprostol (PGE1 analog); 1 μg/ml 16,16 dmPGE2; 0.4 mM protein kinase A (PKA) inhibitor, Rp-cAMP; or 50 ng/ml KGF. *Studies*: 1) epithelial integrity with confocal microscopy; 2) expression of Cox2, EP1-4 receptors, KGF and KGFR using immunostaining and western blotting; 3) In HET-1A cells we quantified: **a)** expression of Cox2, EP receptors1-4, KGF and KGFR and **b)** [i]cAMP (using Biotrack EIA), cAMP response element-binding protein (CREB) and cell proliferation (BrdU assay) prior to and after treatment with PGEs or KGF.

RESULTS: In normal oesophagus, OPC expressed Cox2, EP receptor2 and KGFR; stromal cells expressed KGF. In oesophageal explants, HTL treatment increased Cox2 and KGFR expression in OPC by 69±5 and 72±6% (both $p < 0.01$ vs. placebo). In HET-1A cells, HTL increased Cox2 and KGFR expression by >50% (both $p < 0.01$). PGEs treatment increased in HET-1A cells: c-AMP by >163-fold, P-CREB and cell proliferation by ~64% (all $p < 0.01$). These effects were abolished by pretreatment with PKA inhibitor. KGF stimulated HET-1A cell proliferation by 68% ($p < 0.01$).

CONCLUSION:) This is the first demonstration that Cox2 and EP-2 receptor are expressed and co-localized in oesophageal OPC indicating that Cox2 generated PGEs play an autocrine regulatory role in OPC proliferation and survival via the c-AMP/CREB/PKA signalling pathway. 2) KGFR are expressed in OPC while KGF is expressed in stromal cells reflecting mesenchymal-OPC interactions. 3) HTL treatment significantly upregulates expression of Cox2 and KGFR in OPC. 4) These findings provide new mechanisms regulating OPC, oesophageal mucosal defense and new insight into the protective and healing actions of hydrotalcite.

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Disclosure of Interest: None Declared

Keywords: cAMP, cyclooxygenase2 (Cox2), KGF, oesophageal, progenitor cells, prostaglandins E

P429 IN VIVO, REAL TIME, NON-INVASIVE ASSESSMENT OF GASTRIC MUCOSAL INJURY AND PROTECTION USING CONFOCAL LASER ENDOMICROSCOPY: FOCUS ON MUCOSAL MICROVESSELS AND PROGENITOR CELLS. COMPARISON WITH HISTOLOGY AND EM

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INTRODUCTION: The mechanisms and cellular targets of gastric mucosal injury are not fully defined. Histological assessment of fixed specimens may not fully reflect *in vivo* events. Confocal laser endomicroscopy (CLE), a novel cutting edge technology, enables *in vivo* real-time visualization of mucosal structures at a subcellular resolution – ''virtual biopsy''. This study was aimed to assess using CLE *in vivo* acute gastric injury with a focus on mucosal microvessels and progenitor cells.
AIMS&METHODS: Fischer F344 rats received 1 ml 0.5% fluorescein i.v. followed by ethanol (ETOH, 1 ml 50%) or placebo intragastrically (i.g.). In some rats, either 1 ml of placebo or hydrotalcite (HTL-newest generation antacid) was given i.g. 30 min prior to ETOH. We used CellvizioLAB LSU F400 and Z ProFlex probe, which was inserted i.g. and CLE images were monitored for 20 min before and after ETOH. **Studies** using CLE: 1) glandular epithelium and microvasculature imaging; 2) vascular permeability measurements; 3) mucosal blood flow dynamics; 4) epithelial progenitor zone integrity; 5) VEGFR2 molecular imaging using labeled antibody; 6) detection of labeled bone marrow-derived stem cells (BMDSC) in gastric mucosa after i.v. injection. For comparison we performed quantitative histology and electron microscopy (EM).
RESULTS: At baseline, CLE demonstrated a normal gastric gland pattern, lamina propria and microvasculature, microvascular blood flow and low vascular permeability. ETOH induced exfoliation of surface epithelium within 2-3 min followed by a 550% increase in vascular permeability ($p < 0.001$) at 3-5 min, microvessel rupture within 5-10 min, extensive extravasation of plasma and erythrocytes and vascular stasis. Progenitor zone cells were severely damaged. Histology and EM confirmed these changes. VEGFR2 was visualized in endothelial cells of microvessels. BMDSC were visualized in gastric mucosal microcirculation. Pretreatment with HTL reduced ETOH-induced vascular permeability by $> 55\%$ ($p < 0.01$), preserved mucosal blood flow and reduced extent and severity of injury (all $p < 0.01$), reflecting mucosal protection.
CONCLUSION: 1) CLE enables precise *in vivo*, real time, sequential analysis of events during gastric injury and evaluation of mucosal protection. 2) Microvascular injury and increased vascular permeability occur early and precede progenitor cell damage and deep hemorrhagic erosions. 3) CLE provides a significant advantage over histologic and EM assessment, by allowing real time monitoring of *in vivo* mucosal structure and function, e.g. vascular permeability, and molecular imaging.
Disclosure of Interest: None Declared
Keywords: confocal laser endomicroscopy, gastric injury, molecular imaging, progenitor cells , VEGFR2

P430 OXIDATIVE-ANTIOXIDATIVE BALANCE IN DUODENAL EPITHELIAL CELLS UPON LONG-TERM GASTRIC HYPOCHLORHYDRIA AND ITS CORRECTION WITH MULTIPROBIOTIC "SYMBITER"

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INTRODUCTION: Hypoacidic states of stomach occupy an important place among disorders of gastrointestinal tract (GIT). Long-term gastric hypochlorhydria (LTGH) can lead to digestive disorders, development of dysbiosis and inflammatory processes in GIT [1]. Probiotics are usually used in order to correct structural and functional damages in GIT, since they possess restoration of homeostasis due to normalization of GIT microbiota.
AIMS&METHODS: The purpose of work was to investigate the oxidative-antioxidative balance in rat duodenal epitheliocytes upon LTGH and administration of multiprobiotic ''Symbiter''.
Experiments were performed on white non-strain male rats. Hypoacidic state was reached by abdominal injection of omeprazole (14 mg/kg) once a day during 28 days. The second group simultaneously with omeprazole was treated with multiprobiotic ''Symbiter'' (0,14 ml/kg orally). Duodenal cells were isolated by low-temperature method. The rate of superoxide anion and hydrogen peroxide generation was assessed spectrophotometrically with XTT and xylenol orange, respectively. The content of diene conjugates were determined in heptane-izopropanol extract spectrophotometrically, Schiff bases – by fluorimetric assay. The content of TBA-reactive compounds was determined by reaction with thiobarbituric acid. Statistical processing of experimental data was performed with conventional analysis of variance.
RESULTS: It was shown that upon LTGH the levels of superoxide radical and hydrogen peroxide in duodenal epitheliocytes were increased: in 1.6 and 1.5 times in villus cells, and in 2.8 and 1.4 times in crypt cells as compared to the control, respectively. The level of lipid peroxidation products (diene conjugates, TBA-reactive substances, schiff bases) was elevated upon LTGH: in 1.7, 1.6, 1.5 times in villus epitheliocytes, and in 2.1, 2.3, 1.8 times in crypt epithelial cells in relation to control, respectively. Administration of multiprobiotic ''Symbiter'' to the rats with hypoacidity was associated with normalization of investigated parameters in duodenal cells.
CONCLUSION: Activation of free radical processes in duodenum upon LTGH was observed, thus indicating oxidative stress development in epithelial cells. Multiprobiotic ''Symbiter''contributed to the amelioration of free radical processes activity in duodenal cells of rats with hypoacidity, which can be explained by multifunctional nature of multiprobiotics (antimicrobial, antioxidant, immune-stimulating and other properties).
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Disclosure of Interest: None Declared
Keywords: duodenal epitheliocytes, free radical processes, long-term gastric hypochlorhydria , multiprobiotic

P431 PERITUMORAL ADIPOSE TISSUE MICROENVIRONMENT IN ESOPHAGEAL CANCER.

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INTRODUCTION: Obesity is strictly associated with chronic inflammation of adipose tissue and may influence cancer development, growth and/or invasion. In particular peritumoral adipose tissue may play a role in cancer pathophysiology, affecting tumor behaviour by altering the local microenvironment.
AIMS&METHODS: The peritumoral adipose tissue has been analyzed in patients with esophageal cancer in terms of adipocyte size and inflammation (CD45, CD68), angiogenesis (CD31) and lymphangiogenesis (podoplanin) markers expression. Adipose tissue samples were obtained from peritumoral and omental depots of 50 patients with esophagogastric junction adenocarcinoma or esophageal squamous cell carcinoma undergoing surgical resection. Complete anthropometric data were retrieved. Adipocytes diameter and immunohistochemical expression of CD45, CD68, CD31 and podoplanin was evaluated in haematoxylin and eosin stained sections. Non-parametric statistics were used.
RESULTS: Adipocyte size was directly correlated with CD45, CD68, CD31 and podoplanin expression in both peritumoral and omental adipose tissue. However adipocytes size directly and significantly correlated ($R=0.37$; $p < 0.01$) with positive lymph node involvement only in peritumoral but not omental adipose tissue.
CONCLUSION: Our results suggest that an increased adipocyte size may be related with inflammation and angiogenesis/lymphangiogenesis processes in adipose tissue. Moreover, peritumoral adipose tissue may play a role in alterating tumor microenvironment thus promoting invasiveness in esophageal cancer.
Disclosure of Interest: None Declared
Keywords: adipose tissue, esophageal cancer, inflammation

P432 DETERMINATION OF CXCR7 EXPRESSION IN ESOPHAGEAL CANCER

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INTRODUCTION: The chemokine CXCL12 and its receptor CXCR4 play a major role in tumor invasion, proliferation and metastasis of different malignant diseases, amongst others esophageal carcinoma. CXCR7 was recently identified as a novel alternate receptor for CXCL12. Aim of this study was to evaluate the prognostic impact of the expression of chemokine receptor CXCR7 in patients with esophageal carcinoma (EC).
AIMS&METHODS: Expression of CXCR7 in primary tumors, lymph node and distant metastases of 299 patients with EC was evaluated by immunohistochemistry on a tissue micro array and correlated with clinical and histopathological data.
RESULTS: In esophageal cancer sections CXCR7-specific reactivity was apparent in 45% ($N = 72$) of the squamous cell carcinoma (ESCC), but only occasionally in adenocarcinoma (EAC) (2%, $N = 3$). No correlation between CXCR4 and CXCR7 expression was evident (0.128). We correlated CXCR7 expression with clinical and histopathological characteristics (pT, pN, UICC stage bone marrow metastasis), but could not find any association.
CONCLUSION: In contrast to the other known CXCL12 receptor CXCR4, CXCR7 is expressed in ESCC only, underlining the divergent mechanisms and backgrounds of EAC and ESCC. The results of the study do not indicate a significant functional role of CXCR7 in EAC or ESCC of the esophagus. However, the variable expression in the main two cell types of EC needs to be further investigated.
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Disclosure of Interest: None Declared
Keywords: cxcr7, esophageal cancer, Immunostaining

P433 COMPARATIVE STUDY OF OLGA AND OLGIM STAGING SYSTEM AND RELATIONSHIP WITH CLINICOPATHOLOGICAL CHARACTERISTICS, GASTRITIS STAGE AND INTEROBSERVER AGREEMENT

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INTRODUCTION: Atrophic gastritic remains a difficult histopathologic diagnosis with low interobserver agreement. The Operative Link for Gastritis Assessment [OLGA]) has proposed a system for reporting gastritis in terms of stage, which arranges the histological phenotypes of gastritis along a scale of progressively increasing gastric cancer risk [1]. A recently-proposed OLGIM system basically incorporates the same staging frame, but replaces the atrophy with the histological assessment of intestinal metaplasia (IM) alone [2].
AIMS&METHODS: The aim of our study was to compare gastritis staging, clinicopathological characteristic and interobserver agreement in the assessement of gastritis by OLGA and OLGIM systems.
RESULTS: 837 patients were enrolled in the study. Overall, 280 (33.4%) and 167 (19.9%) patients were classified as stage I-IV according to OLGA and OLGIM, respectively. In addition, the stage III-IV was observed in 25 patients staged by OLGA, but in 24 patients staged by OLGIM. Interobserver agreement for atrophic gastritis was moderate in antrum and incisura angularis (respectively, kappa=0.53 and 0.57, $p<0.0001$), but fair for atrophic gastritis assessement in corpus (kappa = 0.38). However, interobserver agreement was almost perfect for intestinal metaplasia assessement both in antrum, incisura angularis and corpus (respectively, kappa=0.82, 0.80 and 0.81, $p<0.0001$).
There was a significant positive correlation between the patient age and gastritis OLGA and OLGIM stage (Rho=+0.34; $p<0.0001$). In addition, there was a weak negative correlation between the serum pepsinogen-1 level, patients's BMI and gastritis OLGA and OLGIM stage.
CONCLUSION: OLGA and OLGIM staging systems correlated with clinicopathological characteristics such serum pepsinogen-1, patient age and BMI. OLGIM staging system characterized with a highest interobserver agreement, however, substantial proportion of potentially high-risk individuals would have been missed if OLGIM staging is applied only. Therefore we recommend to use a combination of OLGA and OLGIM stages in routine clinical reports.
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Disclosure of Interest: None Declared
Keywords: gastritis stage, OLGA staging, OLGIM staging

P434 LONG-TERM THREE-DIMENSIONAL PRIMARY GASTRIC CULTURE UNDER AN AIR-LIQUID INTERFACE ENVIRONMENT

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INTRODUCTION: With advances in stem cell research, molecular markers of stem and early progenitor cells have been discovered in the small intestine and colon. On the other hand, little is known about stem cells in the stomach because of a lack of specific stem cell markers and an in vitro system that allows long-term culture.
AIMS&METHODS: The aim was to produce a culture system that mimics normal gastric epithelial growth and differentiation. Glandular stomach cells from postnatal day 2 C57BL/6J mice were cultured in our three-dimensional (3D) primary culture system. This culture system maintains the cultured cells that are embedded in a collagen gel under an air-liquid interface environment.
RESULTS: Cultured stomach cells showed outer spindle cells and yielded expanding sphere structures, which grew for three months. The wall of cultured gastric spheres consisted of a monolayer of tall columnar cells with round nuclei at the base and mucus cytoplasm. Immunohistochemistry revealed cells that were positive for MUC5AC, demonstrating differentiation into gastric surface mucous cells. Fewer than 1% of the epithelial cells were positive for enteroendocrine cell marker chromogranin A. Ultrastructural examination revealed fully differentiated microstructures in cultured gastric epithelial cells such as microvilli, junctional complexes, and glycogen and secretory granules. Real-time PCR of cultured gastric spheres revealed mRNA expression of MUC5AC and did not show expression of MUC2 and CDX2. These results showed that cultured cells in our 3D primary gastric culture system maintained the characteristics of the stomach without transformation to the intestinal phenotype.
CONCLUSION: In conclusion, we established a 3D culture system to allow long-term culture of primary stomach cells within the stem cell niche. This culture method should be useful for stem cell research and elucidating the cause of gastric diseases.
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Disclosure of Interest: None Declared
Keywords: stem cell, stomach, three-dimensional primary culture

P435 TELOMERE LENGTH IN NON-NEOPLASTIC GASTRIC MUCOSA CORRELATES WITH H. PYLORI INFECTION, DEGREE OF GASTRITIS AND NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) USE

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INTRODUCTION: Telomere shortening occurs with human aging in many organs and tissues and is accelerated by rapid cell turnover and oxidative injury.
AIMS&METHODS: To clarify the clinical importance of telomere shortening in gastric mucosa, we measured average telomere length using quantitative real-time PCR in non-neoplastic gastric mucosa and assessed its relationship to *H. pylori* related gastritis, ulcer disease, and non-steroidal anti-inflammatory drugs (NSAIDs) usageGastric biopsies were obtained from 150 cancer free subjects including 48 chronic NSAIDs users and 102 non-users. Relative telomere length in genomic DNA was measured by determining the ratio of telomere repeat copy number (T) to single copy gene (S) copy number(T/S ratio) in individual samples relative to a reference pooled DNA from healthy blood samples. *H. pylori* infection status, histological severity of gastritis, and serum pepsinogens (PGs) were also investigated**.** E-cadherin (CDH1) methylation status was determined by methylation-specific PCR (MSP)
RESULTS: Average relative T/S ratios of *H. pylori* infected subjects were significantly reduced when compared to *H. pylori* negative subjects (4.03+/-1.96 *vs.* 2.82+/-1.62 mean+/-SD, $p=0.002$). Reduction of relative T/S ratio was closely associated with all histological parameter of gastritis (acute inflammation: $p=0.004$, chronic inflammation: $p=0.0003$, atrophy: $p=0.0002$, and metaplasia: $p=0.002$) and CDH1 methylation ($p=0.0002$). In *H. pylori* negative subjects, NSAIDs users presented significantly reduced relative T/S ratio than non-users ($p=0.028$). Reduction of relative T/S ratio was also associated with gastric ulcer occurrence in all subjects ($p=0.01$) and NSAIDs user ($p=0.009$)
CONCLUSION: Telomere shortening is closely associated with severity of *H. pylori* induced gastritis and CDH1 methylation status. Also, telomere shortening is accelerated by NSAIDs usage especially in *H. pylori* negative subjects.
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Disclosure of Interest: None Declared
Keywords: DNA methylation, *H. pylori*, NSAIDs, Stomach, Telomere length

P436 CORRELATION BETWEEN THE LEVEL OF SYSTEMIC AND ESOPHAGEAL CD4+ T LYMPHOCYTES IN HIV-INFECTED PATIENTS WITH CANDIDA ESOPHAGITIS

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INTRODUCTION: Several studies have shown that HIV infection is associated with depletion of intestinal CD4+ T cells. However, the esophagus mucosal immune dysfunction has not been described yet. It is known that *Candida* esophagitis rises in incidence in HIV-infected patients with blood CD4+T cells count <200 cells/mm^3. It is not known if this correlation is also seen in the level of CD4+ T cells present in the esophageal mucosa.
AIMS&METHODS: Aim: To conduct a comparative analysis of how *Candida* infection affects CD4+ T cells in the esophageal mucosa and to investigate whether this event correlates with the level of CD4+ T cell depletion as measured in the peripheral blood.
Methods: Immunohistochemistry to CD4+ T cells were performed in histological samples obtained from esophageal endoscopic biopsies in a total of 26 HIV-infected patients including 14 HIV-infected patients with *Candida* esophagitis (5 female and 9 male, mean age 44.6 years) and 12 HIV-infected controls (8 female and 4 male, mean age 51 years) with normal esophagus. Immunostained cells were quantified by counting the number of positive cells for each specimen at X400 magnification using a square grid of 0.0625mm^2. The number of positive cells was compared between the two groups using Graph Pad Prism version 5.00 for Windows (Graph Pad software, San Diego, CA, USA) to perform a Mann-Whitney test with the level for significance set at 95%. The blood CD4 lymphocyte count obtained at the time of endoscopy was also analyzed by flow cytometry. The study conformed to the principles of Declaration of Helsinki and Brazilian governement requirements.
RESULTS: Esophageal CD4+ T cell was lower in the group with *Candida* esophagitis (mean 52.96) compared to the control group (mean 74.53). Mean peripheral blood CD4+ T cell count in HIV-infected patients with *Candida* esophagitis was 96.07 (range 9-180) and in the control group was 359.08 (range 165-577). The difference between the level of CD4+ T cell in the blood was statistically significant ($p<0.0001$). However, this difference was not maintained in the CD4+ T cell count in esophageal mucosa ($p=0.6069$)
CONCLUSION: The level of CD4+ T cell in blood was not directly correlated with the severity of CD4+ T cell depletion in esophageal mucosa. Our results did not show a significant difference in the level of esophageal CD4+ T cells between the *Candida* infection and control group. Therefore, CD4+ T cells could not have a decisive role in the immunopathogenesis of *Candida* esophagitis in HIV-infected patients.
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Disclosure of Interest: None Declared
Keywords: aids, esophageal candidiasis, esophageal CD4+ cells, peripheral blood CD4+ cells

P437 PREVALENCE OF AUTOIMMUNE GASTRITIS IN PATIENTS WITH AUTOIMMUNE DISEASE

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INTRODUCTION: Autoimmune gastritis involves the fundus and corpus of the stomach and characterized by the presence of antiparietal cell antibodies (APCA), leading to mucosal atrophy. Earlier reports have shown high prevalence of *autoimmune gastritis in patients with other autoimmune disease*. We aimed to study the prevalence of autoimmune gastritis in different groups of patients with *autoimmune disorders such as autoimmune thyroiditis and* autoimmune hepatitis 1 type, primary biliary cirrhosis, primary sclerosing cholangitis and overlap syndrome, comparing to control group.
AIMS&METHODS: 104 patients with autoimmune thyroiditis (males/females: 14/90, mean age 59, 79) and 23 patients with autoimmune liver disease (males/females: 6/17, mean age 49, 71) were included in this study. 39 patients without autoimmune disease (males/females: 10/29, mean age 48, 09) were in control group. APCA status was evaluated by enzyme-linked immunosorbent assay (ELISA).
RESULTS: This study demonstrated significant difference in APCA status between these three groups of patients. The highest prevalence (52,9%) of autoimmune gastritis was in patients with autoimmune thyroiditis. In patients with autoimmune liver disease, APCA was positive in 30,4% patients, comparing to 23% in control group ($p<0,01$).
CONCLUSION: This study shows significantly higher prevalence of autoimmune gastritis in patients with autoimmune thyroiditis and autoimmune liver disease, comparing to control group. Results of our study sustaining the hypothesis of an overall association between autoimmune diseases, including GI disorders. Apparently, affected by some autoimmune disease, patients have a higher probability of being affected by a second or several autoimmune disorders.
Disclosure of Interest: None Declared
Keywords: antiparietal cell antibodies, autoimmune disease, autoimmune gastritis

P438 THE EFFECT OF PROTON PUMP INHIBITORS ON THE FUNCTION OF NEUTROPHILS AND MONONUCLEAR CELLS

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INTRODUCTION: Proton pump inhibitors (PPIs) are popular and relatively safe drugs. Apart from inhibition of gastric acid secretion potential anti-inflammatory properties of proton pump inhibitors have been suggested. This effect could probably have therapeutic implications but may also predispose to infectious diseases.
AIMS&METHODS: The aim of this study was evaluation of PPIs effect on function of human neutrophils *in vivo*. Thirty patients without accompanying immunodeficiency were enrolled. A proton pump inhibitor was administered orally for 7 days: 15 patients were treated with omeprazole 20 mg per day and 15 patients with pantoprazole 40 mg per day. Total nitric oxide (NO) in the serum and supernatants obtained from polymorponuclear neutrophils (PMN) and peripheal blood mononuclear cells (PBMC) were measured. The expression of inducible nitric oxide synthase (iNOS) and phospho-p38 mitogen-activated protein kinase (MAPK) were estimated by Western blotting. The generation of superoxide anion radicals by the cells was measured using the cytochrome-c reduction test. The cyclic guanosine monophosphate (cGMP) level in the cell supernatant and plasma was assessed using an enzyme-linked immunosorbent assay kit. Reduction test of spontaneous and reduced of nitrotetralizate blue test (NBT) were performed according to the Park method.
RESULTS: Treatment with omeprazole or pantoprazole did not significant changes in serum NO level. A statistically significant increase in the percentages of activated phagocytes (NBT) was found in the group with omeprazole treatment (16.0 *vs* 27.0%; p=0,04), but not in the group with pantoprazole (21.0 *vs* 16.%; ns). No significant differences were observed in neutrophil supernatant NO and cGMP concentration in both groups. We found significant decrease of mononuclear cell supernatant NO concentration after pantoprazole (30.68 *vs* 19.89 mmol/5x10^6 PBMC/ml; p=0,04), but not after omeprazole treatment (17.05 *vs* 19.32 mmol/5x10^6 PBMC/ml; ns). Treatment with PPI's had no effect on neutrophil iNOS, phospho-p38 expression as well as on generation of superoxide anion radical.
CONCLUSION: Treatment with omeprazole but not pantoprazole stimulates reactivity of neutrophils. However, it is not accompanied by activation of cell inflammatory machinery and may indicate neutrophil malfunctioning. On the other hand, treatment with pantoprazole may decrease antimicrobial and cytotoxic capability of mononuclear cells.
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Disclosure of Interest: None Declared
Keywords: function of neutrophils, proton pump inhibitors

P439 GASTRIC MUCOSAL LYMPHOCYTE SUBPOPULATIONS IN SOME VARIANTS OF THE COURSE AND OUTCOME OF CHRONIC INFLAMMATION OF UPPER GASTROINTESTINAL TRACT

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INTRODUCTION: Gastric mucosal lymphocyte subpopulations may play significant role in course and outcome of chronic inflammation of upper gastrointestinal tract
AIMS&METHODS: 36 patients chronic gastritis, erosive-ulcerative conditions and neoplasia of the stomach were examined. H. Pylori absence was confirmed by immunocytochemical method. According to the histological analysis the groups were formed: 1 (n = 17) - chronic non-atrophic gastritis, 2 (n = 7) - chronic atrophic gastritis, 3 - gastric cancer (n = 7), 4 (n = 5) - erosive-ulcerative conditions of gastric mucosa (GM). Lymphocyte subpopulations (CD45CD3CD4CD8, CD45CD3CD (16 +56) HLADR, CD45CD19, CD45CD3$\alpha\beta$TCR$\gamma\delta$TCR, CD45CD95, Beckman-Coulter, USA), infiltrating the GM derived from biopsy using mechanical disaggregation (Medimachine, Decton Dickinson, USA) were examined by multicolor flow cytometric analysis (FC-500, Beckman-Coulter, USA). The gastric mucosal cell proliferative activity was investigated by DNA cytometry (FC-500, Beckman-Coulter, USA).
RESULTS: Substantially in all groups except the 4th in GM CD3 + T-lymphocytes dominated, among which cytotoxic CD3 + CD8 + prevailed, that greatly differed from the ratio of the peripheral blood lymphocyte subpopulations. The ratio of T-helper to cytotoxic T-lymphocytes in 1, 2 and Group 4 was 0.05 to 0.7 relatively, and only in the 3rd group reached 1. Among the intraepithelial lymphocytes in the 3rd and 4th groups a high percentage of "double-positive" T-lymphocytes revealed. The majority of T cells expressed $\alpha\beta$TCR, the number of lymphocytes CD3 + $\gamma\delta$TCR + ranged from 1.5 to 2.5% in the different groups, reliable differences were found between the 2nd and 4th groups. The NK-cell number (CD3-CD (16 +56) +) expressing HLADR was the lowest in group 1 and the maximum in the 3rd and 4th groups. Ratio of B- cells (CD19 +) averaged 7-13%, except group 4, in which it was 5-fold higher. Markers (HLA DR, CD95) were maximal in patients of group 4. The GM cell proliferative activity ranged from 3 to 11% in different groups and was the highest in group 4.
CONCLUSION: The ratio of gastric mucosal lymphocyte subpopulations differs from that in the peripheral blood significantly. Immune responses in all survey groups have particular features, but they are characterized by prevalence of T-cell immune response, with the exception of group 4. In neoplasia disbalance between proliferation and apoptosis was characterized by the highest index of cell proliferation, which combined with the maximum number of lymphocytes expressing the marker of readiness to apoptosis.
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Disclosure of Interest: None Declared
Keywords: chronic inflammation of upper gastrointestinal tract, Gastric mucosal lymphocyte subpopulations

P440 EVALUATION OF PSORIASIS TREATMENT WITH ESOMEPRAZOL - A PILOT STUDY

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INTRODUCTION: Psoriasis is an inflammatory skin disease that affects 1–3% of Caucasian populations and may be persistent, disfiguring and stigmatising.Proton pump inhibitors (PPIs) are potent blockers of gastric acid secretion. They are widely regarded as the agents of choice for the treatment of acid-peptic disorders. In addition to anti-secretory effects, however, PPIs have been found to have anti-oxidant properties and direct effects on neutrophils, monocytes, endothelial, and epithelial cells that might prevent inflammation. Also PPIs inhibit the expression of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) as well as endothelial-dependent neutrophil adhesion. Those anti-inflammatory effects of the PPIs might influence a variety of inflammatory disorders, both peptic and non-peptic, within and outside of the gastrointestinal tract (1,2). There are few reports about PPI treatment in psoriasis
AIMS&METHODS: Aims: To evaluate the treatment of Psoriasis with Esomeprazole. Methods: Adult patients (18 year or more) with Psoriasis were selected. Exclusion criteria included concomitant use of any treatment for Psoriasis, organic diseases, use of other PPI than Esomeprazole. 10 patients were selected and psoriasis was evaluated by Psoriasis Area and Severity Index(PASI). Patients were medicated with Esomeprazole 40mg B.I.D for 90 days. At the 90th Day the patients were again evaluated by PASI. Paired t test was used for statistical analyses
RESULTS: Results:Statisticaly significant results were seen when compared PASI before and at 90Th Day of treatment :(mean +/- SD x mean +/- SD) (5.52 +/- 2,93 x 0.89 +/- 0.74) $p = 0.0002$.At 90th day of treatment most patients presented no erythema, induration or scaling of plaques with >75% fall in the PASI.
CONCLUSION: Conclusion: The use of Esomeprazole for Psoriasis presented excellent clinical results with important reduction of PASI. These preliminary results warrant further larger randomized controlled studies.
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2. Handa O, Inflamm Res,2006
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Disclosure of Interest: None Declared
Keywords: Esomeprazole, proton pomp inhibitor, Psoriasis

P441 BUFFERING AND ANTIREFLUX EFFICACY OF ALGINATE-ANTACID FORMULATION (GAVISCON DOUBLE ACTION LIQUID) IN PATIENTS WITH GERD

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INTRODUCTION: A postprandial "acid pocket" has recently been described and in patients with GERD it shows greater extension. It is postulated that antacids or alginate-antacids might raise the pH locally and so provide relief from this acid pocket, although at present clinical data are ambiguous
AIMS&METHODS: to assess and compare buffering and antireflux efficacy of Gaviscon Double Action (alginate-antacid) and antacid postprandially in patients with GERD.
10 patients with non-erosive GERD (female - 7 male - 3, mean age - 44 ±11,1 yrs) underwent upper GI endoscopy and pH-monitoring. 3 electrode pH-probe was disposed in corpus, cardia and 5-7cm above lower esophageal sphincter, the arrangement was controlled by X-ray. The effect was assessed by 34 hour pH-monitoring: basal and postprandial acid secretion, number and period of acid reflux were evaluated during 24h without drug consumption, on the second day pts were given alginate-antacid Gaviscon Double Action (group 1) and antacid (group 2). After the first dose of drugs buffering property was assessed during 4 h, than drugs were given after meal in 20min 3 times, so the monitoring has been lasted for 10h.
RESULTS: Buffering effect of both drugs has been lasted for 2h and slightly decreased to baseline pH (1,6 - 2,2). The increase of gastric secretion after drug effect ("rebound effect") wasn't observed in both groups. In group 1 number of acid reflux significantly decreased from 63,4±14,2 to 5,4±2,7 (p=0,000), index DeMeester also diminished from 17,51±2,82 to 1,66±1,17 (p=0,000), that demonstrated antireflux properties of alginate-antacid. In group 2 reflux number reduced from 61,2±10,8 to 48,4±11,2, index DeMeester decreased from 15,82±1,8 to 11,69±4,8, though the difference wasn't statistically significant (p=0,103).
CONCLUSION: alginate-antacid Gaviscon Double Action demonstrates buffering and antireflux properties that emphasizes benefit of both antacid and alginate in patients with GERD.
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Disclosure of Interest: None Declared
Keywords: alginate-antacid formulation , GERD, pH-monitoring

P442 UPPER GASTROINTESTINAL EVENT REDUCTION AND CARDIOVASCULAR SAFETY OF ANTIPLATELET THERAPY WITH PA32540, A TABLET WITH ENTERIC-COATED ASPIRIN AND IMMEDIATE-RELEASE OMEPRAZOLE: RESULTS OF TWO 6-MONTH, PHASE 3 STUDIES

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INTRODUCTION: PPIs can significantly reduce aspirin (ASA)-associated GI symptoms that impact adherence to long-term antiplatelet therapy. PA32540 is a coordinated-delivery tablet of immediate-release (IR) omeprazole 40 mg and enteric-coated (EC) ASA 325 mg. We hypothesized that PA32540 would have fewer gastric ulcers (GU) and fewer upper GI events compared with EC ASA while maintaining the cardiovascular (CV) benefits of ASA.
AIMS&METHODS: Two identical phase 3 double-blind multicenter studies enrolled 1,049 subjects prescribed daily ASA at 325 mg for ≥3 months before study enrollment for secondary prevention of CV events. Subjects were randomly assigned to once-daily treatment with PA32540 or EC ASA 325 mg. The primary endpoint was the cumulative proportion of subjects with endoscopically-confirmed GU (defined as a mucosal break ≥3 mm in diameter with depth) at any time throughout 6 months. Endoscopic assessments were performed at screening and at 1, 3, and 6 months. Upper GI events were prospectively defined. Major adverse CV (MACE) were adjudicated by an independent blinded endpoint committee.
RESULTS: Baseline characteristics and results are shown below. The incidences of GU and upper GI events leading to study discontinuation were significantly lower following administration of PA32540 vs EC aspirin alone over 6 months ($p < 0.05$). No significant difference in MACE was identified.
Baseline Characteristics and Results

Table: P442

BASELINE CHARACTERISTIC (Intent-to-Treat Population)	PA32540 (N=524)	ASA (N=525)
Age, mean (SD), y	66.3 (7.5)	65.7 (7.2)
Male, n (%)	375 (71.6%)	374 (71.2%)
Race, n (%)		
White	470 (89.7%)	473 (90.1%)
African American	49 (9.4%)	42 (8.0%)
Other	5 (0.9%)	10 (1.9%)
History, n (%)		
Diabetes	213 (40.6%)	188 (35.8%)
Previous MI	214 (40.8%)	199 (37.9%)
CVD	102 (19.5%)	113 (21.5%)
Concomitant lipid-lowering therapy, n (%)	439_(83.8%)	430_(81.9%)
***RESULTS AT STUDY END*(6 months)**	**(N=524)**	**(N=525)**
Endoscopic GU, n (%)*	17 (3.2%)	45 (8.6%)
Discontinuation due to upper GI event, n (%)*	8 (1.5%)	43 (8.2%)
*P<0.05		

MACE (Safety Population)	PA32540 (N=521)	**ASA (N=524)**
CV death	0	1
Nonfatal MI	5	3
Acute coronary syndrome	0	5
TIA	1	4
Congestive heart failure	1	1
CAD	1	0
Planned CABG	1	0
Subjects with any MACE events	9 (1.7%)	13 (2.5%)[1]

[1]One subject had 2 events

CONCLUSION: PA32540 was associated with fewer GUs and fewer upper GI symptoms compared with EC ASA 325 mg alone, with no increase in serious CV events. The findings have important implications for the use of PA32540 in the long-term management of patients requiring ASA for secondary CV prevention.
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Keywords: Aspirin, Gastroprotection, Proton pump inhibitors, Secondary cardiovascular prevention

P443 PREDICTION OF MORTALITY IN PATIENTS WITH IN-HOSPITAL UPPER NON VARICEAL BLEEDING: A PROSPECTIVE MULTICENTER STUDY IN ITALY.

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INTRODUCTION: Non variceal upper GI bleeding (NVUGIB) that occurs in patients already hospitalized for another condition is associated with increased mortality, but outcome predictors have not been consistently identified.
AIMS&METHODS: To compare outpatients presenting with NVUGIB to in-hospital bleeders (IHB) and to better identify predictors of mortality from NVUGIB in patients suffering from in-hospital bleeding
Secondary analysis of prospectively collected data from two nationwide multicentric databases (PNED). Descriptive, inferential, and multivariate logistic regression models were carried out in 338 inpatients (68.6±16.4 years, 68% males) and 1,979 outpatients (67.8±17 years, 66% males)
RESULTS: Mortality in patients with in-hospital bleeding was significantly higher than outpatients (8.9% vs. 3.8% - OR 2.44 [95%CI 1.57-3.79], p< 0.0001). Predictors of death were hemodynamic instability on presentation, severe comorbidity, (ASA score 3 or 4), past history of peptic ulcer, recurrent bleeding, failure of endosocpic treatment and low dose aspirin use. The impact of these risk factors was different in the two pooulations of in- and outpatients (see table). As a results the predictive accuracy of the model (AUROC) in IHBs was 85.3% vs.74.0% for outpatients, p<0.02.

Hemodynamic instability	7.31 [2.71 - 19.65]	0.000	2.31 [1.17- 4.59]	0.016
ASA score 3 or 4	6.72 [1.87-24.0]	0.003	3.89 [2.33-6.50]	0.000
Low-dose aspirin's use	0.12 [0.02-0.56]	0.008	0.25 [0.11-0.58]	0.001
Past history of peptic ulcer disease	3.18 1.27-7.95]	0.013	1.54 [0.89-2.64]	0.120
Recurrent bleeding	0.71 0.10-4.94]	0.730	5.22 [2.45-11.10]	<0.000
Failed endoscopic treatment	4.38 [0.69-31.9]	0.145	14.29 [5.22-39.17]	0.000
Gastric + duodenal ulcer at endoscopy	3.72 0.77-17.99]	0.101	0.94 [0.12-7.45]	0.958

CONCLUSION: Patients with in-hospital NVUGIB have a significantly higher risk of death, because they are sicker than outpatients admitted for NVUGIB. There are significant differences in both clinical features and treatment patterns between in-patients and outpatients. Predictors of death have a different impact in the two populations.
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Disclosure of Interest: None Declared
Keywords: in-hospital bleeding, mortality rate, risk factors

P446 COMPARISON BENEFIT OF SECOND-LOOK ENDOSCOPY AFTER INITIAL ENDOSCOPIC HEMOSTASIS IN ACUTE PEPTIC ULCER BLEEDING FACTOR ANALYSIS OF RECURRENT BLEEDING

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INTRODUCTION: Endoscopic hemostatic therapy for gastrointestinal bleeding(GIB) is high effectiveness. But rebleeding occurs in 10% to 25% of cases after initial endoscopic hemostasis. Clinical value of a second-look endoscopy after initial endoscopic hemostasis with high-dose proton pump inhibitor(PPI) infusion therapy is controversial.
AIMS&METHODS: We aim to determine whether routine second-look endoscopy is necessary and to assess predictors of rebleeding after initial endoscopic hemostasis and high dose PPI medication. In addition we make a comparison between Rockall score and AIMS65 score.Both endoscopic and clinical data were analyzed in 101 acute peptic ulcer bleeding patients during August 2008 to June 2012. All peptic ulcer bleeding patients were treated with high-dose PPI infusion therapy after initial endoscopic hemostasis. To know the patients who need second-look endoscopy, we analysed predictors of rebleeding in patients with high risk on second-look endoscopy.
RESULTS: The rebleeding rate after first endoscopic hemostasis and high dose PPI infusion was 11.8%(12/101). The preendoscopic predictors of rebleeding were use of NSAIDs(p<0.01), albumin level (p=0.042), complete Rockall score(p=0.043), Forrest type(I,IIa)(p=0.017), transfusion requirements before endoscopic hemostasis(P=0.013). No significant difference was found for the factors of initial hemoglobin, sex, age, systolic blood pressure, diastolic blood pressure, heart rate, INR level, use of antiplatelet drug, anticoagulant drug, diabetes, liver cirrhosis, cardiovascular disease, chronic kidney disease, malignancy ulcer location, ulcer size≥1cm, AIMS65score. In univariated analysis of high risk group (Forrest type I or IIa), liver cirrhosis(p=0.040) and complete Rockall score ≥ 4 point were the risk factors of rebleeding. The Multivariated analysis of high risk group identified complete Rockall score ≥4 as only statistically significant risk factor(odds ratio, 5.123; 95% Cl, 1587-16.542, p=0.006).
CONCLUSION: In this study, complete Rockall score showed higher specificity and AIMS65 score showed higher sensitivity to predict mortality and recurrent bleeding in non-variceal upper gastrointestinal bleeding. However, both scoring system have insufficient predictive power about death and rebleeding(all AUROC < 0.7), so it is necessary to design new scoring system which have far higher sensitivity and specificity in the future.
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Disclosure of Interest: None Declared
Keywords: endoscopic hemostasis, UGI bleeding

P447 INDEPENDENT RISK FACTORS OF 30-DAY OUTCOMES IN PEPTIC ULCER BLEEDING (PUB'S) BY MULTIVARIATE ANALYSES: IS ULCER SIZE A PREDICTOR OF WORSE OUTCOMES WITH CURRENT TREATMENTS?

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INTRODUCTION: Earlier studies report that large ulcer size is a risk factor for PUB rebleeds. However, with changes in medical therapy (high dose IV PPI's) & newer endoscopic hemostasis – NEH, independent risk factors for rebleeding or other 30 day outcomes have not been reported for PUB's.
AIMS&METHODS: In patients with severe PUB's, our purposes were to determine: 1) independent risk factors of 30-day rebleeding, surgery, & death & 2) whether ulcer size alone or in combination with other risk factors is an independent predictor of major outcomes. A large prospectively studied population of patients hospitalized with severe PUB's between January 1993 & December 2011 at our two tertiary care academic medical centers, stratified by stigmata of recent hemorrhage (SRH) & treated optimally (IV high dose PPI & NEH) were included. Using logistic regression model we analyzed independent risk factors of each outcome up to 30 days.
RESULTS: 1264 patients were included. Major SRH were active arterial bleeding in 126 (10%) patients, oozing in 95 (7.5%), non-bleeding visible vessel in 312 (24.7%), & adherent clot in 155 (12.3%). Minor SRH were spots in 110 (8.7%) & 466 (36.9%) patients had clean ulcers. For ulcers 10 mm or larger, the odds of 30 day rebleeding increased 6% per each 10% increase in ulcer size (OR 1.06, 95%CI 1.02-1.10, p=0.0053). Other risk factors of 30-day rebleeding were major SRH, inpatient start of bleeding, & prior GI bleeding. But female gender, any aspirin use, & endoscopic hemostasis were independent protective factors. Ulcer size was not a predictor of 30-day surgery. Major SRH, prior GI bleeding, & cirrhosis were also predictors of 30-day surgery, whereas aspirin & endoscopic hemostasis were protective factors. Risk factors of 30-day death were major SRH, inpatient bleeding, PTT >35 s & cirrhosis. Combined with major SRH, larger ulcer size was a risk factor for death (OR 1.08 per 10% increase in ulcer size, 95%CI 1.02-1.14, p=0.0095).
CONCLUSION: 1. Increasing ulcer size was an independent risk factor of PUB rebleeding in subset with ulcers 10 mm or larger. 2. Combined with major SRH, increasing ulcer size was also a predictor of death.
Disclosure of Interest: None Declared
Keywords: Bleeding peptic ulcer, Endoscopy, Outcomes

P448 LOCAL IMPLANTATION OF ADIPOSE-DERIVED MESENCHYMAL STEM CELLS ENHANCED HEALING OF GASTROTOMY IN AN ANIMAL MODEL

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INTRODUCTION: Mesenchymal stem cells (MSCs) have high plasticity in differentiation and can secret growth cytokines to accelerate healing. This study aims to investigate the effect of local application of ADMSCs in enhancing healing of gastrotomy.
AIMS&METHODS: MSCs were isolated from the adipose tissue of transgenic-GFP SD rats. A 2-cm incision was created at gastric body and subsequently closed with 5-0 interrupted sutures in wild type SD rats. The animals were divided into four treatment groups, including the control, addition of fibrin glue, fibrin glue with MSCs and MSCs implantation groups. For fibrin glue with MSCs, 5×10^6 MSCs in 70 μl PBS were topically applied on the gastrotomy with a layer of fibrin glue. For MSCs group, MSCs were injected around the gastrotomy. The outcomes assessment included pneumatic bursting pressure, histological analysis, expressions of PCNA, IL-6, TGF-β, Cox-2 and VEGF, and MSCs differentiation.

RESULTS: The gastrostomies in MSCs injection group can withstand significantly higher pneumatic bursting pressure on postoperative day 3 and 5 (P=0.001)(Fig 1 and 2). Histological analysis showed that MSCs injection group had less inflammatory cell infiltration, earlier onset of granulation, epithelialization and more collagen at gastrotomy compared with control and fibrin glue groups. The expression of IL-6 was reduced from day 3 to 7 for MSCs injection group. In contrast, there was a significant increase in IL-6 from day 3 to 7 for the control and fibrin glue groups. Compared with other groups, PCNA and TGF-β expressions were significantly higher in MSCs injection group (MSCs injection vs. control group, PCNA expression: P=0.001 for 3 days, TGF-β expression: P=0.01 and 0.001 for 3 and 5 days, respectively). At 14 and 21 days, MSCs were observed at the gastrotomy with a spindle shape with expression of α-SMA, which indicated the differentiation into muscle cells.
CONCLUSION: : Direct implantation of MSCs can hasten the healing of gastrotomy through enhancing the process of granulation and epithelialization. The results of this study will provide basis for clinical application of MSCs to improve healing of gastrotomy after Natural Orifices Transluminal Endoscopic Surgery.
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Disclosure of Interest: None Declared
Keywords: Healing, stem cell, stomach

P449 PREVALANCE AND INVESTIGATIONAL PATHWAYS OF PATIENTS WITH CONSTIPATION PREDOMINANT IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Our group has previously described investigational pathways that occur in patients with diarrhoea predominant irritable bowel syndrome (IBS-D). Currently, there is a paucity of work undertaken in either primary or secondary care evaluating patients with constipation predominant irritable bowel syndrome (IBS-C).This study evaluates the population prevalence of IBS-C, determining also the investigational pathways that occur in these patients.
AIMS&METHODS: We prospectively collected data from 3 groups of patients between April 2005 and November 2012. Group 1 (n= 1002) were healthy volunteers, Group 2 (n=64) were patients fulfilling Rome III criteria for IBS-C, with Group 3 (n=403) being patients fulfilling Rome III criteria for IBS-D. In Group 1 the prevalence of IBS and its differing subtypes (IBS-D, IBS-C, mixed IBS (IBS-M) and unspecified IBS) were determined using the Rome III Diagnostic Questionnaire. In groups 2 and 3, demographic data and diagnostic yield of any investigations undertaken as part of the diagnostic workup were evaluated. Statistical analysis was performed using SPSS version 17.0 (SPSS Inc, Chicago, IL) with Fisher's exact test used to compare categorical data, and an unpaired T-test used to compare continuous data
RESULTS: IBS prevalence in healthy volunteers (Group 1) was 6% (60/1002), with 80% being female ($p<0.0001$).Mixed IBS was the most common IBS subtype (Table 1), with IBS-C patients being significantly older than other patients with IBS (mean age 45 vs 30 years, p=0.027). When comparing Groups 2 and 3, patients with IBS-C underwent a total of 56 additional investigations (including radiological, endoscopic investigations, breath tests, SeHCAT scan, faecal pancreatic elastase), significantly lower than the number of investigations undertaken in the IBS-D group of 885 ($p<0.001$). Whilst further investigations in Group 3 identified an alternative diagnosis to IBS-D in 25%, the 56 additional tests undertaken in Group 2 did not help establish an alternative diagnosis to IBS-C in any of the patients.
Table 1: Prevalence rates of differing types of IBS in Group 1 (n=1002)

Subytype of IBS	Number of Patients	Prevalence (%)	Sex (F:M)	Mean Age	Standard Deviation
IBS-D	14	1.4	7:7	32	18
IBS-C	7	0.7	6:1	45	21
IBS-M	27	2.7	24:3	32	15
Unspecified IBS	12	1.2	11:1	25	7

CONCLUSION: This is the first study to evaluate the population prevalence of differing IBS subtypes within a UK population. Whilst, further investigation of IBS-D patients may lead to an alternative diagnoses and instigation of an appropriate management strategy, the merits of further investigation in IBS-C patients is to be questioned.
Disclosure of Interest: None Declared
Keywords: constipation, Irritable bowel syndrome

P450 ANXIETY IS DRIVING DYSPEPSIA AND GASTROOESOPHAGEAL REFLUX SYMPROMS IN THE GENERAL POPULATION – THE KALIXANDA STUDY 10 YEAR FOLLOW-UP

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INTRODUCTION: Functional dyspepsia (FD) is associated with anxiety but longitudinal follow-up studies in the general population are not available.
AIMS&METHODS: We aimed to define if anxiety and depression are associated with FD (Rome III definition) and gastro-oesophageal reflux symptoms (GORS) in a population based follow-up study.
The participants (n=3000) were randomly selected from the national population register and surveyed by validated abdominal symptom questionnaire and by hospital anxiety and depression scale (HADS) in 1998. 1000 individuals were then randomly selected 1998-2001 for oesophagogastroduodenoscopy. All eligible subjects from the endoscoped cohort (n=887) were invited to a follow-up study in June-August 2010 with the same questionnaires. The data was analyzed by logistic regression for correlated data (GEE) and by logistic regression in longitudinal analysis.
RESULTS: 703 (79.3%) completed the questionnaires at follow-up. FD was reported by 110 (15.6%) at the baseline and by 93 at follow-up (13.3%); 48 were new cases. GORS without organic disease was reported by 185 indivuals (26.3%) at the basic study and by 203 individuals (28.9%) at follow-up. 75 were new cases. Anxiety was associated with FD (OR 3.14; 95% CI 1.38-7.15) and with GORS (OR 2.58; 95% CI 1.19-5.58) in longitudinal analysis. Anxiety at baseline was associated with new onset FD at follow-up (OR 4.33; 95% CI 1.27-14.82) but not with GORS. Low level of anxiety at follow-up was not linked with loss of FD or GORS.
CONCLUSION: Anxiety is linked with ongoing FD and GORS. Anxiety at baseline is associtaed with new onset FD.
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Disclosure of Interest: None Declared
Keywords: Anxiety, Functional dyspepsia, gastro-esophageal reflux

P451 CHANGE IN DNA METHYLATION PATTERN OF SLC6A4 IN THE GASTRIC MUCOSA MAY HAVE A ROLE FOR DEVELOPING FUNCTIONAL DYSPEPSIA

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INTRODUCTION: The neurochemical serotonin (5-HT) is an important signaling molecule in the gastrointestinal motor and sensory functions. A key regulator of 5-HT levels is the transmembrane serotonin transporter (5-HTT; SLC6A4) that governs the reuptake of 5-HT. Recent studies have indicated 5-HTT expression may be regulated by epigenetic mechanisms.
AIMS&METHODS: We investigated DNA methylation status of *SLC6A4* gene in the gastric mucosa from functional dyspepsia (FD) because of their potential role in dyspeptic symptoms. Endoscopic gastric biopsies were obtained from 78 subjects with no upper abdominal symptoms (mean age, 59.8+/-1.64 SE; female / male, 33/45) and 79 patients with FD (mean age, 57.0+/-1.72 SE; female/male, 42/37). The FD patients consisted of 43 patients with EPS, 24 patients with PDS, and 12 patients with having both EPS and PDS according to the Rome III classification. Bisulfite Pyrosequencing was carried out to determine the methylation status of promoter CpG islands (PCGIs), promoter non CpG islands (PNCGIs) and gene body non CpG islands (NPNCGIs) in the *SLC6A4* gene. Gene expression was examined by real-time PCR.
RESULTS: Methylation level of *SLC6A4* in the gastric mucosa was lowest in PCGIs (5.1+/- 0.29%) and highest in NPNCGIs (60.4+/-1.1%), while PNCGIs presented intermediate methylation level (20.9+/-0.64%). Methylation level of PCGIs and PNCGIs were positively correlated (R=0.22, p=0.005), while inverse correlation in methylation level was found between PCGIs and NPNCGIs (R=-0.59, $p<0.0001$). In overall, methylation level of PCGIs was significantly lower in FD compared to control subjects (4.5+/-0.3% vs. 5.7+/-0.5%, p=0.04). Methylation level of PNCGIs was also tended to be lower in FD compared to controls (19.7+/-0.8% vs. 22.0+/-1.0%, p=0.08). On the other hand, methylation level of NPNCGIs was significantly higher in FD compared to control subjects (62.9+/-1.6% vs. 58.0+/-1.6%, p=0.03). Lower methylation level in PNCGIs was highlighted in the patients with PDS (p=0.01), while higher methylation level in NPNCGIs was more prominent in the patients with EPS (p=0.017). Methylation levels of PCGIs and PNCGIs were inversely correlated, while methylation levels of NPNCGIs was positively correlated with *SLC6A4* mRNA levels in the non-neoplastic gastric mucosa and gastric and colorectal cancer cell lines.
CONCLUSION: Our data suggest that change in DNA methylation pattern of *SLC6A4* in the gastric mucosa may have a role for developing FD. A role of epigenetics for developing FD needs do be further evaluated.
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Disclosure of Interest: None Declared
Keywords: DNA methylation , functional dyspepsia, SLC6A4

P452 EXPRESSION AND FUNCTION OF SLC26A9 MEMBER OF THE SLC26 ANION TRANSPORTER FAMILY IN THE GASTROINTESTINAL TRACT

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INTRODUCTION: We recently identified Slc26a9 as an anion conductance that is upregulated in airway inflammation and prevents bronchial mucus obstruction (Anagnostopoulou et al. JCI 2012). Slc26a9 variants were recently found associated with meconium ileus in cystic fibrosis infants (Sun et al. Nature 2012).
AIMS&METHODS: The association with meconium ileus raises the question where Slc26a9 is expressed in the gastrointestinal tract and what is its function. Acid, HCO_3^-, short circuit current (Isc) measurements were performed in isolated mucosa and acid, HCO_3^- and fluid absorptive and secretory rates were measured by single pass perfusion and back titration in anesthetized Slc26a9 KO and WT mice by inhalation of 2.0% isoflurane. Slc26a9 cellular expression was studied by laser dissection and qPCR, and quantitative morphometry was performed in the different segments of the murine Gastrointestinal tract.

RESULTS: Slc26a9 was found highly expressed in the mucosae of the upper gastrointestinal tract, with abrupt decrease of expression levels to virtually undectable levels beyond the duodenum. As previously reported, Slc26a9 KO mice had completely lost the ability to secrete acid in adulthood. However, Slc26a9 was found highly expressed along the whole gastric gland, even in areas without H^+,K^+-ATPase expression. Proximal duodenal bicarbonate and fluid secretory rates, which are higher in the proximal than the distal duodenum in WT mice, as well as the ability to stimulate these rates with forskolin, were reduced in the absence of Slc26a9 expression. The gastric antrum, as well as the fundus (after omeprazole treatment to rule out any residual acid secretory capacity) was studied to test whether Slc26a9 transports HCO_3^- itself. Gastric antrum, while expressing high Slc26a9 levels in WT mice, had lower basal and forskolin-stimulated HCO_3^- rate as well as lower Isc response in WT than KO mice, arguing against a role of Slc26a9 as a HCO_3^- transporter. Morphometry revealed strongly elongated fundic as well as antral glands, and slightly elongated proximal duodenal villi as well as crypts
CONCLUSION: Slc26a9 expression is necessary for normal gastric acid and proximal duodenal bicarbonate secretion, but it is not expressed in more distal parts of the gastrointestinal mucosa. The increased risk for meconium ileus may be due to loss of digestive function of the stomach and proximal duodenum.
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Disclosure of Interest: None Declared
Keywords: acid and bicarbonate secretion, anion channel, Slc26a9 , upper gastrointestinal tract

P453 EARLY RESULTS OF PERORAL ENDOSCOPIC MYOTOMY USING HYBRID KNIFE TM VS LAPAROSCOPIC HELLER'S MYOTOMY FOR ACHALASIA CARDIA

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INTRODUCTION: Laparoscopic Hellers's cardiomyotomy (LHM) is an established treatment for achalasia cardia. Recently endoscopic myotomy (POEM) has been described as a promising technique with good short term results. Hybrid knife is supposed to shorten the procedure time of POEM. We compared the technical and early functional results of the POEM and LHM.
AIMS&METHODS: Data was collected prospectively for all patients of achalasia cardia. Endoscopy, high resolution manometry and barium swallow was done in all patients to confirm the diagnosis of achalasia cardia. POEM was performed under general anaesthesia using C02 insuffilation . Both the creation of submucosal tunnel and myotomy was done using hybrid knife (ERBE Elektromedizin, GmbH, Germany) capable of injecting and cutting with the same instrument. LHM was done using 4 ports along with anterior Dorr fundoplication . Technical results of both the procedures are given in table.
RESULTS: There were 12 POEM and 20 LHM procedures done in the period 2009 to 2012. The technical and functional results are shown in the table. There was no significant difference in the technical and functional success rates in the two groups. Two patients in the POEM group developed reflux symptoms while one patient in the LHM group developed severe reflux following removal of wrap (due to dysphagia). Two patients in the LHM group required reintervention, one for severe chest pain and other for severe dysphagia. One patient in the POEM developed pneumoperitomeum and pneumomediastinum after the procedure and was treated conservatively. Procedure time and length of hospital stay were significant longer for LHM group (Table).

	POEM	Hellers Cardiomyotomy	p value
Total No. of patients	**12**	**20**	
Mean Eckardt's dysphagia score	**8.1**	**9.2**	
Pretreatment	**1.8**	**1.6**	
Post treatment.			
Technical success rate	**12/12**	**19/20 (95 %)**	
Functional success rate	**12/12**	**17/20 (85 %)**	**0.274**
LES Pressure mm Hg (Mean)	**50.73**	**52**	
Pretreatment	**16.18**	**18**	
Post treatment			
Length of Myotomy (cms)	**10**	**8**	
Mean procedure time (Min)	**65**	**111.5**	**0.0006**
Complications	**1**	**2**	**1.000**
1. **Mucosal tear**	**0**	**0**	**0.375**
2.**Significant blood loss**	**1**	**0**	
3.**Pneumoperitoneum/ Pneumomediatinum**	**0**	**0**	
4.**Death**			
Mean duration of hospital stay (Days)	**2**	**4**	**0.0004**

CONCLUSION: Both POEM and LHM have excellent short term results. However, the procedure time and length of stay were significantly longer for LHM group in our study. It is possible that the use of Hybrid knife reduces the procedure time of POEM.
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Disclosure of Interest: None Declared
Keywords: achalasia,, manometry, POEM

P454 A SURVEY OF THE PREVALENCE AND CHARACTERISTICS OF UNINVESTIGATED DYSPEPSIA IN CHINESE COLLEGE STUDENTS

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INTRODUCTION: Dyspeptic symptoms, defined as the presence of symptoms considered to originate from the gastroduodenal region. Epidemiological studies suggest that uninvestigated dyspepsia (UD) is common. However, there is little data on the prevalence of UD and its overlap with other gastrointestinal diseases in the college student population. The aim of this survey was to investigate UD in college students in the Zhejiang province.
AIMS&METHODS: A total of 2520 college students completed a questionnaire. The diagnosis of UD and irritable bowel syndrome (IBS) was based on the Rome-III criteria. Gastroesophageal reflux disease (GERD) was defined as episodes of heartburn and/or acid regurgitation that occurred at least once a week. General items, such as gender, age and body mass index (BMI), were also included in the questionnaire.
RESULTS: A total of 2520 students were interviewed, and 650 students were excluded due to incomplete questionnaire responses. A total of 1870 students (967 males, mean age 21.34 years) completed the questionnaire. The incidence of UD was higher in females and in senior students. The prevalence of UD, IBS, GERD, UD+GERD overlap and UD+IBS overlap was 108 (5.67%), 129 (6.89%), 17(0.91%), 12 (0.64%) and 18 (0.96%), respectively.
CONCLUSION: The prevalence of UD in college students from the Zhejinag province was 5.67% in this study. Symptoms of dyspepsia occurred most frequently in females and in more senior students. The majority of those affected had postprandial distress syndrome. Overlaps were present, not only between UD and IBS, but also between UD and GERD.
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Disclosure of Interest: None Declared
Keywords: college student, Dyspepsia, gastroesophageal

P455 CLINICAL RELEVANCE OF INEFFECTIVE OESOPHAGEAL MOTILITY IN SECONDARY PERISTALSIS OF PATIENTS WITH GORD

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INTRODUCTION: Secondary peristalsis contributes to oesophageal clearance for retained food bolus and refluxate. Ineffective oesophageal motility (IOM) is common in patients with gastro-oesophageal reflux disease (GORD). We aimed to investigate the hypothesis whether the presence and severity of IOM would affect the physiological characteristics of secondary peristalsis in patients with GORD.
AIMS&METHODS: We aimed to investigate the hypothesis whether the presence and severity of IOM would affect the physiological characteristics of secondary peristalsis in patients with GORD. Secondary peristalsis was performed with slow and rapid air injections into mid-oesophagus of IOM patients and age matched control subjects. IOM severity was defined according to the presence of oesophageal transit abnormalities by application of combined multichannel intraluminal impedance and manometry (MII-EM) with liquid and viscous swallowing, including those without functional abnormalities (i.e., normal bolus transit for both liquid and viscous, IOM-N), and with functional abnormalities (i.e., abnormal bolus transit for liquid and/or viscous, IOM-A).
RESULTS: Eighteen GORD patients with IOM and 15 control subjects participated in this study. IOM patients were further categorized into those with IOM-N ($n = 11$) and IOM-A ($n= 7$). Secondary peristalsis during slow air distension was triggered less frequently in patients with IOM-A (43%) and IOM-N (75%) when compared with control subjects (100%) (both $P < 0.01$), and the difference also occurred between IOM-A and IOM-N ($P < 0.05$). The frequency of secondary peristalsis induced by rapid air distension was significantly lower in IOM-A patients compared to both control subjects (40% vs. 100%, $P < 0.001$) and IOM-N patients (40% vs. 75%, $P = 0.02$). The threshold volume for inducing secondary peristalsis by slow and rapid air distensions didn't differ between control subjects and IOM patients. There were no differences in pressure wave amplitude and duration of secondary peristalsis between control subjects and IOM patients during slow and rapid air distensions.
CONCLUSION: The data suggest that IOM may predispose to impaired activation of secondary peristalsis, but have no effect on motility characteristics of secondary peristalsis. Increased IOM severity is associated with defective triggering of secondary peristalsis which may further impair osophageal clearance.
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Keywords: gastro-oesophageal reflux disease, ineffective oesophageal motility, secondary peristalsis

P456 PRESERVED PROXIMAL STOMACH RESPONSE TO FOOD IN THE HEALTHY, ASYMPTOMATIC ELDERLY.

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INTRODUCTION: It has been suggested that ageing is associated to reduced proximal stomach relaxation in response to food ingestion and impaired gastric accommodation, which might originate upper gastrointestinal symptoms impairing food ingestion and therefore contribute to malnutrition[1-3]. Nevertheless, studies of the process of gastric accommodation after food ingestion in the healthy elderly are scarce, and the frequency of postprandial slow phasic contractions of the proximal stomach in this particular group has not been studied so far.
AIMS&METHODS: This work aimed at both assessing postprandial gastric accommodation and measuring the frequency characteristics of the phasic contractions of the proximal stomach in healthy, asymptomatic elderly volunteers, in comparison to a control group of younger adults. Nine healthy elderly volunteers (5 female) aged 62-70 years and 14 young healthy adults (7 female) aged 21-33 years were included in the study. After fasting overnight, volunteers ingested a standard liquid nutrient test meal (360 mL; 400 Kcal) labeled with Technetium-phytate. Dynamic acquisitions of anterior and posterior images of the stomach were carried out with a gamma camera during meal ingestion and for 10 min thereafter. The values for the area under the activity *versus* time curve for both the proximal and the total stomach were determined, which allowed the calculation of the proportion of the total intragastric activity retained in the proximal stomach, as a measure of gastric accommodation. The dominant frequency of phasic oscillations of the proximal stomach in the study period was determined using Fast Fourier Transform after digital signal processing (MatLab; Mathworks Inc.).
RESULTS: There were no significant differences between groups concerning proximal stomach postprandial function. Indeed, meal residence in the proximal stomach in proportion to that found in the total stomach were similar in both groups (52 ± 14% vs. 48 ± 7%; $p > 0.90$). Also, there were no differences between groups concerning the dominant frequency of proximal stomach slow phasic contractions (1.18±0.44 versus 1.05±0.28; $p > 0{,}90$).
CONCLUSION: Our data do not provide evidence that ageing significantly influences gastric accommodation. It is therefore unlikely that the effects of ageing on proximal stomach motor response to food ingestion are of substantial physiological or clinical significance.
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Keywords: ageing, gastric accomodation, gastric motility

P457 WHAT IS THE TECHNIQUE FOR MEASURING THE LOWER ESOPHAGEAL SPHINCTER PRESSURE THAT BEST CORRESPONDS WITH THE ESOPHAGEAL SYMPTOMS?

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INTRODUCTION: Introduction: Esophageal motor patterns recorded in manometry are defined according to pre established criteria for liquid swallowing. However, there are no internationally accepted benchmarks to analyze the variables and the methods for evaluating lower esophageal sphincter (LES) pressure are still controversial.
AIMS&METHODS: Aims:1. Compare five techniques for measuring the pressure of the LES. 2. To evaluate whether any of them is more useful to explain the symptoms. Methods: We included adults patients who underwent esophageal manometry (EM) for dysphagia and/or heartburn at the Gastroenterology Hospital Motility Lab between for one year.Design: Retrospective, observational, comparative and cross sectional study. Dysphagia and heartburn symptoms were collected from medical records. Manometric tracings were evaluated as follows: Stationary measurements (M) during 10 swallows: M1: average of swallows and inter-swallow interval pressures; M 2: average of inter swallows interval pressures. Slow withdrawal measurements: M 3: average pressure of 4 channels. M 4: Average measures 1 + 3; M 5: Average measures 2 + 3. Statistical analysis: Medcalc 11.21.1.0, ANOVA test.
RESULTS: Results: A total of 120 records were reviewed and finally 104 patients were included, 81 were male (67%), mean age: 51 years (range: 18-81). Symptoms recorded were dysphagia: 25% (n=26), heartburn 33%(n=34) and dysphagia and heartburn 42%(n=44). We evaluated patients with a single symptom. Manometric diagnoses no statistically significant differences were found between the five techniques for measuring the LES pressure in patients with dysphagia (pNS). Statistically significant differences were observed between the five techniques in patients with heartburn (<0.0001). 2. M 1 was more accurate and useful to explain heartburn symptoms.
CONCLUSION: Conclusions: In our study the different techniques for measuring the LES pressure showed no differences in patients with dysphagia, but evidenced different values in patients with heartburn. "M 1" technique, as was called by our team, was the more accurate to explain this symptom. This evidence could help to improve patients diagnostic approach. Limitation: the pressure at the end of expiration was not measured according to standard practice in our laboratory as we consider that it has no clinical relevance in the physiology of the studied conditions.

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Disclosure of Interest: None Declared
Keywords: esophageal manometry, lower esophageal sphincter pressure

P458 CHARACTERISTICS OF ESOPHAGEAL INVOLVEMENT IN SCLERODERMA

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INTRODUCTION: Esophageal involvement is frequent in scleroderma.
AIMS&METHODS: Aim: To precise clinical, endoscopic, pH-metric and manometric features of esophageal involvement in systemic sclerosis (SSc).
Methods: This study was prospective and concerned 227 patients with SSc classified by the 1980 American College of Rheumatology criteria and the 2001 Leroy and Medsger criteria. Mean age was 39,7 ± 13,2 years and sex-ratio of 0,13. Gastroesophageal endoscopy and esophageal manometry were performed in all the cases and a 24-hour esophageal pH monitoring in 89 cases.
RESULTS: Esophageal symptoms were present in 121 cases (53.3%) and were signs of GERD or dysphagia respectively in 98 (43.2%) and 93 patients (40.9%). Reflux esophagitis was found in 76 cases (33.4%); it was mild or moderate in 49 cases (A or B of LA classification) (21.6%) and severe (C or D LA) or complicated with stenosis and/or Barrett esophagus in the remaining cases. Esophageal pH-metry revealed a pathologic acid reflux in 59 cases (66.3%), more often in presence of esophagitis than in its absence: 34 (92%) vs 25 (48%): $p < 0.001$. Rate of acid reflux was also more important in cases with reflux esophagitis : mean percentage of time at $pH < 4/24h = 23 \pm 19$ vs 11 ± 14: $p < 0.001$. Esophageal motor disorders (EMD) and lower esophageal sphincter (LES) incompetence were present respectively in 169 cases (74.4%) and 126 (55.5%). Presence of EMD was not related to age, gender or duration of the disease, but to presence of esophageal complaint and/or reflux esophagitis.
CONCLUSION: Esophageal involvement is frequent in scleroderma. It's symptomatic in 50% of cases and is complicated by a reflux esophagitis in more than 1/3 of cases. EMD, frequent in all forms of SSc, are constant in that with reflux esophagitis.
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Disclosure of Interest: None Declared
Keywords: esophageal motor disorders, GERD, systemic sclerosis

P459 BOTULINUM TOXIN INJECTION FOR SPASTIC AND HYPERTENSIVE ESOPHAGEAL MOTILITY DISORDERS: SAFETY AND EFFICACY

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INTRODUCTION: Esophageal motor disorders such as spastic or hypertensive peristaltic disorders are a rare cause of dysphagia and chest pain. Medical treatment options are limited. Endoscopic botulinum toxin injection (BTX) has been proposed to treat diffuse esophageal spasm (ref 1). It is known as an easy and safe procedure.
AIMS&METHODS: The purpose of this retrospective study was to evaluate the tolerance and the efficacy of BTX in patients with spastic and hypertensive esophageal motility disorders as classified according to the Chicago classification (ref 2) for high resolution manometry (HRM). All patients with spastic or hypertensive motility disorders in HRM and treated with esophageal BTX at 2 different institutions, were included in the study. HRM recordings were systematically re-analyzed and a patient's phone survey was conducted.
RESULTS: 46 patients (23 men, mean age 66 years, range 28-87) with type III achalasia (n=22), Jackhammer esophagus (n=8), distal esophageal spasm (DES) (n=9), and others (n=7), unresponsive to medical therapy, were included. Patients presented with dysphagia (100%), weight loss (65%, mean 8 kg [2-18]) and chest pain (50%). They underwent one BTX session with 80 to 100 IU of Botox° (Allergan) diluted in 10 mL of saline solution into the lower esophageal sphincter (LES) and/or at the lower third of the esophagus.
Safety. Chest pain was reported in 13 cases (28%), requiring morphine administration in 3 cases, and disappeared in less than 7 days in all cases. Two serious adverse effects occurred (4%): aspiration pneumonia, and death following surgery-requiring mediastinitis 3 weeks after BTX. No complication occurred in the remaining 31 cases (68%).

Efficacy. The efficacy was evaluated in 43 patients (2 lost of follow-up, one death). Thirteen patients (28%) did not exhibit any symptom improvement or it lasted less than 2 months. A significant short-term response (symptom-free for more than 2 months) was obtained in 30 cases (65%): 6 Jackhammer (75%), 7 DES (78%), 13 achalasia (59%), 4 others (57%). Twenty-four (52%) remained asymptomatic for more than 6 months: 5 Jackhammer (62%), 5 DES (55%), 11 achalasia (50%), 3 others (43%). Mean symptom-free period in these patients was 14 months [6-23].

CONCLUSION: BTX into the LES and/or lower third of esophagus appears effective in spastic and hypertensive esophageal motility disorders with symptom improvement in 65% of patients. However, severe adverse effects might occur. Prospective randomized trials are required to identify which disorders are likely to benefit the most from BTX treatment, and how safety may be improved.

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Disclosure of Interest: None Declared

Keywords: botulinum toxin injection, Diffuse esophageal spasm, high resolution manometry, hypertensive esophageal motility disorders, Jackhammer, Mediastinitis

P460 UNDERSTANDING THE CAUSE OF PERSISTENT GERD SYMPTOMS DESPITE PROTON PUMP INHIBITOR THERAPY: IMPEDANCE-PH MONITORING REVISITED.

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INTRODUCTION: Patients with persistent reflux symptoms despite proton pump inhibitors (PPIs) and a normal gastroscopy pose a challenge. Impedance-pH (MII-pH) clarifies the symptom profile and evaluates patients objectively for acid-reflux (AR) and non-acid reflux (NAR).

AIMS&METHODS: ***Aim***: Evaluate MII-pH characteristics in PPI non-responders. ***Methods:*** Between January 2009-December 2012, consecutive patients with persistent typical reflux symptoms (group 1); atypical symptoms(group 2) and non-cardiac chest pain (NCCP, group 3) underwent 24 hour MII-pH study after PPI washout for 2 weeks. Abnormal MII-pH study was defined by (1)esophageal acid exposure time (AET)>4.2%; bolus exposure (BE>1.4%), high reflux numbers (RE>73) and/or a positive symptom index (SI ≥50%) and/or symptom association probability (SAP ≥95%). The prevalence of abnormal AET and MII-pH parameters between groups was compared by chi-square and student t-test.

RESULTS: 150 patients (60M, mean age 45.5± 12.8) were studied (Table 1). Group 1 patients had significantly more symptomatic AR and NAR events ($p<0.05$) compared to groups 2 and 3 and increased proximal RE compared to group 3 ($p<0.05$). Patients with a positive symptom association for AR events were more likely to have abnormal BE (p=0.01) and abnormal reflux numbers($p<0.05$).

	Group 1 Typical (N=24M,24F)	Group 2 Atypical (N=31M,48F)	Group 3 Non cardiac chest pain (N=5M,18F)
Raised AET	4/48 (8.3%)	11/79(13.9%)	1/23(4.3%)
No. of AR events (mean, SEM)	24.3 ± 3.3	21.4 ± 2.2	18.6 ± 3.2
No. of NAR events (mean, SEM)	30.9 ± 4.8 *p<0.05 compared to groups 2 and 3*	23.8 ± 1.6	18.4 ± 2.4
No of proximal reflux events (mean,SEM)	29.7± 3.9 *p<0.05 compared to group 3*	23.8 ± 1.8	18.4 ± 3.4
Acid Clearance Time (mean, SEM)	70.5 ± 10.1 *p<0.05 compared to group 2*	111.5 ± 18.1	99.8 ± 30.4
Bolus Clearance Time (mean, SEM)	11.0 ± 0.8 *p<0.05 compared to group 2*	13.7 ± 0.7	11.5 ± 1.0
Positive symptom association for acid reflux	22/48(45.8%) *p<0.05 compared to groups 2*	20/79 (25.3%)	7/23(30.4%)
Positive symptom association for non-acid reflux	25/48 (52.1%) *p<0.05 compared to groups 2 and 3*	30/79(38.0%)	0/23 (0.0%)

CONCLUSION: Both AR and NAR events account for persistent symptoms in PPI non-responders, especially patients with typical reflux symptoms. Therapies beyond PPI may be necessary.

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Disclosure of Interest: None Declared

Keywords: Impedance-pH, Non-acid reflux

P461 IMPEDANCE-PH REFLUX PATTERNS AND POSITIVE SYMPTOM ASSOCIATION PREDICT THE PRESENCE OF MICROSCOPIC ESOPHAGITIS IN NON-EROSIVE REFLUX DISEASE PATIENTS

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INTRODUCTION: Microscopic esophagitis (ME) is frequently encountered in patients with erosive and non-erosive reflux disease (NERD). Recently, this histological finding has been regarded as the potential main mechanism in symptom generation in NERD. Impedance and pH (Imp-pH) testing detects both acid and non-acid reflux and is useful for evaluating symptom-reflux association and overall reflux patterns.

AIMS&METHODS: To determine whether any symptom association or reflux pattern was associated with ME in patients with NERD.

We evaluated 84 (39M/45F; mean age 45) consecutive patients with NERD while off-PPI therapy. During upper endoscopy multiple biopsies were taken at Z-line and 2 cm above it. Basal cell hyperplasia, papillae elongation, dilation of intercellular spaces and eosinophil (Eos) intraepithelial infiltration were measured [0 (absent), 1 (mild or 1=1 Eos), and 2 (marked or 2=>1 eos/HPF)] on hematoxylin–eosin-stained slides by two expert and blinded pathologists. A global score (GS) was calculated by summing up all the scores and dividing by the number of assessed lesions and was considered positive for ME when >0.35. Within 3 days from endoscopy, patients underwent impedance-pH testing. We measured esophageal acid exposure time (AET), mean acid clearance time (MACT), number of impedance-detected reflux episodes (acid, nonacid) and symptom association probability (SAP; positive if ≥95%).

RESULTS: Reflux characteristics are summarized in the Table (univariate analysis). Overall, multivariate analysis showed that the factors associated with the presence of ME were: a positive symptom association probability [OR 3,485 (95%CI 1,045-11,626; p=0,0423], a prolonged MACT [OR 4,322 (95%CI 1,473-12,678; p=0,0077] and an abnormal number of total reflux events [OR 3,485 (95%CI 1,029-8,833; p=0,0443].

Reflux Features (upper limit of normal value)	Median Values (range) **Whole population (n=84)**	Patients with Abnormal Values n (%) **Patients with ME (n=47)**	Patients with Abnormal Values n (%) **Patients without ME (n=37)**	*p value*
Total AET, % (n=4,2%)	2.8 (0.7-5.1)	19 (40%)	6 (17%)	0.0235
MACT total, sec (n=85)	69 (29-125)	27 (57%)	8 (22%)	0.0009
GER total, n (n=54)	51 (35-77)	29 (62%)	9 (24%)	0.0006
Proximal Reflux, n (n=30)	22 (13-47)	23 (49%)	7 (19%)	0.0044
SAP+ all reflux	61	41 (87%)	20 (54%)	0.0007

CONCLUSION: While confirming the importance of acid clearance in favouring the presence of esophageal microscopic damage in patients with NERD, impedance-pH data emphasize the major role of overall reflux episodes in promoting these histological lesions and further support the relevance of ME in symptom generation.

Disclosure of Interest: None Declared

Keywords: GERD, impedance-pH monitoring, Microscopic Esophagitis

P463 THE PROXIMAL EXTENT OF WEAKLY ACIDIC LIQUID AND MIXED LIQUID-GAS REFLUX IS A MAJOR FACTOR ASSOCIATED WITH REFLUX PERCEPTION IN PATIENTS WITH NERD ON PPI THERAPY IN JAPAN: STUDY USING COMBINED IMPEDANCE-PH MONITORING

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INTRODUCTION: The pathogenesis of heartburn and acid regurgitation still remains to be fully elucidated in the non-erosive reflux disease (NERD) patients. Few studies have evaluated association between reflux symptoms and reflux episodes including gas reflux in the NERD patients in Japan.

AIMS&METHODS: The aim of this study is to assess the determinants of reflux perception in patients with NERD on proton pump inhibitor (PPI) therapy in Japan. Seventeen patients with persistent symptoms suggestive gastro-esophageal reflux, despite taking rabeprazole 10mg twice daily for at least 8 weeks, were included in this study. Patients' symptoms were assessed using the questionnaire for the diagnosis of reflux disease, the frequency scale for symptoms of gastro-esophageal reflux disease (FSSG), and all patients were performed ambulatory 24-hour combined impedance-pH monitoring. Reflux episodes were identified and classified as liquid (acid, weakly acidic or weakly alkaline) or gas reflux and were considered symptomatic if patients recorded a symptom within 2 minutes after a reflux episode. Symptom index (SI) was considered to be positive if ≧ 50%, and proximal reflux episodes were determined when reflux reaches 15 cm above the proximal margin of the lower esophageal sphincter (LES).

RESULTS: Of 17 patients, 6 were SI-positive, and 11 were SI-negative. The mean FSSG score of SI-negative (27.5±8.1) tended to be higher than that of SI-positive (18.7±9.5) (p=0.059). In the SI-positive patients, a total of 129 liquid reflux episodes was detected. Overall, 18 (14.0%) reflux were symptomatic, including one (5.5%) acid, 14 (77.8%) weakly acidic, and 3 (16.7%) weakly alkaline reflux. Distal reflux episodes were significantly more frequent (75.2%)

than proximal reflux (24.8%, $p<0.001$). On the contrary, occurrence rate of reflux symptoms in proximal reflux episodes was significantly more frequent (67.4%) than in distal reflux (15.6%) ($p<0.001$). A total of 41 mixed liquid-gas reflux episodes were detected, and 4 (9.7%) were symptomatic. Distal reflux episodes were significantly more frequent (68.3%) than proximal reflux (31.7%, $p<0.001$). In contrast, occurrence rate of reflux symptoms in proximal reflux episodes was significantly more frequent (23.1%) than in distal reflux (6.3%, p=0.013). On the other hand, a total of 323 gas reflux episodes were detected, but only 4 (1.2%) were symptomatic.

CONCLUSION: The proximal extent of weakly acidic liquid and mixed liquid-gas reflux is a major factor associated with reflux perception in SI-positive patients with NERD on PPI therapy.

Disclosure of Interest: None Declared

Keywords: impedance-pH monitoring, liquid reflux, mixed liqid-gas reflux, NERD

P464 COMPARISON OF ESOPHAGEAL MANOMETRY FEATURES OF WEAKLY ACIDIC REFLUX ASSOCIATED HEARTBURN AND FUNCTIONAL HEARTBURN

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INTRODUCTION: Whether esophageal motility disorders play roles in the occurrence of heartburn needs to be elucidated.

AIMS&METHODS: The aims of this study were to analyze the esophageal pressure topography (EPT) findings in the weakly acidic reflux (WAR) associated heartburn and compare them with that of acid reflux (AR) and functional heartburn (FH).

The heartburn patients with over 12 months' history were enrolled. All of them underwent gastroscopy to exclude organic diseases and reflux esophagitis, as well as 24 hour impedance-pH monitoring. The patients were divided into three groups: a, AR: patients with acid exposure time (AET) > 4% but without overload of weakly acid or non-acid; b, WAR: patients with weakly acid events > 18 and normal AET and non-acid events; c, FH: patients with normal range of AET, Symptom index, Symptom association probability, weakly and non-acid reflux. The EPT results were analyzed following Chicago classification criteria 2012

RESULTS: Total 103 patients were enrolled. 46 patients were AR, 36 were WAR and 21 were FH. The percentage of esophageal motility disorder in WAR, AR and FH group was 63.9%, 54.3% and 61.9% respectively ($p>0.05$). The features of motility disorder in the three groups presented significantly difference.(table)

Group %	WAR (a) N=36 52±12 yr	AR (b) N=46 52±15 yr	FH (c) N=21 51±11 yr	P value (chi-square test)
Weak peristalsis	61.1 (22/36)	37.0 (17/46)	23.8 (5/21)	a/b, p=0.045; a/c, p=0.028
Large breaks	36.1 (13/36)	23.9(11/46)	19.4(4/21)	NS
Small breaks	25 (9/36)	13.4(6/46)	4.8(1/21)	a/b, p=0.018; a/c, p=0.010
Normal	36.1(13/36)	45.7(21/46)	38.1(8/21)	NS
Rapid contractions	2.8(1/36)	4.3(2/46)	14.3(3/21)	NS
Distal esophageal spasm (DES)	0	6.5(3/46)	14.3(3/21)	a/c, p=0.045
EGJ outflow obstruction	0	4.3(2/46)	9.5(2/21)	NS
Jackhammer	0	2.2(1/46)	0	NS

CONCLUSION: Peristaltic defect was most frequent motility disorder in WAR heartburn patients. It suggests WAR patients present incomplete bolus transit, which may play a role in the development of heartburn by increasing reflux volume and prolonging the time of reflux content contact with the esophageal mucosa. And DES might be a cause of the symptom in FH patients

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Disclosure of Interest: None Declared

Keywords: Chicago classification criteria, esophageal pressure topography, functional heartburn, high resolution manometry, weakly acidic reflux

P465 RELATIONSHIP BETWEEN POSTPRANDIAL GASTRO-ESOPHAGEAL REFLUX PATTERN AND SEVERITY OF MUCOSAL DAMAGE

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INTRODUCTION: It has been hypothesized that the postprandial increase of gastroesophageal reflux (GER) results from an increase in the rate of transient lower esophageal sphincter relaxations (TLESRs) which occur more frequently after gastric distention. However, few data exist on the characteristics of GER episodes during the post-prandial (PP) period when the amount of acid is reduced (i.e. neutralization of gastric acidity by food) and the acid pocket occurs. Impedance-pH testing, detecting both acid and non-acid GER, can be used in this setting to characterize better than traditional pH-metry PP reflux events.

AIMS&METHODS: To evaluate the PP reflux patterns among healthy volunteers (HVs) and non-erosive reflux disease (NERD), erosive esophagitis (EE) and Barrett esophagus (BE) patients. We studied 30 HVs [8F; median age 25y] and 35 NERD [11F; 49.5y], 35 EE [7F; 43.5y] and 30 BE patients [5F; 59y]. All patients underwent upper endoscopy, esophageal manometry and impedance-pH off-therapy. During the 24-hour study, patients and HVs ate three standard meals.We measured acid exposure time (AET, % time pH < 4), median bolus clearance time (MBCT), mean acid clearance time (MACT), number of acid and non-acid GER events during the first PP hour for each of the three daily meals. Liquid, mixed and gas refluxes were also assessed.

RESULTS: All parameters increased progressively from HVs to BE, with patients with BE and EE having the higher values of AET, number of acid and non-acid GER events, MBCT and MACT compared to HVs and NERD patients ($p<0.05$). Moreover, patients with NERD had higher values of AET, number of acid and non-acid GER events, MACT compared to HVs ($p<0.05$). Finally, a gradual increase in pure liquid and mixed liquid–gas GER episodes was found in the patients with increasing degrees of esophageal damage ($p<0.05$).

	AET	MBCT	MACT	GER ACID	GER non-ACID	Liquid and mixed	Gas
HV	0.8 (0.2-2.4)	12 (9-16)	27 (7.5-49)	6 (3.5-8.5)	9 (4.5-11)	15 (10.5-20)	1 (0-4)
NERD	4.9 (2.4-9)	17 (13-24)	70 (51-105)	11 (6.5-14.5)	6.6 (4-11)	20.5 (14-31)	2 (1-3.5)
EE	10.1 (5.6-16.6)	18.5 (13.5-33)	73 (42-129)	15 (10-24)	7 (3-13)	22.5 (18-36)	2 (1-3)
BE	15.6 (2.8-30.3)	20.5 (15-28)	89 (43-157.5)	18 (5-26)	5.5 (2.5-13.5)	24.5 (18-38)	3.5 (1.5-7)

CONCLUSION: Our findings show that PP impedance-pH parameters increase in parallel with the severity of mucosal damage. We can hypothesize that BE and EE patients may have more TLESRs during the PP period as result of a more impaired gastric accommodation in them. This may favor the backflow of the content of acid pocket into the esophagus and the development of mucosal injuries.

Disclosure of Interest: None Declared

Keywords: Gastroesophageal reflux disease(GERD), impedance-pH monitoring, [illegible]

P466 REFRACTORY GERD: INCREASED BODY MASS INDEX IS ASSOCIATED WITH ONGOING ACID REFLUX BUT NOT WITH HYPERSENSITIVE ESOPHAGUS OR FUNCTIONAL HEARTBURN

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INTRODUCTION: Compare the prevalence of ongoing acid reflux, hypersensitive esophagus and functional heartburn in obese/overweight and normal weight patients referred for multichannel intraluminal impedance and pH monitoring, because of persisting gastroesophageal reflux disease (GERD) symptoms despite therapy with proton pump inhibitors.

AIMS&METHODS: Patients with normal endoscopy and typical GERD symptoms, despite proton pump inhibitor (PPIs) therapy twice daily, underwent 24-hour pH-impedance monitoring. Distal esophageal acid exposure (% time pH < 4) was measured and reflux episodes were classified into acid or non-acid. A positive symptom index (SI) was declared if at least half of symptom events were preceded by reflux episodes. Patients were categorized to those with ongoing acid reflux, those with hypersensitive esophagus and those with functional heartburn. Incidence of ongoing acid reflux, hypersensitive esophagus and functional heartburn between overweight/obese patients (BMI≥25 Kg/m^2) and normal weight patients (BMI < 25 Kg/m^2) was subsequently evaluated.

RESULTS: A total of 246 patients (females: 158, males: 88, increased BMI: 151, normal BMI: 95, mean age 55 - range 18-75 years) were included. Ongoing acid reflux was found in 39 patients (increased BMI: 31, normal BMI: 8), hypersensitive esophagus in 77 patients (increased BMI: 43, normal BMI: 34) and functional heartburn in 118 patients (increased BMI: 69, normal BMI: 49). When comparing BMI among all 3 groups, patients with increased BMI were more likely to have acid reflux than hypersensitive esophagus or functional heartburn (p=0.03).

CONCLUSION: In patients with GERD symptoms refractory to double dose PPI therapy those with increased BMI are more likely to have ongoing acid reflux than hypersensitive esophagus or functional heartburn.

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Disclosure of Interest: None Declared

Keywords: ACID REFLUX, BODY MASS INDEX, GERD

P467 ENHANCED PERCEPTION OF PROXIMAL GASTRO-OESOPHAGEAL REFLUX IN GORD: IMPAIRED MUCOSAL INTEGRITY OR DISTINCT SENSORY INNERVATION?

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INTRODUCTION: In patients with GORD, including refractory disease, reflux events reaching the proximal oesophagus are more likely to be perceived than those

only reaching the distal oesophagus. Experimental data suggests an increased sensitivity of the proximal oesophagus relative to the distal. As such, the proximal oesophagus is likely to be significant in the pathogenesis of GORD symptoms. Reasons for this are unclear, but may include reflux volume, impairment in mucosal integrity (i.e. high permeability and/or low transepithelial electrical resistance, TER) or changes in sensory innervation. The mucosal integrity of the proximal oesophagus is untested in GORD, and little is known about differences in mucosal afferent innervation between distal and proximal oesophagus.

AIMS&METHODS: We **aimed** to characterise mucosal integrity and afferent nerve distribution in the proximal and distal oesophageal mucosa in patients with heartburn without oesophagitis.

We took mucosal biopsies from the distal and proximal oesophagus in 15 patients with heartburn but no oesophagitis, and from 10 healthy volunteers. Biopsies were mounted in an Ussing chamber, and basal and dynamic integrity evaluated by measuring baseline TER and change in TER on exposure of the luminal aspect to a ''test'' pH2 solution containing 1mg/ml pepsin and 1mM taurodeoxycholic acid.

In 9 patients and 10 healthy volunteers, proximal and distal biopsies were examined immunohistochemically for presence and location (number of cells from the luminal aspect of the biopsy) of CGRP-immunoreactive nerve fibres.

RESULTS: There was no difference in baseline TER between the proximal and distal oesophagus in patients or healthy volunteers (179.0±18.2Ω vs. 148.6±21.4Ω (patients) vs. 194.3±22.3 vs. 149.4±22.1 (healthy volunteers), $p>0.05$ for all comparisons). Similarly, there was no significant difference in the change in TER on exposure to the ''test'' solution.

Mucosal afferent nerves were located in more superficial location in the proximal compared to distal oesophagus in both patients and healthy volunteers. Furthermore, fibres were located significantly more superficially in the proximal (but not distal) oesophageal mucosa of patients compared to controls (mean 5.7±0.7 vs. 22.2±2.7 cells from lumen in patients, 13.1±1.1 vs. 23.6±1.3 in healthy volunteers).

CONCLUSION: The enhanced sensitivity of the proximal oesophagus in GORD, is not explained by a distinct impairment of proximal mucosal integrity. However, our results suggest that such increased sensitivity might be associated with a more superficial location of mucosal afferent nerves in the proximal oesophagus of patients with GORD.

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Keywords: Afferent nerve, biopsy, gastroesophageal reflux, Mucosal integrity

P468 ASSOCIATIONS BETWEEN SLEEP DISTURBANCES AND REFRACTORY GERD SYMPTOMS IN PATIENTS RECEIVING ONCE-DAILY PPI AND EFFICACY OF TWICE-DAILY RABEPRAZOLE TREATMENT

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INTRODUCTION: Approximately 20–40% of patients with gastroesophageal reflux disease (GERD) are refractory to the standard regimen of once-daily proton pump inhibitor (PPI) treatment. Nighttime acid reflux that influences refractory symptoms is strongly associated with sleep disturbances.

AIMS&METHODS: The aim of this study was to examine the associations between sleep disturbances and refractory GERD symptoms in patients receiving once daily PPI and the efficacy of twice-daily rabeprazole treatment. In a multicenter survey, 433 GERD patients receiving once-daily PPI treatment completed a self-report questionnaire that included the Frequency Scale for the Symptoms of GERD (FSSG) and questions about sleep disturbances. Study cases were defined as patients with an FSSG score ≥8. Of the 222 study cases, 106 individuals received rabeprazole 10 mg twice daily for 4-8 weeks.

RESULTS: Of the 433 subjects, 222 patients (51.2%) had refractory GERD symptoms. Use of a half dose of PPI (odds ratio [OR], 1.93; 95% confidence intervals [CI], 1.07-3.50), nighttime symptoms (OR, 2.58; 95% CI, 1.78–3.74), arousals during sleep (OR, 2.16; 95% CI, 1.18–3.96), daytime sleepiness (OR, 1.59; 95% CI, 1.00–2.53), and poorer sleep quality (OR, 1.64; 95% CI, 1.25–2.16) were significantly associated with refractory GERD symptoms. Twice-daily rabeprazole treatment significantly improved FSSG scores and sleep disturbances.

CONCLUSION: About 50% of GERD patients receiving once-daily PPI treatment had refractory GERD symptoms. Use of a half dose of PPI and sleep disturbances were significantly associated with refractory GERD symptoms. Twice-daily rabeprazole treatment was effective in such cases.

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Keywords: proton pump inhibitor, rabeprazole, refractory symptom, sleep disturbances

P470 RELATIONSHIP BETWEEN AIR SWALLOW AND GASTROESOPHAGEAL REFLUX DISEASE

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INTRODUCTION: Air swallow is a normal physiological phenomenon in health. Some researchers believed that patients with gastroesophageal reflux disease (GERD) swallowed air more, but there were some contradictory reports.

AIMS&METHODS: We aimed to investigate the relationship between air swallow and GERD by using the 24h multichannel esophageal pH-impedance monitoring.

GERD patients and health volunteers (controls) underwent 24h multichannel intraluminal impedance and pH monitoring. All of the subjects received gastroendoscopy to exclude abnormalities other than erosive esophagitis or chronic superficial gastritis previously. Impedance data was analyzed to record the numbers of air events and the parameters of gastroesophageal reflux. Correlation between the parameters of air events and gastroesophageal reflux was analyzed. P value less than 0.05 was considered statistically significant.

RESULTS: A total of 30 GERD patients (45±13 yrs., m/f=18/12) and 30 controls (41±13 yrs., m/f=10/20) was enrolled. The numbers of air swallow in GERD patients were higher than that in controls (22.6±20.8 vs. 16.1±12.7, $p<0.05$), especially in female GERD patients (GERD vs. controls: f, 23.4±21.5 vs. 14.3±11.3, $p<0.05$; m, 22.1±20.0 vs. 19.9±15.0, $p>0.05$). Air swallow happened mainly between meals (GERD vs. controls, female: between meals: 21.2±20.5 vs. 10.9±9.0, $p<0.05$; during meal: 2.3±2.0 vs. 3.4±3.2, $p>0.05$). Meanwhile, air swallow events were significant correlated with the total events number of air reflux for 24h (R=0.517, p=0.000) and the total mixed reflux time (R=0.442, p=0.000). Furthermore, air swallow events correlated negatively with the total esophageal clearance time in GERD patients (R=-0.361, p=0.05), but not in controls (R=0.173, p=0.361).

CONCLUSION: Air swallow happens more often in GERD patients, especially in female between meals. Air swallow might be a reason of gastroesophageal air reflux and mixed reflux. On the other hand, air swallow may play an important role for esophageal content clearance in GERD patients.

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Disclosure of Interest: None Declared

Keywords: 24h pH-impedance monitoring, air swallow, gastroesophageal reflux disease

P471 SYNCHRONOUS EXPRESSION OF CD147, MONOCARBOXYLATE TRANSPORTER 1 AND THEIR ASSOCIATION WITH CD44 IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: CD147, extracellular matrix metalloproteinase inducer is a glycosylated transmembrane protein that has been identified as a member of the immunoglobulin superfamily, known to induce matrix metalloproteinases. There are evidence for the upregulation of MCTs in tumors, such as colorectal, cervical and lung carcinomas. Recently, it was demonstrated that the prognostic value of CD147 is associated with monocarboxylate transporter 1 (MCT1) co-expression in gastric cancer. It was suggested that constitutive interactions between hyaluronan and CD44 also contribute to regulation of MCT localization and function in breast carcinoma cells.

AIMS&METHODS: The aim of this study was to investigate the relationship between CD147, MCT1, CD44s, CD44v6, MMP9 expression and clinicopathological factors in esophageal squamous cell carcinoma(ESCC). Immunohistochemical analysis of CD147, MCT1, MMP-9, CD44s and CD44v6 was carried out in paraffin-embedded sections of surgically resected 43 cases of ESCC and paired distal normal esophageal tissues. Sections were scored semi-quantitatively for immunoreaction and intensity of staining.

RESULTS: Immunostaining of CD147 and MCT1 was seen in cancer cell surface. Immunostaining of MMP-9 was seen in tumor cell cytoplasm and stromal elements. Overexpression of CD147 was observed in 29 cases (67.4%) of 43 ESCC. MCT1 overexpression was observed in 30 cases (69.7%) of 43 ESCC. In CD147 positive 29 cases, MCT1 positive case was 25 cases (86.2%), MMP-9 positive case was 23 cases (79.3%) and CD44 positive case was 17 cases (58.6%). Significant correlations were observed between CD147/MCT1 co-expression and depth of tumor invasion (T1 33.3%, T2 60.0%, over T3 71.4%), lymph node metastasis (N0 46.1%, N1 63.3%) and disease stage (stage I 37.5%, stage II 41.6%, stage III, IV 73.9%). Immunostaining of CD44 was seen in cancer cell surface and basal cell layer of epithelial cells. Overexpression of CD44 was observed in 24 cases (55.8%) of 43 ESCC. Significant correlations were observed between CD44 overexpression and depth of tumor invasion (T1 41.6%, T2 60.0%, over T3 61.9%), lymph node metastasis (N0 38.4%, N1 63.3%), disease stage (stage I 50.0%, stage II 33.3%, stage III, IV 69.6%) and histological differentiation (well 25.0%, mod. 66.7, por. 100%).

CONCLUSION: In ESCC, co-expression of CD147/MCT1 correlates with expression of MMP-9. The results of this study suggest that CD147 activity is dependent on MCT1 co-expression. Both CD147/MCT1 co-expression and CD44 upregulation correlates with invasive activity and lymph node metastasis. CD44 upregulation correlates with histological differentiation.

Disclosure of Interest: None Declared

Keywords: CD147, CD44s, CD44v6, MCT1, MMP9

P472 LEUKOTRIENE B4 RECEPTOR-1 (BLT-1) AND CYSTEINYL LEUKOTRIENE RECEPTOR-2 (CYSLT-2) ARE DEREGULATED IN BOTH TRANSFORMED AND NON-TRANSFORMED EPITHELIUM OF PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Leukotriene B4 receptors (BLT-1 and BLT-2) and cysteinyl leukotriene receptors (CysLT-1 and CysLT-2) are suggested to contribute to malignant cell transformation and proliferation. The expression of these receptors in esophageal squamous cell carcinoma (ESCC) has not been investigated.
AIMS&METHODS: We aimed to investigate the expression of BLT-1, BLT-2, CysLT-1 and CysLT-2 in ESCC and adjacent non-transformed squamous epithelium of the esophagus (NTSE), as well as in control biopsy samples from esophageal squamous epithelium (CSE) of patients with functional dyspepsia. Nineteen consecutively diagnosed patients with ESCC were prospectively enrolled between March 2010 and January 2011. UICC stage was calculated based on the 7th AJCC/UICC edition. Furthermore, 9 sex- and age-matched patients with functional dyspepsia were included as controls. Expression levels of BLT-1, BLT-2, CysLT-1 and CysLT-2 were analyzed by immunohistochemistry (IHC) and quantitative reverse transcription-polymerase chain reaction (qRT-PCR) in biopsy samples. Spearman correlation, Friedman test, Wilcoxon rang sum test and Mann-Whitney-U-test (2-sided) were used for statistical analysis.
RESULTS: 11/19 (58%) patients with ESCC were at AJCC/UICC stage IV, 8/19 were in stage I to III. BLT-1, BLT-2, CysLT-1 and CysLT-2 were ubiquitously expressed in all biopsy samples. Protein and transcript levels of BLT-1 were significantly increased in both ESCC and NTSE compared to CSE ($p < 0.05$). ESCC showed a significantly increased BLT-2 protein expression compared to NTSE and CSE ($p < 0.05$), whereas BLT-2 transcript levels did not differ among the three groups. The protein expression of CysLT-1 and CysLT-2 was significantly increased in ESCC compared to NTSE and CSE ($p < 0.05$). CysLT-1 mRNA expression was significantly decreased (3.2 fold) in ESCC compared to CSE ($p < 0.05$), but not to NTSE. A significant decrease of CysLT-2 mRNA expression was observed in both ESCC (17 fold) and NTSE (16.1 fold) compared to CSE ($p < 0.05$). Gene expression levels of BLT-1, BLT-2, CysLT-1 and CysLT-2 were not correlated with AJCC/UICC stage.
CONCLUSION: The expression of LT receptors is deregulated in ESCC. Up-regulation of BLT-1 and down-regulation of CysLT-2 gene expression occur already in NTSE of patients with ESCC suggesting a potential role of these receptors in early steps of esophageal carcinogenesis.
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Disclosure of Interest: None Declared
Keywords: esophageal squamous cell cancer, leukotriene receptoors

P473 IMPACT OF HDAC-1 AND MTA-1 EXPRESSION FOR ESOPHAGEAL CARCINOGENESIS

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INTRODUCTION: Animal models are important in the development of novel therapies for esophageal cancer. While the relationship between reflux and esophageal carcinoma has been explored in a number of studies, the molecular mechanisms underlying esophageal carcinogenesis are still not well understood. HDAC1/MTA1 complexes are known to inhibit p53 acetylation, and thus inhibit p53-induced apoptosis.
AIMS&METHODS: The aim of this study is to investigate the role of HDAC1 and MTA1 expression on esophageal carcinogenesis in rats.
Rats underwent a total gastrectomy followed by esophago-jejunostomy to induce chronic duodenal content reflux esophagitis. The animals were sacrificed sequentially at 20, 30, 40 and 50 weeks post-surgery and esophagi were examined. Immuno-histochemical analysis was used to assess the expression and localization of HDAC1 and MTA1.
RESULTS: At 20 weeks post-surgery, squamous proliferative hyperplasia and Barrett's metaplasia were observed. Adenocarcinoma associated Barrett's metaplasia and squamous cell carcinoma were observed 30-50 weeks post-surgery. Nuclear expression of HDAC1 and MTA1 were seen in all stages of squamous cell carcinogenesis and adenocarcinogenesis, but not in normal esophageal epithelium.
CONCLUSION: The expression of HDAC1 and MTA1 may play a role in duodeno-esophageal reflux induced neoplastic transformation of esophageal mucosa to cancer cells with squamous differentiation and adeno differentiation.
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Disclosure of Interest: None Declared
Keywords: Barrett's esophagus, esophageal adenocarcinoma, esophageal carcinogenesis, esophageal squamous cell carcinoma, histone deacetylases, metastasis-associated gene

P474 A COMPARATIVE STUDY OF NARROW-BAND IMAGING AND LUGOL IODINE STAINING IN THE DIAGNOSIS OF EARLY ESOPHAGEAL CANCER AND PRECANCEROUS LESION

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INTRODUCTION: Esophageal (esophageal cancer, EC) is the eighth most common cancers and the sixth most common cause of death from cancer. Surgical resection is the treatment of early esophageal cancer, and esophageal cancers carry a high mortality mainly due to its late diagnosis, with a five-year survival of less than 10%.More than 70% of diagnosis are made in patients presenting with dysphagia and weight loss, clinical findings frequently observed in patients in at least stage II.
AIMS&METHODS: Objective: To observe the esophageal through the narrow-band imaging techniques (NBI) and Lugol iodine staining, and then compare the efficacies of two methods in the diagnosis of early esophageal cancer and precancerous lesion.
Method: 103 patients were enrolled from January 2010 to January 2013. Conventional endoscopic white light imaging (WLI) with NBI and Lugol iodine staining were consecutively performed, and the discovered lesions were confirmed by pathologic diagnosis as the gold standard, NBI and iodine staining scale was compared with pathologic diagnosis. Then compared the value of WLI, NBI and Lugol iodine staining.
RESULTS: (1) 125 lesions were found in 103 patients. 96 lesions were detected with WLI, 120 lesions were detected with NBI endoscopy, 125 lesions were detected with iodine staining. There was no significant difference between NBI and iodine staining in detecting rate ($p > 0.05$). The detection rate of WLI was lower than NBI and iodine staining.($p < 0.01, p < 0.01$).
(2)The sensitivity for severe dysplasia and early esophageal of NBI and iodine staining was 100%, 100% ($p > 0.05$), which were higher than WLI ($p < 0.05$). There was no significant difference in detecting mild and moderate dysplasia between NBI and iodine staining (94.20% vs 100%, $p > 0.05$); which were higher than WLI (73.91%, $p < 0.01, p < 0.01$).
(3) The NBI classification for Severe dysplasia and early esophageal cancer was,I,90% (36/40);II and III, 10%(4/40); for mild and moderate dysplasia,I, 2.90%(2/69); II andIII, 94.20% (65/69); The iodine staining grading for Severe dysplasia and early esophageal cancer was,I, 95%(38/40);II and III, 5%(2/40); for mild and moderate dysplasia,I, 5.80%(4/69); II and III, 94.20%(65/69).
CONCLUSION: NBI appears as effective as Lugol iodine staining to detect early esophageal cancer and precancerous lesions. Although NBI is more technically easy to perform, less time-consuming, and Lugol iodine staining is cheaper, especially for the screening for early esophageal cancer and precancerous lesions in the undeveloped areas. Therefore, these two methods can't replace each other, and still be ideal complementary diagnostic tool.
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Disclosure of Interest: None Declared
Keywords: Diagnose, Early esophageal cancer and precancerous lesions, Lugol staining, Narrow-band imaging

P475 H.PYLORI INFECTION IN PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: H.Pylori is a gram negative, spiral shaped, multiple unipolar flagellated and urease producing bacteria. Esophageal squamous cell carcinoma (ESCC) is one of the most agressive digestive system tumour in rural areas of Asia. A clear association has been showed between Helicobacter pylori infection and gastric cancer (1,2). However, there are conflicting reports the relationship between ESCC and *H.pylori* (3). The aim of this study examined the prevalence of *H.pylori* in patients with esophageal squamous cell carcinoma.
AIMS&METHODS: 65 ESCC patients (43 women, aged 32-92 years) were evaluated in our clinic from April 2010 to April 2013. All of the patients were diagnosed by esophagogastroscopy and histopathological examination. 26 of them had esophagectomy. Esophagogastroscopy with antral biopsy was performed for each patient. Gastric biopsy samples are tested for urease activity by using a commercial hp fast test, which has an urea containing medium and a pH reagent. The control group comprised 100 dyspeptic subjects (60 women and 40 men, aged 30-85 years) Antrum biopsies with normal endoscopic evaluation were examined for *H.pylori* by the same method. Comparisions between two groups were performed by the Mann- Whitney U-test.
RESULTS: The mean age was 45.96 ±1.61 in control (dyspeptic) group and was 59.43±1.90 in ESCC group. *H.pylori* infection was observed in 49 of 65 (75.3%) ESCC patients. In dyspeptic group, *H.pylori* infection was found in 53 of 100 (53%) patients. We found significantly higher infection with *H.pylori* in patients with ESCC compared to the dyspeptic population (p=0.002).

CONCLUSION: These results suggested that *H.pylori* infection could be an ethiological factor in patients with ESCC.

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Disclosure of Interest: None Declared

Keywords: esophageal cancer, h.pylori

P476 USEFULNESS OF ORAL PREDNISOLONE IN THE TREATMENT OF ESOPHAGEAL STRICTURE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA.

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INTRODUCTION: Endoscopic subumucosal dissection (ESD) permits en bloc removal of superficial esophageal squamous cell carcinoma. A circumferential mucosal defect involving over three fourths the circumference of the esophagus after ESD was significantly associated with the subsequent development of esophageal stenosis. So, it is necessary to prevent postprocedure stricture after ESD. We analyzed that frequent endoscopic balloon dilation (EBD) was required in the treatment of the stenosis after semicircular ESD, treated with pre-emptive EBD. The number of EBD required was 5.3(4-8) in the pre-emptive group. 50% of them had complications, perforation and deep laceration of the muscular layer, related to EBD itself.

AIMS&METHODS: To evaluate the effectiveness of oral prednisolone in controlling postprocedure esophageal stricture. Design: Retrospective study. Setting: Endoscopy department in our hospital. 22 superficial esophageal lesions in 21 patients who underwent semicircular ESD for esophageal squamous cell carcinoma involving over three fourths defect of the lumen from November 2011 to January 2013 were retrospectively studied. Intervention: Pre-emptive EBD was not started until stenosis occurs. Esophageal stenosis was defined when a standard endoscope (9.8mm in diameter) failed to pass through the stenosis. Oral prednisolone was started at 30 mg/day on the first day post-ESD. The prednisolone gradually tapered off and then was canceled eight weeks. The quantity of drug and schedules referred to an existing report.

RESULTS: 8 of 22 lesions (38.4%) was occurred stricture. The number of EBD required was 3.6(0-16) on these lesions. The number of EBD sessions tended to be greater (5.3 v.s.3.6) in the pre-emptive EBD group than in the oral prednisolone group (Table2). The risk factor of stricture was ''cervical esophagus'', ''chemoradiotherapy or systemic chemotherapy history''. There was one perforation related to EBD itself in 21 patients. And an attempted suicide occurred, could not deny related to oral prednisolone.

CONCLUSION: Oral prednisolone may therefore potentially reduce the overall cost and complications associated with mechanical luminal dilation and may offer a useful preventive option for post-ESD esophageal stricture.

Disclosure of Interest: None Declared

Keywords: Endoscopic subumucosal dissection (ESD), oral prednisolone, treatment of esophageal stricture

P477 THE VALUE OF AIR INSUFFLATION CT ON DIAGNOSIS OF ESOPHAGEAL SUBMUCOSAL TUMORS

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INTRODUCTION: with the advantage of both endoscopy and ultrasound, EUS has emerged as a reliable detection method for evaluating these lesions under both direct vision and satisfactory ultrasonic field .

However, the limitations of EUS include not only poor observation of the anatomic features of the adjacent structures but also the demand of special instruments and experienced endoscopists.

Esophageal lumen is closed during conventional CT scan and it is difficult to distinguish SMTs clearly from esophageal wall and surrounding tissue.

So the application of conventional CT in detecting esophageal SMTs was limitad. Because SMTs could be showed more clearly in air insufflated esophageal lumen during gastroscopy, this study was conducted to determin the value and effective of air insufflation CT on diagnosis of esophageal SMTs.

AIMS&METHODS: To determine the value and sensitivity of air insufflation computed tomography (CT) on diagnosis of esophageal submucosal tumors (SMTs).

Conventional CT and air insufflation CT were performed on 40 patients who had been confirmed esophageal SMTs by gastroscopy and endoscopic ultrasonography (EUS).

Air insufflation CT procedure:

1) patient fasted for 4-6 h;

2) inserting a nasogatric tube into esophageal lumen 30 cm from the incisors;

3) connecting a air bag to nasogatric tube and insufflating air continually by pressuring the air bag;

4) performing chest CT scan after 5 seconds with patient's mouth closed.

RESULTS: he sensitivity for detecting esophageal SMTs of conventional CT was 57.5% (23/40) compared with that of air insufflation CT (90.0%, 36/40), the difference was of statistical significance (X^2=15.21, $P<0.05$). Furthermore, lesions were showed more clearly by air insufflation CT.

Compared lesion size on air insufflation CT with that after resection, 9 cases revealed measurement error more than 30%, but EUS finding matched excisional specimen in 4/9 cases; compared lesion size on EUS with that after resection, 8 cases revealed measurement error more than 30%, but air insufflation CT finding matched excisional specimen in 3/8 cases.

CONCLUSION: Air insufflation CT is more effective and significant than conventional CT on diagnosis of esophageal SMTs. Combined with EUS, air insufflation CT has added value in evaluating the origin of esophageal SMTs and the anatomic features of adjacent structures which benefit to predict the risk of endoscopic treatment and surgery.

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Disclosure of Interest: None Declared

Keywords: CT, diagnosis, EUS, SMTs

P478 TYPE OF LUGOL-VOIDING LESIONS IS AN IMPORTANT CLINICAL PREDICTOR FOR RECURRENT SYNCHRONOUS/METACHRONOUS NEOPLASM AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR PRIMARY ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is an advanced endoscopic procedure to resect early esophageal neoplasm; however, new synchronous/metachronous neoplasm may occur in the preserved esophageal mucosa.

AIMS&METHODS: This study assessed the risk of developing recurrent synchronous/metachronous esophageal neoplasm in patients receiving ESD for primary esophageal squamous cell carcinoma based on multiplicity of Lugol-voiding lesions (LVLs) observed by chromoendoscopy and patient characteristics. Fifty-three patients with early esophageal squamous cell carcinoma who underwent curative ESD were recruited. We collected individual factors, including the demographic characteristics, social habits, *co-morbidity*, and initial tumor characters to identify risk factors associated with the development of recurrent synchronous/metachronous esophageal neoplasm using the Cox proportional hazards regression models. According to previous study by M Muto, et al., Iodine staining pattern of background mucosa at initial ESD were divided into 4 groups as follows : Group A, no LVLs; B, several ($\leqq$10) small LVLs; C, many ($>$10) small LVLs; and D, many ($>$10) irregular-shaped multiform LVLs. We defined group A and B as low-risk group (type 1) while group C and D as high-risk group (type 2). Patients were followed by endoscopy with narrow-band imaging and iodine staining.

RESULTS: A total of 53 patients (mean age $\pm$ standard deviation: 51.7 $\pm$ 9.4 years) were followed up (mean follow-up interval: 88.9 $\pm$ 53.6 weeks). There were 15 (28.3%) patients having recurrent esophageal neoplasm during follow-up. Univariate analyses showed that the presence of type 2 background mucosa and multi-focal neoplastic lesions at initial ESD were potential risk factors, and regression analyses confirmed that only type 2 Iodine staining pattern (hazard ratio: 9.10, 95% CI: 1.17-70.49, p=0.035) was significantly associated with recurrent esophageal neoplasm.

CONCLUSION: The presence of numerous, irregular-shaped, multiform Lugol-voiding lesions is an important clinical predictor for recurrent synchronous/metachronous esophageal neoplasm after ESD for primary esophageal squamous cell carcinoma. Long-term, intensive endoscopic surveillance is required and further possible chemo-prevention seems to be warranted for these patients.

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Disclosure of Interest: None Declared

Keywords: Endoscopic submucosal dissection (ESD), Esophageal neoplasm, Metachronous, Recurrence, Squamous cell carcinoma, Synchronous

P479 MICROVASCULAR CALIBER CHANGES IN INTRAMUCOSAL AND SUBMUCOSALLY INVASIVE ESOPHAGEAL CANCER

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INTRODUCTION: Intrapapillary capillary loops (IPCLs) show distinct pattern changes which correlate with tumor progression and depth of invasion important for the in-vivo characterization of superficial squamous cell carcinoma (SCCA).
AIMS&METHODS: We aim to correlate histopathologic diameter of IPCLs in resected SCCA and invasion depth. Methods: We conducted a prospective study to evaluate the diameter of abnormal IPCL using light microscopy and immunohistochemical staining in superficial SCCA resected by endoscopic submucosal dissection (ESD). Prior to resection, IPCL patterns were identified by magnification endoscopy (ME) with NBI. Twenty tissue samples (IPCL-V1,10; IPCL-VN,10) from patients who underwent ESD for superficial SCCA with IPCL-V1 and IPCL-VN (IPCL-I,103; IPCL-V1,113; IPCL-VN,100) were examined. Samples were stained with haematoxylin and eosin, CD34 and Desmin. Measurement of vessel diameter at light microscopy was averaged over 10 high-power fields at x200 magnification.
RESULTS: Histopathologic caliber of IPCL-V1, which corresponds to tumor limited to the mucosa (T1a-EP), was significantly dilated compared with caliber in the normal esophageal mucosa (IPCL-I (7.7+2.8um vs. 21.9+7.4um, $p<0.001$); whereas, caliber of IPCL-VN corresponding to tumors invading into the submucosa (T1b) were significantly larger than the caliber of T1a-EP lesions (21.9+7.4um vs. 65.2+22.9um, $p<0.001$).
CONCLUSION: Caliber of surface vessels in SCCA gradually increases according to depth of invasion. These changes in IPCL can be observed with ME, allowing in vivo discrimination between intramucosal from submucosally-invasive cancer allowing the endoscopist to make real-time assessment of tumor depth and aids in the decision whether a patient should undergo surgery or a less invasive treatment such as EMR/ESD.
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Keywords: ESD (endoscopic submucosal dossection), IPCL, magnifying endoscopy, Oesophageal carcinoma

P480 CLINICAL IMPACT OF SURVEILLANCE AND EARLY INTERVENTION FOR HEAD AND NECK SQUAMOUS CELL CARCINOMA IN PATIENTS WITH ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Narrow-band Imaging (NBI) is effective in detecting synchronously and metachronously superficial head and neck squamous cell carcinoma (HNSCC) in patients with esophageal squamous cell carcinoma (ESCC), and most of these lesions can be treated endoscopically. However, it has not been clarified whether early detection and intervention for early HNSCC in ESCC patients decrease serious events related to presence of metachronous HNSCC or not.
AIMS&METHODS: Since the beginning of 2006, we have introduced the intensive surveillance for HN region using NBI for all ESCC patients before treatment, and during follow-up evaluation. The patients criteria was as follows: (1) newly diagnosed ESCC received definitive treatments (endoscopic resection (ER), surgery or chemoradiotherapy); (2) clinical stage I to III; (3) no history of any HNSCC; (4) absence of synchronously advanced cancer; (5) followed-up period over 6 months after treatment for ESCC. The patients were classified into two groups, such as Group A before the intervention of NBI surveillance between October 1992 and December 2000, and Group B after the intervention of that between January 2006 and December 2008. In these two groups, we examined the detection rate of superficial HNSCC, and the serious events related to metachronous HNSCC, which was frequency of loss of laryngopharyngeal function and death due to HNSCC during the follow-up periods.
RESULTS: A total of 698 patients (median age 65) consisting of 328 in Group A and 370 in Group B were recruited from our database. Synchronously superficial HNSCCs were found in only 1 patient (0.3%) in Group A, while those were found in 14 (3.8%) in Group B ($p=0.001$).
Of these 698 patients, 254 in group A and 307 in group B were followed up over 1 year. Metachronous HNSCCs were detected more frequently in group B (26 patients of 307; 8.5%) than in group A (9 of 254; 3.5%, $p=0.02$). Although all of the HNSCC lesions in group B were detected as early cancers with 38 lesions (81%) treated by ER, 60% of the lesions in group A were detected in advanced stage (III/IV) ($p<0.001$). Laryngopharyngeal dysfunction and death due to metachronous HNSCC were more frequent in Group A than in group B (1.6% v 0%, $p=0.048$; 2.0% v 0%, $p=0.018$). There was no serious problem related to ER for superficial HNSCC.
CONCLUSION: After the intervention of surveillance for HN region using NBI endoscopy, detection rate of early HNSCC was increased in ESCC patients. For early treatment, occurrence of metachronously advanced HNSCC and serious events related to metachronous HNSCC were decreased.
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Disclosure of Interest: None Declared
Keywords: esophageal squamous cell carcinoma, head and neck cancer, NBI, synchronous and metachronous HNSCC

P481 HISTOLOGIC EVALUATION OF RESECTION SPECIMENS IN PATIENTS WITH ESOPHAGEAL NEOPLASIA: TYPE OF LESION DOES NOT PREDICT HISTOLOGY AND STAGING

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INTRODUCTION: It remains controversial whether the macroscopic classification of the esophageal lesions (in contrast to early gastric cancer) according to the Japanese criteria has a prognostic value with regard to endoscopic therapy. The aim of this prospective, single-center study was to evaluate the clinical role of this macroscopic classification in patients with early esophageal neoplasia.
AIMS&METHODS: A total of 69 patients with 78 suspect esophageal lesions who were referred between January 2009 and April 2013 for endoscopic therapy were prospectively included in the study. A trimodal endoscopy with targeted biopsies prior to endoscopic resection/dissection included assessment of the macroscopic type according to the Japanese classification. Histology (both from biopsy specimen and resection specimen) was correlated with macroscopic assessment.
RESULTS: The overall distribution of the lesions by gross type was as follows: type Is, n = 6 (8%); type IIa, n = 34 (44%); type IIb, n = 29 (37%); type IIc, n = 4 (5%); type IIa+b, n = 3 (4%); type IIa+c, n = 2 (2%). Histology revealed no neoplasia in 8 lesions, low grade intraepithelial neoplasia (LGIN) in 18 lesions, high grade intraepithelial neoplasia (HGIN) in 13 lesions, early adenocarcinoma (EAC) in 35 lesions and early squamous carcinoma (ESC) in 4 lesions. The distribution of different macroscopic types was as follows: LGIN – Is 0%, IIa 22%, IIb 72%, IIc 0%, IIa + b 6%; HGIN- Is 15%, IIa 31%, IIb 38%, IIc 8%, IIa + c 8%; EAC + ESC – Is 8%, IIa 56%, IIb 23%, IIc 5%, IIa + b 5%, IIa + c 3%. Macroscopic type did not predict advanced cancers (G2 or 3, n=8) and penetration to the submucosa (n=9).

Histology of ER/ESD specimens (compared with prior forceps biopsy) led to a change in diagnosis in 43% of the focal lesions and a relevant change in the management in 26% of patients.
CONCLUSION: Most endoscopically resected early esophageal neoplasia are 0-IIa and 0-IIb types. Macroscopic type does not reliably predict histology, grading and penetration depth. Targeted biopsies of focal lesions are not accurate enough for precise diagnosis.
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Disclosure of Interest: None Declared
Keywords: Barrett's esophageal cancer, endoscopic resection, Targeted biopsies

P482 USEFULNESS OF NEEDLE KNIFE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION IN SUPERFICIAL ESOPHAGEAL NEOPLASMS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is commonly performed for large superficial GI tract lesions. Many kinds of device are used for ESD: the IT-knife, Hook knife, and Flush knife, however, the needle knife has been considered to cause a high rate of complications in ESD for esophageal lesions because of its shape. On the other hand, endoscopic mucosal resection with a cap (EMR-C) has been applied for superficial esophageal lesions since the 1980's. Only a few reports have compared EMR-C and ESD using a needle knife; therefore, in this study, we compared these two methods for esophageal lesions.
AIMS&METHODS: To compare the efficacy, usefulness, and complications between conventional EMR-C and ESD using a needle knife for superficial esophageal neoplasms. (Methods) Between 2001 and 2010, patients with superficial esophageal neoplasms were treated by EMR-C or ESD using a needle knife. For the EMR-C, using a cap to the top of the endoscope, the targeted lesion was resected with conventional EMR method. For the ESD method, attachment was used and, after the injection of sodium hyaluronate under the submucosal layer, using the needle knife, ESD was performed.
RESULTS: From the database, we collected a total of 87 patients who underwent esophageal treatment endoscopically. Complete resection was achieved in all 87 patients. Twenty-one patients were treated by EMR-C (19 males/ 2 females, mean age: 66.0), and 66 patients were treated by ESD using a needle knife (62 males/ 4 females, mean age: 67.5). The mean resected specimen size was 21.4 mm in the EMR-C group and 30.6 mm in the ESD group. The en-bloc resection rate was 61.9% in the EMR-C group and 98.5% in the ESD group. The negative horizontal margin rate was 85.7% in the EMR-C group and 90.9% in the ESD group. The negative vertical margin rate was 95.2% in the EMR-C group and 90.9% in the ESD group. There was no complication in the EMR-C group but 9 cases of complication in the ESD group (4 cases of stenosis, 3 cases of mediastinal emphysema, and 1 case of perforation). During the observation period, 2 patients, died of pneumonia and 1 died from acute myocardial infarction in the EMR-C group, and 1 patient died from pancreatic cancer and 1 died from liver cirrhosis in the ESD group.
CONCLUSION: ESD using the needle knife for esophageal neoplasms facilitated resection and achieved a larger resection than EMR-C. There are some problems regarding complications; however, ESD using the needle knife has a marked advantage for desirable en-bloc resection of esophageal neoplasms. Further investigations to evaluate the various other devices are needed.
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Disclosure of Interest: None Declared
Keywords: EMR, ESD (endoscopic submucosal dossection)

P483 PLACEMENT OF BILIARY METAL STENTS FOR UPPER ESOPHAGEAL STRICTURES

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INTRODUCTION: The treatment of strictures of the cervical esophagus remains a challenge. Endoscopic dilation is the standard of care, but refractory or tumoral stenoses require some form of stenting. Placement of self-expanding metal stents (SEMS) has been considered impractical for cervical strictures. Metal stents placed near the upper esophageal sphincter cause problems like severe cervical pain, globus sensation, bleeding or compression of the trachea. Expansive force and diameter of regular esophageal stents are difficult to tolerate in the cricopharyngeal region. We report our results with the use of biliary SEMS in the upper esophagus, which have a smaller diameter and less expansive force.
AIMS&METHODS: We retrospectively reviewed all patients in our center between July 2011 and August 2012 who received a biliary metal stent because of a refractory stenosis in the cervical esophagus. All patients were informed about off-label-use and alternative treatments. We implanted covered biliary SEMS (Wallflex, Boston scientific) with a diameter of 1cm and length of 6-8cm. Technical and clinical success and duration of stenting were evaluated retrospectively using the clinical records. Results are presented as summary statistics.
RESULTS: Seven patients were treated with biliary SEMS in the upper esophagus. Strictures were located between 10 and 19cm from incisor teeth. We treated 2 patients with benign and 5 with malignant stenoses. Stent placement was successful in all (7/7) patients. One patient with the most proximal stricture was unable to tolerate the stent because of pain and globus sensation. This stent had to be extracted on the same day. All other patients (6/6) had good clinical success and were able to take up liquid and in some cases even solid food. We had no major complications and stent tolerability was good. . In one patient with a refractory postradiogenic stricture the stent was changed every three months on a regular basis. In patients with malignant strictures the stent was left in place as long as clinically successful. Median duration of stenting was 66 days.
CONCLUSION: In our series we report good clinical success with immediate improvement of dysphagia and no major complications. These results were received in complicated strictures refractory to other treatments. Stent tolerability, which has been a major concern in this situation, was good in 86% of patients. This compares favourably to other series using regular esophageal stents, where up to 45% of patients complain of chest and neck pain.
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Disclosure of Interest: None Declared
Keywords: Biliary stent, esophageal stricture

P485 CLINICOPATHOLOGICAL STUDIES OF ESOPHAGEAL CARCINOMA IN ACHALASIA: ANALYSIS OF ITS CANCERATION AND RISK FOLLOWING SURGICALLY TREATED ACHALASIA

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INTRODUCTION: Achalasia of the esophagus is a benign disease, and an esophageal motor disorder characterized by insufficient relaxation of the lower esophageal sphincter. Esophageal carcinoma is the most serious late complication of achalasia clinically. Chronic inflammatory irritation by retained food may induce carcinogenesis of the esophageal squamous epithelium. However, the detailed mechanism of carcinogenesis in achalasia patients has not been clarified histopathologically.
AIMS&METHODS: We analyzed nineteen cases of achalasia-associated carcinoma of the esophagus clinicopathologically. We examined nine cases of achalasia-associated squamous cell carcinoma, surgically or endoscopically resected, using histological and immunohistochemical procedures. The invasive parts of each carcinoma, in situ carcinoma, dysplasia as well as hyperplasia were examined for histological mapping, and with immunohistochemical expression for p53 protein.
RESULTS: The patients ranged in age from 46 to 76 years, with a mean age of 61 years. The mean interval between the diagnosis of achalasia and carcinoma was 22.3 years. Nine of the nineteen cases were superficial cancers, and the other ten cases were advanced cancers. Radiographically, nine cases were sigmoid type, the other ten cases were flask type and none were spindle type. Six cases were grade III, the other thirteen cases were grade II and none were grade I. Endoscopically, eight carcinomas were protruding type, and the others were superficial depressed type and ulcerative type. Eighteen cases were composed of squamous cell carcinoma and the other one was basaloid-squamous carcinoma. Histological mapping of the resected specimens demonstrated marked hyperplastic changes of stratified squamous epithelium and multiple foci of dysplastic changes. The squamous cell carcinomas showed well to moderately differentiated type with low-grade atypia, closely associated with dysplastic foci. Immunohistochemical overexpression of p53 was detected in the invasive parts of the carcinoma, in situ carcinoma, and dysplasia.
CONCLUSION: Chronic inflammatory irritation by retained food may induce chronic hyperplastic esophagitis and eventually malignant transformation of esophageal epithelial cells, associated with dysplasia-carcinoma sequence. Achalasia seems to be a risk factor for developing squamous cell carcinoma of the esophagus, even if after surgically treated. Long-term follow-up for patients with achalasia by endoscopic screening with iodine staining is recommended.
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Disclosure of Interest: None Declared
Keywords: achalasia, esophageal cancer, esophageal carcinogenesis

P486 PALLIATIVE OESOPHAGEAL STENTING- THE EXPERIENCE OF A DISTRICT GENERAL HOPSITAL

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INTRODUCTION: Oesophageal cancer is often diagnosed late in it pathological process, resulting in limited options for curative treatment. As a consequence management is usually targeted at symptom control, with palliative oesophageal stenting an important procedure allowing for improved nutrition, hydration and comfort. This cohort of patients is usually elderly, with comorbidities and so striking the balance between symptom control and the risk of complications can be difficult. The aim of this study was to evaluate the use of oesophageal stenting in the setting of a large district general hospital.
AIMS&METHODS: We retrospectively reviewed all patients who underwent palliative oesophageal stenting between June 2010 and July 2012 across the North East Hertfordshire NHS trust. These cases were reviewed with respect to patient demographics, techniques employed, mortality at days seven, fourteen and thirty as well as complications with in the three months post procedure.
RESULTS: During this two year period 40 patients underwent palliative oesophageal stenting. There was a male preponderance, with the average age of 74 years old. The majority of tumours were adenocarcinomas, with squamous cell carcinomas accounting for approxiamately third of cases.
All procedures were carried out under fluoroscopic guidance, with successful deployment of covered metal stents (Boston Ultra-flex). A single endoscopist carried out 24 of the 40 procedures; however the remaining stents were performed by four different endoscopists, with the mean number of stents per consultant being four per year.

Short term mortality was 5% at day 7, 7.5% at day 14 and 15% at day 30, with the cause of deterioration due to background medical problems rather than as a direct consequence of this intervention.
The most common reason for failure of success of stent placement within 3 months was tumour infiltration, affecting 10% of patients in this time period. There were complications in a minority of patients, with food bolus obstruction in 5%, stent migration in 2.5%, and no cases of perforation and haemorrhage.
CONCLUSION: Our data has demonstrated that oesophageal stenting remains a safe option for symptom control in palliative oesophageal cancer. Mortality and morbidity rates are below that of the national average as described in the national oesophago-gastric cancer audit, this is likely to represent better patient selection and increased use of alternative palliative procedures such a laser therapy and dilatation. Complication rates are low despite the small numbers carried out per endoscopist, making the district general hospital a suitable environment to carry out such interventions.
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Disclosure of Interest: None Declared
Keywords: oesophageal adenocarcinoma, oesophageal stent

P487 THE SALVAGE ENDOSCOPIC TREATMENT(SET) FOR THE THE SUPERFICIAL HEAD & NECK SQUAMOUS CELL CARCINOMA (SHESCC) FOUND IN THE RADIOTHERAPY FIELD

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INTRODUCTION: The most of the squamous cell carcinoma in the head & neck region(HNSCC) is usually found at advanced stage. Surgical treatment is invasive and is greatly undermined the postoperative QOL. So the chemo-radiation therapy(CRT) has been globally accepted for the first treatment. The HNSCC has tendency for metachronous cancer, and some HNSCC had CRT resistance. So we often find the second cancer in the radiotherapy field. For such a patient, total laryngectomy is only the last treatment.If the second cancer is limited in local area, minimally invasive treatment should be a desirable. It has been known that some of the recurrent superficial esophageal cancer after CRT can be cured by endoscopic treatment (ET). So the second superficial-HNSCC(SHNSCC) without metastasis may be cured by endoscopic treatment, and it must be a very good for patients.
AIMS&METHODS: The purpose of this study is to assess the effectiveness of the SET for the second SHNSCC found in the radiotherapy field.The SHNSCC is defined as a carcinoma that the depth of invasion is within the sub-epithelial layer. From Jan 2000 to Feb 2013, we have 314patients (570lesions) of the SHNSCC. Of the 314patients, 253patients (475lesions) had been treated by ET. Of the 253cases, 22 patients were the SET cases. The indication of the SET is that the second HNSCC was superficial type and had no metastasis. For those SET cases, we investigated their clinical and pathological data.
RESULTS: Among 22patients,20 were men and 2 were women, mean age at first treatment was 68.9 years (range 57-84).10 have received CRT/RT for esophageal cancer, and 12 have received CRT/RT for HNSCC. Average dose of RT was 59.9Gy. 5Fu+CDDP had been given to 9patients and TAT had been given to 3patients as a chemotherapy.We could performed Endoscopic Laryngo-Pharyngeal Surgery(ELPS)safely and succeeded in complete en-bloc resection in all cases. We had 2 cases of postoperative bleeding, 2 of postoperative laryngeal edema and 1 of postoperative stenosis, but there were no fatal complications. After the ELPS, swallowing and vocal function was completely preserved in all cases, and QOL of patients was very good. Among the 22patients, 15(68.2%) are alive, 7(31.8%) died (2 for HNSCC, 5 for other disease).
CONCLUSION: The result of our trail indicated the usefulness and effectiveness of the SET for the second SHNSCC found in the radiotherapy field. For this purpose, gastrointestinal endoscopist should also focus on the SHNSCC detection
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Disclosure of Interest: None Declared
Keywords: Endoscopic treatment, The salvage treatment, The the superficial head & neck squamous cell carcinoma

P488 DIAGNOSIS AND TREATMENT FOR EARLY PRIMARY MALIGNANT MELANOMA OF THE ESOPHAGUS (PMME)

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INTRODUCTION: Primary malignant melanoma of the esophagus (PMME) is a rare disease. Treatment for advanced PMME is basically esophagectomyor CRT, but treatment effect is very poor and it's prognosis is extremely poor. It is well-known fact endoscopic resection (ER; ESD/EMR) is the first treatment of the early GI tract cancer, and can cure the early cancer. Early PMME is more rare than advanced PMME and is very difficult to find because we do not know collect endoscopic findings. But there is a possibility early PMME has no metastasis just same as early cancer in theGI tract. With this fact and speculation, if we find the early PMME, ER
may also be effective for early PMME instead of operation.
AIMS&METHODS: The purpose of this study is to examine the effectiveness of the ER for the early PMME. From Jan 2000 to Feb 2013, we experienced 3 cases of early PMME. For those 3 cases, we investigated their clinical and pathological data.
RESULTS: 1 case was a 57y.o female, 2 cases were 65 and 57y.o male. There ware no symptoms in all cases, and all cases were found by screening endoscopy. Lesions were located in all part of esophagus. The size of lesion was 3-25mm, the shape was flat(0-IIb). The color of pigmented spots was a very clear black and the spots was composed of large and small size. The demarcation line was irregular, ill-defined and faded in color. Case1:A 65y.o men with 1 lesion. He was treated by total esophagectomy with LN dissection. Pathological diagnosis revealed the lesion was PMME and the depth of invasion was T1a-LPM and no lymphatic-vascular invasion, no LN metastasis. He died of pneumonia in five years after surgery, but there wasno recurrence of cancer.Case2:A 57y.o female with 4 lesions. After the CT examination showing no metastasis, ER was performed, as the patient chose ER rather than operation that was the standard therapy we suggested. Pathological diagnosis revealed the lesions ware PMME and the depth of invasion were T1a-LPM and no lymphatic and vascular invasion. We followed up every 6months by endoscopy, and went through 6 ERs in total for new early PMMEs during the follow-up period. 6.5 years has passed since the first treatment, the patient is still alive and free from disease.Case3:A 57-year old male with 2 lesions. After the informed consent that ER was an option to operation, 2 lesions were removed by ER. The pathological diagnosis revealed the lesions were PMME and the depth of invasion were T1a-LPM and no lymphatic and vascular invasion.
CONCLUSION: Our 3 cases indicate the possibility to cure early PMME by ER, and ER can be an adequate optional treatment for early PMME.
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Disclosure of Interest: None Declared
Keywords: Endoscopic resection, Esophageal malignant melanoma

P489 A REQUIREMENT OF PROPHYLACTIC TREATMENT AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR SUPERFICIAL ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESCC).

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INTRODUCTION: Since the ESD for superficial ESCC can now resect the lesions collectively, it has become possible to more detailed pathological evaluation. There is a lymph node metastasis of 10-20% in T1a-MM and T1b-SM1 ESCC, there is a approximately 40% in T1b-SM2 ESCC. When pathological examination of the ESD specimen confirms T1a-MM or T1b ESCC, it is necessary to provide the prophylactic treatment, chemoradiotherapy (CRT) or surgical resection. However, some patients are over-treated by the prophylactic treatment because it is not so high rate of metastasis for T1a-MM and T1b-SM1 ESCC.
AIMS&METHODS: The aim of this study is to inspect a requirement of the prophylactic treatment and a pathological risk factor of metastasis of T1a-MM and T1b ESCC. In the cases of pathological T1a-MM or T1b ESCC undergoing ESD in our hospital, I examined the relations with metastasis of vascular invasion and Droplet infiltration (DI), and more, I examined the presence or absence of the prophylactic treatment and the outcome of the cases. The DI, the infiltrative growth pattern that the nest of cancer infiltrates, is thought that it is one of the risk factor of metastasis.
RESULTS: In 40 cases of T1a-MM ESCC, there were 6 cases (15%) of vascular invasion-positive, 7 cases (18%) of DI-positive, and 3 cases (8%) were positive both. CRT was performed in 3 cases and surgical resection was performed in 2 cases and the other 5 cases are followed up without the prophylactic treatment. 30 cases without risk factor were followed up without the prophylactic treatment, but lymph node recurrence was observed in 1 case. In 4 cases of T1b-SM1 ESCC, there was 1 case (25%) of vascular invasion-positive, and CRT was performed. The other cases were negative of risk factor and followed up without the prophylactic treatment. In 11 cases of T1b-SM2 ESCC, there were 6 cases (55%) of vascular invasion-positive, 5 cases (46%) of DI-positive, and 5 cases (9%) were positive both. CRT was performed in 2 cases and surgical resection was performed in 6 cases. In 6 cases undergoing surgical resection, there were 2 cases (33%) of lymph node metastasis. 3 cases were not performed the prophylactic treatment for the elderly. In all cases of T1a-MM and T1b ESCC, death from original disease has not been seen.
CONCLUSION: For T1a-MM and T1b-SM1 ESCC without metastasis clinically, ESD is performed actively, it should be determined whether it is necessary to the prophylactic treatment by pathological evaluation. Although ESD indication may be expanded to T1b-SM2 ESCC, it is a theme which the prophylactic treatment is selected.
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Disclosure of Interest: None Declared
Keywords: ESD, esophageal squamous cell carcinoma, pathological risk factor of metastasis, prophylactic treatment

P490 THE REPRESENTATIVE CHARACTERISTICS OF SUPERFICIAL BARRETT'S ESOPHAGEAL CANCER ARE A REDDISH AREA LOCATED ON THE ANTERIOR TO RIGHT SIDE WALL IN JAPANESE PATIENTS.

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INTRODUCTION: Barrett's esophageal cancer (BC) is less common in Japan than in Western countries, so few clinical studies of this condition have been

conducted in this country. The aim of this study was to evaluate the clinicopathological characteristics of BC in Japanese patients.
AIMS&METHODS: Thirty four patients (36 lesions) with superficial BC (34 male (100%), mean age 66.5yr) and 43 patients with endoscopically detected Barrett's esophagus (BE) with a length of more than 2 cm (34 male (79.1%), mean age 64.0yr) were enrolled in this study. We evaluated clinicopathological factors, the body mass index (BMI), and the presence of reflux esophagitis (RE), specialized intestinal metaplasia (IM), hiatal hernia (HH), and *Helicobacter pylori* (HP) infection, and assessed gastric acid secretion using the endoscopic gastrin test (EGT) (mEq/10 min) (Am J Gastroenterol 1998).
RESULTS: Thirty one (86.1%) of 36 BC were visualized as a reddish lesion, 28 (77.8%) were located on the anterior to right side wall. Intestinal type adenocarcinoma was common in BC (94.4%). Most of BC was derived from short segment BE (85.2%). BMI in patients with BC (22.9) was not significant differences in those with BE (24.2). The prevalence of IM in patients with BC (73.5%) was not significant differences in those with BE (72.1%). The prevalence of RE in patients with BC (29.4%) was not significant differences in those with BE (37.2%). The prevalence of HH (52.9%) in patients with BC was not significant differences in those with BE (34.9%). The HP infection rate in patients with BC (38.3%) was not significant differences in those with BE (25.6%). EGT values in patients with BC (4.3mEq/min) was not significant differences in those with BE (5.7).
CONCLUSION: The representative characteristics of superficial BC are a reddish area located on the anterior to right side wall in Japanese patients. Additionally, most of the BC in Japan is derived from short segment BE.
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Disclosure of Interest: None Declared
Keywords: Barrett's esophageal cancer, Clinicopathological characteristics

P491 PREVENTING ESOPHAGEAL STRICTURE BY COVERING MUCOSAL DEFECTS WITH POLYGLYCOLIC ACID SHEETS FOLLOWING ENDOSCOPIC SUBMUCOSAL DISSECTION: A NOVEL APPROACH

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INTRODUCTION: Endoscopic submucosal dissection (ESD) for superficial esophageal cancer is widespread. However, esophageal stricture following ESD can occur as a major complication in cases of larger mucosal defects and leads to a decrease in quality of life. The incidence of esophageal stricture at our hospital is 28% (n=231 cases) with mucosal defect size ranging from 2/3 to 11/12 the esophageal circumference. Although steroid injection into the submucoal layer and oral administration of prednisolone have recently been reported as preventive measures, ulcer formation due to steroid injection or severe pneumonia due to oral prednisolone has been experienced. Therefore, we examined the efficacy of polyglycolic acid sheets (Neovel®) for mucosal defects.
AIMS&METHODS: Of 104 patients with 116 lesions resected by ESD from May 2012 to March 2013, 10 patients were enrolled. All patients had a mucosal defect with an esophageal circumference of 2/3 to 11/12 and gave informed consent to participate. After confirming the size of the mucosal defect, Neovel sheets were cut into patches measuring 5 × 10 mm. As a first step, a small amount of fibrinogen, one part of fibrin sealant, was sprayed onto the artificial ulcer, and the Neovel patches were placed without overlapping. Remnant fibrinogen and thrombin were then sprayed onto the Neovel patches. The prevalence of esophageal stricture, remaining Neovel at one and two weeks after ESD, and adverse events were investigated.
RESULTS: Mean age was 66.7 years old, and 80% of the subjects were men. Invasion depth was confirmed by histological examination as follows: m1, n=1; m2, n=7; m3, n=1, and sm2, 1. Two patients who were diagnosed with m3 and sm2 were excluded because they underwent surgical resection after ESD. Mucosal defect circumference was as follows: 7/12, n=2; 8/12, n=4; 9/12, n=1, and 11/12, n=1. Residual Neovel was 87.5% at one week and 50% at two weeks after ESD. No esophageal stricture or adverse events were observed. As a minor complication, post-ESD bleeding occurred in 1 case, but was treated successfully by conservative treatment. No serious complications or treatment-related deaths were noted.
CONCLUSION: The present treatment resulted in no esophageal strictures and appeared to have a high level of safety. Therefore, polyglycolic acid sheets have the potential to prevent esophageal stricture. Nevertheless, the procedures are rather cumbersome, so further investigations are warranted.
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Disclosure of Interest: None Declared
Keywords: ESD (endoscopic submucosal dossection), esophageal stricture, novel method, polyglycolic acid sheets

P492 SUITABLE SETTING OF A TARGET-CONTROLLED INFUSION SYSTEM WITH A BISPECTRAL INDEX MONITOR FOR PROPOFOL SEDATION ADMINISTERED BY A NON-ANESTHESIOLOGIST DURING ESD

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INTRODUCTION: Propofol administration via a target-controlled infusion system with a bispectral index monitor (BIS/TCI system) is expected to prevent complications of sedation during complex and long endoscopic procedures such as gastric and oesophageal endoscopic submucosal dissection (ESD). There is a need for a suitable and safe method of propofol administration by non-anesthesiologists in order to maintain a moderate to deep sedation during procedures.
AIMS&METHODS: We evaluated the settings of the BIS/TCI system with propofol sedation during ESD. From May 2009 to Feb 2013, 250 patients with oesophagogastric neoplasms were treated with ESD using the BIS/TCI system of propofol sedation. In the TCI system, the initial target blood concentration of propofol was 1.2μg/ml. The titration speed of propofol was adjusted by increasing or decreasing the blood concentration of propofol by 0.2μg/ml according to the BIS score and the movement of the patients. The BIS target level ranged from moderate to deep sedation, at which a stable BIS score between 60 and 80 was obtained. In addition, the frequencies of oxygen desaturation (SpO2 < 90) and hypotension (BP < 90 mmHg) were evaluated during the procedures.
RESULTS: The mean procedure time was 89±59 min, and the mean dose of propofol was 4.19±1.32 mg/kg/h. In 80.4% of cases it was possible to maintain stable sedation with blood concentration of less than 1.6μg/ml using TCI. The default setting of ideal blood concentration for propofol was 1.2μg/ml because the medians of lower and upper bounds of the blood concentration were 1.2 (range 0.6-1.8)μg/ml and 1.4 (range 1.0-3.8)μg/ml, respectively. Although hypotension occurred in 27 cases (10.8%), oxygen desaturation occurred in only 9 cases (3.6%). All cases were resolved through conservative therapy or by increasing the concentration of supplied oxygen. There were no severe adverse events involving propofol sedation during the ESD procedures.
CONCLUSION: It was possible for a non-anesthesiologist using our settings to maintain stable sedation during a time-consuming endoscopic procedure through propofol sedation with a BIS/TCI system.
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Disclosure of Interest: None Declared
Keywords: bispectral index monitor, propofol, sedation, target-controlled infusion

P493 CARCINOMATOSIS MATTERS: CLINICAL OUTCOMES AND PROGNOSTIC FACTORS FOR CLINICAL SUCCESS OF STENT PLACEMENT IN MALIGNANT GASTRIC OUTLET OBSTRUCTION

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INTRODUCTION: Although one recent retrospective study has shown that carcinomatosis is not a contraindication to stenting in selected patients with malignant gastric outlet obstruction (GOO), associate factors for clinical success rate of self-expandable metallic stent (SEMS) placement in GOO patients with carcinomatosis have not been fully characterized.
AIMS&METHODS: We analyzed a total 228 patients who were scheduled for SEMS placement for malignant GOO in tertiary-care academic medical center. All patients were treated with an uncovered or covered SEMS by using the over-the wire placement procedure. We retrospectively evaluated clinical outcomes of SEMS placement.
RESULTS: Technical success was achieved in all patients. Patients were categorized into two groups according to the presence of carcinomatosis. Clinical success rates of patients without carcinomatosis group and with carcinomatosis group were 93.9% (92/98) and 80.8% (105/130), respectively ($P = 0.004$). Poor performance status (ECOG $\geq$ 3, $P < 0.001$) and carcinomatosis ($P = 0.016$) were independent poor predictive factors for clinical success of SEMS placement. In subgroup analysis in patients with carcinomatosis group, clinical success rates of patients without ascites group and with ascites group were 92.1% (70/76) and 64.8% (35/54), respectively ($P < 0.001$). Poor performance status (ECOG $\geq$ 3, $P = 0.025$) and ascites ($P = 0.002$) were independent poor predictive factors for clinical success of SEMS placement in carcinomatosis subgroup.
CONCLUSION: In palliation for malignant GOO, the status of carcinomatosis with ascites is a significant poor predictive factor for clinical success of SEMS placement.
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Disclosure of Interest: None Declared
Keywords: ascites, Carcinomatosis, Gastric outlet obstruction, Self Expanding Metal Stent

P494 PROTECTION OF CHEMOTHERAPY-INDUCED MUCOSITIS BY EMU OIL: AN EXPERIMENTAL STUDY

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INTRODUCTION: Emu oil, which is extracted from the subcutaneous or retroperitoneal fat of the emu, is mainly composed of fatty acids like oleic acid, linoleic acid, and linolenic acid. Recentrly, one study suggested that emu oil can decrease intestinal inflammation in mucositis rat model. Mucositis is one of the serious complications of cancer chemotherapy with no effective treatments.
AIMS&METHODS: The aim of this study is to validate the protective effect of emu oil on chemotherapy induced mucositis. Male Sprague dawley rats (n 36; 235-265g) were ramdomly allocated to one of the following groups (n 12), water and saline; water and 5-fluorouracil (5-FU); emu oil and 5-FU. The rats were orogastrically gavaged with emu oil (1ml) or water (1ml) for 5days before intraperitoneal injection of 5-FU (150mg/kg) or saline (control), and orogastric gavage with emu or water was continued up to the day of sacrifice (96h post 5-FU administration). Histologic parameters (inflammatory cell infiltration, villus height, crypt depth), myeloperoxidase (MPO) activity, which is a indicator of inflammation, by enzyme-linked immunosorbent assay were measured in intestinal tissues collected at sacrifice.

RESULTS: All 5-FU injected rats did not gain weight for the duration of the trial compared with saline injected controls. But MPO activity in the small bowel was decreased by emu oil compared with 5-FU treated controls 96 h post 5-FU administration. There were also increases in crypt depth in the small bowel of rats that receivied emu oil compared with 5-FU-treated controls.
CONCLUSION: This study suggest that emu oil has protective effect on chemotherapy induced mucositis. Further studies are required to define specific mechanisms of protective effect of emu oil on intestinal mucositis.
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Disclosure of Interest: None Declared
Keywords: chemotherapy, emu oil, mucositis

P495 IMPACT OF METABOLIC SYNDROME ON THE ONCOLOGIC OUTCOME AFTER RADICAL GASTRECTOMY FOR GASTRIC CANCER

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INTRODUCTION: Several studies have shown that metabolic syndrome (MS) was a risk factor for colorectal cancer, breast cancer and prostate cancer. But few studies have reported the relationship between MS and the prognosis of gastric cancer.
AIMS&METHODS: Data were collected from 555 patients underwent radical gastrectomy for gastric cancer between January 2006 and December 2007 for pilot study. The patients with inadequate or missing data were excluded. Remaining 204 patients were divided into 2 groups based on the presence of MS. We tested the prognostic value of MS in the patients.
RESULTS: No significant differences were observed in tumor staging and grade of tumor differentiation between the 2 groups, MS (n = 60) and non-MS (n = 144) groups. Median follow-up periods were 53.2±23.5 and 54.7±22.1 months in MS and non-MS groups, respectively ($P = 0.677$). 17 (28.3%) and 21 (14.6%) patients showed recurrence of tumor in MS and non-MS group, respectively ($P = 0.022$). In addition, disease-free survival of the patients in MS group was inferior to those in non-MS group ($P = 0.036$). Cox regression hazard model demonstrated that advanced tumor stage (stage III or IV, HR = 13.9, 95% CI = 6.5 to 29.7) and presence of MS (HR = 2.4, 95% CI = 1.2 to 4.5) were independent risk factors for recurrence. Body mass index was the major factor with the influence on patients with gastric cancer accompanied by MS.
CONCLUSION: MS may be an important prognostic factor for gastric cancer. Control of metabolic syndrome would improve the therapeutic efficacy of gastric cancer.
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Disclosure of Interest: None Declared
Keywords: disease free survival, gastric cancer, Metabolic syndrome

P496 FEASIBILITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR TYPE I GASTRIC CARCINOIDS COMPARED WITH ENDOSCOPIC SUBMUCOSAL RESECTION

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INTRODUCTION: Conventional endoscopic submucosal resection (EMR) of carcinoid tumors is often associated with involvement of the resection margin, which necessitates further intervention. Endoscopic submucosal dissection (ESD) is a novel technique for the removal of carcinoid tumors.
AIMS&METHODS: The aim of the present study was to compare the clinical usefulness of ESD with that of EMR for the complete resection of gastric carcinoid tumors. Between January 2001 and October 2010, a total of 41 patients with 54 type I gastric carcinoid tumors that were estimated to be 10 mm or less in diameter and that were resected either using ESD or EMR were investigated for this study. The complete resection rate and complications associated with these two procedures were analyzed.
RESULTS: Among the 54 lesions, 36 were resected using EMR, and 18 lesions were resected using ESD. There were no significant differences between the EMR and ESD groups in terms of the location or the size of the tumors. The overall ESD complete resection rate was higher than that of EMR (88.9% vs. 75.0%, respectively, P=0.301). A lower vertical margin involvement rate was obtained when ESD was performed compared to that when EMR was performed (5.6% vs. 16.7%, respectively, P=0.403). However, there was no statistical difference. The complication rate was not significantly different between the two groups.
CONCLUSION: ESD showed higher complete resection rate, especially in vertical margin despite lack of statistical significance.
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Disclosure of Interest: None Declared
Keywords: Carcinoid tumor, Endoscopic submucocsal resection, Ligation device

P497 MANAGEMENT OF URGENT UPPER GI REFERRALS: TIME FOR A RETHINK

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INTRODUCTION: Patients in the UK with upper gastrointestinal (UGI) symptoms suggestive of cancer are referred to hospital under the 'Two week wait (2WW)' pathway. Those patients with 'alarm' symptoms thought to indicate the presence of a gastric or oesophageal (GO) cancer are sent directly for an upper GI endoscopy (OGD), but the cost-effectiveness of this approach is uncertain. It is also uncertain whether dyspepsia should be included as an 'alarm symptom', although the NICE referral guidelines suggest patients aged >55 years with recent onset dyspepsia should be referred under the 2WW pathway. We reviewed our practice to establish the value of the 'direct to test' approach for upper GI 2WW patients.
AIMS&METHODS: Aim- To determine the frequency of GO carcinoma in 2WW patients with different combinations of symptoms.
Method - Patients referred with UGI symptoms on the 2WW pathway between April 2008 and January 2013 were identified. The frequency of a 'tumour' found in patients with a combinations of symptoms was determined; these include weight loss, dysphagia, vomiting, haematesis or malaena, anaemia and/or dyspepsia. To establish whether dyspepsia alone was of any value in identifying patients with gastric cancer, we expanded our search to determine the likelihood of finding a cancer in any patient (including non-2WW urgent and routine referrals)
RESULTS: In total, 154 GO cancers (92 in patients referred under 2WW) were identified in 14572 OGDs, performed during April 2008 and January 2013 (48% male, mean age 63 (18-99 years)).
No symptom (or symptom combination) yielded a cancer diagnosis rate of over 7%. GO cancer was most likely to be detected patients with dysphagia. To examine further the value of uncomplicated dyspepsia (dyspepsia alone) in detecting patients with cancer we looked at all patients referred over the same time period. Of 4168 patients referred with dyspepsia, 19 (0.46%) had cancers. After removing those patients who also had anaemia, weight loss or dysphagia and discounting those patients where biopsies of the 'tumour or mass' were negative on histology, only three patients with tumours were found: one leiomyoma, one GIST and a squamous cell carcinoma of the oesophagus. No gastric carcinomas were found in any patient with uncomplicated dyspepsia.
CONCLUSION: Summary
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1.Over 96% of patients referred on the upper GI 2WW pathway have no evidence of cancer at endoscopy 2.Only one cancer was identified in any patient with dyspepsia as the only clinical feature
Conclusion
Patients referred on the upper GI 2WW pathway should be reviewed in the clinic prior to endoscopy to ensure more efficient use of resources.
Dyspepsia is of no value in identifying patients with upper GI cancer and should be removed from 2WW referral proformas.
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Disclosure of Interest: None Declared
Keywords: Dyspepsia, UGI malignancies, Urgent OGDs

P498 ANALYSIS OF LYMPH NODE METASTASES AFTER ADDITIONAL SURGERY FOR EARLY GASTRIC CANCER TREATED BY ESD WITH PATHOLOGICAL LYMPHATIC INVASIONS

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INTRODUCTION: If resected specimens have lymphatic invasions after ESD (Endoscopic Submucosal Dissection) for early gastric cancers, they are considered as non-curative and additional surgery is recommended. But the result of additional surgeries is not investigated enough.
AIMS&METHODS: The risk of lymph node metastases after additional surgery for early gastric cancers treated by ESD with pathological lymphatic invasions, is analysed. From January 2002 to December 2012, 611 cases (662 lesions) of early gastric cancers were treated by ESD at Yamagata Prefectural Central Hospital. Resected specimens were pathologically diagnosed with 2mm width step serial sections. If lymphatic invasions were diagnosed, such cases were recommended to be treated by additional surgery. Lymphatic invasions were confirmed by D2-40 immuno-staining.
RESULTS: 1) Out of 611 cases of early gastric cancers treated by ESD, lymphatic invasions were pathologically diagnosed in 20 cases (3.3%). All 20 cases were

given surgical treatments. 2) Out of 20 cases, lymph node metastases were pathologically diagnosed in 5 cases (25%).
CONCLUSION: After additional surgery, lymph node metastases were diagnosed in only 5 cases (25%). This result means that 75% of cases were overtreated by surgery. We need to research more diagnostic factors of lymphatic invasion patterns which indicate the risk factor for lymph node metastases.
Disclosure of Interest: None Declared
Keywords: additional surgery, ESD (endoscopic submucosal dossection), lymph node metastases, lymphatic invasion

P499 PROGNOSTIC SIGNIFICANCE OF GLASGOW PROGNOSTIC SCORE IN PATIENTS WITH INCURABLE GASTRIC CANCER

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INTRODUCTION: Systemic inflammation has been proved to be correlated with poor survival in many cancers. Recently, the inflammation based Glasgow prognostic score (GPS), based on serum levels of C-reactive protein (CRP) and albumin, has been used to predict survival in cancer, including gastric cancer. However, the significance of GPS in incurable gastric cancer has not been known. This study investigates the significance of the modified Glasgow prognostic score (mGPS) for the survival in patients with incurable gastric cancer.
AIMS&METHODS: The mGPS (albumin <35 g /L $=1$ and CRP >10 mg/L$=1$) was calculated on the basis of the data for 448 patients with metastastic gastric cancer. Patients were given an mGPS of 0, 1, or 2 according to the score. The prognostic significance was analyzed by univariate analyses.
RESULTS: Significant correlations were found between overall survival and CEA, CA19-9, CRP, Albumin,TNM stage and mGPS. Sex, white cell count, neutrophils, CEA, tumor stage were each significantly correlated with the mGPS. Univariate analysis showed that CEA, CA19-9,tumor stage and mGPS were significantly associated with overall survival, while multivariate analysis showed that only mGPS was significantly associated with overall survival (OR, 1.658; 95% CI, 1.203–2.286; $P=0.002$). Kaplan-Meier analysis demonstrated significant differences among patients with mGPS of 0, 1 and 2 ($P<0.001$), with the mortality rate higher for patients with a higher mGPS.
CONCLUSION: The inflammation based score, modified Glasgow prognostic score (mGPS), can predict survival in patients with incurable gastric cancer.
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Disclosure of Interest: None Declared
Keywords: gastric cancer, Glasgow prognostic score, metastasis, Prognosis

P500 PROGNOSTIC FACTORS OF THE PATIENTS WITH STAGE I / II GASTRIC CANCER

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INTRODUCTION: According to the recent report of Japanese nationwide registry[1, 2], 5-year survival rates of patients with stage I/II gastric cancer were satisfactory. The primary cause of death of the stage I patients were not cancer recurrence. Japanese Gastric Cancer Association (JGCA) guideline recommends that patients with stage I and T3N0 (stage II) cancer receive no adjuvant chemotherapy. However, it would be still important to select high risk patients for recurrence when applying modified surgery.
AIMS&METHODS: To investigate prognostic factors in stage I/II gastric cancer, clinical and pathological factors of consecutive 357 patients who received curative surgery for primary gastric cancer from 2001 to 2005 were analyzed retrospectively. Prognostic factors included age, sex, histological differentiation, size and depth of tumor, capillary invasion and number of node metastasis. Postoperative survival rates were calculated by Kaplan-Meier method. Cox regression model were used to search significant prognostic factors. JGCA (13th edition) and TNM (5th edition) classifications were used for definition of prognostic factors.
RESULTS: Among 357 patients, 298 were stage IA, IB and II. Overall 5-year survival rates were 91.8%, 85.4% and 62.1% respectively. Fourteen of 298 stage I/II patients died of recurrence. Median survival time of them was 32 months. Seven peritoneal, 5 liver, 3 local and 3 distant metastases were observed. Advanced age, male, JGCA-N (lymph node station) and undifferentiated tumor were selected as significant prognostic factors by Cox regression analysis.
CONCLUSION: Though the number of patients was too small, these data suggested that age, sex, lymph node metastasis and histological differentiation might be risk factors in stage I/II gastric cancer. Further study using a larger dataset seems to be needed.
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Disclosure of Interest: None Declared
Keywords: Gastric cancer, prognostic factor, surgical treatment

P501 ENDOSCOPIC LIGATION AND RESECTION FOR GASTROINTESTINAL SUBMUCOSAL TUMORS SMALLER THAN 3 CM

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INTRODUCTION: For gastrointestinal (GI) submucosal tumors (SMTs) <3 cm, endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) may obtain inadequate tissue for a conclusive diagnosis and their optimal treatment is controversial sometimes. We studied a relative safe endoscopic treatment with sufficient tissue retrieved for pathological diagnosis of these tumors.
AIMS&METHODS: Since Jan. 2010 till Mar. 2013, patients with GI SMTs <3 cm found by upper or lower GI endoscopy and confirmed by EUS without evidence of metastasis were enrolled to analyze the diagnostic yield and outcome of endoscopic ligation and resection (ELR). An endoscopic ligator with rubber band for tumor <1.2 cm or a detachable endoloop for tumor >1.2 cm was used to tighten around the tumor base, then, after EUS to confirm the lesion was located above the band or endoloop, endoscopic resection and retrieval of upper portion of the ligated tumor for pathological study was performed. The remnant portion was left for a spontaneous sloughing and follow-up EUS at 1 month and 6 months after ELR and every 12 months thereafter were scheduled. Further surgical intervention was carried out for those residual SMTs found during follow-up period and diagnosed as intermediate or high malignant potential.
RESULTS: A total of 23 patients (16 women, mean age 59.8 $\pm$ 11.1 years) with 27 GI SMTs <3 cm were treated by ELR and received follow-up period ranged from 1 to 39 (mean 15.6) months. The tumors number and location were 10 at gastric body, 8 at gastric fundus, 2 at gastric antrum, 3 at duodenum , 2 at esophagus and 2 at colon-rectum. The tumors size ranged from 0.3 to 2.9 (mean 1.3 $\pm$ 0.8) cm included 19 tumors were <1.2 cm, 4 tumors were 1.2 to 2 cm and 4 tumors were >2 cm. Pathological diagnosis of these tumors included 17 (62.9%) gastrointestinal stromal tumors (GISTs), 4 (14.8%) lipomas, 2 (7.4%) leiomyomas , 2 carcinoids, 1 (3.7%) Brunner's gland hyperplasia and 1 mesenchymal tumor. Two larger (2.6 and 2.9 cm) GISTs received further surgical resection due to >5 mitoses per 50 high power fields were found and residual tumors still existed during follow-up period. The other GI SMTs revealed complete sloughed without severe complications after ELR and all patients were still alive without recurrent tumors till last follow-up.
CONCLUSION: Our preliminary results support that ELR may provide a good diagnostic yield and may be considered as a safe alternative treatment for patients with localized low malignant potential GI SMTs <3 cm.
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Disclosure of Interest: None Declared
Keywords: Endoscopic ligation therapy, Submucosal tumor

MONDAY, OCTOBER 14, 2013 9:00–17:00
***H. PYLORI* I – Poster Area**

P502 EPIDEMIOLOGY OF HELICOBACTER PYLORI INFECTION: THE SORBO SAN BASILE STUDY

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INTRODUCTION: In 2001, a prospective study was planned in Sorbo San Basile, a small town in southern Italy (932 inhabitants).
AIMS&METHODS: The study started in 2002 (n.595, 64% representative participants) and continued in 2012 when subjects with no evidence of active *H. pylori* infection in 2002 were recruited (n.157, 76% representative participants). Blood was drawn from 518 (87%) and 117 (75%) participants in 2002 and 2012, respectively. A structured questionnaire dealing with sanitary and socioeconomic issues was administered (e.g.: breastfeeding, dyspepsia, smoking, antibiotics and alcohol consumption, parental occupation and education, social class, crowding). Active *H. pylori* infection was assessed by 13C-UBT. Serum VacA and CagA antibodies were determined by western blotting. IL-2, IL-10, IL-12, and IFN-g functional polymorphisms were genotyped. Data were analyzed by multivariable logistic regression analysis.
RESULTS: Active *H. pylori* infection was found in 351 (59%) of 595 participants (264M, 3-97 yr). Age (OR 1.06) and people per room (OR 2.18) were independent risk factors. Of 518 subjects, 479 (92%) and 369 (71%) were VacA and CagA positive, respectively, whereas 310 (60%) UBT positive. Age (OR 1.11), BMI (OR 0.91), and breastfeeding (OR 2.68) were independent risk factors for subjects serology positive and UBT positive or negative (n.479; 92%) compared to those serology and UBT negative (n.39; 8%) while age (OR 1.04) and female gender (OR 1.70) were for subjects serology and UBT positive (n.310; 60%) compared to those serology positive and UBT negative (n.169; 32%). Furthermore, age (OR 1.10) and IL-10 polymorphism (OR 2.72) were independent risk factors for subjects VacA, CagA, and UBT positive compared to those VacA positive and CagA and UBT negative. Ten years later, of 157 subjects only 4 (0.26%/yr) became UBT positive. BMI, social class, household people, and people per room significantly improved (p=0.00) in the 157 subjects. Of 117 subjects, 13 (5%/yr) and 50 (5.3%/yr), and 7 (0.8%/yr) and 2 (0.9%/yr) had VacA and CagA seroconversion and seroreversion, respectively.
CONCLUSION: In this general population, age and crowding at home are major determinants of active *H. pylori* infection while socioeconomic

improvement paralleled a very low incidence rate. Crosstabulation of serology and UBT indicates: 1. a very high exposure to *H. pylori* (up to 92%), particularly in older subjects, those with lower BMI and who had breastfeeding; 2. a dynamic infection with wide range of spontaneous clearance (14 to 84%), higher in the last 10 years, first decades of life, and males. 3. that polymorphism of IL-10 (high production) is associated with active CagA positive infection.

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Disclosure of Interest: None Declared

Keywords: cagA gene, cytokine polymorphisms, Helicobacter pylori, urea breath test, VacA

P503 EFFECTS OF SMOKING ON HELICOBACTER PYLORI-ASSOCIATED CHRONIC GASTRITIS AND THE DEVELOPMENT OF GASTRIC CANCER

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INTRODUCTION: Smoking, as a lifestyle factor, is considered to be deeply involved in gastric cancer (GC) development. Since the intra-gastric environment alters with progression of *Helicobacter pylori* (HP)-associated gastritis, it is reasonable to speculate that the effects of smoking on GC development differ at different stages of HP-associated gastritis.

AIMS&METHODS: Thus, the effects of smoking on GC development during the course of HP-associated gastritis were investigated.An occupational cohort of 4,585 healthy middle-aged men were followed for a mean (SD) period of 11.7 (4.4) years. The stage of HP-associated gastritis was evaluated with serum levels of HP antibodies and pepsinogen. The effects of smoking on gastritis activity level, extent of chronic atrophic gastritis (CAG), and GC development were investigated for each stage of the gastritis.

RESULTS: In an HP-uninfected group, smoking promoted exocrine gastric secretions, whereas in the infected group, smoking significantly reduced inflammation in mild CAG. In extensive CAG, smoking acted on the progression of atrophy in a positive dose-dependent manner with the number of cigarettes. In extensive CAG, smoking led to an increased cancer risk, and in the group excluding end-stage gastritis, a significant risk elevation correlating with the number of cigarettes was seen.

CONCLUSION: The effects of smoking on HP-associated gastritis and the cancer development differ depending on the stage of the HP-associated gastritis. Smoking reduced the gastritis activity level in mild CAG, strongly suggesting the possibility that smoking is involved in the progression of CAG, and enhanced the cancer development in extensive CAG, not including those in the terminal stage.

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Keywords: chronic gastritis, gastric cancer, Helicobacter pylori, smoking

P504 HELICOBACTER PYLORI PREVALENCE REMAINS HIGH IN MIDDLE AGED HEALTHY, SOUTH-EAST HUNGARIAN, RURAL MALES. A POPULATION BASED STUDY.

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INTRODUCTION: Epidemiologic studies indicate a decrease in prevalence of HP infection in Western Europe. In contrast, little is known about Central Europe, where substantial part of the population still lives outside of cities.

AIMS&METHODS: The **aim** of the study was to obtain data on the HP prevalence in Csongrád and Békés County in Hungary and to compare this value with the data collected 15 years ago in Vas County. The secondary aim was to study the differences between the prevalence of HP infection in people living in large cities and in the countryside.

Methods: Six-hundred and thirty-seven healthy blood donor volunteers (M/F: 319/318, mean age: 40 (19-65) years) were enrolled. Demographic data collection and clinical symptom analysis was carried out by means of a questionnaire. All subjects were tested for HP IgG antibody positivity by enzyme linked immuno assay. Subgroup analysis by age, gender, smoking habits, alcohol consumption, urban and non-urban population was also performed.

RESULTS: During the last 15 years the overall prevalence of HP infection is halved (65 vs. 32%) in the studied healthy subjects. It was higher in males (35 vs. 30%), as well as in rural people (37 vs. 27%). In contrast similar prevalence was found in younger (<40 years) urban and rural females. The highest prevalence was found in rural males over forty years (55%). Linear association was established according to age in both sexes ($p < 0.01$). Smoking and alcohol consumption were not related to HP infection.

CONCLUSION: The overall prevalence of HP infection is decreasing in South-East Hungary similarly to the Western countries, although it is still high in middle aged rural males. This increased HP prevalence in non-urban males and the age distribution of the HP positive subjects may be explained by hygienic circumstances.

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Disclosure of Interest: None Declared

Keywords: epidemiology, Helicobacter pylori

P505 CONSISTENCY IN SOCIAL PATTERNING OF HELICOBACTER PYLORI INFECTION OVER A 10-YEAR PERIOD. A PROSPECTIVE MULTI-CENTRE EPIDEMIOLOGICAL STUDY IN THE CZECH REPUBLIC

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INTRODUCTION: Prevalence of Helicobacter pylori (Hp) infection decreased significantly in the Czech Republic from 2001 (41.7%) to 2011 (23.5%) (1,2).

AIMS&METHODS: The aim of this project was to evaluate the effect of social and demographic characteristics on Hp infection. Two prospective multi-centre studies were accomplished in 2001 and 2011 using the same methods in a representative sample of general unselected population from the same geographical areas. A total of 2,509 persons (aged 5-100) were randomly selected out of 30,012 in 2001 and 1,837 subjects (aged 5-98 years) randomly selected out of 38,147 people, took part in the study in 2011. Hp status was investigated by means of 13C-urea breath test (INFAI, Köln, Germany). Breath samples were analysed by isotope ratio mass spectrometry (AP 2003, Analytical Precision Products, Cambridge, UK).

RESULTS: The prevalence of Hp increased with age, with grater relative differences in 2001 (OR 11.5 for age 65-74 compared to 5-14 years) than in 2011 (OR 2.3 respectively) (both $p < 0.001$). The absolute prevalence decreased significantly in all birth cohorts over the period of the study, e.g. 36.7% for age 25-34 in 2001 and 25.1% for age 35-44 in 2011 ($p < 0.001$). Hp infection was associated with low education of father (OR 2.6 in 2001 and OR 3.2 in 2011) and mother (OR 2.6 and 1.9), three or more siblings (OR 3.3 and 3.6), crowding in childhood with more siblings or parents (OR 3.1 and 3.4) and low own education (OR 2.4 in 2001 and OR 2.5 in 2011). Inaccessibility of running warm water in childhood was less important risk factor of Hp infection in 2011 (OR 1.1) compared to 2001 (OR 1.4, p=0.026). Never married adult subjects were at lower risk of Hp infection in 2011 (OR 0.66) compared to married, divorced or widowed persons. There was no significant difference between the prevalence of Hp in higher or middle social class compared to lower social class (OR 1.03 in 2001 and 1.07 in 2011). Place of residence in childhood in villages was associated with higher risk of Hp infection in 2001 (OR 1.6) but not in 2011 and current place of residence did not show statistically significant association with Hp prevalence in analyses adjusted for other social characteristics in either period.

CONCLUSION: We found a general consistency in how social and demographic characteristics affect Hp infection despite the significant decrease of its prevalence in the Czech Republic from 2001 to 2011.

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Disclosure of Interest: None Declared

Keywords: Czech Republic, epidemiology, Helicobacter pylori, prospective multicentre study, social patterning

P506 ETHNIC FEATURES OF ATROPHIC GASTRITIS PREVALENCE AND GASTRIC CANCER INCIDENCE IN THE POPULATION OF EASTERN SIBERIA.

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INTRODUCTION: It is known that atrophic gastritis is an independent risk factor for noncardial stomach cancer [1]. The determination of serum pepsinogens and *H. pylori* was recommended as screening method for stomach precancerous lesions [2].

AIMS&METHODS: Aim. To study prevalence of atrophic gastritis in Mongoloids and Europoids of Eastern Siberia using determination of serum pepsinogens and to compare data with gastric cancer incidence.

Methods. The screening of atrophic gastritis was performed in Evenkia, Tyva and Krasnoyarsk city. For the study we selected 801 persons (387 males, 414 females) in Krasnoyarsk, 527 Evenks (225 males, 302 females) in Evenkia, 466 Tyvins (203 males, 263 females) in Tyva aged over 45 years old by random sampling. In all patients we performed clinical examination and determination of pepsinogen-1, pepsinogen-2 and antibodies to Helicobacter pylori in blood serum by immunoassay method using test kits "GastroPanel" ("Biohit", Finland) and ''Vector Best'' (Russia). As a marker of severe atrophy of gastric body mucosa we considered the level of pepsinogen-1 less than 25 μg/L and the ratio pepsinogen-1/pepsinogen-2 less than 3. Data on gastric cancer incidence were collected from the file-data of the regional oncology registries of the three involved regions.

RESULTS: The prevalence of *H. pylori* infection among surveyed populations was equally high – about 90.0%. The prevalence of severe gastric body atrophic gastritis and gastric cancer incidence were lower in Evenks in comparison to Europoids and Tyvins (Table). Risk factor for severe atrophic gastritis in Europoids was age older 55 years (OR=1.7, CI 1.07-2.76; p=0,03), in Evenks and Tyvins - age older 50 years (OR = 0,18; CI 0,02-0,93; p=0,03).

Table. The prevalence of atrophic gastritis and gastric cancer incidence in Eastern Siberia.

Population	Atrophic gastritis		H. pylori		Gastric cancer incidence per 100 000
	Abs.	%	Abs.	%	
1.Evenks, n=527	27	5.3	496	94.1	20.2
2.Tyvins, n=466	44	9.4	436	93.5	50.7
3.Europoids, n=801	87	10.9	721	90.0	33.2
OR; CI; p_{1-2}	0.52; 0.32-0.85; 0.01		1.10; 0.66-1.84; 0.81		0.39; 0.23-0.66; <0.001
OR; CI; p_{1-3}	0.45; 0.29-0.70; 0.004		1.76; 1.15-2.70; 0.01		1.65; 0.95-2.88; 0,09

CONCLUSION: We found ethnic differences of atrophic gastritis prevalence and gastric cancer incidence in Mongoloids and Europoids of Eastern Siberia.
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Disclosure of Interest: None Declared
Keywords: atrophic gastritis, gastric cancer , *H. pylori* , pepsinogens

P507 HELICOBACTER PYLORI ERADICATION AND TYPE 2 DIABETES MELLITUS: IS THERE A LINK?

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INTRODUCTION: The relationship between diabetes mellitus (DM) and infection by Helicobacter pylori (Hp) is controversial. However, a large number of studies have shown that eradication rates are lower in diabetic patients than in the general population.
AIMS&METHODS: To determine the rate of eradication of Helicobacter pylori infection in morbidly obese patients with type 2 DM compared with a control group not diabetic. PATIENTS AND METHODS: Retrospective analysis of patients followed in the outpatient medical morbid obesity. Included 80 patients: 40 with DM (95% female, mean age 49.5 ± 8.8, mean BMI 48 ± 3.5 kg / m^2, HgA1c average 7.3 ± 1.5%) and 40 non-diabetic patients (87 , 5% female, mean age 46.4 ± 7.9, mean BMI 46 ± 6.5 kg / m^2). All patients underwent gastric biopsy for research Hp. Patients with positive results in a histopathological study underwent triple therapy with amoxicillin (1g 2i.d.), clarithromycin (500mg 2i.d.) and omeprazole (20mg 2i.d) for 14 days. Eradication was determined by urease breath test 34 ± 5.7 days after completing treatment regimen.
RESULTS: The prevalence of Hp was 65% (n = 52). The difference in prevalence of Helicobacter pylori infection was not statistically significant between the two groups (62.5% (n = 25) in patients with DM, 70% (n = 27) in nondiabetics, p > .05). The eradication rate was 75% (n = 39). Hp was eradicated in 60% (n = 15) for patients with diabetes and in 88.8% (n = 24) of patients without diabetes. The eradication rate was significantly lower in patients with DM compared to the control group. The average duration of diabetes (5.3 ± 3.8 years vs 5.1 ± 3.6 years) and HgA1c average value (7.2 ± 1.2% vs 7.2 ± 1.4%) was not significantly different between diabetic patients with or without Hp eradication.
CONCLUSION: In this group of morbidly obese patients the rate of eradication of Hp was significantly lower in diabetic patients
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Disclosure of Interest: None Declared
Keywords: Helicobacter pylori eradication, type 2 diabetes mellitus

P508 HELICOBACTER PYLORI INFECTION AND TYPE 2 DIABETES MELLITUS: THERE AN ASSOCIATION?

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INTRODUCTION: The relationship between diabetes mellitus (DM) and infection by Helicobacter pylori (Hp) is controversial. In recent years, some studies indicate an increased incidence of infection, particularly in patients with long duration of disease, poor control diabetic, hypertensive, obese, female and cardiovascular autonomic neuropathy. However, other studies indicate that there is no difference in the prevalence of *H. pylori* infection among diabetics and non-diabetics
AIMS&METHODS: To determine the prevalence of Hp infection in morbidly obese patients with type 2 DM and to evaluate the relationship between Hp infection and glycemic control. Patients and methods: included retrospectively 80 patients with morbid obesity. Forty patients with DM (95% female, mean age 49.5 ± 8.8, mean BMI 48 ± 3.5 kg / m^2, HgA1c average 7.3 ± 1.5%) and 40 non-diabetics (87.5% female, mean age 46.4 ± 7.9, mean BMI 46 ± 6.5 kg / m^2). Endoscopy and gastric biopsies for research Hp were performed in all patients.
RESULTS: The prevalence of Hp was 65% (n = 52). The difference in prevalence of Helicobacter pylori infection was not statistically significant between the two groups (62.5% (n = 25) in patients with DM, 70% (n = 27) in nondiabetics, p > .05). The mean plasma glucose (219 ± 27.5 mg / dl vs 227 ± 22.3 mg / dl), the average level of HgA1c (7.2 ± 1.7% vs 7.3 ± 1.3%) and the average duration of DM (5.2 ± 2.8 years vs 4.9 ± 2.3 years) did not differ significantly (p > 0.05) between diabetic patients with and without Hp. There was no increased prevalence of Hp infection in DM patients with poor diabetic control (HgA1c > 7%) compared to patients with appropriate control (15 (60%) of 25 patients vs 10 (66.6%) of 15 patients, respectively).
CONCLUSION: The results of this study showed no significant difference in the prevalence of *H. pylori* infection among diabetic patients and the control group, not indicating association between *H. pylori* infection and DM.
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Keywords: Helicobacter pylori eradication, type 2 diabetes mellitus

P509 EXTRAGASTRIC PATHOGENICITY OF HELICOBACTER SUIS IN IDIOPATHIC PARKINSONISM: EXAMINATION OF ALL-CAUSE MORTALITY AND BLOOD INDICES.

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INTRODUCTION: Relative frequency of *Helicobacter suis cf pylori* was 10 times greater in the first archived DNA-extract from gastric-biopsies in 60 patients with idiopathic parkinsonism (IP), than in 256 'controls' from UK gastroenterology-services.
AIMS&METHODS: We explore the pathological significance of *H. suis* in IP. DNA-extracts from gastric-biopsies had been examined for *H. suis* using a *ureA*-based species-specific qPCR, subsequent to routine culture for *H. pylori*, and, if negative, PCR targeting 16S rRNA and *vacA*.
RESULTS: *H. suis* was present in the first sample from 16/60 IP-patients. Of 20 follow-ups:- Co-existent *H. pylori* had been eradicated in 5/6 previously *H. suis*-positive: 4 remained *H. suis*-positive, as did the patient without *H. pylori*. *H. pylori* had been eradicated in 12/14 previously *H. suis*-negative: 3 became *H.* suis-positive afterwards, 2 remaining negative for both species. Risk of death during follow-up was 8.0 (95% CI 1.3, 47.4) times greater with *H. suis*-positivity at anytime (6/19), compared with those negative throughout (2/40 (one lost to follow-up)) (Cox proportional-hazards model, adjusted for age-at-diagnosis, gender: p=0.02). Independent effects of both species on blood indices were assessed in same regression model. With *H. suis*-positivity, platelet count tended to be lower (by 10 (-1, 20)%, p=0.06) whilst mean platelet volume was higher (0.83 (0.02, 1.6) fL, p=0.04), *H. pylori* having no effect. Total lymphocyte count was lower with *H. pylori* (0.19 (0.04, 0.34) $x10^9$/L, p=0.02), but not significantly so with *H. suis*. B-cell count was lower with each species (30 (3, 57)/μL, p=0.03; 42 (8, 77), p=0.02).
CONCLUSION: All-cause mortality associated with *H. suis* in IP requires further investigation. Usual anti-*H. pylori* therapy may be ineffective against *H. suis* and promote recrudescence. Fewer larger platelets implies destruction. Relative lymphopenia of IP could be related to *H. pylori*. Lower B-cell count, associated with both species, may signify acquired immune tolerance.
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Disclosure of Interest: None Declared
Keywords: all-cause mortality, blood indices, Helicobacter pylori, Helicobacter suis, Idiopathic parkinsonism

P510 CLINICOPATHOLOGICAL STUDY OF THREE GENERATIONS OF NODULAR GASTRITIS - WHEN SHOULD NODULAR GASTRITIS BE ERADICATED?

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INTRODUCTION: Nodular gastritis (NG) is typically and frequently found in children who are infected with *Helicobacter pylori* (HP). NG has been recognized in adults infected with HP as well, and although it is considered to be a pangastritis, NG has been strongly associated with diffuse-type gastric cancer of the corpus as well. The natural history of NG remains elusive. Thus, we aimed to evaluate the clinicopathological hallmarks of NG over three generations of patients.
AIMS&METHODS: We recruited 103 patients (average age: 29 years, range: 4-79 years) who were diagnosed as having NG by upper gastrointestinal endoscopy at our hospital. The subjects were divided into three groups: 13 patients aged younger than 15 years (9 female; average age: 10.5 years) were assigned to the pediatric group, 50 patients aged between 16 and 30 (25 female; average age: 19.1

years) were classified into the young group, and 40 patients older than 31 years of age (29 female; average age: 47.7 years) comprised the elder group. We evaluated the clinical, endoscopic, and pathological features of NG among these three generations. Pathological features were evaluated using the updated Sydney System (USS).
RESULTS: NG was more frequently found in women in the pediatric and elder groups. Although the endoscopic finding of atrophic gastritis tended to increase with age, it was generally mild in our cohort. There was no significant difference among the three groups regarding scores for mononuclear cell infiltration in the greater curvature of the antrum. However, scores for mononuclear cell infiltration in the greater curvature of the gastric body was significantly higher in the elder group than in the pediatric and young groups (1.31 vs. 1.36 and 1.98, both $P<0.001$). Scores for neutrophil infiltration in the greater curvature of the gastric body were also significantly higher in the elder group than in the other two groups (0.92 vs. 1.08 and 1.65, both $P<0.001$), but those for neutrophil infiltration in the greater curvature of the antrum were comparable among the groups. The scores for atrophy, intestinal metaplasia, and HP infection did not differ significantly in our study.
CONCLUSION: In pediatric and young patients, inflammatory cell infiltration in the gastric body is milder than in elder patients. As pangastritis is considered to be a risk factor for diffuse-type gastric cancer, HP eradication therapy in younger people, especially before 30 years of age, may prevent this type of cancer of the corpus.
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Disclosure of Interest: None Declared
Keywords: eradication, nodular gastritis

P511 IMPROVEMENT OF GASTRIC ATROPHY AND INTESTINAL METAPLASIA 10 YEARS AFTER HELICOBACTER PYLORI ERADICATION

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INTRODUCTION: *Helicobacter pylori* (*Hp*) infection cause the gastric atrophy and intestinal metaplasia (IM) , both of which are considered precancerous change. Improvement of gastric atrophy and intestinal metaplasia after *Hp* eradication is controversial, because long term follow-up studies are few. We herein investigated the improvement of gastric atrophy and IM histologically and endoscopically for 10 years after *Hp* eradication.
AIMS&METHODS: We investigated the patients who were taken biopsy specimens from the greater curvatures of the gastric antrum and the corpus before and 10 years after *Hp* eradication. The histological findings of these specimens were analyzed according to updated Sydney's system. Gastric atrophy was also estimated endoscopically based on Kimura-Takemoto classification[1)]. In addition we divided into two groups according to age (<60 or over), then those scores were also compared. Statistical analysis was performed using R software.
RESULTS: This study included 46 patients (33 men, 13 women; mean age at *Hp* eradication: 55.7 ± 9.3, mean follow-up period: 4899 ± 816 days). Reasons of eradication were gastric ulcer: 22, duodenal ulcer: 14, gastroduodenal ulcer: 5, gastric adenocarcinoma: 2, others: 3. Scores of atrophy and IM at gastric antrum and corpus were improved significantly 10 years after *Hp* eradication (Table). Endoscopic atrophy was not improved significantly ($p = 0.413$). When we divided the patients into two groups, the atrophy and IM at the gastric antrum in the younger group were only improved significantly.

	Antrum		Corpus	
	Atrophy	IM	Atrophy	IM
Before *Hp* eradication	1, 1.1 ± 1.1	0, 0.8 ± 1.0	0, 0.4 ±0.8	0, 0.4± 0.9
10yr After *Hp* eradication	0, 0.5 ± 0.8	0, 0.4 ± 0.8	0, 0.1± 0.3	0, 0.1 ±0.3
p value	0.018	0.003	0.001	0.020

IM: intestinal metaplasia , (Median, Mean ± Standard deviation)
CONCLUSION: *Hp* eradication improved the gastric atrophy and IM after 10 years follow-up, especially in the gastric antrum in younger patients. This improvement needs long term follow-up, but could contribute the reduction of gastric adenocarcinoma.
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Disclosure of Interest: None Declared
Keywords: eradication, Helicobacter pylori, intestinal metaplasia

P512 EFFICACY OF «TEST&TREAT» STRATEGY: IS THERE THE DIFFERENCE BETWEEN MALE AND FEMALE PATIENTS?

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INTRODUCTION: A «test-and-treat» strategy is appropriate for uninvestigated dyspepsia (UD) in populations where the *H. pylori* (Hp) prevalence is high (1). This approach is subject to cost-benefit considerations, but clinical efficacy is variable in different subgroups of patients with uninvestigated dyspepsia (2). There are no adequate data of *H. pylori* prevalence among dyspeptic patients in Ukraine and the clinical efficacy of «test-and-treat» approach is not investigated..
AIMS&METHODS: Our aims were to analyze the strategy viability in male and female patients. 312 UD-patients (Caucasians - 156 male (m) and 156 female (f), without alarm signs, age <39 y.o., determined according to local cancer risk) were recruited in 4 centers. Hp status was established using 13C-urea breath test (UBT). 220 (70,5%±2,6%) was Hp-positive (119 (76,3%±3,4%)-m, 101 (64,7%±3,8%)-f). Hp-negative were 92 persons (m-37, f-55). Symptoms were assessed by scale 0 to 5 point before and after treatment. Hp-positive (group1) patients were treated with standard 10-days triple therapy, according to Maastricht-4 recommendations. Hp-negative patients (group 2) received standard dose of proton pump inhibitor (PPI) once daily for 4 weeks. Assessment of residual symptoms frequency and severity was performed after 1 month and 1 year after treatment finish. Eradication success was controlled by UBT after 1 month after end of the treatment.
RESULTS: Successful eradication was achieved in group 1: m -108 (90,8%±2,6%,), f- 88 (87,1%±3,3%), $p>0,05$. Complete or significant symptoms relief have noticed 92 (85,1%±3,4%) of successful treated male patients (OR 4.8 (95% CI 3,9-5,7)), this topic in female was 49 (55,7%±5,3%), OR =1,2 (95% CI=0,8–1,9). Clinically this approach is more effective in male patients (p=0,0076). After 1 year this results were not changed significantly ($p_i>0,05$). The effectiveness of PPI in group 2 was enough (significant symptomatic improvement) in 63,0%±5,0% of cases (m-64,9%±7,8%, f-61.8%±6,6%, $p>0,05$). After 1 year this results were not changed significantly ($p_i>0,05$), but relapses of dyspepsia appeared in 76.1%±4,4% of patients during the year.
CONCLUSION: The prevalence of Hp in UD-patients is high in Ukraine. A «test-and-treat» strategy is clinically effective and strongly appropriate for UD male patients of age <39 (in Ukraine) without alarm signs. The efficacy in female is significantly lower, possibly because of functional dyspepsia high prevalence in this subgroup.
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Disclosure of Interest: None Declared
Keywords: 13C-urea breath test, test and treat strategy, gender differences

P513 HELICOBACTER PYLORI COLONIZATION AND PREECLAMPSIA: THE GENERATION R STUDY

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INTRODUCTION: Preeclampsia (PE) is characterized by endothelial dysfunction and related hypertension and coagulative disorders. It is a leading cause of perinatal and maternal morbidity and mortality. Although the exact pathogenesis is still unknown, certain infectious agents seem to play a role. *Helicobacter pylori (H. pylori)* has been reported to induce platelet aggregation, and we therefore hypothesized that this bacterium could be associated with PE.
AIMS&METHODS: The objective of this study was to assess the association between *H. pylori* colonization and PE. We measured IgG anti-*H. pylori* and CagA-antibodies in serum of pregnant women of the Generation R study, a population-based prospective cohort study in Rotterdam, the Netherlands. Delivery and medical records were retrieved for identification of subjects with PE, which were defined according to standard criteria. Information on demographics, education, and maternal risk factors was collected by questionnaires. Only women with a live born singleton pregnancy were included. Subjects with chronic hypertension, systemic lupus erythematosus, lupus anticoagulants or chronic heart disease were excluded from analyses. Odds ratios (OR) of PE for *H. pylori* colonization were calculated using logistic regression analyses after adjustment for potential confounders including maternal age, ethnicity, parity, smoking, body mass index and education level.
RESULTS: Serum of 6348 pregnant women was analyzed (mean age 29.7 ± SD 5.3). In total, 2923 women were *H. pylori* positive (46%) and 1028 of them were CagA-positive (35%). For 132 women pregnancy was complicated with PE (2.1%). *H. pylori* colonization rate in women with PE was 56% compared to 44% in subjects without PE (p=0.02). CagA-positivity rate was 20% in women with and 16% in women without PE (p=0.30). Adjusted for potential confounding effects, women colonized with *H. pylori* were more likely to develop PE (final OR 1.53; 95% confidence interval 1.04-2.26). CagA-positivity was not associated with PE.
CONCLUSION: Our data demonstrate that *H. pylori* colonization in pregnant women is associated with PE. *H. pylori* may be involved in different inflammatory mechanisms, which might potentially affect the pathogenesis of PE. Understanding and further validation of this association may contribute to effective intervention (e.g. *H. pylori* eradication treatment) for reducing morbidity and mortality from this disease.
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Disclosure of Interest: None Declared
Keywords: epidemiology, Helicobacter pylori, Preeclampsia

P514 HELICOBACTER PYLORI INFECTION IS ASSOCIATED WITH THYROID NODULE PREVALENCE IN EUTHYROID POPULATION

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INTRODUCTION: Gastric epithelial cells are injuried by *Helicobacter pylori (H. pylori)* inducing autoantibodies, it is the same that it appears cross-reactivity through molecular modeling between *H. pylori* and thyroid tissue antigens, and it could result in pathological damage of thyroid tissue[1]. When *H. pylori* antigen is presented to T cells, the body produces cross-reactive immune response, it could cause immune injury to thyroid tissue. There were some reports which had shown a positive correlation between *H. pylori* infection and autoimmune thyroid diseases (ATDs)[2] , in clinical works, many patients who were diagnosed as thyroid nodules with normal thyroid function were found, but the risk factor for thyroid nodules among euthyroid population has not yet been fully clarified.
AIMS&METHODS: The aim of this study was to investigate the association of *H.pylori* infection with thyroid nodule in euthyroid population. A cross-sectional study was performed among 988 euthyroid chinese who underwent general health screening including thyroid ultrasonography, fasting ^{13}C urea breath test and laboratory data at International Health Care Center, the First Affiliated Hospital of Zhejiang University College of Medicine.
RESULTS: A total of 435 (44.0%) subjects were diagnosed as thyroid nodule and a total of 486 (49.2%) were . diagnosed as *H.pylori* infection. The thyroid nodule prevalence was significantly higher in *H.pylori* infection group than the control group (49.0% *vs.* 39.2%, $P = 0.002$). Age, gender, body mass index (BMI), systolic and diastolic blood pressure (SBP and DBP) status–adjusted correlation analysis showed that thyroid nodule was positively correlated with *H.pylori* infection [odds ratio (OR): 5.939, $P = 0.015$]. Stepwise logistic regression analysis was performed to evaluate the risk factors for thyroid nodule using the dichotomous variable logistic regression model. Nineteen variables including age, gender, SBP, DBP, BMI, serum thyroid- stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3) and *H.pylori* infection. It showed that thyroid nodule was significantly associated with age, female, serum thyroid-stimulating hormone (TSH), BMI, *H.pylori* infection (all $P < 0.05$).
Table1. Risk factors for thyroid node in euthyroid Chinese

Variables	Wald chi-squared	*P*	OR(95%CI)
female	35.953	0.000	2.578(1.892-3.514)
age	73.581	0.000	1.056(1.043-1.070)
TSH	8.630	0.003	0.784(0.667-0.922)
BMI	8.851	0.003	1.075(1.025-1.128)
H.pylori infection	5.633	0.018	1.390(1.059-1.824)

CONCLUSION: *H.pylori* infection is significantly associated with thyroid nodule prevalence in euthyroid population.
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Disclosure of Interest: None Declared
Keywords: euthyroid population, Helicobacter pylori infection, thyroid nodule

P515 LOCAL EXPERIENCE WITH NON-BISMUTH QUADRUPLE THERAPY AS FIRST LINE TREATMENT FOR HELICOBACTER PYLORI ERADICATION

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INTRODUCTION: In a previous study about effectiveness of eradication therapies for Helicobacter pylori (HP) prescribed in our area, we found that the first line combination most widely used (Amoxicillin + Clarithromycin + PPI) had a low efficacy (61.9% "per intention to treat" and 63.9% "per protocol"). In areas of high clarithromycin resistance recent guidelines recommend quadruple treatments, bismuth containing or not depending on the availability of this medicine. According to our previous data and the lack of availability of bismuth in Spain, in mid 2012 we started to prescribe a non-bismuth quadruple therapy (Amoxicillin + Clarithromycin + Metronidazole + PPI for 10 days).
AIMS&METHODS: Aim: To analyse the efficacy of the classical triple eradication therapy for HP and the non-bismuth quadruple combination, in the first year of its prescription in our area.
Methods: Retrospective observational study of all therapies prescribed in our hospital for HP eradication between 1st of January and 31st of December 2012 and their efficacy. Eradication was confirmed with ^{13}C-urea breath test at least 5 weeks after completion of treatment.
RESULTS: During 2012, 446 breath tests were made in our centre in 303 new patients, who constituted the study population. 56.9% were women, and the medium age was 47.9 years (SD 17.6 years). Among all those patients 198 (65.4%) got at least a first line therapy, that in 111 cases was the classical triple therapy (Amoxicillin + Clarithromycin + PPI) for 7-14 days. This combination was prescribed for 7 days in 62.2% of cases, while a 30.6% of patients (n=34) had a treatment duration of 10 days. Meanwhile, 75 patients (37.6%) received a first line therapy with non-Bismouth quadruple therapy. This quadruple combination showed a higher efficacy than the classical triple therapy, in both "per intention to treat" (86.1% vs. 69.2%, p=0.012) and "per protocol" analysis (89.9% vs. 69.8%, p=0.002). The sequence of Amoxicillin + Clarithromycin + PPI and Levofloxacin + Amoxicillin + PPI for 10 days as second-line therapy was used in 24 cases with an efficacy of 79.2%, while the combination of non-Bismouth quadruple therapy followed by Levofloxacin + Amoxicillin + PPI for 10 days was used only in 4 cases with a 75% of success.
CONCLUSION: In our area, non-Bismuth quadruple therapy has a high efficacy as first-line therapy for HP eradication, showing much better results than standard triple therapy with Amoxicillin + Clarithromycin + PPI.
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Disclosure of Interest: None Declared
Keywords: Helicobacter pylori, Non-bismuth quadruple therapy

P516 THE EFFECT OF EMPIRICAL RESCUE THERAPY FOR TWO OR MORE CONSECUTIVE H. PYLORI ERADICATION FAILURES

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INTRODUCTION: The eradication rate of first and second-line therapies have been decreasing progressively due to increasing antimicrobial resistance of Helicobacter pylori. After two or more consecutive *H. pylori* eradication failures, clinicians have faced the dilemma of determining which of the following therapy would be the most appropriate. The aim of this study was to elucidate clinical course and treatment strategies of refractory *H. pylori* infection.
AIMS&METHODS: From 2003 to 2012, total 123 (mean age 63.9: male 58, female 65) patients who had experienced at least two consecutive *H. pylori* eradication failures were enrolled at the Seoul National University Bundang Hospital. Efficacy of different rescue regimens was compared by confirming of eradication rate. *H. pylori* status was evaluated by histologic finding, campylobacter-like organism test and 13C urea breath test. Antibiotic susceptibility test for *H. pylori* was not done in all cases.
RESULTS: The clinical & endoscopic findings were as follows : 84 patients (67.7%) had erosive or atrophic gastritis and functional dyspepsia, 15 patients (12.1%) - gastric ulcer, 6 patients (4.8%) - duodenal ulcer, 10 patients (8.1%) - DU + GU, 18 patients - other findings (12 Tubular adenoma, 5 Gastric adenocarcinoma, 1 MALT lymphoma). There was no significant difference in the eradication rate between each rescue regimens. *H. pylori* eradication rates with the 3rd, 4th and 5th-line rescue regimens were 51.6% (62/120), 48.7% (20/41), and 20.0% (2/10), respectively. Finally, cumulative *H. pylori* eradication rate with the 3~7th rescue regimens (mean 3.51 times) was 73.0% (84/115). The cumulative incidence rate of gastric cancers did not differ between the eradicated group and failed group (mean observation period: 42.9 months).
CONCLUSION: Even with the consecutive treatments of refractory *H. pylori* infection using empirical regimens, *H. pylori* eradication rate was gradually declining. Finally, cumulative overall eradication rate could not achieve over 75%. Now that repeated empirical treatment without culture cause a significant limitation for effective eradication in the future, we should consider careful treatment strategies in refractory *H. pylori* infection.
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Disclosure of Interest: None Declared
Keywords: Cumulative eradication rate, Helicobacter pylori, Rescue regimen, Treatment Failure

P517 THE EFFICACY OF HYBRID AND SEQUENTIAL THERAPIES AS FIRST-LINE TREATMENT FOR H. PYLORI INFECTION IN KOREA

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INTRODUCTION: Recent prospective studies have shown sequential therapy has not achieved 85% *H. pylori* eradication rates in Korea. The aim of this study was to assess the efficacy of hybrid therapy as first-line treatment for *H. pylori* eradication.
AIMS&METHODS: From December 2012 to April 2013, A total 84 (mean age 57.6: male 29, female 55) patients who proven *H. pylori* infection were randomized to received either 14 day-Hybrid therapy (rabeprazole 20 mg b.i.d. and amoxicillin 1 g b.i.d. for 14 days plus clarithromycin 500 mg b.i.d. and metronidazole 500 mg b.i.d. for the remaining 7 days) or 14 day-sequential therapy (rabeprazole 20 mg b.i.d. and amoxicillin 1 g b.i.d. for the first 7 days, followed by rabeprazole 20 mg b.i.d., clarithromycin 500 mg b.i.d., metronidazole 500mg b.i.d. for the remaining 7days). Outcome of eradication was evaluated by the 13C-UBT at least 4 weeks later after cessation of treatment.
RESULTS: 84 patients (44 patients in the hybrid group and 40 patients in the sequential group) completed the study. The eradication rates of hybrid treatment group and sequential treatment group were 81.8% (36/44) (95% CI = 70.4 - 93.2%) and 80.0% (32/40) (95% CI = 67.6 – 92.4%) by intention-to-treat analysis (p=0.832). By the per-protocol, eradication rates were 83.7% (36/43) (95% CI = 72.6 - 94.7%) and 84.2% (32/38) (95% CI = 72.6 – 84.2%) (p = 0.952). There were no significant between-group differences in compliance and discontinuation due to severe side-effects.
CONCLUSION: 14 day-hybrid therapy failed to achieve significantly higher eradication rates than 14 day-sequential therapy. Both of them cannot achieve

over 85% of eradication rate. So, further studies are needed to find alternative first-line treatment for better eradication rate for Korean population.
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Disclosure of Interest: None Declared
Keywords: Eradication rate, Helicobacter pylori, Hybrid therapy, Sequential therapy

P518 ERADICATION RATE OF HELICOBACTER PYLORI INFECTION ACCORDING TO THE STAGES OF PEPTIC ULCER DISEASE

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INTRODUCTION: The eradication rate of *Helicobacter pylori* infection might be affected by the inflammatory status of gastric mucosa and virulence factors such as CagA and VacA. The inflammatory status of gastric mucosa is different according to the stages of peptic ulcer disease. To our knowledge, there have been few studies about the eradication rate according to the peptic ulcer stages.
AIMS&METHODS: The aim of this study was to evaluate the eradication rate of *H. pylori* infection according to the stages of peptic ulcer disease. A total of 1,187 patients with peptic ulcer disease (382 gastric ulcer, 719 duodenal ulcer and 86 combined ulcer) who received proton pump inhibitor (PPI)-based triple therapy for 7 days were retrospectively included from January 2004 to December 2011. *H. pylori* eradication status was evaluated by ^{13}C urea breath test at 4~6 week after the completion of therapy. The patients were sorted into three groups by the ulcer stage and then the eradiation rates were compared.
RESULTS: The overall *H. pylori* eradication rate was 81.8%. There was no statistical difference in the eradication rate between gastric and duodenal ulcer (P=0.428; 80.1% *vs*. 82.1%). The eradication rates in active stage (n=330), healing stage (n=278) and scar stage (n=579) were 85.8%, 83.8% and 80.3%, respectively (P=0.016). In univariate analysis, active ulcer (P=0.028; 85.8% *vs*. 80.3%) and age < 50 (P=0.028; 84.5% *vs*. 79.5%) were associated with higher eradication rate. In multivariate analysis, active ulcer was a significantly independent predictor of successful eradication (Odd ratio; 3.04, 95% CI; 1.711-5.392, P=0.0001).
CONCLUSION: There was a significant difference in eradication rate according to the ulcer stages. Different eradication regimen or treatment duration in patients with scar stage ulcer might be necessary. Further prospective studies are warranted.
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Disclosure of Interest: None Declared
Keywords: Helicobacter pylori eradication, stage, ulcer

P519 INITIAL EMPIRICAL TREATMENT FOR HELICOBACTER PYLORI ERADICATION IN ROUTINE CLINICAL PRACTICE. NON BISMUTH SEQUENTIAL OR CONCOMITANT REGIMEN? A PRELIMINARY PROSPECTIVE COMPARATIVE STUDY IN SPARTA GREECE.

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INTRODUCTION: In areas of high clarithromycin resistance, the recent European guidelines recommend bismuth based regimens or if the bismuth is not available, non bismuth quadruple ''sequential'' or ''concomitant'' regimens
AIMS&METHODS: To assess the effectiveness, safety and acceptability of ten days sequential (ST) and concomitant (CT) therapies as first line empirical treatment for *H.pylori* eradication. In Greece the reported clarithromycin resistance approximates 20% or even higher.Prospective randomized 1:1, aaccording the number of endoscopy, single center study of two years duration. All patients included in the study were diagnosed with peptic ulcer disease, erosions or non ulcer dyspepsia by endoscopy. Helicobacter pylori infection was documented by at least two positive tests among rapid urease test, gastric histology, 13C Urea Breath test. Patients were randomly assigned to one of the following therapies: A. ST consisting of Omeprazole 20 mg and Amoxicillin 1000 mg for the first five days following by Omeprazole 20 mg, Clarithromycin 500 mg and Metronidazole 500 mg for the remaining five days, all twice daily. B. CT same four drugs taken concomitantly for ten days. Helicobacter pylori eradication was checked using a 13C Urea Breath test 8 weeks after treatment and histology for gastric lesions. Intention to treat (ITT) and per protocol (PP) eradication rates were determinate. Adverse events and treatment compliance (cut off 90%) were evaluated using specific questionnaire and residual medical count.
RESULTS: 102 patients per arm of therapy, 60% men, mean age 49,4 +/- 10,8 years in ST and 48,2 +/- 9,2 years in CT (p NS). In each arm, 49% had peptic ulcer, 25% erosions and the remaining non ulcer dyspepsia, while 31% were smokers. Eradication was achieved in 87/96 who returned for the follow up (2 lost 4 incomplete treatment) in the ST thus ITT was 85, 29% (95 %CI 83, 6- 92, 7%) and PP was 90, 62% (95 %CI 83, 3- 94%). In CT eradication was achieved in 88/95 (4 lost 3 incomplete treatment) who returned for the follow up thus ITT was 86,27% (95 %CI 82.1 – 91,9%) and PP was 92,63% (95 %CI 85,8 – 95,7%). Difference in ITT 0, 98% (95 %CI 0, 5 – 1, 2%) and in PP 2, 01% (95 %CI 1, 5-2, 9%). Adverse events were 28% in the ST, 30% in the CT (p NS). Drugs compliance was 95% and 96% in the two treatment groups.
CONCLUSION: In our area the two regimens appear to be equal effective, achieving 90% PP eradication rate, and well tolerated as first line empirical treatment for *H.pylori* eradication
Disclosure of Interest: None Declared
Keywords: Concomitant therapy, Non bimuth quadruple therapy, Sequential therapy

P520 LACTOBACILLUS REUTERI IN MANAGEMENT OF HELICOBACTER PYLORI INFECTION IN DYSPEPTIC PATIENTS: A DOUBLE BLIND PLACEBO CONTROLLED RANDOMIZED CLINICAL TRIAL

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INTRODUCTION: The eradication rate of *Helicobacter pylori* after the standard triple therapy is declining and this may necessitates introduction of new antimicrobial agents.
AIMS&METHODS: This study was conducted to test the assumption that addition of *Lactobacillus reuteri* to the standard triple therapy improves eradication rate, clinical and pathological aspects in *H. pylori* infection. Seventy patients were enrolled and were randomly assigned into, group A the *L. reuteri* treated group and group B, the placebo control group. All patients were treated by the standard triple therapy for two weeks and either *L. reuteri* or placebo for four weeks. They were examined by symptom questionnaire, *H. pylori* antigen in stool, upper endoscopy with biopsies for rapid urease test and histopathological examination before and 4 weeks after treatment.
RESULTS: The eradication rate of *H. pylori* infection was 74.3% (26/35) and 65.7% (23/35) for both *L. reuteri* and placebo treated groups respectively (p =0.603). There was a significant difference regarding the reported side effects (p=0.002), patients treated with *L. reuteri* reported less diarrhea and taste disorders than placebo group. A significant difference within each group was noted after treatment for Gastrointestinal Rating Scale (GSRS) scores, patients treated with *L. reuteri* showed more improvement of gastrointestinal symptoms than placebo treated group (p < 0.000). The severity and activity of *H. pylori*-associated gastritis was reduced after 4-weeks of therapy in both groups. *L. reuteri* treated group showed significant improvement than placebo treated group (P < 0.000 and 0.034 respectively).
CONCLUSION: Eradication triple therapy of *H. pylori* supplemented by *L. reuteri* increased eradication rate by 8.6% (non significant), improved GSRS score (significant), reduced side effects (significant) and improved histological features (significant) in *H. pylori* infection when compared with triple therapy supplemented with placebo.
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Disclosure of Interest: M. Emara : none, S. Mohamed : none, H. Abdel-Aziz : none
Keywords: Eradication rate, Gastritis, Gastrointestinal Rating Scale, Helicobacter pylori, Lactobacillus reuteri, triple therapy

P521 EFFECTIVENESS OF HELICOBACTER ERADICATION IN THE TREATMENT OF GASTRIC MALTOMA

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INTRODUCTION: *Helicobacter pylori* eradication induces remission in most patients with gastric mucosa-associated lymphoid tissue (MALT) lymphoma. However, there have been few reports about the effect of bacterial treatment on the gastric MALToma in Korea, a well-known *H. pylori* endemic area.
AIMS&METHODS: From January 2000 to December 2011, consecutive patients with stage-I gastric MALToma were enrolled in single centre retrospectively.
RESULTS: A total of 52 patients were enrolled and median age of the patients was 58 years (36-81 years). There were fewer male than female (M:F, 18:34) and male to female ratio was 1:1.9. The macroscopic tumour type was determined according to the classification of Watanabe, as follows : (1) ulceration (46.1%); (2) protruding (13.5%); (3) granular (9.6%); (4) infiltrative (25.0%); and (5) mixed (5.8%). Most of lesions were single (73.1%) and 68.4% of the neoplasm was located in body, 26.3% in antrum, and 5.3% in cardia or fundus. The median time of follow-up was 37.2 months (range 5–96 months). Among 51 of 52 patients who checked status of *H. pylori,* 33 (63.5%) was positive in *H. pylori* test. Eradication was done in 25 of 33 with *H. pylori*-positive. Among 23 of 25 assessable patients, 22 (96%) showed successful eradication. During the follow-up period, all of 22 showed CR (86.4%) or PR. Eight of 18 *H. pylori*-negative MALToma had eradication. Among them, seven patients showed CR and one showed no change.
CONCLUSION: In conclusion, irrespective of the existence of bacteria, *H. pylori* eradication is effective in the treatment of gastric MALToma.
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Disclosure of Interest: None Declared
Keywords: Helicobacter pylori, MALToma, stomach, treatment

P522 EFFICACY OF TWO LEVOFLOXACIN-CONTAINING SECOND-LINE THERAPIES FOR HELICOBACTER PYLORI: A PILOT STUDY

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INTRODUCTION: An ideal second-line therapeutic regimen for the treatment of patients who do not respond to standard triple therapy is currently being investigated
AIMS&METHODS: We aimed to investigate the efficacy of two levofloxacin-containing second-line therapies for *Helicobacter pylori* (*H. pylori*).
148 consecutive *H. pylori*-positive patients who did not respond to the standard triple therapy (77 female, 71 male) were enrolled in the study. The patients were randomized consecutively to two second-line therapy groups; 73 to the

levofloxacin-containing sequential (LCS) and 75 to the levofloxacin-containing quadruple (LCQ) therapy group. The LCS therapy group received pantoprazole 40 mg and amoxicillin 1,000 mg twice daily for 5 days followed by pantoprazole 40 mg twice daily and metronidazole 500 mg three times daily and levofloxacin 500 mg one time daily for 7 days. The LCQ therapy group received pantoprazole 40 mg twice daily, tetracycline 500 mg four times daily, bismuth subcitrate 300 mg four times daily and levofloxacin 500 mg one time daily for 10 days. *H. pylori* eradication was confirmed by stool antigen testing at least 6 weeks after cessation of therapy. Side-effects and compliance were assessed by a questionnaire.
RESULTS: Per protocol cure rates were: 85.7% (95%CI; 75-92) and 93.1% (95%CI; 85-98) in the LCS and LCQ therapy, respectively. Intention-to-treat cure rates were: 82.2% (95%CI; 73-91) and 90.6% (95%CI; 79-95) in the LCS and LCQ therapy, respectively. No statistically significant difference was found between two groups (p=0.1). No differences in compliance or adverse effects were demonstrated between two groups.
CONCLUSION: This prospective trial demonstrates that both levofloxacin-containing sequential therapy and levofloxacin-containing quadruple therapy regimens have higher *H. pylori* eradication rates and are well tolerated. The levofloxacin-containing quadruple therapy is likely the best treatment option for a second-line therapy, at least in the Turkish population.
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Disclosure of Interest: None Declared
Keywords: Helicobacter pylori, levofloxacin, second line therapy

MONDAY, OCTOBER 14, 2013 9:00-17:00
SMALL INTESTINAL I - Poster Area

P523 HUMAN ENTEROGLIAL CELLS-DERIVED SOLUBLE FACTORS MEDIATE PATHOGENIC AND PROBIOTIC BACTERIA EFFECTS ON INTESTINAL EPITHELIAL CELLS VIA A RAGE-DEPENDENT MECHANISM.

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INTRODUCTION: We have previously demonstrated that human enteroglial cells (EGCs) express TLRs and can release S100B, a neurotrophin which effects are mediated mainly by the receptor for advanced glycation endproducts (RAGE). The putative effects of mediators released by EGCs, after bacteria stimulation, on the surrounding cells have not been explored yet.
AIMS&METHODS: We aim to evaluate: 1) the effect of soluble factors released by EGCs, upon probiotic and pathogenic bacteria stimulation, on intestinal epithelial cells (IECs) viability and differentiation; 2) whether these effects are mediated by RAGE. Human EGCs were exposed to probiotic (Lactobacillus Paracasei F19, 10^8 bacteria/mL) and pathogenic (Enteroinvasive Escherichia Coli, 10^8 bacteria/mL) bacteria. After a 24 h incubation, conditioned media (CM) from these cultures were used to challange CaCo2 cells cultured to confluence, in presence or absence of a specific anti-RAGE antibody. CaCo2 viability and differentiation after 24 h were studied by MTT vitality test and lactase and sucrase enzyme activity test, respectively. CaCo2 cells with medium alone were used as control. Data are expressed as mean±SD of 3 independent experiments.
RESULTS: CM from EGCs alone and from EGCs stimulated with both probiotic and pathogenic bacteria did not affect CaCo2 cells viability (0.79±0.26, 0.85±0.36, 0.89±0.24 vs 0.89±0.31 $\lambda_{540\ -\ 630}$; p=NS). CM from EGCs alone and from probiotics stimulated EGCs significantly increased lactase (1.15±0.17 and 1.29±0.19 fold increase vs control; $p < 0.05$) as well as sucrase activity (2.09±0.30 and 1.95±0.23 vs control; $p < 0.05$), as compared to untreated CaCo2 cells. These effects are abolished when Caco2 cells are pre-treated with anti-RAGE. CM from pathogens stimulated EGCs has no effects on both lactase (0.85±0.23 fold increase vs control; p=NS)) and sucrase activity (0.55±0.15 fold increase vs control; p=NS).
CONCLUSION: We show that EGCs conditioned medium, with both pathogen and probiotic bacteria, may differently modulate IECs differentiation without exerting cytotoxic effects, with a mechanism involving RAGE stimulation on IECs. Our preliminary results provide further evidence on the role of EGCs in mediating the host-bacteria interaction and put forward the major contribution of EGCs in the control of epithelial barrier function.
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Disclosure of Interest: None Declared
Keywords: enteric glial cells, Intestinal epithelial cells, RAGE

P524 LINEAGE-SPECIFIC EXPRESSION OF BESTROPHIN-2 AND BESTROPHIN-4 IS REGULATED BY NOTCH SIGNALING IN HUMAN INTESTINAL EPITHELIAL CELLS.

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INTRODUCTION: Bestrophins are newly identified family of ion channels, that can function either as Ca^{2+}-activated Cl^- channels or as HCO_3^- channels. Former study has indicated that, among four bestrophin genes, bestrophin-2 (BEST2) and bestrophin-4 (BEST4) might be expressed within the human intestinal tissue. However, their precise expression within the human intestine, or the mechanism regulating their expression remains largely unknown.
AIMS&METHODS: We aimed to clarify the cell population that expresses BEST2 or BEST4, and also the molecular mechanism regulating their expression, within the human intestine. Expression of BEST2 and BEST4 *in vivo* was identified by immunohistochemical analysis (IHC) using normal human intestinal tissues, or those from ulcerative colitis (UC) patients. Lineage-specific expression was further analyzed *in vitro*, by employing established human intestinal epithelial cell (IEC) line models of goblet cell differentiation or enterocyte differentiation. Involvement of Notch signaling was examined by using a cell-line in which Notch activation can be induced by a Doxycycline-dependent manner. Gene expression in those cell-lines was evaluated by both quantitative RT-PCR and immunocytochemistry.
RESULTS: In the normal human intestine, both BEST2 and BEST4 were expressed at the basolateral membrane of post-mitotic IECs. However, co-staining analysis revealed that BEST2 is expressed exclusively in MUC2-positive colonic goblet cells, whereas BEST4 is expressed exclusively in Villin-positive enterocytes of both small intestine and the colon. In UC patients, BEST2 expression was markedly downregulated in goblet cell-depleted crypts, which confirmed goblet cell-restricted expression of BEST2 under both normal and pathological conditions. Consistently, *in vitro* induction of enterocyte differentiation significantly upregulated expression of both Villin and BEST4, but not BEST2, in Caco-2 cells. Conversely, induction of goblet cell differentiation by a Notch inhibitor, LY411575, significantly upregulated expression of both MUC2 and BEST2, but not BEST4, in HT-29 cells. In sharp contrast, forced activation of Notch signaling, which is a key molecular event for enterocyte differentiation, significantly upregulated expression of both Villin and BEST4, but not BEST2, in LS174T cells.
CONCLUSION: Goblet cell-specific expression of BEST2, as well as enterocyte-specific expression of BEST4 is regulated by the activity of Notch signaling in human IECs. Results suggest the potential contribution of BEST2 and BEST4 to lineage specific functions of IECs, such as mucin secretion or nutrition absorption.
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Disclosure of Interest: None Declared
Keywords: BEST2, BEST4, Chloride channel, Enterocytes, Goblet cells, Notch signaling

P525 COMPLETE CONVERSION OF CRYPT PROGENITOR CELLS INTO ATOH1-POSITIVE CELLS BY TARGETED DELETION OF DLL1 AND DLL4 IN LGR5-POSITIVE INTESTINAL STEM CELLS.

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INTRODUCTION: Notch ligands Dll1 and Dll4 are functionally redundant, and both are required for the proper maintenance of the intestinal epithelium. These ligands have been shown to activate Notch signaling at both stem- and progenitor-cell level, and thereby contribute to maintain $LGR5^+$ intestinal stem cells (ISCs), as well as $Hes1^+$ or $Atoh1^+$ progenitor cells. However, whether an ISC that is deficient of both genes can maintain its stem cell function, and give rise to both $Hes1^+$ and $Atoh1^+$ progenitor cells, has never been identified.
AIMS&METHODS: In this study, we aimed to analyze the effect of Dll1 and Dll4 deficiency in $LGR5^+$ ISCs. Mice harboring the EGFP-Ires-creERT2 knock-in allele at the LGR5 locus ($LGR5^{EGFP\text{-}Ires\text{-}CreERT2}$) was crossed with both Dll1-floxed and Dll4-floxed mice to generate $LGR5^{EGFP\text{-}Ires\text{-}CreERT2}/Dll1^{flox/flox}Dll4^{flox/flox}$ mice. A control strain was also generated by crossing those CreERT2 mice with Rosa26-lacZ reporter mice ($LGR5^{EGFP\text{-}Ires\text{-}CreERT2}$/LacZ mice). These mice were subjected to Cre-mediated gene recombination by intraperitoneal injection of Tamoxifen (TMX) for 5 consecutive days. Mice were sacrificed at various days post induction, and their intestinal tissues were analyzed by immunohistochemistry (IHC).
RESULTS: Analysis of $LGR5^{EGFP\text{-}Ires\text{-}CreERT2}$/LacZ mice showed that in the small intestine, progeny of $LacZ^+$ $LGR5^+$ ISCs can completely replace the whole crypt, including Paneth cells, within 5 days post induction. In these mice, both $Hes1^+$ and $Atoh1^+$ cells were clearly observed in the crypts, which did not change upon TMX treatment. Small intestinal tissue of $LGR5^{EGFP\text{-}Ires\text{-}CreERT2}/Dll1^{flox/flox}Dll4^{flox/flox}$ mice collected at 5 days post induction revealed that the number of $EGFP^+$ ISCs remained unchanged, compared to control mice. IHC analysis showed that number of Paneth cells also remained unchanged, suggesting that the stem cell niche is insusceptible to Dll1 and Dll4 loss-of-function at this experimental period. However, in sharp contrast, IHC analysis also revealed that marked increase of $Muc2^+$ goblet cells can be observed exclusively in the villus extending from crypts containing $EGFP^+$ ISCs. Consistently in those $EGFP^+$ crypts, no $Hes1^+$ cell could be observed, but the progenitor region appeared to be completely dominated by $Atoh1^+$ cells, as confirmed by double immunostaining of Hes1 or Atoh1 with EGFP.
CONCLUSION: Targeted deletion of Dll1 and Dll4 in $LGR5^+$ ISCs can completely convert crypt progenitor cell population into $ATOH1^+$ cells. Compared to the stem cell compartment, progenitor cells may be more susceptible to loss-of-function of Dll1 and Dll4.
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Disclosure of Interest: None Declared
Keywords: ATOH1, Lgr5, notch pathway

P526 HUMAN SMALL INTESTINAL BARRIER FUNCTION AND TIGHT JUNCTION INTEGRITY DURING ISCHEMIA REPERFUSION

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INTRODUCTION: The small intestine is lined with epithelial cells interconnected by tight junctions (TJ) to prevent exposure of the host interior to potentially harmful luminal content. Intestinal ischemia and reperfusion (IR) is associated with damage to this barrier which can lead to bacterial translocation, systemic inflammation, and eventually multiple organ failure. Previous studies showed that the human small intestine is able to morphologically restore IR-induced damage after 30 minutes of ischemia. However, it is unknown if the barrier is also functionally resealed within this time frame. This study aimed to assess intestinal barrier function during intestinal IR.
AIMS&METHODS: In a human experimental model 6 cm of jejunum, to be removed for surgical reasons, was selectively exposed to 30 minutes of ischemia (I) followed by 30 and 120 minutes of reperfusion (R). Before induction of ischemia, lactulose (L) and rhamnose (R) were injected into the lumen of the isolated bowel segment to assess intestinal permeability. A sham procedure without IR was performed in 3 patients. Blood and tissue were sampled at all time points. Arteriovenous (V-A) concentration differences of plasma sugars were measured using HPLC-MS and L/R ratios were calculated. Tissue was stained for ZO-1/occludin and analyzed by electron microscopy (EM) to visualize TJs.
RESULTS: Plasma L/R ratio significantly increased at 30I30R compared to control (0.75±0.10 vs 0.20±0.09, P < .05), indicating increased intestinal permeability after short reperfusion. At 30I120R, the ratio normalized to 0.17±0.06 and was not significantly different from control or sham. ZO-1/occludin staining showed continuous staining in control tissue, while at 30I, distortion of staining was observed, indicating TJ loss. An intact lining of ZO-1/occludin was observed at 120R. EM analysis revealed disrupted TJs after 30I, which are restored after 120R.
CONCLUSION: The human small intestinal barrier is damaged after ischemia followed by 30 minutes of reperfusion. Morphological and functional recovery of this barrier occurs within 120 minutes of reperfusion, highlighting the unique ability of the human gut to withstand short ischemic events.
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Disclosure of Interest: None Declared
Keywords: ischemia reperfusion, small intestine, tight juntions

P527 NEURAL MODULATION OF GLUCOSE ABSORPTION IN RAT JEJUNUM VIA SGLT1 AND GLUT2: DEPENDENCE ON INTRALUMINAL GLUCOSE CONCENTRATION

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INTRODUCTION: Intestinal glucose absorption is a critical component of glucose homeostasis. This study aims to determine the role of capsaicin sensitive primary afferents (CSPA) in regulating rat jejunal glucose absorption and to determine if this regulation occurs via SGLT1 and/or GLUT2.
AIMS&METHODS: Glucose absorption was measured in-vivo by intrajejunal perfusion of various concentrations of glucose in control rats and rats desensitized to capsaicin. The effects of adding capsaicin, phlorizin or phloretin to the perfusate were determined. The effect of capsaicin, with and without phlorizin, phloretin or tetrodotoxin on glucose uptake by jejunal strips was also measured in-vitro.
RESULTS: Absorption of 0.1 to 50 mM glucose in vivo was saturable, and increased from 0.09+0.002 to 29.8±2.4 μmoles/hour/cm. Intaluminal perfusion of 1 mM phlorizin or phloritin reduced the absorption of 50 mM glucose by 34 and 21%, respectively ($P < 0.05$). Intrajejunal perfusion of 400μM capsaicin had no effect on the absorption of 0.1mM, 1mM, 5mM, or 20mM glucose, but absorption of 50 mM glucose was reduced by 50% ($p < 0.05$). Systemic desensitization to capsaicin decreased absorption of 20 and 50 mM glucose by 21% and 47%, respectively. The decrease of 50 mM glucose absorption was fully reversed by phloretin, but was accentuated by phlorizin. In vitro, SGLT-1 mediated steady state glucose uptake (1 and 20 mM) by jejunal strips was inhibited by capsaicin in a dose-dependent manner. This effect was more pronounced with lower concentration of glucose and was reduced by tetrodotoxin. In normal rats, one minute uptake of 1-50 mM glucose by strips was also saturable and increased from 2.97±0.02 to 40.1± 2.3μmoles/minute-gram dry weight. This uptake was reduced substantially in the presence of 10 or 25 μM phlorizin or phloretin, an effect that was more pronounced with the lower concentration of glucose. Systemic desensitization to capsaicin reduced basal 1-20 mM, but not 50 mM unidirectional glucose uptake. Low dose phloretin decreased unidirectional uptake of 50 mM glucose by 35% in normal rats, but had no effect in rats desensitized to capsaicin.
CONCLUSION: CSPA fibers are involved in regulating intestinal glucose transport. This regulation seems to depend on the intraluminal glucose concentration, and is at least partially mediated by both SGLT1 and GLUT2.
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Disclosure of Interest: None Declared
Keywords: glucose absorption, GLUT2, neural regulation, SGLT1

P528 THE EFFECTS OF ALCOHOL ON GUT WALL INTEGRITY AS MEASURED BY I-FABP, L-FABP AND LBP.

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INTRODUCTION: The aim of this study is to determine the immediate effects of oral alcohol consumption on gut wall integrity. The gut wall integrity will be assessed using intestinal- and liver-fatty acid binding proteins (I-FABP and L-FABP) as a measure of the integrity of the enterocyt. Lipopolysaccharide Binding Protein (LBP), a protein that binds lipopolysaccharides (LPS), will serve as a measure of endotoxemia.
AIMS&METHODS: A clinical trial in randomized cross-over design, including fifteen healthy adult male volunteers was conducted. Seven blood samples were taken. One blood sample was collected pre-consumption, five hourly post-consumption and one 24 hours later. Each volunteer consumed alcohol (1g/kg) on the one day and water on another. Volunteers fasted during 6 hours pre-consumption to obtain a reproducible alcohol uptake. Concentrations I-FABP, L-FABP and LBP in blood plasma were analyzed using ELISA.
RESULTS: Fifteen males were included, median age 21 years (18-41). The mean IFABP (ng/ml) of all samples was significantly higher after drinking alcohol than after drinking water, 1.64 (0.81-5.63) vs. 1.15 (0.52-1.81) resp. p=0.001. The mean of the highest single IFABP samples per volunteer was also higher on the alcohol day compared to the water day 3.16 (1.31-13.29) vs. 1.80 (0.77-2.68) p=0.001 resp. The mean L-FABP (ng/ml) was significantly higher on the alcohol day 18.99 (9.25-37.19) vs. 16.16 (10.52-30.52) p=0.012. As was the mean of the highest single LFABP sample per volunteer on the alcohol day 31.70 (13.90-73.72) vs. 24.24 (16.98-36.80) p=0.009. The mean LBP (µg/ml) showed no significant difference between the alcohol and water group 15.13 [9.44 – 23.16] vs. 15.74 [9.20-41.39] resp. p=0.394 nor did the highest single LBP sample per volunteer: alcohol 20.50 [11.28-28.60] vs. water 20.32 [11.98-48.28] p=0.570.
The correlation between I-FABP and L-FABP was ρ=0.843, p=0.000. The correlation between LBP and I-FABP was 0.148, p=0.033 and LBP and L-FABP was 0.209, p=0.003. The highest concentrations of LBP per volunteer did not correlate significantly with highest I-FABP/L-FABP levels 0.479, p=0.071 and 0.211, p=0.451 resp.
I-FABP and L-FABP concentrations increase significantly during the first 3 hours after drinking alcohol. Levels then decrease significantly.
CONCLUSION: Acute alcohol consumption immediately effects the gut wall integrity, as measured with damage markers I-FABP and L-FABP and continues to do so up to three hours. LBP concentrations do not increase significantly so translocation of bacterial products does not seem likely after acute alcohol consumption.
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Disclosure of Interest: None Declared
Keywords: Alcohol, Gut microbiota

P529 PHOSPHORYLATION OF SMAD2/3 IN STEM CELLS OF SMALL INTESTINE

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INTRODUCTION: The stem cells of intestine are ultimately responsible for the renewal of tissues undergoing continuous turnover and is possibly in the CBC cells and the +4 cell position from the bottom of crypts. We have previously identified the significant expression of Smad2/3, phosphorylated at specific linker threonine residues (pSmad2/3L-Thr), in specific epithelial cells of the murine stomach and have suggested these cells to be epithelial stem cells. In the present study, we explore whether pSmad2/3L-Thr can serve as a marker for stem cells of murine intestine.
AIMS&METHODS: The small intestines from C57BL/6 mice were examined. Double immunofluorescent staining of pSmad2/3L-Thr with Ki67, CDK4, and chromograninA was performed, to show the characteristics of pSmad2/3L-Thr positive cells. To study other supposed stem cell biomarkers expression, we perfomed double immunofluorescent staining of pSmad2/3L-Thr with DCAMKL1, MSI-1, Lgr5. After immunofluorescent staining, we stained the same sections with hematoxylin–eosin and observed these cells under a light microscope.
For BrdU label-retaining assay, mice were injected with BrdU 3 times a day for 2 days. At various times (5, 10, and 15 days) after labeling, each group of mice was sacrificed. We performed immunofluorescent staining of the pSmad2/3L-Thr with BrdU.
RESULTS: In the small intestine, pSmad2/3L-Thr positive cells were significantly confirmed in the CBCs or +4 cell position. Although pSmad2/3L-Thr positive cells were detected between the Ki67 cells, immunohistochemical co-localization of pSmad2/3L-Thr with Ki67 was never observed. pSmad2/3L-Thr positive cells showed co-localization with CDK4 positive cells, and didn't show co-localization with chromograninA positive cells Under a light microscope, pSmad2/3L-Thr positive cells indicated undifferentiated morphological features and were confirmed in the CBCs and +4 cell position. pSmad2/3L-Thr positive cells were co-localized with MSI-1, and adjacent localization with DCAMKL1 positive cells. In Lgr5-EGFP knock-in mice, some but not all pSmad2/3L-Thr cells showed co-localization with Lgr5.
For label-retention studies, on 5,10,15-day, a part of BrdU label-retaining cells were co-localized with pSmad2/3L-Thr.
CONCLUSION: We have identified the significant expression of pSmad2/3L-Thr in specific epithelial cells of the murine small intestine. We suggest these cells to be intestinal stem cells. These cells might be in the phase of cell cycle just before undergoing cell division.
Disclosure of Interest: None Declared
Keywords: smad2/3, small intestine, stem cells

P530 ACTIVITY OF RIFAXIMIN AGAINST BACTERIAL STRAINS ISOLATED FROM DUODENAL ASPIRATES OF PATIENTS WITH INTESTINAL BACTERIAL OVERGROWTH

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INTRODUCTION: In a recent publication on 320 patients, we confirmed a relationship between small intestinal bacterial overgrowth (SIBO) and irritable bowel syndrome (IBS) (Pyleris et *al*. DDS 2012). In this study, we extend this investigation to include 800 patients and analyze the in vitro activity of rifaximin on SIBO colonizers.
AIMS&METHODS: Duodenal aspirates were collected from 800 outpatients subjected to upper GI endoscopy and quantitatively cultured under aerobic conditions. SIBO was diagnosed in 159 based on the isolation of at least one coliform $>10^3$ cfu/ml. Identification of Gram-negative bacteria was made by API20E and API20NE systems. Minimum inhibitory concentrations (MICs) of rifaximin, ampicillin, cefuroxime, gentamycin and levofloxacin were performed by a microdilution technique at a final volume of 0.1ml using a log-phase inoculum of $5x10^5$ cfu/ml of the isolates. Strain ATCC 25922 (*E. coli*) was tested as a control. Time-kill studies were performed exposing a log-phase inoculum of $1x10^6$ cfu/ml of 29 isolates to various concentrations of rifaximin; 11 were *Escherichia coli* and 3 *Enterococcus faecalis*. Any >3log10 decrease of viable cells was considered significant killing effect.
RESULTS: MIC50/MIC90 (mg/l) of rifaximin (no of tested isolates in parethesss) were: on *E.coli* (n= 48) 16/64; on *Klebsiella pneumoniae* (n= 32) 64/128; on *Enterobacter* spp (n= 23) 64/128; on *Klebsiella oxytoca* (n= 7) 64/64; on *Enterococcus* spp (n= 14) 8/16; on *Staphylococcus aureus* (n= 12) 0.12 and 0.12; on other *Enterobacteriaceae** (n= 11) 32/64; and on non-*Enterobacteriaceae*** (n= 23) 16 and >256. According to the CLSI breakpoints, ampicillin, cefuroxime, gentamycin, levofloxacin and rifaximin inhibited 25.9, 46.5, 74.1, 85.3 and 89.6% of the total tested isolates respectively. The killing effect was 27.5% of isolates by the 500 mg/l concentration on *E.coli* after 4 hours; 36.4% after 6 hours; and 81.8% after 24 hours. This was 100% after 24 hours for *E.faecalis* and 33.3% for the non-*E.coli* isolates.
*species of *Citrobacter freundii*, *Proteus mirabilis*, *P. vulgaris* and *Serratia marcenscens;*
**species of *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia* and *Moraxella spp*.
CONCLUSION: As rifaximin is poorly absorbed and reaches its maximum concentration in the small intestine, MIC values for most of the tested aerobes corroborate clinical data on the clinical efficacy of rifaximin in IBS (Pimentel et *al*. N Eng J Med 2011; 364). The time-kill effect of rifaximin indicates the most promising effect of rifaximin on *E.coli* and *E.faecalis in vitro*.
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Keywords: IBS, Rifaximin, SIBO

P531 MIRNA-MRNA PAIRING ANALYSIS IDENTIFIES THE INFLAMMATORY RESPONSE AND INTESTINAL PERMEABILITY AS POTENTIALLY DYSREGULATED FUNCTIONS IN THE JEJUNAL MUCOSA OF IBS-D PATIENTS

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INTRODUCTION: There is growing evidence that miRNAs are aberrantly expressed in chronic inflammatory diseases, but their involvement in the development and symptom generation in irritable bowel syndrome (IBS) have not been fully explored to date.
AIMS&METHODS: Our aims were (1) to identify miRNAs differentially expressed in the small bowel mucosa of IBS-D patients and (2) to explore putative targets and identify genes controlled by specific dysregulated IBS-D miRNAs.
Healthy volunteers (n=9) and non-allergic, non-celiac, naïve participants fulfilling IBS-D Rome III (n=14) were studied. Total RNA isolated from jejunal biopsies was submitted to microarray analysis (Agilent's Unrestricted_Human_miRNA_V16.0 and Affymetrix Human Genome U133 Plus 2.0 GeneChips). Combined analysis of miRNA and mRNA profiles was subsequently carried out by investigating the co-expression profile of miRNA-mRNA pairs. Targets were then selected based on inversed expression (up-regulation of miRNA and down-regulation of the target mRNA, and vice versa) and further evaluated using the Ingenuity Pathway Analysis software to identify biological networks, functions and pathways most significant to those targets.
RESULTS: 30 miRNAs and 286 mRNAs were differentially expressed ($p<0.05$) between healthy and IBS-D samples. miRNA-mRNA pairing analysis identified 155 genes that were experimentally observed or predicted with a moderate/high score to be targets of the differentially expressed miRNAs. Pathway analysis of the target genes revealed their implication in biological functions related to gastrointestinal disease ($p<0,001$), inflammatory disease ($p<0,001$) and inflammatory response ($p<0,001$). Top molecular and cellular functions associated with the target genes related to cell growth and proliferation ($p<0,00001$) and cell assembly and organization ($p<0,00001$). Interestingly, three networks (score>37, $p<10^{-37}$) of potentially interacting target genes implicated in significant biological functions related to intestinal permeability, secretory diarrhea and caveolar-mediated endocytosis signaling were also identified.
CONCLUSION: Substantial differences in miRNA and mRNA expression exist between healthy and IBS-D jejunal mucosa. miRNA-mRNA pairing analysis will help us to select a battery of distinctive molecular targets for future studies aimed at promoting innovative treatment and prevention strategies for IBS management.
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Disclosure of Interest: None Declared
Keywords: intestinal inflammation, intestinal permeability, Irritable bowel syndrome, miRNAs

P532 EOSINOPHILIC ACTIVATION BY NEUROMEDIATORS REPRESENTS A MECHANISM LEADING TO IMMUNE ACTIVATION AND BARRIER DYSFUNCTION IN IBS

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INTRODUCTION: In irritable bowel syndrome (IBS), the mechanisms underlying altered bowel habit and visceral hypersensitivity remain unestablished, although barrier dysfunction mediated by neuro-immune interactions involving eosinophils and mast cells may contribute. The impact on immune function of neuropeptides, such as substance P (SP) and its receptor (NKR1), remains unexplored in these patients.
AIMS&METHODS: We study the immunomodulatory role of SP and acetylcholine on the eosinophil (Eo), a key regulator of barrier function. Healthy(H) subjects (n=12) and age-matched, naïve participants fulfilling diarrhea-prone IBS(IBS-D) Rome III (n=17) were included. Jejunal biopsies were obtained by Watson's capsule in all participants. Mucosal Eos counts, ultrastructure, activation and secretory activity (SNAP-23) were evaluated by immunohistochemistry (MBP), transmission electron microscopy or gene expression. The Eo cell line AML14.3D10 was stimulated with SP (10^{-6}M) or Carbachol (CCh, 10^{-4}M), gene and protein expression were assessed by qRT-PCR, immunofluorescence, or flow cytometry.
RESULTS: The number of MBP^+cells was similar in both groups (H:44±7; IBS-D:83±19 cells/mm^2). However, we observed Eos peacemeal degranulation, increased SNAP-23 expression, unchanged MBP, and decreased eotaxin, EDN and ECP gene expression ($P<0.05$) in IBS-D. The Eo cell line expressed NKR1 and responded to SP by upregulating IL-8, NFKB and MBP, downregulating CCL21 and without changing EDN and EPO gene expression ($P<0.05$). Moreover, Eos expressed M1, M2 and M3 muscarinic receptors and responded to CCh stimulation by upregulating IL-8, NFKB and CCL21 and downregulating EPO, MBP and EDN gene expression ($P<0.05$). Secretory activity was confirmed by localization of SNAP-23 on the membrane surface only in stimulated cells.
CONCLUSION: Similar to IBS-D intestinal mucosa, decreased Eo classical proinflammatory profile is identified by neuromediator stimulation of the Eo cell line. The relevance of neuroimmune activation of mucosal Eos in IBS warrants further investigation.
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Disclosure of Interest: None Declared
Keywords: CARBACHOL, EOSINOPHIL, IBS, SUBSTANCE P

P533 REDUCED NUMBERS OF MAST CELLS IN THE JEJUNUM OF PATIENTS WITH IBS-D COMPARED TO HEALTHY VOLUNTEERS.

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INTRODUCTION: Mast cells are part of the innate immunity of the gut. The pathogenesis behind irritable bowel syndrome (IBS) is still unknown, but alterations in the mucosal immune system might have a role in development of the disease. Increase of mast cells has previously been described in duodenum, jejunum and colon of patients with IBS. However there are also studies that have been unable to detect differences and even decrease of mast cells has been reported[1]. The methods used in the different studies have not been unifying.
AIMS&METHODS: The aim of this study was to develop a standardized method for mast cell morphometry and to identify alterations in the prevalence of mast cells.
Jejunal biopsies were taken with a Watson capsule from 27 patients with IBS and 45 healthy volunteers (HV) and duodenal biopsies were taken with gastroscopy from 10 patients. Biopsies were paraffin embedded after fixation in formalin and stained by immunohistochemistry for tryptase and CD117. Stained cells were manually counted per mm^2 mucosa in lamina propria, intraepithelial and total. The area was calculated via image analysis program (Nikon NiS elements BR 3,22). Unpaired t-test with Bonferroni's correction was used for statistical analyses.
RESULTS: We found no difference in total numbers or mast cells using tryptase or CD117 between IBS patients and HV. When analysing subgroups of IBS, patients with IBS-D have significantly lower intraepithelial CD117-positive mast cells ($p<0.0125$) but not intraepithelial tryptase-positive cells compared to HV. Duodenal biopsies from patients exhibited significantly more mast cells than jejunum biopsies both for tryptase ($p<0.001$) and CD117 ($p<0.001$) stained biopsies.
CONCLUSION: In contrast to many other studies we found no increase of jejunal mast cells in IBS but possibly a decrease in jejunal intraepithelial mast cells in patients with IBS-D. The intraepithelial mast cells have previously not been described in IBS but since they are in direct contact with the gut lumen, they might have a role in IBS pathogenesis. We counted mast cells per mucosal area.

Others have mostly counted mast cells per high power field (hpf). Counting per hpf includes areas without mucosa and is therefore difficult to standardize for comparison. The number of mast cells in the duodenum was greater than in the jejunum. Further studies with a larger cohort are needed to confirm this finding.

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Keywords: CD117, IBS, Jejunum, MAST CELL

P534 MESENCHYMAL STEM CELL-DERIVED MOLECULES PROTECT AGAINST RADIATION-INDUCED INTESTINAL INJURY THROUGH MODULATION OF ENDOGENOUS CELL HOMEOSTASIS AND INHIBITION OF SYSTEMIC AND LOCAL INFLAMMATION

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INTRODUCTION: Intestinal injury induced by radiotherapy can affect patient's quality of life and may be life threatening. Mesenchymal stem cells (MSC)-derived molecules have been shown to provide protection from intestinal injury. However, the mechanisms involved are barely understood. In this study, we evaluated the therapeutic capability of MSC-derived molecules after radiation-induced intestinal injury and identified the potential mechanisms invovled.

AIMS&METHODS: To study this, rats were exposed to a 10 Gy abdominal irradiation, MSC-conditioned medium (MSC-CM) was then delivered to rats by tail intravenous injection. Blood and tissue samples were collected for various measurements. The levels of various inflammatory cytokines were determined in small intestine and blood to assess the amelioration of inflammation. Parallel studies were performed in rat intestinal epithelial cells (IEC-6) co-coltured with MSCs after radiation. Proteomic analysis were performed to identify the key biomolecules correlated with the therapeutic effects in MSC-CM.

RESULTS: We report that systemic infusion of MSC-CM significantly ameliorated the clinical and histopathological severity of intestinal injury in rats, abrogating weight loss and inflammation, restituting intestinal structure and xylose absorption, increasing survival. We observed that the delivery of MSCs secretions leads to an intestinal cytoprotective effect by both stimulating regeneration and inhibiting death of irradiated intestinal epithelial cells *in vivo and vitro*. MSC-CM treatment also accelerates $Lgr5^+$ intestinal stem cells (ISCs) regeneration in the early stage of rehabilitation. In addition, we demonstrate that MSC-CM treatment has an inhibitory effect on inflammation response by down-regulation of pro-inflammatory cytokines and up-regulation of anti-inflammatory cytokines at both systemic and local levels. Conditioned medium from MSCs stimulated by radiation-induced inflammatory products ($MSC\text{-}CM^{IR}$) was more effective than conditioned medium from MSCs incubated under normal conditions ($MSC\text{-}CM^{NOR}$), an observation partly explained by its higher content of growth factors and chemokines, such as basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF).

CONCLUSION: Our results suggests that MSC-CM treatment provides therapeutic benefits to the injuried intestine by reducing apoptosis and increasing proliferation of intestinal epithelial cells, accelerating resident $Lgr5^+$ ISCs regeneration, limiting systemic and local inflammation and could be used as an attractive candidate for the treatments of radiation-induce intestinal injury.

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Disclosure of Interest: None Declared

Keywords: mesenchymal stem cells, paracrine factors, radiation, regeneration, small intestinal damage

P535 SELECTIVE ADENOSINE RECEPTOR MODULATORS: NEW APPROACHES FOR PREVENTION OF INFLAMMATION-INDUCED DISTURBED GASTROINTESTINAL MOTILITY

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INTRODUCTION: The purine nucleoside adenosine, which is involved in a variety of physiological functions, regulates immune and inflammatory responses and acts as a modulator of gut functions. By activation of different receptor subtypes adenosine is able to induce anti-inflammatory or pro-inflammatory impacts.

AIMS&METHODS: The current study examined the impact of the adenosine A_{2A} receptor ($A_{2A}R$) agonist CGS 21680 and the A_{2B} antagonist ($A_{2B}R$) PSB-1115 on acute inflammation in rat ileum/jejunum preparations. Further it focused on interactions of the multi-herbal drug STW 5 and its component *Iberis amara* (STW 6) with $A_{2A}R$ as a possible mechanism of the protective effect of STW 5 in gastrointestinal disorders.

Inflammation was induced by intraluminal instillation of 2,4,6-trinitrobenzene sulfonic acid (TNBS). Contractions were measured isometrically in an organ bath set up. Gene expression was determined using qRT-PCR. Radioligand binding assays (competition experiments) were carried out with rat brain homogenates. Morphological changes were estimated after van Gieson staining.

RESULTS: CGS 21680 (0.1-10 μM) restored concentration-dependently the TNBS-induced inhibition of the ACh-contractions. PSB-1115 (100 μM) diminished the contraction in TNBS-preincubated preparations. A significant amelioration of the TNBS-diminished contractions was found after combined application of CGS 21680 and PSB-1115 in subthresholds, which was in the same range as the effect of 1 μM methotrexate. STW 5 (64-512 μg/ml) and STW 6(3-24 μg/ml) reduced concentration-dependently the TNBS-induced morphological disturbances and in parallel the ACh-induced contractions. STW 5 but not STW 6 interacted with $A_{2A}R$ and inhibited the TNBS- increased TNFα gene expression which was blocked by the $A_{2A}R$ antagonist CSC (0.2 mM).

CONCLUSION: Our results demonstrate that the activation of A_{2A} or the blockade of A_{2B} receptors can decrease the inflammation-induced disturbance in small intestinal preparations. STW 5 but not STW 6 interacts with $A_{2A}R$ contributing to the inhibition of the TNFα gene expression which could be responsible for inhibition of TNBS-induced disturbed contractions.

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Keywords: Adenosine , herbal drug, Motility Disorders, tumor necrosis factor-alpha

P536 ROLE OF ENDOGENOUS GLP-2 IN THE RECOVERY PHASE OF DSS-INDUCED COLITIS IN MICE

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INTRODUCTION: Glucagon-like peptide-2 (GLP-2) is a potent intestinotrophic growth factor that has been shown to stimulate intestinal growth and reduce disease severity. Dipeptidyl peptidase-4 (DPP-4) inhibition reduces GLP-2 degradation and enhances the intestinotrophic effect of exogenous GLP-2. GLP-2 and DPP-4 inhibitor may therefore have curative properties against colitis via the enhancement of endogenous GLP-2. In a previous study, we reported that anagliptin, a DPP-4 inhibitor, had little influence on the development of DSS (dextran sodium sulfate)-induced colitis in mice, but improved recovery from this colitis by enhancing the proliferation of colonic epithelial cells. We conjectured that this enhancement of the recovery phase was facilitated by an effect of GLP-2. In this study, to confirm the influence of the recovery phase in the absence of GLP-2, we evaluate DSS-induced colitis in mice deficient in GLP-2.

AIMS&METHODS: Mice deficient GLP-2 were established by disrupting Glucagon gene (Gcg) by the introduction of green fluorescent protein (GFP) cDNA in a knock-in mouse line. $Gcg^{gfp/gfp}$ mice were deprived of pro-Glucagon hormone, GLP-1 and GLP-2. Twelve-week-old $Gcg^{gfp/gfp}$ and $Gcg^{+/+}$ mice were individually housed with ad libitum access to drinking water containing 3.0% DSS for 6 days. DSS-containing water was replaced with filtered water without DSS on day 6. Severity of colitis was assessed daily by body weight (BW) loss and disease activity index (DAI).

RESULTS: On Day 9, after 3 days from restart of water without DSS, there was no significant difference in BW loss or DAI ($Gcg^{gfp/gfp}$ group, BW -15.9±4.4%, DAI 3.8±1.8; $Gcg^{+/+}$ group, BW -14.9±3.8%, DAI 4.1±3.3; NS, n=4 each). From day 10 to day 22, BW of the $Gcg^{gfp/gfp}$ group was lower than that of the $Gcg^{+/+}$ group within the range of 1.0 to 5.1%.

CONCLUSION: In our previous study, we reported a significant improvement in BW loss and DAI on day 10, after 3 days from restart of water without DSS, in the anagliptin-treated group compared to the untreated group (untreated group, BW -20.7±7.4%, DAI 7.0±1.8; anagliptin-treated group, BW-12.2±7.0%, DAI 3.9±3.0; $P<0.01$, n=15 each). In the present study, however, we saw only a minor difference between $Gcg^{gfp/gfp}$ mice and $Gcg^{+/+}$ in the degree of DSS colitis. On day 10, average BW in the $Gcg^{+/+}$ mice was only 2% higher than that of the $Gcg^{gfp/gfp}$ mice. We therefore conclude that GLP-2 and DPP-4 inhibitor may have curative properties against colitis, but that the absence of GLP-2 does not exacerbate the recovery phase of DSS-induced colitis in mice.

Disclosure of Interest: None Declared

Keywords: colitis, DPP4-inhibitor, GLP-2

P537 PHENOTYPIC AND FUNCTIONAL CHARACTERIZATION OF INTRAEPITHELIAL AND LAMINA PROPRIA INFLAMMATORY CELL INFILTRATE IN AUTOIMMUNE ENTEROPATHY.

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INTRODUCTION: Autoimmune enteropathy (AE) is a rare disease characterized by diarrhea, malabsorption, and association with other autoimmune conditions. Histological hallmarks of AE include villous atrophy, lamina propria infiltration by T lymphocytes and increased intraepithelial lymphocytes (IELs). Few data exist regarding functional and phenotypic characterization of mucosal inflammatory cells in the small intestine during AE.

AIMS&METHODS: Duodenal biopsies were obtained from a 26-year old female diagnosed with AE, at baseline and following steroid therapy. Biopsies were treated with DTT, EDTA and collagenase to extract IELs and lamina propria mononuclear cells (LPMCs). Cells were analyzed for surface marker expression and intracellular cytokine profile by flow cytometry and immunohistochemistry.

RESULTS: The majority of IELs were CD8+CD103+ and produced interferon(IFN)-γ; noteworthy, a relevant amount of them co-produced interleukin(IL)-17. Steroid treatment reduced IL-17 production by IELs. Analysis of LP T cells revealed a similar proportion of CD4+ and CD8+ lymphocytes. Most of LP $CD4^+$ T cells exhibited a memory phenotype ($IL7R^{high}CD25^{low}$),while a low percentage of Tregs ($CD4^+CD25^{high}FoxP3^+$) was observed. Within CD4+ memory compartment, Th1 ($CXCR3^+$) and Th17 ($CCR6^+$) cells were equally represented; interestingly, a significant proportion of $CXCR3^+CCR6^+$ cells was observed. Prednisone treatment reduced CCR6+ and $CXCR3^+CCR6^+$ cells, while increasing the expression of $FoxP3^+$ in$CD4^+CD25^{high}$ cells. Upon stimulation, LP CD4+ T cells expressed IFN-γ, IL-17 and IL-22, while CD8+ cells mostly expressed IFN-γ. Prednisone treatment markedly reduced the production of IFN-γ by LP CD4+ cells. Phenotypic analysis of LP dendritic cells revealed that a small fraction of them expressed the myeloid cell marker CD11c and CD103. A significant number of CD11c- DCs expressing fractalkine receptor (CX3CR1) was found within the LP. Immunohistochemistry data confirmed the results.
CONCLUSION: These data demonstrate a massive infiltration by Th1 and Th17 cells, and activated CD8+ lymphocytes, in the small intestinal LP during AE. Noteworthy, LP Treg infiltration at baseline was remarkably low. The majority of IEL were CD103+IFN-γ+ CD8+ cells; among these, a relevant proportion co-produced IL-17. Most of these phenotypic and functional alterations were corrected by steroid therapy. These results could be relevant for the identification of novel therapeutic targets in patients with AE.
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Keywords: Autoimmune enteropathy, Intraepithelial lymphocytes

P538 DOES HIGH DOSE IRRADIATION AFFECT FUNCTIONS OF THE INTERSTITIAL CELLS OF CAJAL IN THE MURINE SMALL INTESTINE?

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INTRODUCTION: Motility of murine small intestine is composed of migrating motor complex (MMC) from enteric nervous system and phasic contraction from slow waves originating in interstitial cells of Cajal (ICC). ICC have plasticity, meaning that they can be reduced and recovered in various stages of diverse gastrointestinal disorders. High dose irradiation has been known to alter the intestinal motility by neurotransmitter related to inflammation. However, detailed analysis of changes in ICC functions after high dose irradiation is lacking.
AIMS&METHODS: We sought to determine whether high dose irradiation affects the plasticity of ICC. High dose of irradiation (13Gy) was given to 8-12 week old female C3H/HeN mice. Tension recordings for MMCs and phasic contractions from small intestinal segment and conventional microelectrode recordings for slow waves were performed at 0, 1, 3 and 5 day after irradiation with compared to sham mice.
RESULTS: Amplitude, area under the curve (AUC), and frequency of MMCs were 4.31 ± 1.59 mN, 61.94 ± 17.42 sec×mN/wave and 0.52 ± 0.09 /min in sham mice (N=6). Frequency of MMCs were faster at day 0 (0.88 ± 0.24 /min, p=0.009, N=4) and day 1 (0.73 ± 0.14 /min, p=0.013, N=5). MMCs almost disappeared at day 3 (N=3) with lower amplitude (0.86 ± 0.01 mN, p=0.009) and AUC (5.88 ± 0.20 sec×mN/wave, p=0.001). MMCs were recovered at day 5 (N=4) with no difference in amplitude (3.08 ± 0.75 mN), AUC (45.43 ± 17.42 sec×mN/wave) and frequency (0.52 ± 0.05 /min) compared to sham mice.
Amplitude, area under the curve (AUC), and frequency of phasic contractions were 0.47 ± 0.11 mN, 0.25 ± 0.06 sec×mN/wave, 36.25 ± 5.76 /min in sham mice (N=6). The phasic contractions were sustained at day 0, 1, 3 and 5 and were not significantly different from the sham mice. Resting membrane potential (RMP), amplitude, spike amplitude and frequency of slow waves were -54.32 ± 10.41 mV, 7.87 ± 3.46 mV, 15.48 ± 12.60 mV, 46.49 ± 6.92 /min in sham mice (N=5). The slow waves were also preserved at day 0, 1, 3 and 5 and were not significantly different compared to the sham mice. Mucosal inflammation was confirmed by H&E staining and c-kit immunohistochemistry confirmed the presence of ICC at day 0, 1, 3 and 5. Expressions of c-kit were not different at each day compared to sham mice.
CONCLUSION: There were changes in MMCs related to enteric nervous system after high dose irradiation. But, in contrast to our expectations, there were no changes in phasic contraction and slow waves, suggesting radiation resistance of the ICC
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Keywords: Interstitial cells of Cajal, Irradiation, migrating motor complex, motility, small intestine

P539 REDUCTION OF NSAID-INDUCED ENTEROPATHY IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING ANTI-TUMOR NECROSIS FACTOR THERAPY: A PROPENSITY-MATCHED ANALYSIS

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INTRODUCTION: The role of tumor necrosis factor-α (TNF-α) in the pathogenesis of nonsteroidal anti-inflammatory drug (NSAID)-induced small intestinal damage remains unclear. Biologics that antagonize the biological activity of TNF-α are being increasingly used in patients with rheumatoid arthritis (RA), and these drugs have the potential to induce mucosal healing in patients with intestinal diseases.
AIMS&METHODS: The aim of this study was to evaluate the preventive effect of anti-TNF therapy against small intestinal damage due to chronic NSAID use in RA patients. Capsule endoscopy was performed in 95 consecutive RA patients who received NSAIDs for more than 3 months, with or without anti-TNF therapy over a period of 3 months. The findings were scored from 0 to 4: 0, normal; 1, red spots; 2, 1 to 4 erosions; 3, >4 erosions; and 4, large erosions/ulcers. The relationship between the use of anti-TNF therapy and the risk of severe damage (score 3 or 4) or the most severe damage (score 4) was assessed using multiple logistic regression analysis. Furthermore, a propensity-score matching analysis was performed to reduce the effects of TNF-selection bias.
RESULTS: By stratifying the patients on the basis of anti-TNF therapy, we obtained crude odds ratios of 0.23 for severe damage (95% confidence interval [CI], 0.09 to 0.65) and 0.37 for the most severe damage (95% CI, 0.16 to 0.86). This protective effect of anti-TNF therapy remained robust to adjustments for baseline characteristics, with the adjusted odds ratios for severe damage and most severe damage ranging from 0.23 to 0.26 and 0.06 to 0.41, respectively. Propensity score matching yielded similar results and showed the protective effects of anti-TNF therapy against severe and most severe damage.
CONCLUSION: Anti-TNF therapy may protect against NSAID-induced small intestinal damage in RA patients. Drugs targeting TNF-α may be effective in the treatment of NSAID-induced enteropathy.
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Disclosure of Interest: None Declared
Keywords: capsule endoscopy, non-steroidal anti-inflammatory drug, propensity-score matching analysis, tumor necrosis factor

P540 RIFAXIMIN FOR TREATMENT OF SMALL INTESTINE BACTERIAL OVERGROWTH (SIBO): A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: SIBO is a condition caused by an increased number and/or abnormal type of bacteria (i.e. oropharyngeal or colonic type bacteria) in the small bowel. Eradication of SIBO relies on antibiotic therapy that must cover both aerobic and anaerobic enteric bacteria. Rifaximin is a poorly absorbable antibiotic, with a broad spectrum of antibacterial activity, covering Gram-positive and Gram-negative micro-organisms, both aerobes and anaerobes.
AIMS&METHODS: To investigate the efficacy of rifaximin to eradicate SIBO performing a systematic review and meta-analysis. MEDLINE, EMBASE, the CCRCT as well as abstract from the DDW, ACG, AGA, UEGW, BSG as well as Asian Pacific Digestive Week were searched up to November 2012. Case series, open label studies, cross-over and RCTs in adult patients with proven SIBO, treated with rifaximin, were eligible. The proportion of individuals eradicated was combined from all studies to give a pooled eradication rate using a random effects model in order to provide a more conservative estimate.
RESULTS: 28 studies were identified containing 921 subjects. 7 studies were RCTs: 2 compared rifaximin to placebo, 2 to systemic antibiotics, and 2 compared different doses of rifaximin. Finally the last RCT compared rifaximin 1200 mg/daily for 10 days vs. rifaximin 1200 mg/daily plus partially hydrolysed guar gum 5 g/ day for 10 days. To diagnose and follow-up the patients 16 studies used the hydrogen-glucose breath test and 12 the hydrogen-lactulose breath test. Pooled eradication rate was 67.0% (95% CI: 59.1 to 69.8) with evidence of heterogeneity ($I^2 = 78.17\%$). In the 2 RCTs comparing rifaximin to placebo, the pooled eradication rates for rifaximin was of 89.7% vs. 7.4% for placebo, with a difference of 82.3% (95% CI: 63.1 to 91.8). In the 2 RCTs comparing rifaximin to other antibiotics, the pooled eradication rates for rifaximin was of 64.1% vs. 41% for placebo, with a difference of 22.7% (95% CI: 7.4 to 37). It was possible to perform sensitivity analysis only in trials using rifaximin at the dosage of 1200 mg/daily according to the duration of treatment. Treatments lasting 10 days eradicated 10.9% (95% CI: 3 to 18.6) more than treatments lasting 7 days. Similarly, therapies lasting 14 days eradicated 26.3% (95% CI: 18.5 to 33.6) and 15.4% (95% CI: 7.7 to 22.7) more than treatment lasting 7 and 10 days respectively. Pooled prevalence of adverse events was 10.3%.
CONCLUSION: Rfaximin is effective and safe for treating SIBO, with an efficacy that appears to be time-dependent. However, large and well-performed RCTs are needed to substantiate these findings and establish the optimal regimen (daily dose and, especially, duration) of therapy.
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Keywords: eradication, Rifaximin, SIBO

P541 DO ENDOSCOPISTS ALWAYS RECOGNIZE SEVERE CASES OF CELIAC DISEASE?

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INTRODUCTION: Human IgA class antibodies against tissue transglutaminase (TTGA) and endomysium (EMA) are sensitive and specific markers for celiac disease (CD). Strongly positive titers of these antibodies (>10 times above the upper limit of normal) have been shown to significantly correlate with Marsh type 3 lesions in histopathological evaluation of duodenal biopsies and are currently considered to be sufficient for the diagnosis of CD in pediatric patients. In adult patients a duodenal biopsy during upper gastrointestinal (GI) endoscopy remains the gold standard in diagnosing CD. The presence of endoscopic markers of CD is a reliable indicator of histological villous atrophy that helps select patients for duodenal biopsies. However, it is not clear if advanced histopathological findings typical for CD are always associated with macroscopic changes of the duodenal mucosa.
AIMS&METHODS: To assess the relationship between duodenal histology and high levels of TTGA and EMA with endoscopic markers in adult patients with CD. Thirty two suspected CD patients with the titers of TTGA or EMA at least 10 times above the upper limit of normal were included in the study. All the patients underwent routine upper GI endoscopy with duodenal biopsies. The endoscopists were not informed about the high levels of antibodies, but the suspicion of CD was mentioned as a cause for referring the patients for endoscopy.
RESULTS: Based on the histopathological evaluation, in 30 patients (94%) Marsh type 3 lesions were described, while 2 patients (6%) had Marsh type 2 lesions. The endoscopists reported a normal endoscopic appearance of the duodenum in 20 out of 32 patients (62.5%). In 12 patients (37.5%) at least one endoscopic marker of CD was present: reduction or loss of Kerckring's folds (n=6), scalloping of the folds (n=6), coexisting reduction and scalloping of the folds (n=3), a micronodular appearance of the duodenal bulb mucosa (n=1), and duodenal erosions (n=2).
CONCLUSION: High titers of TTGA and EMA strongly correlate with histopathological but not endoscopic findings in CD. A normal endoscopic duodenal mucosal appearance does not exclude villous atrophy. Despite careful inspection of the duodenum during upper GI endoscopy, lack of endoscopic findings in patients with the suspicion of CD may be misleading, therefore duodenal biopsies with histopathological evaluation in adult CD patients are always required.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, endoscopic findings

P542 INTESTINAL INTRAEPITHELIAL LYMPHOGRAM AND SUBEPITHELIAL DEPOSITS OF ANTI-TISSUE TRANSGLUTAMINASE IGA FOR COELIAC DISEASE DIAGNOSIS IN LYMPHOCYTIC DUODENOSIS

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INTRODUCTION: Lymphocytic Duodenosis (LD) may have multiple aetiologies and the differential diagnosis is complex. It has been suggested that $\gamma\delta$+ intraepithelial lymphocytes (IEL) studies by immunohistochemistry or flow cytometry (FCM) or the presence of subepithelial deposits of transglutaminase IgA (TGd) by immunofluorescence could be useful for the diagnosis of coeliac disease (CD) in these patients. Data on these issues are scarce.
AIMS&METHODS: To evaluate the diagnostic utility of the celiac FCM IEL pattern (increase in $\gamma\delta$+IEL) in comparison with TGd and serum anti-TG IgA (TGs) in patients with LD.
We prospectively included 200 patients with clinical suspicion of CD and positive genetics (DQ2 and/or DQ8). 73% women; 28.5±1.4 years. Duodenal biopsies were taken for histopathological studies (LD was defined as >25% IEL), FCM and TGd. TGs cut-offs (Celikey, Varelissa) were: TGs<2u negative; between 2-7 u doubtful; and >7u positive. In doubtful TGs titres, EmA were evaluated. Gold standard was considered the presence of one of the following: 1) atrophy or LD with TGs+ (Doubtful TGs with EmA+); 2) atrophy or LD with TGs-, TGd+ and/either FCM+. TGd were blindly analyzed 2 different times by the same experienced observer and the intra-observer concordance degree was analyzed. Only moderate to high intensity TGd were considered as positive (since low intensity TGd are frequently seen in non-celiac controls). Sensitivity (95% CI) to detect CD was computed. Concordance degree was studied using Kappa statistics.
RESULTS: Concordance degree between both readings of TGd was moderate (K=0.56). There were 13 doubtful cases (moderate intensity in only one of both readings) which were considered as positive. Fifty patients had atrophy and all them fulfilled the gold standard criteria: Sensitivity of $\gamma\delta$+IEL, TGd and TGs were 96% (CI, 85-99) in each case. Sixty-five patients had LD and 27 (41.5%) fulfilled the gold standard criteria: Sensitivity of $\gamma\delta$+IEL, TGd and TGs were 85% (CI, 65-95), 54% (CI, 34-73), and 30% (CI, 14.5-50), respectively. Concordance between TGd and TGs was excellent (K=0.82).
CONCLUSION: Celiac FCM IEL pattern is a reliable parameter to diagnose CD among patients with LD with higher sensitivity than both TGd and TGs. FCM seem also better than TGd assay since the latter is cumbersome and user-dependent and repeated analyses show only moderate reproducibility.
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Disclosure of Interest: None Declared
Keywords: coeliac disease, flow cytometry, Lymphocytic duodenosis, TCR Gammadelta intraepithelial lymphocytes, transglutaminase deposits

P543 A RAPID AND SENSITIVE METHOD TO DETECT HLA CLASS II ALLELES IN THE SALIVA ASSOCIATED WITH CELIAC DISEASE

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INTRODUCTION: The major predisposing genes in celiac disease (CD) are the HLA- DQ2 and DQ8 genotypes, found in at least 95% of patients. HLA typing is increasingly performed in CD-at-risk categories and in cases of uncertain CD diagnoses.
AIMS&METHODS: To evaluate a new rapid method for HLA typing using saliva samples and oral swabs. Patients and Methods: Sixty-five newly diagnosed CD patients (28M, 37F), mean age (+SD) 15.4 + 8.1 years were included. All patients showed serum positive IgA anti-transglutaminase antibodies and intestinal villi atrophy. The determination of CD-related HLA genotypes was performed using: a) a drop of whole blood taken by a lancet device and absorbed on filter paper, b) in 0.5ml of saliva and c) on an oral swab. Samples were stored at -20°C, and then sent to the Biodiagene laboratory within one month. A DQ-CD Typing Plus kit (Biodiagene, Palermo, Italy) was used for the identification of HLA class II alleles DQA1*0201, *03, *05, DQB1*02, *0301/04, *0302, DRB1*03, *04, *07, *11, *12 and DQB1*02 homozygosis. This kit allows rapid DNA extraction from dried blood absorbed onto filter paper and we developed a modified method using oral swab or saliva.
RESULTS: In whole blood absorbed on filter paper we found that 50 patients carried the alleles codifying for the DQ2 genotype, 9 patients carried both the DQ2 and the DQ8 genotypes and 6 patients carried the DQ8 genotype. In the saliva samples we found a concordance with the results obtained on blood in all 65 samples (100%), while no results were obtained in two samples. Using the oral swabs we observed concordant results with the assays performed on whole blood in 39 of 65 samples (60%), while no results were obtained in 26 samples.
CONCLUSION: These preliminary data showed that HLA typing for DQ2 and DQ8 genotypes can be performed with excellent efficiency using saliva samples but not with oral swabs. The rapid method used in this study allowed HLA typing, while saving time and avoiding the more invasive taking of blood samples.
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Disclosure of Interest: None Declared
Keywords: celiac disease, HLA, saliva

P544 IMPACT OF HLA TYPE II ON CLINICAL EXPRESSION OF CELIAC DISEASE

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INTRODUCTION: Celiac disease occurs in genetically predisposed people having HLA-DQ2 and /or HLA-DQ8 genotyping in 90-95% and 5-10% of cases, respectively. It has been suggested that patients with two copies of HLA-DQ2 are more at risk of developing celiac disease than patients having only one copy. It remains unknown whether the type and number of copy of HLA- DQ2/DQ8 modify expression of celiac disease.
AIMS&METHODS: Aim: to assess impact of HLA of type II on clinical, biological and histological features of celiac disease (CD).
Patients and Methods: Analysis of computer database of European Georges Pompidou Hospital in Paris listed 655 patients with possible diagnosis of CD registered between 2000 and 2012. Up to date we analyzed retrospectively 376 medical files (57% of the series) ascertaining diagnosis of CD in 297 patients. HLA of type II genotyping had been performed 222 (75%) of these patients who were considered for statistical analysis.
RESULTS: Among the 222 patients (158 F, 64M, mean age at diagnosis of CD: 28 years), 211 (95%) and 28 (13%) patients had HLA-DQ2 and HLA-DQ8 genotyping, respectively. Eighteen patients (8%) were homozygous for HLA-DQ2 (DQ2/DQ2) and 16 (7%) were DQ2/DQ8. Frequency of patients with anaemia and low serum albumin levels at diagnosis did not significantly differ between HLA-DQ2 and HLA-DQ8 patients. In contrast HLA-DQ2 patients had more frequently severe villous atrophy (subtotal or total) (72%) than HLA-DQ8 patients (42%) who had more frequently partial villous atrophy ($p = 0.001$). Frequency of associated autoimmune diseases at diagnosis (autoimmune thyroiditis, type I diabetes, autoimmune hepatitis...) was similar in patients HLA-DQ2 (23%) and HLA-DQ8 (18%) (N.S). In contrast, patients developing intestinal T cell lymphoproliferative disorder (refractory celiac diseases, high grade T cell lymphoma, large granular lymphocytic leukemia) were all HLA-DQ2 with higher rate of homozygosity DQ2 (22%) than uncomplicated celiac patients (8%) ($p = 0.05$).

CONCLUSION: This preliminary study performed on half of our series suggests that HLA type II genotyping impacts the degree of villous atrophy of celiac disease with less severe villous atrophy in patients with HLA-DQ8. In contrast with frequency of autoimmune diseases not impacted by the number of copy DQ2, lymphomatous complications appear more frequently in celiac patients homozygous for HLA-DQ2.
Disclosure of Interest: None Declared
Keywords: celiac disease, HLA-DQ2/DQ8

P545 COMBINED CLINICAL, SEROLOGICAL AND DIET ADHERENCE ASSESSMENT WITH HISTOLOGICAL EVALUATION AFTER 1 YEAR OF GLUTEN-FREE DIET: AN INNOVATIVE FOLLOW-UP APPROACH IN CELIAC PATIENTS.

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INTRODUCTION: Adherence to a gluten-free diet (GFD) is the only effective treatment for celiac disease (CD). It has been recommended that patients be followed up by regular visits and serological markers of CD, although a follow-up procedure has not been standardized.
AIMS&METHODS: This study aimed to evaluate the usefulness of a combined clinical, serological and diet adherence assessment together with histological evaluation of duodenal mucosa after one year of GFD. Between 2009 and 2012 we enrolled 61 consecutive adult patients (70% F; median age 37 yrs, range 17-70) with biopsy-proven atrophic CD. Patients were reevaluated after 12-15 months of GFD with duodenal histology, serology (Ab IgA to anti-tissue transglutaminase and to anti-endomysium) and a dietary interview based on a validated structured questionnaire considering as strict or no adherence to GFD a score of 3-4 or 0-2, respectively (Biagi et al., Br J Nutr 2009). Clinical status was assessed considering well-being a complete resolution of the sign/symptom that brought to diagnosis and improvement a partial resolution of their signs/symptoms. Histology was scored following Marsh classification.
RESULTS: At 1 yr-follow-up, strict adherence to GFD was found in 49 (80%) patients (F 71,5%) (Group 1), while no adherence to GFD in 12 (20%) patients (F 67%) (Group 2). The two groups were similar with regard to age, gender, sign/symptom of diagnosis, comorbidity, positivity to antibodies and Marsh score at diagnosis time. At 1-yr follow-up, 35 Group 1 patients had normal duodenal histology compared to none in Group 2 ($p < 0.0001$), and 42 Group 1 pts yielded clinical well-being compared to 2 Group 2 pts ($p < 0.0005$), but the proportion of pts with positive serology was similar in the two groups (10 in Group 1 (20,5%) pts vs 3 in Group 2 (25%) pts; p=0.682). Positive serology was found in 7 (20%) of the 35 pts with normal duodenal histology after 1 year of strict adherence to GFD.
CONCLUSION: After 1 year of strict adherence to GFD, evaluated by a validated dietary questionnaire, the majority of celiac patients (72%) shows a total histological recovery from duodenal damage. The clinical status keeps in step with histological recovery, but serology seems to be a poor predictor for strict adherence to GFD. In patients with strict adherence to GFD the histological evaluation of duodenal biopsies seems to be a valid approach to assess the efficacy of GFD.
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Disclosure of Interest: None Declared
Keywords: celiac disease, gluten free diet, histological follow-up

P546 MORPHOLOGICAL FEATURES OF ENDOTHELIAL CELLS OF ENDOMETRIUM BEFORE AND AFTER INCUBATION WITH ANTI-TRANSGLUTAMINASE ANTIBODIES IN BOTH HEALTHY AND CELIAC WOMEN

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INTRODUCTION: Celiac disease is a well-known cause of recurrent miscarriage. Previous studies have evaluated the effect of the tissue transglutaminase antibody (tTGA) on the differentiation of endometrial endothelium (that plays a main role in the development of the fetus), in terms of angiogenesis, cytoskeleton structure, fluidity and strength of membranes.
AIMS&METHODS: Aim of the study is to investigate if the tTGA may induce damage of endothelial cells in both healthy and celiac women.
The endometrial tissue obtained from 5 healthy fertile women and 2 celiac ones was incubated in a M199 culture medium. The cell suspension was centrifuged and the cells placed in a endothelium-specific medium, then detached and subjected to magnetic immunoselection and plated on glass slides with Matrigel; finally, it was incubated with tTGA and held in fixative solution. After post-fixation and a further fixation in a mixture of acetone and EPON, it was cut into section of about 0.5 uM, for the study on the optical microscope (confocal microscope, also with fluorescence and phase contrast) and, respectively, of 70 ηm for the study to the transmission electron microscope (TEM). Five parameters have been evaluated: connection among cells, plasmatic membrane, nuclei, cytoplasm, pseudopods.
RESULTS: Results are summarized in the table below.

	HEALTHY WOMEN		CELIAC WOMEN	
	BASELINE	*tTGA INCUBATION*	*BASELINE*	*tTGA INCUBATION*
CONNECTION AMONG CELLS	Present	Reduced	Present	Almost disappeared
PLASMATIC MEMBRANE	Well defined	Reduction of protofilaments. Presence of collagenous structures	Not well defined	Only collagenous structures
NUCLEI	Compact	Widely fragmented	Less defined, with multiple breaks	Not defined, higher number of breaks
CYTOPLASM	Abundance of rybosomes	Leakage of rybosomes	Decreased No of rybosomes	Rybosomes almost absent
PSEUDOPODS	Present. Branching structures	Shortened	Reduced in No, lenght, elasticity	Not displayed (isolated cells)

CONCLUSION: In healthy women endothelial cells of endometrium show, at incubation with tTGA, morphological damages that may play a role in modifying motility and cell adhesion. In celiac women, even at baseline, there are alterations of both nuclear and cytoplasmatic structures. At incubation with tTGA, these differences become deeper, with disappearance of pseudopodes, that lead to cell isolation. These modifications may lead to angiogenesis abnormalities that could bring to recurrent episodes of miscarriage.
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Keywords: celiac disease, electron microscope, endothelial cells, recurrent miscarriage, transglutaminase antibodies

P547 THE DIAGNOSTIC UTILITY OF COELIAC SEROLOGY IN LYMPHOCYTIC DUODENOSIS

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INTRODUCTION: Lymphocytic duodenosis (LD) is defined by normal villous architecture and intraepithelial lymphocytes (IELs) >25 per 100 enterocytes. Such patients should not be diagnosed with coeliac disease (CD), solely by histology, as recent studies have suggested other associations with LD. Coeliac serology (tissue transglutaminase [TTG] and/or endomysial antibodies [EMA]) may play a useful role although their diagnostic value in such settings is unknown.
AIMS&METHODS: We aimed to provide diagnostic outcomes in our cohort of LD patients whilst also assessing the clinical utility of coeliac serology.
Two hundred patients with LD were rigorously investigated for CD and other known associations of LD, by means of revisiting the patient's history and recent investigations including the initial coeliac serology, followed by a combination of gluten challenge, HLA typing, repeat duodenal biopsies, and exclusion of infection/inflammatory bowel disease.
In the absence of an alternative cause, a diagnosis of CD was based on the persistence or progression of LD on a gluten-containing diet, the presence of HLA DQ2 or DQ8, and a clinical response to a gluten free diet.
RESULTS: 150 female, 50 male, mean age 49, SD 16, age range 17-83
An identifiable association was found in 70% of patients: CD (20%), NSAIDs (17%) and *H.pylori* (16%) accounting for the majority. In 30% no cause was found, although reassuringly 2/3rd normalised their histology. The role of coeliac serology in LD for diagnosing CD is shown in table 1.
Table 1: Evaluation of coeliac serology for diagnosing CD

LD coeliac serology test result (n 200)	PPV	NPV	Sensitivity	Specificity
If only TTG performed	54%	92%	70%	85%
If only EMA performed	95%	89%	50%	99%
Both TTG and EMA normal	6%	44%	20%	16%
TTG raised but EMA normal	33%	83%	30%	85%
TTG normal but EMA positive	80%	82%	10%	99%
Both TTG and EMA raised	100%	87%	40%	100%

CONCLUSION: As a single test, EMA has a greater diagnostic accuracy than TTG when assessing patients with LD.
As a combination test, only the presence of both a positive EMA and a raised TTG has a 100% predictive value for CD.

Therefore, although coeliac serology is useful in LD, most cases still require further work-up for diagnostic confirmation.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, Coeliac serology, Lymphocytic duodenosis

MONDAY, OCTOBER 14, 2013 9:00–17:00
NUTRITION I – Poster Area

P548 WHITE MULBERRY SUPPLEMENTATION AS ADJUVANT TREATMENT OF OBESITY.

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INTRODUCTION: Body weight is partially controlled by our genes, and managed by a neuro-hormonal system, in particular by insulin and glucagon. The extract of Japanese white mulberry is known to inhibit the alpha-glucosidase and then the intestinal hydrolysis of polysaccharides, thereby reducing the glycemic index of carbohydrates.
AIMS&METHODS: Our aim was to evaluate the slimming effect of the extract of white Japanese mulberry as an adjuvant of the dietary treatment of obese or overweight subjects.
In this randomised, placebo-controlled trial, 46 overweight patients (F:M/40:6 – range 35-55 yo) were enrolled and divided into two subgroups (A and B). Both subgroups were given an identical balanced diet of 1300 kcal. Group A received 2400 mg of white Japanese mulberry extract (800 mg three times at day) for 3 months; group B received instead an identical dose of placebo. Each subgroup had a follow-up visit every 30 days until day 90 of treatment. During every follow-up visit, body weight and waist circumference in all the subjects and, only in women, thigh circumference, were measured. The following blood tests were performed during each follow-up visit: blood glucose curve and insulin glucose load, complete blood count, blood urea nitrogen, creatinine and electrolytes.
RESULTS: In group A, weight loss was about 9 kg in three months, equal to approximately 10% of the initial weight. Plasma insulin and glucose curves in group A at the end of the trial were significantly lower than baseline. In the 20 women of group B, treated with only low-calorie diet and placebo, weight reduction was globally of 3.2 kg, approximately equal to 3% of the initial weight; moreover, the blood glucose curves and the insulin curves showed a slight decline compared to baseline, but not so significantly as group A. Waist circumference and thigh circumference (in women) decreased in all participants, obviously more evidently in subjects who had a deeper weight loss.
CONCLUSION: The extract of white Japanese mulberry may represent a reliable adjuvant therapy of the dietary treatment for obesity and overweight. Further studies, with an adequate sample size, are needed to confirm this results.
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Keywords: dietary intervention, insulin, Nutrition, obesity

P549 ONE YEAR WEIGHT LOSS OUTCOMES USING INCISIONLESS ENDOSCOPIC SURGERY FOR PRIMARY OBESITY: THE POSE PROCEDURE

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INTRODUCTION: Background: Obesity is a multifaceted, metabolic condition in which excess body fat has accumulated to the extent that it has an adverse effect on health. Bariatric surgical procedures provide the most consistent and long-lasting weight lossoutcomes. However, risks associated with bariatric surgerygive rise to the need for less invasive and safer alternatives. The POSE procedure (Primary, Obesity, Surgery,Endolumenal) utilizes the Incisionless Operating Platform (IOP) to durably plicate gastric tissue endoscopically.
AIMS&METHODS: Objective: The purpose of this analysis was to quantify weight loss, body mass index (BMI) and the incidence of complications up to one year after the POSE procedure forthe treatment of primary obesity.
Methods: A descriptive analysis was conducted based on all patients having received a POSE procedure during the time period of July 11, 2011 to January 23, 2013 at a single center,private hospital in Madrid, Spain. Weight loss results were summarized and presented as mean averages for weight loss, % excess weight loss, and % total body weight loss.
RESULTS: Results: A total of 147 patients were included in this analysis: 69% female and 31% male with a mean age of 45. At baseline: mean weight (kg) 106.8, SD 18.2; body mass index (BMI, kg/m2kg) 38.2 (28.1-50.2). Three-month mean weight was 95.6, SD 15.9, Twelve-month mean weight was 92, SD 16.38; BMI decreased to 33.3 (22.4-44.4); EWL was 42.7%; TBWL, 14.6%. Adherence to follow patients was 100% at 3 months, 91% at 6 months and 79% at 12 months. All operations were performed by the same endoscopist. Each patient and procedure is unique unto itself, but on average, the POSE procedure took about 35 minutes from the time the transport is inserted until the time removed. On average, 7 - 8 suture anchors were placed in the fundus of the stomach and 3-4 suture anchors were placed in the distal body. Oropharyngeal pain and dyspepsia was observed in 80% of patients only on the first day postoperatively. Mortality rate was 0%. Patients reported less hunger and earlier satiety post procedure.
CONCLUSION: Conclusions: At 12-month follow-up, the POSE procedure has demonstrated that it is a safe and effective weight loss treatment option without the recovery issues associated with open and laparoscopic bariatric surgery.Overall, weight loss at one year post POSE procedure is promising and combined with a multi-disciplinary team approach may support long term improvement in patient health outcomes. Further research is needed to determine optimal patient profiles and ongoing support needed to assist patients in sustaining lifelong health.
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Disclosure of Interest: None Declared
Keywords: Endoscopy in obesity, Obesity, Pose procedure, weight loss

P550 RISKS OF COLORECTAL ADENOMA AND LIFE TIME ANTHROPOMETRY. A PROSPECTIVE STUDY IN GREECE.

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INTRODUCTION: Obesity has been recognized as a risk factor for colorectal adenoma, but the influence of weight changes, adipose tissue distribution, and possible differences between genders remains unanswered, as the results of previous studies show considerable heterogeneity due possibly to ethnic/ racial differences and probably aren't reproducible in Greece.
AIMS&METHODS: To assess the association between adiposity and weight changes from early adulthood and colorectal adenoma risk, in a well predefine population in Sparta area in Greece. Prospective, single centre study, three years duration. Colonoscopies were conducted on 700 patients regardless of symptoms, whose mean age at colonoscopy was 62 +/- 7, 8 years, 45% men. During colonoscopy the number, size and location of each polyp were recorded. A detailed history was obtained from each subject, using clothing size to assess early adulthood body weight at age 20, at age 30, and weight change over the 5 and/or 10-year period before colonoscopy. Multivariate logistic regression analyses were used to assess the association between change in body weight at various age intervals and adenomas of any size, including advanced neoplasm (adenomas >10mm or any adenoma with villous histology, high-grade dysplasia).
RESULTS: Obesity, measured at the time of colonoscopy, was positively associated with risk of colorectal adenomas (OR 2.06; 95% CI, 1.13-3.14), was stronger in women (OR 1, 95; 95% CI, 1.23- 3, 17) than in men (OR 1. 56; 95% CI, 0.52-3.07). The prevalence of adenomas was 11% in individuals whose BMI was normal at age 20 and remained normal at present, 19% and 30% in those who became overweight/obese at present, 25% in those who they were stable overweight and 31% in those who have been consistently obese. The risk of adenomas increased among participants who gained weight compared with those who maintained weight over the previous 5 years (OR 1, 75; 95% CI, 1.25-3.22) and 10 years (OR 2.12; 95% CI, 1.25-3.62). These associations were similar for both advanced and nonadvanced adenomas.
CONCLUSION: In our area these results suggest a positive association between colorectal adenoma risk and actual obesity, recent and from early adulthood weight gaining. Given the endemic of childhood obesity in our country further evaluation of adiposity as a modifiable risk factor against colon cancer are warranted.
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Disclosure of Interest: None Declared
Keywords: colorectal adenoma, Obesity

P551 ANALYSIS OF 1050 PATIENTS SUBMITTED TO ENDOSCOPIC TREATMENT OF EXCESS WEIGHT WITH AN INTRAGASTRIC BALLOON

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INTRODUCTION: Endoscopic methods, especially the intragastric balloon (IGB), have been shown to be effective for the treatment of excess weight.
AIMS&METHODS: AIMS: To assess the efficacy and complications of excess weight treatment with an IGB in patients seen at the Endogastro Med Service clinic. METHODS: A total of 1050 patients were analyzed. An Allergan IGB (BIB®) with a volume of 600 to 700 ml was used. The patients had a minimum initial body mass index (BMI) of 27 kg/m2 and were followed up by a multidisciplinary team consisting of a nutritionist, a doctor and a psychologist.

For statistical analysis, the patients were divided into groups according to sex and degree of excess weight (overweight and grade I, II and III obesity). Data were analyzed using descriptive statistical methods, the Student t-test, Spearman correlation, and analysis of variance followed by the Tukey post-test. The level of significance was set at $p<0.05$.
RESULTS: 75 patients were excluded from the analysis: 45 (4,28%) due to early IGB removal, 9 (0.85%) due to absence of weight loss, 10 (0.95%) due to weight gain, 10 (0,95%) due to incomplete data and 01 due to pregnancy (0,09%). The incidence of fungus was 0.38% (n=4) and the incidence of leakage was 0.47% (n=5). Of the 975 remaining patients, 764 were women and 211 were men. Mean age was 38.09 years. The patients showed a significant weight loss, with a significantly lower final BMI (mean: 29.78±4.86 kg/m2; range: 19.14-57.39) than the initial BMI (mean: 36.72±5.36 kg/m2; range: 26.77-69.29) ($p<0.0001$). Mean BMI reduction was 6.95±2.99 kg/m2 (range: 0.36-20.52). Mean percent weight loss was 18.83±7.20% and mean percent excess weight loss was 67.55±36.81% (range: 3,86-336,14). Regarding percent initial weight loss there was a higher reduction in patients with grade III obesity than patients with overweight and grade I obesity ($p<0,05$) and there was a higher BMI reduction in men then in women (p=0.0147). There was a positive correlation between the numbers of visits to a nutritionist and a greater loss of initial weight (p=0.0001).
CONCLUSION: Endoscopic treatment of excess weight with an IGB has been established as an excellent therapeutic option for patients of both genders with overweight or different degrees of obesity.
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Disclosure of Interest: None Declared
Keywords: bariatric endoscopy, intragastric balloon, obesity treatment

P552 PRIMARY OBESITY SURGERY ENDOLUMENAL (POSE): WEIGHT, SATIATION, AND METABOLIC CHANGES IN A PROSPECTIVE COHORT OF OBESE PATIENTS.

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INTRODUCTION: The Incisionless Operating Platform™ (USGI Medical, San Clemente, CA, USA) utilizes the g-Cath EZ ™ suture anchor, which has demonstrated the ability to durably plicate gastric tissue endoscopically at 2+ years. Prior work at our institution for primary obesity revealed mean total % excess weight loss (%EWL) of 60.6% at 1 year (N=21).This study evaluates possible mechanisms of weight loss and predictors for success.
AIMS&METHODS: A prospective, single site study was initiated with Ethics approval. Enrolled patients were aged 21-60 with a BMI of ≥ 30 and ≤ 40 and no history of bariatric procedure. Diet was advanced post procedure to full solids over 4-6 weeks to allow time for suture plication healing. Serial nuclear gastric images over 3 hours (solid meal) were done pre-procedure and at 2/6 months. Serial peptide levels were recorded over 2 hours both pre-procedure and at 2/6 months in response to a standard solid meal. 6 month peptides pending. A validated intake capacity test (kcals) was done before and at 2/6 months. Weights were recorded regularly through 12 months. Regression modeling assessed variables that influenced % EWL (BMI25 method). Models were selected based on higher R^2 with lowest degrees of freedom. Data reported in means (95% CI).
RESULTS: 18 patients were enrolled (78%F/22%M). Mean age =39.1. Baseline mean body mass index (BMI) = 36.3±2.3. A total mean 13.6 plications were placed in the fundus and gastric body. Mean operative time, 51±9.0 minutes. No significant operative or post-op adverse events. Mean 6, 9 & 12 month %EWL to date was 56.6±27 (N=18), 60.5±29 (n=17) and 69.9±22 (n=11) respectively. Mean time to satiation decreased significantly from baseline at both 2&6M post-POSE ($p<0,001$), as did mean kcal intake at 2&6 months [from 901Kcal to 473 and 574 respectively ($p<0,001$)]. Gastric retention rate at 30 minutes increased significantly post-POSE at 2 months ($p<0,03$) but was not significant at 6 months. Glucose/Insulin ratio improved 2&6M post-POSE (all $p<0,05$). Postprandial ↓ in Ghrelin was enhanced post-POSE compared to pre-POSE (-21 [-2; -40] vs. -59 [-22; -95]; p=0.03) as well as postprandial ← in PYY (6 [0; 13] vs. 14 [7; 20]; p=0.001). Regression-modeling showed that gender ($p<0,01$), weight (p=0,03) and pre-POSE GE ($p<0,01$) were independent predictors of %EWL at 6M (R^2 :54%).
CONCLUSION: POSE is followed by significant weight loss, improved glucose-homeostasis and satiation-peptide responses. Weight loss post-POSE might be enhanced selecting subjects with slower pre-POSE gastric emptying. Further study is required.
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Keywords: gastric emptying, ghrelin, obesity treatment , Peptide YY, satiety

P553 GIP- AGONIST IMPROVES OBESITY-INDUCED FAT INFLAMMATION

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INTRODUCTION: Obesity gives rise to low-grade chronic inflammation, manifested by pro-inflammatory polarization of adipose tissue innate and adaptive resident and recruited immune cells that contribute to development of insulin resistance (IR). The glucose-dependent insulinotropic polypeptide (GIP) incretin hormone is responsible for mediating 50-70% of the postprandial insulin secretion. The recent past has seen differences of opinion concerning GIP having a deleterious or beneficial role in IR
AIMS&METHODS: Here, we aimed to decipher the metabolic and immunoregulatory role of GIP in diet- induced obesity (DIO) using the long-acting GIP analogue [d-Ala^2]GIP.
RESULTS: Treatment with [d-Ala^2]GIP improved insulin sensitivity. Treated mice had increased levels of adipose tissue lipid droplet proteins, indicating better lipid storage capacity. Moreover, [d-Ala^2]GIP- treated mice exhibited reduced numbers of circulating neutrophils and pro-inflammatory $Ly6C^{hi}$ monocytes and their $Ly6C^{hi}$ macrophage descendents within the adipose tissue. Importantly, [d-Ala2]GIP treatment significantly reduced adipose tissue $Ly6C^{lo}CD11c^{+}$ $F4/80^{hi}$ macrophage population, reported to be associated with IR. Furthermore, infiltration of IFNγ - producing $CD8^{+}$ and $CD4^{+}$ T cells was strongly attenuated. Lastly, [d-Ala2]GIP treatment induced a favorable adipokine profile, with prominent reduction in TNFα and inflammatory chemokines and enhanced adiponectin expression.
CONCLUSION: Our results show that augmentation of GIP improves DIO insulin sensitivity and ameliorates adipose tissue inflammation
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Disclosure of Interest: None Declared
Keywords: adiopse tissue , glucose-dependent insulinotropic polypeptide , Insulin resisrance

P554 MULTIPROBIOTIC THERAPY PREVENTS THE DEVELOPMENT OF EXPERIMENTAL OBESITY

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INTRODUCTION: World Health Organization (WHO) declared obesity a global epidemic and took him under its control. WHO experts predict that the number of those suffering from this disease will reach 300 millionby 2025. Therefore, the search of new non-toxic drugs for preventing the development of obesity is the most important challenge of modern science. The question about impact of probiotics on fat metabolism and obesity is being actively debated in the scientific literature. One of the indicators of metabolic syndrome is the adiponectin concentration decrease in the blood. In connection with mentioned above the aim of the study was to investigate the effect of multiprobiotic "Symbiter acidophilic concentrated" on adiponectin level in the rats serum under experimental obesity.
AIMS&METHODS: The study was carried out on 36white rats, that were divided into 6 groups (I-III – males, IV-VI – females). I and IV groups were intact control (4-month old rats). Newborn rats of groups II and III subcutaneously in volume 8 µl/g were administered a placebo (saline) or monosodium glutamate (MSG) (4 mg/g) at 2, 4, 6, 8, 10 days of life. Since the age of 1 month, rats of III and V group had been injected with water in a volume of 0.25 ml/100 g (placebo), rats III and VI groups-multiprobiotic "Symbiter acidophilic concentrated" in a dose of 140 mg/kg dissolved in water of a volume 0.25 ml/100 g. Introduction had been performed with two-week course for 3 months. After 4 months in the blood serum of all groups adiponectin level was measured with ELISA.
RESULTS: In male rats, there were more pronounced changes - body weight and visceral fat exceeded benchmarks in 3 ($p\leq0.001$) and 5 ($p\leq0.001$) times, respectively. Body weight and visceral fat of female rats in group III was higher by 125% ($p\leq0.001$) and 338% ($p\leq0.001$), respectively. It was established that under condition of obesity caused by the introduction of MSG, the level of adiponectin in serum decreased in male rats by 59% ($p\leq0,05$) and 23% ($p\leq0,05$) in females compared with intact rats. The use of probiotic therapy led to recovery of adiponectin level: its concentration in serum grew in 1.9 times ($p\leq0,05$) in males and in 1.4 times ($p \leq 0,05$) in females which were treated with multiprobiotic compared with rats injected with placebo.
CONCLUSION: Thus, the introduction of multiprobiotic increased adiponectin levels in animals injected with MSG, that shows the effectiveness of probiotic therapy for the prevention of obesity.
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Disclosure of Interest: None Declared
Keywords: monosodium glutamate , multiprobiotic , obesity

P555 UK HPN DATA SUGGEST A CONTINUED RISE IN PAEDIATRIC HPN USE: A REPORT ON BEHALF OF THE BSPGHAN/BAPS BRITISH INTESTINAL FAILURE SURVEY WORKING GROUP

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INTRODUCTION: Paediatric HPN (PHPN) usage has risen within the UK in the last 2 decades (1). Studies reporting improved outcomes for patients with intestinal failure due to advancing surgical technique and novel medical therapies would suggest short term increases in the requirements for PHPN. Due to the large requirement for health resources for such patients, accurate PHPN epidemiology is vital for service planning. The British Society for Paediatric Gastroenterology Hepatology and Nutrition (BSPGHAN) and British Association of Paediatric Surgeons (BAPS) collate UK PHPN data through the British Intestinal Failure survey (BIFS).
AIMS&METHODS: We aimed to perform a PHPN point prevalence survey and compare this with previously published data (1). The BIFS administrator

contacted the 32 recognised PHPN UK centres for data relating to 26.11.2012. Anonymysed data were collected on patients ≤16yr receiving HPN (or being trained for imminent discharge) including demographics, diagnosis and duration of PN. Publicly available population statistics were used to account for missing data and to provide point prevalence figures.

RESULTS:

Year	Centres	Patients	Calculated point prev/million	SBS (%)	Enterocyte (%)	Neuro (%)	Other (%)
1993	21	46	4.4	18 (27)	12 (18)	12 (18)	24 (37)
2010	25	145	13.7	-	-	-	-
2012	25	172	15.9	84 (46)	40 (23)	36 (20)	12 (6)

25/32 PHPN responded corresponding to approximately 92% of the UK population under 16yrs (10.9 million). There was a 19.3% rise in PHPN patients from 145 in 2010 to 172 in 2012. This represents an increase in point prevalence of 13.9/million in 2010 to 15.9/million in 2012 and a signicant rise from the 1993 figure previously reported (1). The relative proportion of patients with short bowel syndrome (SBS) rose from 27% in 1993 to 46% in 2012.

CONCLUSION: BIFS data suggest that UK PHPN point prevalence has risen significantly in the short term, in-line with inidividual centres reporting improved early survivial in intestinal failure. Increased survival from neonatal surgical procedures also appear to be reflected by increased numbers and proportions of SBS patients. The limitations of point prevalence surveys in terms of service planning have been previously highlighted (2). Improvements in the ascertainment of the prospective arm of BIFS are warranted to gather accurate incidence, period prevalence and outcomes for UK PHPN.

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Disclosure of Interest: None Declared

Keywords: epidemiology, intestinal failure , parenteral nutrition

P556 LAPAROSCOPIC GASTROSTOMY IS SAFER THAN PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN CHILDREN: RESULTS OF A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: A gastrostomy is frequently performed in children who require long-term enteral feeding. Nowadays gastrostomy placement is a minimally invasive procedure via either percutaneous endoscopic gastrostomy (PEG) or laparoscopic assisted gastrostomy (LAG). Both procedures are widely used in pediatric patients. However, no consensus exists on which type of approach is best practice in these patients.

AIMS&METHODS: The aim of this study was to determine if PEG or LAG is the most effective and safe procedure in pediatric patients requiring a gastrostomy. A systematic review and meta-analysis was performed according to the guidelines in the PRISMA-statement. PubMed, EMBASE, and the Cochrane Library were searched to identify eligible articles. Results were pooled in meta-analyses and expressed as risk ratios (RR).

RESULTS: Our extensive literature search provided 2,342 articles. After title, abstract and full-text screening five original studies comparing PEG to LAG placement in children were identified. All studies had retrospective study designs. The completion rate (PEG 98% *vs*. LAG 100%) and time to full-enteral feeds (PEG 0.7 *vs*. LAG 0.8 days) of both procedures were similar. No studies reported data comparing the efficacy of feeding via the gastrostomy or its effect on developing gastroesophageal reflux (GER). Intraperitoneal leakage (RR 0.28; p=0.36; and after tube exchange RR 3.14; p=0.28) was as frequently encountered after both PEG and LAG. However, PEG was associated with significantly more adjacent bowel injuries (RR=5.55; p=0.05) and early tube dislodgements (RR=7.44; p=0.02). Moreover, overall rate of all reinterventions that require general anesthesia (RR=2.79; p=0.0008) was significantly higher after PEG. The risk of developing minor complications was similar after both procedures.

CONCLUSION: This systematic review and meta-analysis demonstrates that PEG and LAG are equally effective; however, LAG was associated with significantly less complications such as adjacent bowel injury, early tube dislodgements and a lower rate of all reinterventions that require general anesthesia. Therefore, we conclude that LAG is the safest approach and should be the first choice in children requiring gastrostomy placement.

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Disclosure of Interest: None Declared

Keywords: Gastrostomy, laparoscopic gastrostomy, Meta-analysis, PEG

P557 STOOL SECRETORY IGA LEVELS IN PRETERM INFANTS WITH AND WITHOUT NECROTISING ENTEROCOLITIS

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INTRODUCTION: Secretory Immunoglobulin A (SIgA) is the most prolific immunoglobulin of the GI tract, and high levels in preterm infants may prevent necrotising enterocolitis, the most devastating disease of the gut of early life. Our aim was to determine and compare the levels of SIgA in stool samples of preterm neonates and breast milk in their mothers.

AIMS&METHODS: We sequentially recruited infants <32 weeks gestation and <1.5Kg birth weight within week 1. NEC was staged according to Bell's Criteria. SIgA titres of 34 preterm neonates and 9 mothers were determined from 100 mg of stool and 100 µl of milk collected weekly for the first month using an enzyme linked immunosorbant assay.

RESULTS: Among all preterm infants (n=34), stool sIgA concentration were significantly higher in week 3 (p=0.020) and week 4 (p=0.027) than week 1. There were no significant differences in stool sIgA concentration between infants with NEC and those who did not ($p > 0.05$) within all the four weeks. A significant increase in mean stool sIgA concentration appeared from week 2 to week 3 (p=0.0485) in NEC infants and from week 1 to week 2 (p=0.005) for those without NEC. For all breastfed preterm neonates (n=6) in the first four weeks, the level of milk sIgA was significant higher on week 1 (colostrum) than week 2 (p=0.021) and week 3 (p=0.034).

CONCLUSION: Our study illustrates immunological adaptation of maternal milk sIgA level for the preterm newborn and that exclusive breast milk feeding may increase stool sIgA more than mixed breast milk and formula. Levels found in stool and milk are significantly higher than for infants and mothers at term.

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Disclosure of Interest: None Declared

Keywords: necrotising enterocolitis, Preterm, Secretory Ig A

P558 TRANSIENT TEMPERATURE GEL ELECTROPHORESIS OF STOOL SAMPLES OF PRETERM INFANTS WITH AND WITHOUT NECROTISING ENTEROCOLITIS IN A MULTICENTRE OBSERVATIONAL STUDY

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INTRODUCTION: Despite the effect of enteral feeding on the development of intestinal microbiota in preterm infants remaining poorly understood, trials aiming to prevent necrotising enterocolitis (NEC) using probiotics are well-established. Exclusively breast milk fed preterm infants have a reduced risk of developing NEC and this may be linked with a more 'beneficial' gut microbiota.

AIMS&METHODS: We sequentially recruited infants <32 weeks and <1.5Kg birth weight. Non-meconium faecal samples from the first and fourth weeks of life in 22 VLBW preterm neonates, 12 with NEC, were analysed by PCR-TTGE using universal bacterial primers. Species richness and similarities were compared between infants according to feed type.

RESULTS: There was large variability between number (1-17) and species diversity (25-36 different species). Number of predominant bacterial species did not increase between the 1st and 4th week of life. Bacterial composition varied largely between the 2 sample points, No difference in species richness or similarity within the 2 feeding groups was observed. 4 bands were identified in >50% of infants. Intra-individual similarity varied greatly and ranged from a similarity index (Cs) of 0% to 66.8%. There was no statistical difference between the similarity indices of the feeding groups (p=0.8852) or between those with and without NEC (p=0.1719).

CONCLUSION: Microbial community of preterm neonates undergoes several changes during their first month of life. The feeding mode did not seem to have a major impact on the development of bacterial diversity, but data was insufficient to comment on significant differences with regard to NEC.

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Disclosure of Interest: None Declared

Keywords: gel electrophoresis, necrotising enterocolitis, Preterm

P559 NEW TRENDS IN NUTRITIONAL STATUS ASSESSMENT IN A GROUP OF CHILDREN WITH CANCER FROM ROMANIA

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INTRODUCTION: Nutritional status is an important considerant in the treatment of pediatric cancer patients because it is linked to poor outcomes. There are still controversies regarding the criteria used to assess nutritional status in children with cancer.

AIMS&METHODS: We proposed to define the best modalities to assess nutritional status in children with cancer using anthropometric and biochemical parameters.A prospective study was performed on 64 children hospitalized and diagnosed with cancer in the Pediatric Clinic Targu-Mures, Romania, between 2009- 2012. We evaluated anthropometric and biochemical parameters: weight, height, body mass index (BMI), middle-upper arm circumference (MUAC), triceps skin fold thickness (TSF), total protein, albumin and Insulin-like growth factor-1 (IGF-1). The values of anthropometric parameters were converted in Standard Deviation (SD) for age and sex using Switzerland Growth Chart 1989.

RESULTS: Of the 64 children with cancer, 40,6% were diagnosed with leukemias, 28,1% with lymphomas and 31,2% with solid tumors. Medium valus of weight, height and BMI were -0.26 SD, -0.19 SD, and -0.36 SD. Assesssing arms anthropometry, we found lower values of MUAC (-0.56 SD) and TSF (-0.77 SD) than weight and height indicators. At the onset of malignant disease, 28.1% of patients had low serum protein values and 25% had low levels of serum albumin. IGF-1 was decreased in 65,6% of patients. We found a good correlation, statistically significant between MUAC and serum proteins (r=0.30; p=0.01), MUAC and albumins (r=0.27; p=0.02) and MUAC and IGF-1 (r=0.40; p=0.001) and

between TSF and albumins (r=0.28; p=0.02), TSF and IGF-1 (r=0.38 ; p=0.002).
CONCLUSION: The arms anthropometry better identify malnutrition in children with cancer than simply assessing weight or height measurements. MUAC and TSF in conjunction with serum protein, albumin and IGF-1 most accurately characterizing the nutritional status.
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Disclosure of Interest: None Declared
Keywords: cancer, children, nutritional status

P560 IL-6-572 G/C GENE POLYMORPHISM IN A ROMANIAN POPULATION OF OBESE AND MALNOURISHED CHILDREN

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INTRODUCTION: Genetic variation in the human IL-6-572 gene (G allele or C allele) has been associated with many heritable traits, including nutritional disorders, expecialy malnutrition and obesity. In malnutrition and obesity multiple anomalies occur including cytokine production, which increse the severity and frequency of infections
AIMS&METHODS: ***To*** study the clinical and genetic factors in children with obesity and malnutrition. IL-6-572 genotype is correlated with cashexia. We examined whether obese and malnourished subjects differ from IL-6-572 genotype distribution, and whether this genotypes polimorfism is correlated with the anthropometric parameters (upper arm anthropometry - skinfold thicknesses) or the degrees of body mass index (BMI) and biochemical characteristics.The study included three comparable age and sex groups of children: 120 malnourished children (39,5%), 83 children with obesity (27,3%) and 101 (33,2%) with normal body weight/ random controls. We assessed anthropometric indices, lipid profile. All children were genotyped for IL-6-572 G/C gene polymorphism which was determined by the polymerase chain reaction using specific primers.
RESULTS: The median age was 74,72 ± 59.68 months in malnutrition group and 117.2 ± 57.93 months in obese group. The distribution of IL-6-572 CC, CG and GG genotypes in malnourished patients were 4.16; 27.50 and 68.33%, respectively; the corresponding numbers for the obese group were 49.39; 50.60 and 0.00%, while for the control group were 7.92; 25.74 and 66.33% respectively. Comparing the obese group with control group we obtained a 11.25 higher risk for the allele C to develop obesity ($p = 0.001$) and 13.53 higher risk comparing the obese group with the malnourished group ($p = 0.001$). Although the age, the protein, cholesterol concentrations and anthropometric parameters differ between random control and obese and malnutrished children, IL-6-572 G/C genotype did not differ. Also we observed an association of alleles CC with obese children, comparing with malnourished children ($p = 0.0001$, 22.45 times higher risk), while the presence of allele G (CG/GG) is more frequent associated with malnutrition.
CONCLUSION: IL-6-572 G/C gene polymorphism is a significant factor for nutritional disorders and alleles CC is associated with obesity, while the presence of allele G is associated with malnutrition in children from central part of Romania. Further studies are warranted to investigate the genetics of fatness and failure to thrive phenotypes in romanian children.
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Disclosure of Interest: None Declared
Keywords: children, IL-6 572 G/C, malnurished, obese

P561 DIFFERENCES IN GLUTEN CONSUMPTION AT EARLY AGE AMONG INFANTS FROM DIFFERENT EUROPEAN COUNTRIES. THE PREVENT-CD COHORTS.

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INTRODUCTION: OBJECTIVES: To evaluate mean daily gluten intake (MDGI) in children DQ2/DQ8 positive with a 1st degree relative with CD recruited from 2007-2010 shortly after birth (EU-PreventCD project,www.preventcd.com)
AIMS&METHODS: Methods: A prospective evaluation of MDGI in 11-36 months old infants in the PreventCD cohorts from Spain (Valencia, Madrid, Reus), Italy, Germany and the Netherlands, was accomplished by specific previously developed food records (FR), adapted to local dietary habits. All of FR corresponds to a period of 7 days and these were completed at 11, 12, 14, 16, 18, 22, 24, 28, 30, 34 and 36 months of age. The MDGI was calculated by the accepted method of multiplying the grams of vegetable protein, derived from gluten-containing cereals according to the food product composition, by 0.80.
RESULTS: Results: 3423 FRs (2-3 per child) were evaluated. MDGI increased progressively from 12 months onwards in all centers, the highest MDGI being registered in the older age group (25-36months). MDGI (in grams) for Valencia, Madrid, Reus, The Netherlands,Germany and Italy are respectively: 2.95, 3.26, 2.09, 5.82, 4.09, 5.44 (11-12months); 4.35, 4.11, 4.75, 7.81, 6.54, 8.14(14-18 months); 4.80, 4.28, 4.77, 8.33, 7.21, 10.46 (20-24months) and 5.18, 4.14, 4.63, 8.91, 7.94, 12.15 (25-36months).
Differences in MDGI are statistically significant between Spanish children and those from Italy, The Netherlands and Germany ($p < 0.001$), for all age groups
Differences in MDGI between Italy and Germany is SS for all age groups; between Italy and The Netherlands, differences however is SS only in the group of 25-36 months of age
The highest MDGI is obtained for Italy at any age and at 25-36 m of age double MDGI from Spain
CONCLUSION: CONCLUSION: In 4 different European countries MDGI increases sharply in-between 12 and 18 months of age, but it remains quite constant thereafter, except for Italy. However, The Netherlands and Italy have overall the highest gluten consumption at any age. Further analysis including genetics and breast feeding as well as longer follow up of this cohort is mandatory to ascertain the true relevance of gluten intake at early ages in the natural history of CD in European children.
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Disclosure of Interest: None Declared
Keywords: European children, Gluten intake

P562 CHARACTERIZATION OF MUCOSA-ASSOCIATED AND FECAL MICROBIOTA OF CHILDREN WITH AUSTISM SPECTRUM DISORDER

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INTRODUCTION: It has often been suggested that there might be an intriguing relation between the gut microbiota and ASD (Autism Spectrum Disorder), and some authors have previously addressed the existence of a possible disbiosis in gut microbiota of autistic children. Our aim was to evaluate duodenal mucosa-associated and fecal microbiota of autistic children compared to age-matched controls.
AIMS&METHODS: 11 autistic patients and 8 controls underwent upper GI endoscopy and stool collection. All upper GI endoscopies were performed because of alarm symptoms (unexplained iron-deficiency anaemia; food impaction; weight loss; vomiting; chronic diarrhoea). Samples of total DNA were extracted both from duodenal biopsies' and stools. PCR with species-specific primers and ''Temperal Temperature Gel Elettrophoresis'' (TTGE) were employed to analyze the composition of dominant intestinal microbiota. In particular, the primers GCclamp-U968 (5'GCclamp-GAA CGC GAAGAACCT TAC) and L1401 (5'GCG TGT GTA CAA GAC CC) were used to amplify the V6 to V8 regions of bacterial 16S rRNA. TTGE profiles were then analyzed through PLS-DA (Partial Least Square Discriminant Analysis).
RESULTS: Preliminary results showed a significant (p=0.001) partition of fecal TTGE profiles from autistic patients and fecal TTGE profiles of control group. In addition, species specific PCR analysis disclosed the absence of Parabacteroides Distasonis among autistic children, while it was present in 75% of controls. No significant difference was disclosed as regard to mucosa-associated TTGE profiles.
CONCLUSION: The difference of TTGE profiles might be interpreted as a possible dysbiotic event in the intestinal microbiota in ASD; moreover, the lack among autistic patients of Parabacteroides Distasonis, previously described as a beneficial strain in the gut microbiota for its anti-inflammatory effects, warrants further investigations.
Disclosure of Interest: None Declared
Keywords: autism spectrum disorder, GI symptoms, gluten free diet, microbiota

TUESDAY, OCTOBER 15, 2013 9:00-17:00
POSTER PLUS VIDEO II - Poster Area

P563 NEW TECHNOLOGY THERAPY USING HIGH-INTENSITY FOCUSED ULTRASOUND (HIFU) FOR PANCREATIC CANCER

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INTRODUCTION: Recently, High-intensity focused ultrasound (HIFU) is most expected as new advanced therapy for pancreatic cancer (PC). HIFU therapy with chemotherapy is being promoted as new method to control local advance by cauterizing tumor and achieve relief of pain caused by PC.
AIMS&METHODS: We have evaluated the therapeutic effect and applicability of HIFU therapy in locally advanced and metastatic PC. We treated PC patients using HIFU therapy 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 (China Medical Technologies Co.LTD., China). The subjects were 54 PC patients, i.e. 35 cases in stage III, 19 cases in stage IV.

RESULTS: All tumors were visualized by HIFU monitor system. Treatment data in Stage III and IV were followed; mean tumor size was 34.4 vs 30.8 mm, mean treatment sessions: 3.0 vs 2.5 times, mean total treatment time: 2.6 vs 2.1 hours, mean total number of irradiation: 3024 vs 1838 shots, respectively. There was no significant difference in treatment data between two groups. The effects of HIFU therapy in Stage III and IV were the following; the rate of complete tumor ablation was 85.7 vs 63.2%, the rate of symptom relief effect was 65 vs 58%, the effectiveness of primary lesion was CR:0, PR:4, SD:29, PD:2 vs CR:0, PR:3, SD:14, PD:2, primary disease control rate (DCR) more than SD was 94.3% vs 89.5%. Comparison of mean survival time (MST) after diagnosis in Stage III and IV was 35.0 vs 15.2 months, respectively ($p<0.05$, $p=0.021$). MST after diagnosis in HIFU with chemotherapy and chemotherapy alone (38 patients in our hospital) was 29.3 vs 12.2 months, respectively ($p<0.001$). 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.
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Disclosure of Interest: None Declared
Keywords: High-Intensity Focused Ultrasound (HIFU), Pancreatic cancer

P564 ENDOSCOPIC SUBMUCOSAL DISSECTION BY USING A NOVEL VERSATILE KNIFE: AN ANIMAL FEASIBILITY STUDY

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INTRODUCTION: Endoscopic submucosal dissection (ESD) with a knife is technically difficult and requires special skills and a long time for the quality controlled procedure. To overcome these problems, ESD may require several different knives and frequent change of knives, depending on the location and shape of the tumor. For the purpose of reducing the procedure time and the number of accessory changing, we developed a novel versatile knife (Optimos® knife), which has combined advantages of several conventional knives (Performing several steps of ESD; marking, circumferential incision and cutting, dissection, vessel coagulation and water injection function).
AIMS&METHODS: The aim of this study was to introduce the Optimos knife and evaluate its efficacy and safety in ESD, compared to when using several conventional knives.
This was a prospective, animal case control trial comparing 2 different modalities (Optimos knife and combination of conventional knives) for the removal of target mucosal lesions. Two micro-pigs were to undergo 18 removals of the stomach mucosa, with target resected specimen size around 3 x 3cm squares. The ESD procedure was repeated by using the assigned ESD knife. Completion time of each resection was documented, and the resected specimen was retrieved and evaluated for completeness. To assess quality control of ESD procedures and procedure-related complications, detailed histopathological examinations were performed.
RESULTS: We resected a total of 18 ESD specimens safely and easily (9 specimens by using the Optimos knife; 9 specimens by mixing conventional knifes). There was no significant difference in the procedure time and cutting speed between the two groups. Significant bleeding occurred with equal frequency (1 vs. 1). There was no perforation in the two groups (endoscopic and histological). Histologic quality analysis of both resected specimen and remaining gastric bed tissue revealed no statistical difference.
CONCLUSION: New Optimos knife, the multifunctional knife developed by combining advantages of various conventional knives, can carry out multiple steps of ESD procedure, and is deemed quite helpful when performing quality controlled ESD safely and rapidly. Further large-scaled, prospective clinical studies are required for more accurate determination of its safety and efficacy.
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Disclosure of Interest: C.-I. Kwon Other: Dr. Chang-Il Kwon invented the Optimos knife in conjunction with Taewoong Medical Company., G.-I. Kim: None Declared, I.-K. Chung: None Declared, W. H. Kim: None Declared, S. P. Hong: None Declared, S. Jeong: None Declared, D. H. Lee: None Declared
Keywords: Endoscopy, ESD, Experimental animal models

P565 A NEW PROTOTYPE USING INDOCYANIN GREEN (ICG) AS A CONTRAST AGENT FOR PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY (PCLE)

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INTRODUCTION: Probe-based Confocal Laser Endomicroscopy (pCLE) is a new imaging technology, enabling in vivo microscopic evaluation in real-time. However the system currently available (blue laser after injection of fluorescein) has some limitations: (1) fluorescein exposes a few patients at risk to allergic reactions, and (2) the depth of exploration is limited.
AIMS&METHODS: Our aim was to develop a new system encompassing two lasers and indo cyanine green (ICG) as a fluorescent agent.
We used a porcine model, with first injection of ICG (5ml at 5mg/ml at 785nm, and an additional 15ml at 3.3 mg/ml at 640nm). Images of the esophageal, duodenal, biliary and hepatic tissues were collected using standard pCLE probes working with the 785nm system. Then, the same procedure was repeated after fluorescein injection with the 488nm system. Images were compared qualitatively for each tissue site.
RESULTS: Good quality images could be obtained using intravenous ICG in all organs. Appropriate fluorescence signal levels could be visualized based on the dosages used. The fluorescence signal was very low at 640nm and close to the lower detection threshold of the system, even after a repeat injection of ICG. The fluorescence signal was acceptable at 785nm. Dynamics of ICG appeared radically different than that of fluorescein, with a rapid extravasation, enabling the observation of microarchitectural structures as a negative signal. Repeat injection enabled further visualization of microarchitectural and cellular details. Image quality was similar after repeated injections.
CONCLUSION: This study provided promising perspectives on future combinations between optical biopsy devices and contrast agent, especially with new near-infrared molecules being developed. Since a 785nm wavelength can penetrate deeper into the tissue, provided chromatic probes are developed in the future, it might be possible to obtain pCLE images at increased depths with the 785 nm system.
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Disclosure of Interest: None Declared
Keywords: endomicroscopy, indocyanin green

P566 IS OVER-THE-SCOPE CLIP A PERMANENTLY IMPLANTED DEVICE? OUTCOME AND FOLLOW UP OF CLIP DELIVERY FOR FISTULAS, PERFORATIONS AND BLEEDING

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INTRODUCTION: Over-the-Scope Clip (OTSC) is a new clipping device providing strong grasping and compression of tissue without provoking ischemia and laceration, proposed for the closure of gastrointestinal defects iatrogenic visceral perforation or bleeding. Once applied, OTSC® remains attached to the mucosa, and cannot be removed, but like standard clips it may be bound to fall over time.
AIMS&METHODS: The aim of this study was to report our experience of the outcome of OTSC® placement in GI fistulas, perforations and bleeding and to evaluate spontaneous detachment rate.Between 10/2010 - 4/2013, 31 OTSC® were placed in 29 patients (15F), median age 62.62 years (20-88), 10 (32%) for iatrogenic visceral perforation, 4(13%) for bleeding and 17 (55%) for leaks following surgery. Anatomic position was: esophagus, n=11, stomach, n=3, duodenum, n=9 and colon, n=8. The median (range) timespan from the primum movens to OTSC® implantation was 71 days (0-570), with 112 days (7-570) for leaks, 30 days (0-90) for bleeding, and 2 days (0-15) for perforation. The size of OTSC® used was 9mm in 27 cases and 14mm in 4. Outcome was evaluated by clinical follow-up and detachment rate by radiological imaging or endoscopy at distant time.
RESULTS: All 31 OTSC® were delivered with no procedure-related complication. The treatment was successful in 21 patients (72,4%) at 15 months (1-32) follow up and the clip was still in place after a median of 195,80 days (30-570). 8pts (27,6%) clipped for surgical leak required repeat endoscopic interventions for persistence of fistula a median of 120 days (33-240) after the clip application. In 2 out of 6 patients OTSC® was not found at repeat endoscopy (122 and 160 days after OTCS® placement). One leak was treated by stenting and the other one by a second OTSC®, which was again not in place at the time of endoscopic control for persistence of the leak. In 1 out 8 patients, the misplaced clip was removed with a foreign body forceps 200 days later, this patient was definitively treated with stenting. In the last 5 patients OTSC® was found to be present but misplaced at the time of second endoscopy after a median of 82,6days (10-240). 3 of these patients underwent surgery and the other 2 are still under stent treatment.
CONCLUSION: OTSC® looks successful for the treatment of iatrogenic acute visceral perforation, gastrointestinal bleeding and leaks follows surgery. Clips seem to remain in place for a long time if rightly placed with clinical efficiency; by contrast OTSC® may slough off spontaneously in case of inefficient application and/or misplacement.
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Disclosure of Interest: None Declared
Keywords: Bleeding, endoscopic clipping, Endoscopic closure, GI fistulae, iatrogenic perforation, OTSC (over-the-scope clip)

P567 USEFULNESS OF THE INFRARED ENDOSCOPY (IRE) IN ASSESSMENT OF BARRETT'S EARLY NEOPLASIA: PRELIMINARY RESULTS FROM A PILOT STUDY.

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INTRODUCTION: An accurate staging of early Barrett's cancer is mandatory to identify patients with neoplasia limited to the mucosa, who can be candidates for endoscopic treatment. Infrared endoscopy (IRE) using indocyanine green (ICG) as a fluorescence marker has been shown to be useful in detecting submucosal (SM) invasion in early gastric cancer. Its role in the endoscopic assessment of Barrett's neoplasia has not been reported.
AIMS&METHODS: To evaluate the utility of IRE in the endoscopic assessment of Barrett's early neoplasia.
Patients with dysplastic Barrett's oesophagus (BO) referred for endoscopic therapy were prospectively enrolled in the study. White light High Resolution Endoscopy, Narrow Band Imaging and IRE were sequentially performed using

an Infrared endoscope prototype (GIF-RQ260Z; Olympus Optical Co.). 2 mg/kg of ICG was intravenously administered before the IRE. Characteristics of BO and any visible lesion (VL) were recorded. IRE findings were classified as no stain, faint stain and dense stain. Biopsies were obtained from flat Barrett's segment. Endoscopic mucosal resection (EMR) was performed for all VL if appropriate. Final histology by biopsies/EMR/surgery was included for analysis.
RESULTS: 21 patients were included (median age 69 years, 86% men); median length of BO 5 cm (range 1-16 cm). Biopsy results from 7 patients with flat BO and 16 VL (Is=1, 0-IIa=9, 0-IIa+c=2, 0-IIb=4) from 14 patients were analyzed. IRE findings after ICG injection (median dose 160 mg) and its correlation with final histology are summarized in Table 1.

Table 1. IRE Staining and final histology

NO STAIN=7				STAIN=16			
≤LGD	HGD	IMC	SMC	≤LGD	HGD	IMC	SMC
5	1	1	0	1	6	5	4

STAIN=16							
FAINT=11				DENSE=5			
≤LGD	HGD	IMC	SMC	≤LGD	HGD	IMC	SMC
1	6	2	2	0	1	2	2

No stain was noted in 7 cases; histology was <HGD in 5 (71%) and ≥HGD in 2 (29%). Staining was noted in 16 cases; 15 (94%) had at least HGD. There was statistically significant difference between cases with no stain and any staining on IRE with regard to the presence of at least HGD [2/7 (29%) vs. 15/16 (94%) p=0.005].
Stain was reported as faint in 11 cases and dense in 5. There was no statistically significant difference between cases with faint and dense staining on IRE with regard to the presence of SM invasion [2/11 (18%) vs. 2/5 (40%) p=0.755].
CONCLUSION: IRE can provide additional information to the currently available imaging techniques for detecting HGD in BO. The presence of inflammation and hypervascularization within the BO makes the accurate visualization of SM vessels challenging. IRE may not have role to predict SM invasion in early Barrett's neoplasia.
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Disclosure of Interest: J. Ortiz-Fernández-Sordo: None Declared, S. Sami: None Declared, V. Subramanian: None Declared, J. Mannath: None Declared, E. Telakis: None Declared, K. Ragunath Financial support for research from: From Olympus-Keymed UK and Intromedic Ltd, Lecture fee(s) from: From Olympus-Keymed UK
Keywords: BARRETTS ESOPHAGUS, Endoscopy, image enhanced endoscopy

P568 USEFULNESS OF RADIAL EUS SCANNING TO ASSESS ADEQUACY OF ENDOSCOPIC RESECTION OF GASTRODUODENAL CARCINOID TUMORS (GDCT)

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INTRODUCTION: Gastroduodenal carcinoid tumors are rare neuroendocrine tumors, usually present as foregut submucosal tumor or polypoid lesions. Accurate diagnosis and endoscopic resection remain a challenge.
AIMS&METHODS: To evaluate the accuracy, diagnostic features, and role of EUS radial scanning in the therapeutic decision making in patients with gastroduodenal carcinoid tumors. From September 2006 to January 2012, 52 patients were identified as having suspected gastric or duodenal carcinoids by our endoscopic services. After excluding obvious subepithelial tumors, ampullary location, and inconclusive pathology a total of 27 patients remained and were analyzed based upon EUS images/video by endoscopists blinded to final clinical and pathological outcomes.
RESULTS: 27 patients with 44 GDCT (30 GCT and 14 DCT) were analyzed. EUS showed GDCT in the second layer in 100% and were homogeneous and hypoechoic in 93%. The median size of GCT was 11 mm (5-18 mm) and DCT was 7mm (6-16 mm). Based on EUS staging; 23 uT1 (85%) underwent ER and 4 uT2 (15%) underwent surgery. We performed 29 ER (16 GCT and 13 DCT) using polypectomy snare in 19 after submucosal injection in 7 and the by band ligation / snare resection (3). ER was complete in 23/29 (79.3%). Accuracy of EUS to determine the correct indication surgery (uT2) or ER (uT1) was 79.3%. Early adverse events (AEs) occurred in 2 patients (6.8%): pain [1] and perforation [1], the latter treated surgically. The mortality rate was 3.4%. Recurrence occurred in 3/23 (13%).
CONCLUSION: Most GDCT are less than 10mm in size, with well-defined margins and hypoechoic nature present in deep mucosal and submucosal layers. Tumor locations (eg. proximal stomach and duodenal bulb) and EUS features are factors predictive of GDCT. EUS provides information to assist ER. GCT located in the middle and distal portion and DCT in the second portion are difficult to be precisely evaluated by EUS.
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Disclosure of Interest: None Declared
Keywords: Carcinoid tumor, Endoscopic treatment, endosonography, Polipectomy, Staging

P569 DIAGNOSTIC PERFORMANCE AND LIMITATIONS OF MAGNIFYING NARROW-BAND IMAGING IN SCREENING ENDOSCOPY OF EARLY GASTRIC CANCER: A PROSPECTIVE MULTICENTER FEASIBILITY STUDY

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INTRODUCTION: Curative treatment of the patient with gastric cancer requires reliable detection of early gastric cancer. Magnifying endoscopy with narrow-band imaging (M-NBI) is useful for the accurate diagnosis of early gastric cancer [1, 2]. However, the role of M-NBI in screening endoscopy has not yet been established.
AIMS&METHODS: The aims of this study were to investigate the feasibility and the limitations of M-NBI in screening endoscopy. We conducted a multicenter prospective uncontrolled trial of patients undergoing routine screening endoscopy. We determined the diagnostic accuracy, sensitivity and specificity of M-NBI according to the degree of certainty and need for biopsy as assessed using the VS (vessel plus surface) classification system [1]. We analyzed the endoscopic and histopathological characteristics of both false negative and false positive cases which were diagnosed using M-NBI with a high degree of confidence. We then developed a provisional diagnostic strategy based on the diagnostic performance and limitations identified in this study.
RESULTS: A total of 1094 patients were enrolled in the study. We analyzed 371 detected lesions (20 cancers and 351 non-cancers). The accuracy, sensitivity and specificity of M-NBI diagnoses with a high degree of confidence were 98.1%, 85.7% and 99.4%, respectively. The false negative lesion was a pale mucosal lesion with a tissue diagnosis of signet-ring cell carcinoma. When we excluded pale mucosal lesions, the accuracy, sensitivity and specificity of M-NBI diagnoses with a high degree of confidence increased to 98.1%, 100% and 99.4%, respectively. We therefore propose a practical strategy for targeting non-pale mucosal lesions.
CONCLUSION: With a refined strategy considering its limitations, M-NBI can act as an "optical biopsy" in screening endoscopies.
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2. Ezoe Y, Muto M, Uedo N, et al. Magnifying narrowband imaging is more accurate than conventional white-light imaging in diagnosis of gastric mucosal cancer. Gastroenterology 2011;141:2017-25.
Disclosure of Interest: None Declared
Keywords: Diagnosis, Early gastric cancer, Magnifying endoscopy, Narrow-band imaging, Screenig, VS classification

P570 ESOPHAGEAL REGENERATION WITH CELL SHEETS FOLLOWING ESD: DEVELOPMENT OF ENDOSCOPIC DELIVERY DEVICES FOR CELL SHEETS

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INTRODUCTION: We have developed a novel strategy for regenerative medicine to recover tissue functions using temperature-responsive cell culture surfaces. To overcome of conventional methods such as the usage of single-cell suspension injection, we have applied transplantable cell sheets fabricated with temperature-responsive culture surfaces for cell delivery. In the field of gastroenterology, these regenerative medicine and tissue engineering approaches have attempted to prevent postoperative stricture by structurally and functionally reconstructing normal tissues through the promotion of early re-epithelialization after endoscopic large size mucosal resection. Our group previously reported a method of regenerative therapy involving the transplantation of fabricated autologous oral mucosal epithelial cell sheets in a canine model and demonstrated its human clinical application. So far, the endoscopic technique of cell sheet transplantation was not easily procedure. Presently, we are developing two types of novel endoscopic device for cell sheets transplantation, and we also show recent our research for esophageal regeneration using cell sheet engineering after circumferential endoscopic large size mucosal resection. We examined allogeneic epidermal cell sheet transplantation using a novel endoscopic delivery device in porcine.
AIMS&METHODS: The novel devices were designed with a computer-aided design system, and the three-dimensional data were transferred to a 3D printer. And then, primary epidermal cells were isolated from the lower abdominal skin of miniature pigs, cultured for 18 days at 37°C on temperature-responsive culture inserts. Transplantable cell sheets were harvested from the inserts by reducing temperature to 20°C. Immediately after creating full circumferential esophageal endoscopic submucosal dissection (ESD), an allogeneic epidermal cell sheet was endoscopically transplanted to the ulcer site. The pigs were endoscopically monitored, and sacrificed 2 weeks after transplantation.

RESULTS: 2-3 pieces of the epidermal cell sheets (20mm in diameter) were successfully transplanted onto the ulcer site after circumferential ESD. In addition, early epithelialization and moderate stricture were observed by a number of transplanted cell sheets.
CONCLUSION: These endoscopic delivery devices for cell sheet would enable easily transplantation of cell sheets onto the lumen of the esophagus. Additionally, fabricated allogeneic epidermal cell sheets might be useful for prevention of stricture after esophageal ESD as well as autologous oral mucosa epithelial cell sheets in swine model.
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Disclosure of Interest: N. Kanai: None Declared, S. Kobayashi: None Declared, T. Ohki: None Declared, N. Tanaka: None Declared, M. Yamato Consultancy for: Cellseed, T. Okano Consultancy for: Cellseed
Keywords: cell sheet, cell therapy, ESD (endoscopic submucosal dossection), Regenerative medicine, stenosis

P571 DOUBLE TYPE METALLIC STENTS FOR MANAGEMENT OF POST-OPERATIVE FISTULA AND LEAKAGE OF THE UPPER GASTROINTESTINAL TRACT

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INTRODUCTION: Post-operative anastomotic leakage and fistula of the upper GI tract are still challenging to manage. Because of the need of removability, fully covered stents are used with a high risk of migration in patients with usually severe conditions and sepsis. The aim of our study was to evaluate the effectiveness of a new type of endoscopic stenting in post-operative GI leakage or fistula. The secondary endpoint was to determine the ability to withdraw the stent.
AIMS&METHODS: Thirty patients treated for upper GI fistula with a double type stent (Taewong, Seoul, Korea) were included in this retrospective study. Eighteen were indicated for post-operative fistula or leakage. Double type stents were used because they added to an inner fully covered stent, an outer uncovered spherical metallic stent. Thus, the inner part ensured the tightness of the stent whereas the outer part decreased the risk of migration. Double type metallic stent (DTMS) were planned to be retrieved after 4 postoperative weeks.
RESULTS: Twelve patients had a post-operative fistula (Sleeve gastrectomy in 8 cases), six had an anastomotic leakage. Eight patients out of the eighteen have undergone a previous failed stenting and eight an associated treatment with OTSC clips. A complete healing was obtained in fifteen among eighteen patients (83%). Those patients were healed with primary success (one session) in 12 cases and required a second treatment session in 3 cases. Among patients with fistulas (12), the success rate was 75% (9/12) and it was 100% (6/6) in patients with anastomotic leakages. All the stents were withdrawn without any complications after a median stenting time of 33 days. The spontaneous migration rate of the stent was 16%.
CONCLUSION: This new double type stent is a new and efficient method to treat post-operative fistulas and leakages of the upper GI tract. The stents were always removable despite the external uncovered part with a low migration rate
Disclosure of Interest: None Declared
Keywords: esophageal fistula, esophageal leakage, Stent

P572 EXPERIMENTAL EVALUATION OF PHOTOCROSSLINKABLE CHITOSAN HYDROGEL AS INJECTION SOLUTION FOR ENDOSCOPIC RESECTION

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INTRODUCTION: Saline and sodium hyaluronate as injection solution for endoscopic resection techniques have several disadvantages such as short lasting effect leading to a potentially higher risk of bleeding and perforation. The new substance of photocrosslinkable chitosan hydrogel in a DMEM/F12 medium (PCH) can be converted into an insoluble hydrogel by ultraviolet (UV) irradiation for 30 seconds. So, we think PCH can maintain submucosal thickness and reduce bleeding and perforation after mucosal resection.
AIMS&METHODS: First, The gastric submucosal layer of rats was injected with PCH (which was then irradiated with ultraviolet light to form a hydrogel), or with sodium hyaluronate, or hypertonic saline, and two investigations about the thickness of the layer and the amount of bleeding were done, using three different sets of rats, respectively. Second, twelve pigs were divided in the two groups: endoscopic submucosal dissections (ESD) were performed with either PCH or hypertonic saline. Thirdly, the effects of both agents on wound healing were examined endoscopically and histologically using six pig stomachs.
RESULTS: Gastric submucosal layers of chitosan hydrogel-treated animals remained significantly thicker than those of other groups for at least 6 h after injection. The total amount of bleeding 20 min after mechanical mucosal resection was 170.0±20.0mg, 678.3±226.3mg, and 1020.0±104.1mg in the PCH, sodium hyaluronate, and hypertonic saline groups, respectively. PCH injection led to a longer lasting elevation with clearer margins as compared with hypertonic saline, thus enabling precise ESD along the margins of the elevated mucosa. The endoscopic aspect after ESD was similar in both groups. PCH biodegradation was completed within 8 weeks on endoscopic and histologic analyses.
CONCLUSION: PCH is a promising agent for submucosal injection prior to various techniques of endoresection. It should be evaluated in clinical trials.
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Disclosure of Interest: None Declared
Keywords: endoscopic submucosal dissection, photocrosslinkable chitisan hydrogel

P573 SERRATED POLYPOSIS: ENDOSCOPIC, PATHOLOGICAL AND CLINICAL DATA FROM A COHORT OF ITALIAN PATIENTS.

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INTRODUCTION: Serrated polyposis syndrome (SPS) is a recently identified colonic polyposis associated to an increased risk of colorectal cancer (CRC). According to World Health Organization (WHO) diagnostic criteria for SPS are: 1) at least 5 serrated polyps (SP) proximal to sigmoid colon, of which 2 are greater than 10 mm in diameter, or 2) any number of SP occurring proximal to sigmoid colon in an individual who has a first-degree relative (FDR) with SPS, or 3) greater than 20 SP distributed throughout the colon. Polyps occurring in SPS are part of a spectrum of SP including hyperplastic polyps (HP), traditional serrated adenomas (TSA), sessile serrated adenomas (SSA). Little is known about SPS genetics, inheritance and clinical manifestations. Few dozens of SPS cases have been described all over the world, especially from Australia, U.S.A and northern Europe. No data on SPS patients from Italy are known.
AIMS&METHODS: We report the first Italian cohort of 15 SPS patients (from 13 different families) identified at our Endoscopy Unit between 2009 and 2012.
RESULTS: Six patients (40%) met the WHO criterion n.1; 2 patients (13,3%) the n.2 and 7 (46,7%) the n.3. 12 (80%) were males; the mean age was 64,2 years (range 52-77). A total number of 592 polyps were removed during 55 colonoscopies performed with high-definition scopes and indigo carmine or electronic chromoendoscopy in case of known SPS. 501 polyps (84,6%) were SP, 91 were tubular or tubular-villous adenomas; 66 polyps (11,1%) were greater than 1 cm in diameter. Regarding SP, 442 (88,2%) were HP, 39 (7,9%) were SSA and 20 (3,9%) were TSA. Regarding the anatomical distribution of all the polyps, 183 (30,9%) were found in the right colon, 304 (51,4%) in the left colon and 105 (17,7%) in the rectum; taking into account the SP only, 118 (23,5%) were located in the right colon, 282 (56,3%) in the left colon and 101 (20,2%) in the rectum. Interestingly, no polyps with high grade dysplasia were found. We observed only one patient with CRC (6,7%), located in the rectum. A familial history of CRC was recorded in 7,7% of cases. 33,3% of SPS patients had an extraintestinal previous cancer. We also observed an high incidence of any cancer (23,8%) in 42 FDR investigated.
CONCLUSION: Our study shows some differences with previous series: high percentage of male patients; low rate of CRC; low incidence of CRC familial history but high incidence of cancer in FDR; SPS distal presentation predominance. Larger studies are needed to confirm these findings.
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Disclosure of Interest: None Declared
Keywords: cancer incidence, Endoscopy, serrated polyposis

P574 EFFICACY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN AN EUROPEAN CENTER

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is gaining acceptance in the West as a therapeutic technique for removal of epithelial and subepitelial gastrointestinal lesions. It allows en bloc resection but demands skilful endoscopic teams. Comparing to endoscopic mucosal resection, it is associated with prolonged procedure time and increased risks of perforation and bleeding. European reports on ESD are scarce and limited in size.
AIMS&METHODS: In this prospective study, we aim to evaluate the efficacy and safety of this technique in our center. Consecutive patients with gastrointestinal lesions referred for ESD were invited to participate in this study, between November 2010 and February 2013. The study was approved by the Ethical Committee of our Institution and each patient gave written informed consent. All ESDs were performed in the endoscopy unit under propofol sedation using IT-knife 2, IT-knife nano and Dual-knife according to lesions localization. Follow-up endoscopies were performed 2 months after ESD and subsequently each 6-12 months, according to pathology result.
RESULTS: 104 patients (45 female, mean age 63,7 ± 13 years-old) were invited to participate in the study. The corresponding 109 lesions were located in the esophagus (n=5), stomach (n=77), duodenum (n=3), colon (n=6) and rectum (n=18). En bloc resection and R0 resection were obtained in 94% and 81% of cases, respectively. The specimens size ranged between 17-140mm (mean 36± 18 mm), corresponding to lesions with 9-105mm (mean 28± 18mm). The median procedure length was 94 ± 80 minutes. Six lesions were subepithelial, being the remaining epithelial. The most frequent pathological results were low-grade dysplasia (n=35), high-grade dysplasia (n=26), intramucosal adenocarcinoma (n=14), invasive carcinoma (n=7). Two patients had acute surgery due to perforation (n=1) and bleeding (n=1). One patient had emphysema and 6 patients had delayed bleeding, all treated conservatively. In 69% of cases ESD was performed in an outpatient basis, being all patients discharged in up to 7 days. Three patients were operated electively due to non curative ESD and one patient had a second ESD because of residual neoplastic tissue in the scar on follow-up. The remaining patients had no recurrence on a strict follow-up protocol.
CONCLUSION: In this prospective study, ESD enabled accurate resection, with low rate of complications and no mortality.
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Disclosure of Interest: None Declared
Keywords: Endoscopic submucosal dissection (ESD), neoplasia, safety

P575 ENDOSCOPIC MANAGEMENT FOR PATIENTS WITH SERRATED POLYPOSIS SYNDROME IS FEASIBLE AND EFFECTIVE : A PROSPECTIVE OBSERVATIONAL STUDY AT A TERTIARY CENTER.

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INTRODUCTION: Serrated polyposis syndrome is a rare condition with multiple serrated lesions all over the colon and is believed to have an increased risk for developing cancer. The recognition of these polyps as well as the clinical and pathological classification is important to determine treatment and surveillance strategy. However, clinical strategy remains unclear as prospective data based on large numbers of patients are scarce

AIMS&METHODS: The aim of this study was to investigate the feasibility of endoscopic treatment and standardized surveillance in patients with this increasingly recognized syndrome. From september 2010 to april 2013 we included consecutive patients in this prospective study. All patients underwent chromoendoscopy at first presentation and during surveillance. The strategy included initial complete resection of all colonic lesions > 5mm. Follow-up was performed in 3-6 months until complete remission was achieved. Afterwards , patients entered a standardized surveillance protocol with chromoendoscopic colonoscopy in annual period.

RESULTS: In 24 patients, 79 colonoscopies, with endoscopic resection of 369 lesions were undertaken. In 22 patients (91.6%) total remission could be accomplished after 2.51 (1-8) colonoscopies. Histology revealed predominantly diminutive hyperplastic polyps (81.7%),31 (8.4%) sessile serrated adenomas and 33 (8.9%) low-grade adenomas and one patient with advanced colorectal cancer. Only 9 (38%) patients had serrated polyps > 10 mm in size. During surveillance period 63 additional lesions were detected and resected. The mean follow-up time was 17.99 months (2-31). No interval carcinoma was detected during surveillance.

CONCLUSION: The present study indicates that endoscopic management in patients fulfilling the diagniostic criteria of serrated polyposis syndrome is feasible and safe. We cannot confirm the previously described association between serrated polyposis syndrom and colonic cancer in general. As the predominant phenotype was small hyperplastic polyps (WHO III◦), it appears likely that cancer risk is associated with larger serrated lesions rather than small hyperplastic polyps itself.

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Disclosure of Interest: None Declared

Keywords: hyperplastic polyp, hyperplastic polyposis, serrated polyposis

P576 COLORECTAL SESSILE SERRATED ADENOMA/POLYP WITH DYSPLASIA MAY LOSE TYPICAL MUCOUS-CAP APPEARANCE

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INTRODUCTION: The colorectal serrated polyp is morphologically conspicuous and the diagnosis by endoscopy is difficult, although mucous-cap is most often mentioned for sessile serrated adenoma/polyps (SSA/P). In pathology, the diagnosis and terminology among each subtypes remains a debate. The ambiguity of diagnosis in endoscopy and pathology may impede the well recognition of serrated polyp and may account for inferior protection of colonoscopy for right-sided colon cancer. Latest differentiation about serrated polyps was released in 2010. Our pathology unit also adjusted and followed the classifications since then.

AIMS&METHODS: To improve our understanding about endoscopic diagnostic capability and clinical features according to the latest pathological proposal for colorectal serrated polyps.

From 2011/01 to 2012/12, diagnosis with sessile serrated adenoma/polyps (SSA/P) and traditional serrated adenoma (TSA) in colorectum were selected from the pathology database. Basic demographic data were reviewed and compared between SSA/P and TSA. SSA/P with cell dysplasia was also selected. The endoscopic pictures of each polyps were reviewed again by one endoscopist to judge whether mucous-cap appearance was shown in SSA/P. In TSA, polyps with villiform pit appearance in white-light endoscopy were regarded as endoscopy-diagnosis capable cases.

RESULTS: A total of 34 SSA/P and 17 TSA were enrolled for study. There were no difference in age (59.0/59.18), gender ratio (men, 52.9%/76.5%, p= 0.187), and polyp size (8.9/9.2, mm) between SSA/P and TSA. Same to current report, SSA/P appeared more frequently in right-sided colon (67.6%) whereas TSA was more common in left-sided colon (76.5%). Common characteristics of serrated polyps in endoscopy were seen in 50% (17/34) and 41.2% (7/17) of SSA/P and TSA, respectively. Ten of SSA/P (29.4%) presented with cell dysplasia. In SSA/P with cell dysplasia, the polyp size tended to be larger than SSA/P without dysplasia, though not statistically significant (1.160/0.783, cm, p=0.31). Besides, SSA/P with dysplasia seldom reveal mucous-cap appearance when comparing to SSA/P without dysplasia (without mucous-cap, 90%/33.3%, p= 0.008).

CONCLUSION: Our result showed that SSA/P with dysplasia seldom presented with mucus-cap appearance. We assumed the process of dysplasia would be associated with mucous secretion. The endoscopic diagnostic capability was not good for SSA/P and TSA. All sessile polyps at right-sided colon should be removed even without mucous-cap appearance if technically available.

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Disclosure of Interest: None Declared

Keywords: colon cancer, serrated adenoma/polyp, Traditional serrated adenoma

P577 SAFE EN BLOC RESECTION PROCEDURE WITH ESD AND LAPAROSCOPY ENDOSCOPY COOPERATIVE SURGERY (LECS) FOR COLORECTAL TUMORS ACCOMPANIED WITH FIBROSIS IN SUBMUCOSAL LAYER

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INTRODUCTION: The possibility of en bloc resection of colorectal tumor using endoscopic submucosal dissection (ESD) sometime depends on the existence of fibrosis in the submucosal layer (SM). In these cases, submucosal dissection by using endoscopic devices will becomes more difficult due to the risk of muscular injury and perforation. We developed safe technique of ESD and its applied laparoscopy endoscopy cooperative surgery (LECS) to complete en bloc resection for tumors accompanied with firm fibrosis in SM.

AIMS&METHODS: ESD was performed for 565cases of tumor in 551 patients (male: female = 329:222; mean age, 66.2years). Among these, 135 cases were accompanied with fibrosis in SM. We analyzed these lesions in order to establish a safe en bloc resection procedure.

RESULTS: ESD cases were divided into three groups, absent with fibrosis: type A, fibrosis due to benign causes: type B, and fibrosis due to SM cancer invasion: type C. We classified endoscopic findings of mild degree as B-1and C-1. moderate degree as B-2 and C-2, and screen-like firm fibrosis as B-3 and C-3. We performed en bloc resection for 529 (93.6%) cases of 565 ESD cases, and experienced only one case (0.18%) with perforation, which was accompanied with fibrosis. En bloc resection rate of the tumor without fibrosis (type A) was 96.7% (416/430), and the tumor accompanied with fibrosis was 83.7% (113/135). En bloc resection rate of type B (n=96) and type C (n=39) were as follows, type B; B-1: 48/51(94.1%), B-2:20/23(87.0%), B-3:14/22 (63.6%), type C; C-1:19/19(100%, average SM depth:884 micron), C-2:4/5(80%, average SM depth:2,474 micron), C-3:8/15(53.3%, average SM depth:3,377micron). These results of B-3 and C-3 were significantly lower than type A statistically. From these results, we designed a safe ESD technique by using endo-clips to prevent perforation in 2 cases with type B-3. In cases accompanied with more wide and firm fibrosis in SM, en bloc resection will become more difficult due to the risk of perforation. From these reasons, we established LECS procedure applied ESD technique. And we have completed safe en bloc resection with adequate surgical margin, and performed LECS for 4 cases of colorectal tumors.

CONCLUSION: We have developed safe ESD technique with very low rate of perforation (0.18%) and its applied LECS procedure in order to complete curative en bloc resection for tumors accompanied with firm fibrosis in submucosal layer.And we will present safe ESD technique and LECS procedure for above mentioned colorectal tumors.

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Disclosure of Interest: None Declared

Keywords: COLORECTAL CANCER, ESD (endoscopic submucosal dossection), LECS

P578 EUS IMPROVES QUALITY OF ERCP IN PATIENTS WITH SUSPECTED CHOLODOCHOLITHIASIS

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INTRODUCTION: EUS is a sensitive diagnostic modality to detect choledocholithiasis. Beyond standard therapeutic ERCP, improving quality of ERCP is important by minimizing radiation exposure, reducing therapeutic procedures and preventing ERCP-related pancreatitis. For suspected choledocholithiasis, performing EUS before ERCP potentially makes it possible for endoscopists to determine necessity of ERCP in patients without any biliary disorder on EUS, minimize biliary procedures and therapeutic devices on EUS findings when choledocholithiasis seen on EUS.

AIMS&METHODS: Aim: To analyze the efficacy of EUS on minimizing radiation exposure, avoiding ERCP-related pancreatitis and reducing therapeutic procedures/devices in patients with suspected choledocholithiasis. Method: From 2011 March to 2012 March, 82 Japanese patients with suspected choledcolithiasis(elevated liver enzyme upper than three times of normal limits and acute onset of right upper abdominal pain) were prospectively enrolled in our study.

RESULTS: Results: 41 patients (EUS group: 25 female, mean 55 year old) underwent EUS before ERCP and 41 (ERCP group: 28 female, mean 62 year old) underwent ERCP. All procedures were performed by experienced endoscopists at our single tertiary medical center. In EUS group, 8 patients were found to have no choledocholithiasis on EUS. 6 patients were considered as passing stone and did not proceed to ERCP. 2 patients were complicated by biliary pancreatitis and proceeded to required only biliary sphincterectomy. 33 patients were found to have choledocholithiasis(single stone to three stones) on EUS and underwent ERCP. Of 33 patients undergoing ERCP, 30 patients underwent basket stone removal followed by biliary sphincterectomy and 3 patients required biliary stenting due to cholangitis. ERCP-related pancreatitis occurred in 2 patinents (4.8%). Mean radiation time is 1minutes 31 seconds in EUS group. In ERCP group, 41 patients underwent biliary sphincterectomy, basket stone removal and balloon occlusion cholangiography in a standard way. 5 patients were found to have no biliary stones and considered as passing stone. 36 patients were found to have single to three stones on cholangiography. 2 patients required biliary stenting in addition because of cholangitis. ERCP-related pancreatitis occurred in 4 patients (9.8%). Mean radiation time is 6 minutes 49 seconds in ERCP group. No recurrence was seen in both groups within observation period (55-302 days). EUS group avoided 8 ERCPs and 41 balloon catheters in comparing with ERCP group.

CONCLUSION: Performing EUS before ERCP in patients with suspected choledocholithiasis is significantly beneficial to minimizing radiation exposure, lowering incidence of ERCP-related pancreatitis and reducing therapeutic procedures.

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Disclosure of Interest: None Declared
Keywords: Combined EUS and ERCP, radiation exposure

P579 EVALUATION OF 4 PUBLICLY AVAILABLE 3D RECONSTRUCTION ALGORITHMS FOR CAPSULE ENDOSCOPY

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INTRODUCTION: Three-dimensional (3D) imaging is gaining popularity; it has been already adopted in laparoscopic/robotic surgery but has yet to be applied widely in gastrointestinal endoscopy. Furthermore, due to current technological limitations, 3D imaging in capsule endoscopy (CE) is yet to be available. To overcome this, a software approach [called Shape-from-Shading (S/S)] has been proposed [1,2]. Essentially, S/S is a large family of software algorithms which attempt to extract the 3D shape of structures or lesions by minimising image constraints (e.g. lighting, surface reflectance, texture) present in every CE frame. At present, there are 4 freely available S/S algorithms for CE [3-6]. If there are to be applied in CE, the prime question is which S/S algorithm is more appealing to CE reviewers.
AIMS&METHODS: We aim to assess 4 publicly available (Tsai,Imperial,Fourier,Barron) 3D reconstruction algortihms in CE. Carefully selected CE frames of bowel structures and/or lesions were evaluated by 3 reviewers -blind to others- with extensive experience in CE review in a Matlab environment (**fig. 1**). Each image was 3D reconstructed with all 4 S/S algorithms.The reviewers were advised to select for each image the best performing (in regard to structure/texture enhancement) S/S algorithm. Scores were tallied (**max** 162) and inter-observer agreement was calculated witht the free-marginal ***Kappa*** (K) coefficient [7].
RESULTS: Overall, a total of 54 CE images (26 PillCam®/28 MiroCam®: 23 luminal protrusion, 16 inflammatory lesion, 15 vascular lesion) were evaluated. Of the 4 S/S algorithms, Tsai's 3D algorithm outperformed the rest in 45/54 images (125 selections) , followed by Imperial's (7/54 images; 31 selections) and Fourier's (1/54 image; 6 selections); there was a single image for which each reviewer selected (as best performing) a different 3D algorithm. Of note, Barron's 3D algorithm was evaluated as not offering imporvement. In 26/54 images, Tsai's algorithm was unanimously selected as the best performing 3D reconstruction software. Tsai's 3D algorithm superiority was independent of lesion category (protrusion/inflammatory/vascular; ***P***: 0.678) and/or CE system used to obtain the 2D images (MiroCam®/PillCam®; ***P***: 0.558). Lastly, the inter-observer agreement was good (K: 0.55).
CONCLUSION: Of the 4 evaluated (S/S) algorithms, Tsai's 3D reconstruction algorithm is the best performing 3D representation software in CE.
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Keywords: capsule endoscopy, evaluation, software, three-dimensional

P580 TREATMENT OF ANASTOMOTIC COMPLICATIONS AFTER COLORECTAL RESECTION WITH SELF EXPANDING METAL STENTS.

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INTRODUCTION: The role of self expandable metallic stents (SEMS) in patients with colorectal obstruction due to benign disease is controversial and high complication rates have been reported in this clinical setting, especially a significant incidence of stent migration. SEMS can also be adopted to treat patients with symptomatic anastomotic complications after colorectal resection.
AIMS&METHODS: All patients who had SEMS placement for anastomotic stricture and/or fistula were included in this study. No patient was excluded. During a 8 year period 16 consecutive patients had SEMS placement for anastomotic stricture after anterior rectal resection and they represent the basis of our study. Patients were prospectively analysed. Seven patients (mean age = 71.7 y; F=2).had "simple" anastomotic stricture. In the remaining 9 patients a fistula was associated to the stricture.
RESULTS: SEMS was placed successfully in all patients with resolution of the symptoms of obstruction (technical success 100%). There was no case of mortality or major morbidity. Two patients complained of anorectal pain, easily under control with light pain medications. Overall symptoms of obstruction were completely relieved in 10 out of 16 patients (62.5%). Four patients (25%) required balloon dilatation for recurrent symptoms of obstruction. In 2 patients the fistula did not heal and the ileostomy was not closed. Overall the fistula healed in 7 out 9 patients (77.7%) The two patients with persistent fistula had a permanent ileostomy.
CONCLUSION: In patients with fistula and stricture, endoscopic stenting with covered stents has many potential leading to healing of the fistula in the majority of the cases. In this scenario, a covered stent should be used, with the creation of a proximal diverting stoma. Thus, SEMS represent a valid adjunctive to treat patients with symptomatic anastomotic complications after colorectal resection for cancer.
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Disclosure of Interest: None Declared
Keywords: anastomosis stenosis, Stenting, surgery

P581 DIGITAL HOLOGRAPHIC MICROSCOPY TO ASSESS INFLAMMATION IN CROHN'S DISEASE AND TO MONITOR INTESTINAL WOUND HEALING IN VITRO

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INTRODUCTION: The current therapeutic armamentarium for treating Crohn's disease (CD) is limited due to severe side effects and loss of efficacy over the course of disease. Preclinical evaluation of new anti-inflammatory drugs is usually performed in wound healing assays *in vitro*. In CD patients, quantitative read out parameters to assess intestinal inflammation are limited and objective measurement of wound healing is rather complex. Digital holographic microscopy (DHM) enables stain-free quantitative phase contrast imaging and provides tissue density by measuring optical path length delay (OPD) and accordingly refractive index (RI).
The aim of this study was to evaluate DHM for assessment of severity of CD in humans as well as intestinal epithelial wound healing *in vitro*.
AIMS&METHODS: Cryostat biopsies of patients with CD (n=6) and healthy controls (n=6 per group) were examined via DHM. To quantify tissue density, segmental OPD/RI was performed according to anatomic structure (epithelium (e), submucosa (sm) and stroma (st)). Moreover, proliferation and migration of Caco-2 cells were studied in wound healing assays in the presence of stimulating epithelial growth factor (EGF) and inhibiting mitomycin c and were assessed in time-lapse series for 48 hrs (digital holograms were recorded every 3 min).
RESULTS: In human IBD patients, average RI differed significantly in all parts of the colonic wall between active disease and healthy control (e: 1.352 ± 0.002 vs. 1.355 ± 0.003; $P < 0.001$, sm: 1.360 ± 0.007 vs. 1.364 ± 0.005; $P < 0.001$, st: 1.350 ± 0.004 vs. 1.360 ± 0.008 vs.; $P < 0.001$). Assessment of wound assays via DHM as reflected by the area covered by living *Caco-2 cells* detected significantly stimulated growth in plane axis (EGF-stimulated : T1(12h)=0.043 mm^2, T2(24h)=0.074 mm^2 und T3(36h)=0.112 mm^2, vs. mitomycin c-inhibited : T1(12h)=0.070 mm^2, T2(24h)=0.202 mm^2 und T3(36h)=0.382 mm^2; $P < 0.001$, n=3). The cellular dry mass showed significant differences between stimulated and inhibited cells ($P < 0.05$) and realtime thickness profiles of cell cultures were obtained.
CONCLUSION: DHM reliably assesses density changes of the colonic wall in CD patients and therefore can quantify the inflammatory damage. This technique enables automated histological examinations in terms of "digital pathology" in the future. In addition, DHM facilitates preclinical evaluation of drug candidates and assessment of their impact on intestinal cell migration and proliferation *in vitro*.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, instestinal epithelial cells

TUESDAY, OCTOBER 15, 2013 9:00–17:00
GENETICS OF GI AND LIVER DISEASES II – Poster Area

P582 STUDY OF THE SIGNIFICANCE BETWEEN PURINE INDUCED LYMPHOPENIA AND INFLAMMATORY BOWEL DISEASE RELAPSES

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INTRODUCTION: Purines are used as second-line immunosuppressive agents in maintaining remission of inflammatory bowel disease(IBD). Studies looking at leukopenia/neutropenia to predict the treatment efficacy of purines have shown mixed results. As lymphocytes play important roles in the pathogenesis of IBD relapses, we aim to evaluate the significance between purine induced lymphopenia and IBD relapses

AIMS&METHODS: Retrospective study of IBD patients under the follow up of a tertiary IBD centre. Patients on purines for a minimum 6 months were included. Information collected included lowest lymphocyte level within first 4 months of therapy, purine doses, types of complications and number of relapses per year. Relapse was defined as flare of symptoms , or surgical intervention was required (eg for fistula or stricture). Surgical interventions for complications (eg abscess or adhesions) were excluded. Lymphocytes level of $<1.0x10*9/L$ was used to define lymphopenia and to divide patients into 2 groups for subsequent analysis using Mann-Whitney U test.
Patients on infliximab/ methotrexate , non-compliant or lymphopenia from other secondary causes were excluded.
RESULTS: 300 patients were screened with total 46 patients eligible. This included 24 Crohn's Disease, 21 Ulcerative Colitis and 1 Indeterminate Colitis. Duration of treatment ranged from 6 months to 12 years (median 4.5 years). Median Azathioprine dose was 2.0mg/kg. There was no statistical significance effect between achieving lymphopenia and the rate of IBD relapses (p=0.98). Further subgroup analysis based on type of IBD revealed similar result for Crohn's Disease (p=0.93). Subgroup analysis for Ulcerative Colitis suggested positive association between lymphopenia with higher rate of flares (p=0.019) but this may possibly be confounded by the small sample size.
CONCLUSION: Lymphopenia during purine treatment does not predict the rate of IBD relapses. This may be limited by our small sample size or possibly the main pathway of IBD inflammation is not mediated through lymphocytes.
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Disclosure of Interest: None Declared
Keywords: inflamatory bowel disease, purine

P583 GENOME-WIDE COPY NUMBER VARIATION SCAN IDENTIFIES COMPLEMENT COMPONENT C4 AS NOVEL SUSCEPTIBILITY GENE FOR CROHN'S DISEASE

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INTRODUCTION: Genome-wide association studies and meta-analyses have identified 140 loci associated with Crohn's disease (CD). Even this large number of loci explains only a minority of the variance in disease risk, suggesting other factors such as copy number variation (CNV) make substantial contributions to disease pathogenesis.
AIMS&METHODS: The aim was to identify CNV regions associated with CD using array comparative genomic hybridization (aCGH). 848 CD patients and 486 healthy controls were included for aCGH. They were assembled in pools of 5 cases - each of identical gender and disease location - and a gender and age matched 5-sample control pool. Eligible regions were finemapped using MAQ (Multiplex Amplicon Quantification). Validation of CNVs was done with qRT-PCR on 2 independent Belgian validation cohorts for a total of 1549 CD and 784 controls. C4 serum levels were determined in 60 CD patients and 116 controls using nephelometry. Statistical analysis was done in R.
RESULTS: The average $\log_2$ ratio per clone was ranked from high (duplicated) to low (deleted). Three of the 10 lowest ranked clones ($\log_2 \leq -15$) were located on 6p21, in the central MHC. MAQ confirmed copy number differences for this region and suggested that the CNV was centered on the RCCX module, containing the *RP*, *C4*, *CYP21* and *TNX* genes. The *C4* gene (either *C4A* or *C4B*) can be present in 1-8 copies, and can occur in two sizes: short (*C4-S*) or long (*C4-L*). qRT-PCR validation showed a shift towards a lower *C4*-L copy number for CD patients compared to controls ($p_{Mann\text{-}Whitney}$=4.38e-03). *C4A* and *C4B* copy number distribution was not different. C4 serum levels were correlated with the C4 copy number, both in cases and controls (p_{ANOVA}=2.81e-4 and p_{ANOVA}=3.39e-10). There were no differences in C4 serum levels between cases and controls ($median_{CD}$=0.33g/L, $median_{CON}$=0.32g/L).
CONCLUSION: A delicate balance exists between a well-regulated immune response against infections, and an over-exuberant response that can lead to (auto)immune disease. C4 is part of the classical pathway that can activate the complement system cascade. We showed that low copy number of *C4-L* is one of the genetic risk factors that can tip the balance towards CD. A low copy number for *C4-L* has also been shown to be a risk for systemic lupus erythematosus.
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Keywords: complement C4, copy number variation, crohn's disease, Genetic susceptibility

P584 CYTOKINE PROFILES IN PERIPHERAL BLOOD OF IBD PATIENTS; THE KEY TO CONNECTING GENOTYPE TO PHENOTYPE.

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INTRODUCTION: Inflammatory bowel diseases (IBD), comprised of ulcerative colitis (UC) and Crohn's disease (CD), are increasingly recognized as a rather heterogeneous group of conditions with distinct pathogenetic pathways. A variable range of cytokines are involved, perhaps influenced by different therapeutic approaches. As key messengers in the immune system, cytokines are known to participate in the disregulation of otherwise controlled inflammation in the gut. In previous studies we observed differently regulated cytokines in IBD, involved in diverse pathways. Currently, we aim to assess these functional differences in the immune response of IBD patients and correlate them to genetic susceptibility loci for IBD, as established by genome-wide association studies (GWAS), as well as to phenotypic patient profiles. More in-depth analysis will then be performed, possibly leading to novel insights in pathways linking these together.
AIMS&METHODS: Whole blood of 40 CD patients was stimulated with aCD3/ aCD28 antibodies and LPS/MDP to mimic the adaptive and innate responses. Twenty-eight cytokines were measured with a multiplex cytokine assay. Genotyping by use of a customized Illumina GWAS chip (Immunochip) includes the single nucleotide polymorphisms (SNPs) from recent GWAS meta-analyses. The phenotype of patients was assessed using the Montreal classification.
RESULTS: Counter to regarding the CD patient population as a whole, we did find cytokine levels to be significantly up- or downregulated when stratifying for the presence of IBD-associated risk alleles. For instance, IL-10 expression drops significantly (p=0.0024), while TNFa expression doubles (p=0.02) when both risk alleles for SNPX resp. SNPY are present. Independent of this cytokine association, this genetic variance also correlates to a worse clinical phenotype, underlining the idea that a causal relationship between genetic variance and clinical phenotype can be identified.
CONCLUSION: Our aim is to unravel the heterogeneous background of IBD, by linking genetic variation to the immunological and clinical phenotype, subsequently elucidating causally involved pathways, contributing to developing patient-specific therapies based on genetic profiling. By firstly correlating altered cytokine expression to IBD risk alleles, we can then study the effects of this SNP in the gene it is physically linked to, and assess its functionality or find epigenetic changes that alter gene expression. When the SNP is correlated to a specific disease phenotype, hypotheses can be built upon linking altered gene expression to the phenotype via altered immunological responses. This route can be applied to our multiple interesting SNP-cytokine associations.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, cytokine profile, genetic polymorphisms, IBD, phenotype

P585 GENE EXPRESSION PROFILES OF ILEAL INFLAMMATORY BOWEL DISEASE CORRELATE WITH DISEASE PHENOTYPE AND ADVANCE UNDERSTANDING OF ITS IMMUNOPATHOGENESIS

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INTRODUCTION: The etiology of inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC) is yet unknown. Inflammation in UC is limited to the large bowel, thus large bowel resection may be curative. In most UC patients undergoing proctocolectomy due to intractable disease an ileal pouch is created. Inflammation of the pouch (pouchitis) develops in most of these patients.
AIMS&METHODS: We aimed to evaluate the *de-novo* inflammation developing in the ileal pouch, hypothesizing it may be similar to ileitis in Crohn's disease (CD).
UC pouch patients were prospectively recruited, stratified according to disease behavior into normal pouch (NP), chronic pouchitis (CP), and Crohn's-like disease of the pouch (CLDP) groups, and compared to controls. Gene expression analysis was performed using microarrays, validated by real-time PCR. Gene ontology and clustering were evaluated using bioinformatic tools.
RESULTS: Sixty six subjects were recruited. While in UC ileum there were no significant gene expression alterations, NP patients had 168 significant alterations (fold change $\geq$2, corrected p value $\leq$ 0.05). In CP and CLDP 490 and 1152 alterations were detected, respectively. High degree of overlap in gene expression alterations between the pouch subgroups was demonstrated. The magnitude of change correlated with pouch disease behavior. Gene expression profiles were more reflective of disease behavior compared to inflammatory indices. CD ileitis had 358 alterations, with a 90% overlap with pouchitis.
Gene ontology analyses revealed multiple biological processes associated with pouch inflammation, including response to chemical stimulus, small molecule metabolic and immune system processes and specific infectious-related pathways such as *staphylococcus aureus*, leishmaniasis and tuberculosis.
CONCLUSION: Gene alterations in pouch inflammation and CD overlap, suggesting that IBD is a spectrum, rather than distinct diseases. Pouchitis may serve as a model of CD. The novel pathways associated with IBD may decipher pathophysiology and suggest targets for intervention.

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Keywords: crohn's disease, gene expression, IBD, imflammatory pathways, pouchitis, ulcerative colitis

P586 ASSOCIATION BETWEEN FUNCTIONEL POLYMORPHISMS IN THE NFKB SIGNALLING PATHWAYS AND RESPONSE TO ANTI-TNF TREATMENT IN DANISH PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Anti-tumor necrosis factor-α (TNF-α) is used for treatment of severe cases of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). However, one-third of the patients do not respond to the treatment. Genetic markers may predict individual response to anti-TNF therapy.
AIMS&METHODS: Thirtynine functional single nucleotide polymorphisms (SNPs) in 26 genes involved in the inflammatory NFκB pathway were assessed in 738 prior TNF-α naive Danish patients with IBD. The results were analysed using logistic regression (crude and adjusted for age, gender and smoking status).
RESULTS: Nineteen functional polymorphisms which modify the activity of NFκB (*TLR2* (rs3804099, rs11938228, rs1816702, rs4696480), *TLR4* (rs5030728, rs1554973), *TLR9* (rs187084), *LY96*(MD-2) (rs11465996), *CD14* (rs2569190), *MAP3K14*(NIK) (rs7222094)), TNF-α (*TNFA*(TNF-α) (rs1800630, rs361525), *TNFRSF1A*(TNFR1) (rs4149570), *TNFAIP3*(A20) (rs6927172)) and other cytokines regulated by NFκB (*IL1B* (rs4848306), *IL1RN* (rs4251961), *IL6* (rs10499563), *IL17A* (rs2275913), *IFNG* (rs2430561)) were associated with response to TNF-α inhibitors among patients with CD, UC or IBD ($p < 0.05$).
CONCLUSION: Patients with genetically determined strong TNF-α mediated inflammation had higher response rates to anti-TNF therapy. Furtheremore, the results suggest that genes regulating inflammation through NFκB are important predictors for the response to anti-TNF therapy among patients with IBD. In addition, the cytokines IL-1β, IL-6 and IFN-γ may be potential targets for treating patients with IBD who do not respond to anti-TNF therapy. Confirmation of these findings in an independent cohort are required before clinical decisions based on this study can be drawn.
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Keywords: adalimumab, inflammatory bowel disease, infliximab, single nucleotide polymorphism

P587 GENETIC POLYMORPHISM OF MYD88 GENE (RS7744) IS CLOSELY ASSOCIATED WITH THE SUSCEPTIBILITY TO ULCERATIVE COLITIS

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INTRODUCTION: Toll-like receptors activation firstly recruits myeloid differentiation primary response gene (88) (MyD88) protein, a common adaptor protein that is fundamental in the innate immune response activation. There is not the other polymorphism except rs7744, with above 0.01 of HWE p value and above 0.05 of minor allele frequency, within 10kbp around MyD88. In addition, there are binding sites of several microRNAs (miRs) nearby rs7744, including miR-29b-2-5p, miR-150-3p and miR-1236. Therefore, we attempted to clarify the association of MYD88 gene polymorphism (rs7744, *1244 A>G) with susceptibility to UC.
AIMS&METHODS: The studied population comprised 922 subjects, including patients with UC (UC cases, n=200), who were enrolled Fujita Health University Hospital, and the healthy subjects without UC (controls, n=722). We employed the PCR-SSCP method to detect a gene polymorphism.
RESULTS: In controls, mean age was 54.5 years old and male/female ratio was 424/298. In UC cases, mean age was 40.0 years old, mean age of onset was 32.7 years old and male/female ratio was 113/87. The distribution of rs7744 genotype in controls was 320AA, 331AG and 71GG (HWE p=0.31), whereas the distribution in UC cases was 63AA, 100AG and 37GG. The genotype frequency of rs7744 AA homozygote was significantly lower and those of GG homozygote was significantly higher in UC cases than in controls (p=0.0012 and 0.0012, respectively). The minor allele frequency of rs7744 were 32.8% and 43.5% in controls and UC cases, respectively ($p < 0.0001$). By logistic regression analysis after adjustment for gender and age, the rs7744 minor allele was significantly associated with the increased risk for UC using both dominant (AG+GG vs. AA) and recessive (GG vs. AA+AG) genetic models (OR, 1.64; 95%CI, 1.15-2.34; p=0.0063 and OR, 1.87; 95%CI, 1.17-3.00; p=0.0094, respectively). These associations were found in male subjects, not in female subjects. In addition, rs7744 minor allele was closely associated with the risk of not chronic continuous phenotype, cases developed after 30 years old, not total colitis type and steroid needless cases using both dominant and recessive genetic models.
CONCLUSION: Our results provided the first evidence that MYD88 gene polymorphism was significantly associated with the development of UC. The genetic polymorphism of MYD88 gene (rs7744) influences the susceptibility to and pathophysiological features of UC.
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Keywords: Gene polymorphism, MYD88, ulcerative colitis

P588 NFKB1 POLYMORPHISM (RS28362941, -94 ATTG INS/DEL) IS ASSOCIATED WITH THE SUSCEPTIBILITY TO ULCERATIVE COLITIS

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INTRODUCTION: Nuclear factor-kappa-B (NF-kB) plays a role in inflammation and carcinogenesis in various organ tissues by inducing translation of many key molecules. A polymorphism -94 ATTG ins/del (rs28362941) is identified. Many studies have reported the association between rs28362491 and various inflammatory diseases. However, these results do not always lead to the same conclusions. We attempted to clarify the associations between ulcerative colitis (UC) and this polymorphism in Japanese population.
AIMS&METHODS: The studied population comprised 949 subjects, including patients with UC (UC cases, n=198), who were enrolled Fujita Health University Hospital, and the healthy subjects without UC (controls, n=751). We employed the PCR-SSCP method to detect a gene polymorphism.
RESULTS: In controls, mean age was 57.0 years old and male/female ratio was 439/312. In UC cases, mean age was 41.7 years old, mean age of onset was 33.1 years old and male/female ratio was 115/83. The distribution of rs28362941 genotype in controls was 283ins/ins, 383ins/del and 85del/del, whereas the distribution in UC cases was 77ins/ins, 84ins/del and 37del/del. The rs28362941 minor allele frequencies in controls and UC cases were 36.8% and 39.9%, respectively (p=0.27). The ratio of del/del homozygote in UC cases was significantly higher than that in controls (p=0.008), and del/del homozygote has a significant risk for the development of UC (OR, 1.83; 95%CI, 1.15-2.92; p=0.011). The male del/del homozygote had an increased risk for the development of UC (OR, 2.03; 95%CI, 1.11-3.73; p=0.022). In female subjects, however, there was no significant difference of genotype distribution between controls and UC cases. In addition, del/del homozygote was closely associated with the risk of not total colitis phenotype. (OR, 1.88; 95%CI, 1.07-3.30, p=0.028), cases developed before 20 years old (OR, 3.62; 95%CI, 1.42-9.26, p=0.0072), not chronic continuous type (OR, 2.01; 95%CI, 1.16-3.47; p=0.012), having no hospitalization (OR, 2.08; 95%CI, 1.23-3.52; p=0.0062) and steroid independent or needless cases (OR, 1.77; 95%CI, 1.05-2.97; p=0.031).
CONCLUSION: Our results provided the evidence that NFKB1 gene polymorphism rs28362941 was significantly associated with the development of UC in Japanese. NFKB1 -94 ATTG del/del homozygote influences the susceptibility to and pathophysiological features of UC.
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Keywords: Gene polymorphism, NFKB1, ulcerative colitis

P589 X-LINKED INHIBITOR OF APOPTOSIS PROTEIN IN THE PATHOGENESIS OF EARLY-ONSET INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The genetic contribution to inflammatory bowel disease (IBD) is only partially understood and it has been suggested that rare variants that escape detection by genome-wide association studies contribute to the genetic risk in IBD.
AIMS&METHODS: Exome-sequencing and functional studies were performed in cases of familial and sporadic early-onset IBD with the aim to discover rare high penetrance variants and novel candidate genes involved in disease etiology.
RESULTS: Exome sequencing revealed a novel hemizygous nonsense mutation (E99X) in the gene encoding for the X-linked inhibitor of apoptosis protein (*XIAP*) in a three-year old patient with a one-year history of colonic, stricturing and fistulizing CD refractory to treatment with corticosteroids, immunosuppressants, and anti-TNFα antibodies. XIAP was not detectable by flow cytometry in various peripheral blood mononuclear cell (PBMC) populations. Lack of XIAP protein expression in the patient was confirmed by western blot analysis. Relative and absolute frequencies of PBMC subsets, T cell proliferation, apoptosis, and immunoglobulin levels were unaltered in the patient. However, while responses to toll-like receptor 2, 3, 4, 7, and 9 stimulation and NLRP3-dependent IL-1β secretion were unimpaired in XIAP-deficient PBMCs and monocytes, NOD2-dependent IL-8 and IL-1β release were not detectable across a range of muramyl dipeptide (MDP) concentrations. Furthermore, wildtype but not E99X XIAP associated with NOD2 in a RIP2-dependent manner as revealed by co-immunoprecipitation. Lentiviral *XIAP* reconstitution in primary monocyte-derived dendritic cells restored MDP-induced NOD2 signaling thus confirming a critical role of XIAP deficiency in the observed NOD2 defects.
CONCLUSION: Our studies reveal a novel *XIAP* mutation associated with early-onset IBD and suggest that *XIAP* deficiency may contribute to disease pathogenesis via impaired NOD2 signaling. In addition, given the central role of *XIAP* deficiency in XLP, these results support the concept that at least a subset of IBD cases may result from congenital or acquired immunodeficiency, potentially in a NOD2-dependent manner.
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Keywords: genetics, IBD

P590 MITOCHONDRIAL NEUROGASTROINTESTINAL ENCEPHALOMYOPATHY (MNGIE): THE LIVER AS A NEW SOURCE OF THYMIDINE PHOSPHORYLASE

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INTRODUCTION: MNGIE is a rare autosomal recessive disease associated with the nuclear *TYMP* gene mutation. As a result, the thymidine phosphorylase (TP) enzyme activity is markedly reduced (or completely deficient) and this leads to mitochondrial DNA mutation and multiple deletions. On a clinical standpoint, MNGIE is characterized by severe gastrointestinal (GI) dysmotility (gastroparesis and intestinal pseudo-obstruction) and neurological impairment. The onset is usually between the second and fifth decades and life expectancy and quality of life are rather poor. So far, there are no established therapeutic options for MNGIE. In the attempt to restore a normal TP activity, allogenic hematopoietic stem cell transplantation (AHSC) has been used as a cellular source of TP. Current data obtained on about 20 MNGIE patients undergone AHSC showed GI and neurological improvement, although 5-year survival rate is roughly 50%.
AIMS&METHODS: In this work, we tested whether the liver may serve as an alternative source of TP. A number of n= 11 patients (7 males; age range: 35-55 years) undergone hepatic resection for focal disorders (i.e., uncomplicated tumors in non-cirrhotic liver) were included. Margins of normal liver tissue were processed for a variety of methodological approaches aimed to identify, quantify and localize TP protein, i.e. WB, ELISA, and immunohistochemistry (IHC). *TYMP* mRNA specific expression has been evaluated via qPCR. Bone marrow and intestinal mucosa were used as positive controls while skeletal muscle as negative control.
RESULTS: WB showed the presence of TP protein in liver tissue with a densitometric ratio TP/GAPDH of 0.9 ± 0.5 A.U. ELISA estimates TP content as 0.5 ± 0.07 ng/μg total proteins. The liver localization of TP with IHC was identified in the nuclei and cytoplasm of hepatocytes and reticular cells. *TYMP* mRNA specific liver expression has been detected in the liver tissue providing evidence of in situ synthesis.
CONCLUSION: The results of this study demonstrate that the liver is an important source of TP. Likewise AHSC, also orthotopic liver transplantation might be a therapeutic alternative for MNGIE patients, hopefully with a better outcome in terms of survival rate.
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Keywords: Liver transplantation, mitochondrial disorders, MNGIE, thymidine phosphorylase

P591 ANTI-PROLIFERATIVE EFFECTS OF BUTYRATE DURING THE POSTNATAL MATURATION OF THE ENTERIC GLIAL NETWORK.

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INTRODUCTION: The postnatal period is crucial for the development of gastrointestinal (GI) functions. The enteric nervous system is a key regulator of GI functions. Increasing evidences demonstrate that 1) postnatal maturation of enteric neurons participate in the control of the development of GI functions (De Vries, *et al*., 2010), and 2) microbiota derived short chain fatty acid can be involved in this maturation (Suply, *et al*., 2012). Although enteric glial cells (EGC) are central regulators of GI functions (Neunlist, *et al*., 2013), the postnatal evolution of their phenotype remains unknown.
AIMS&METHODS: We aimed to characterize 1) the postnatal evolution of EGC phenotype in the colon of rat pups 2) the impact of SCFAs upon their maturation and 3) the postnatal evolution of transcriptional networks involved in neuro-glial embryogenesis.
Enteric glial markers evolution, EGC proliferation and specific transcription factors evolution in colonic myenteric plexus of rat pups were assessed by immunohistochemistry and RT-qPCR betweeen 1 and 36 days after birth. Impact of butyrate on EGC phenotype and proliferation was analysed in EGC culture *in vitro* and by performing acute and chronic butyrate enemas *in vivo*.
RESULTS: In rat pups, we showed that mRNA and protein expressions of the glial markers GFAP and S100β strongly increased within five weeks after birth and the glial network appears fully organized by 36 days after birth. We showed that butyrate enemas significantly inhibited the proliferation of EGC both *in vivo* and *in vitro* but had no impact upon glial markers expression. Furthermore, we showed that transcription factors involved in the control of embryonic development of the ENS continued to be expressed after birth. Furthermore, PCA analysis showed that their global expression within the distal colon was characteristic of the stage of maturation.
CONCLUSION: These results demonstrate that the EGC network continues to set up after birth. The factors, in particular of nutritional origins, and the mechanisms responsible for EGC maturation *in vivo* remain to be identified.
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Keywords: butyrate, enteric glial cells, postnatal maturation

P592 MICROBIOTA ANALYSIS IN IBS AND IBD/NON-IBD PATIENTS AND NORMAL SUBJECTS

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INTRODUCTION: The increasing awareness of the gut microbiota's effect on our health has triggered the need for tools to monitor these microbes. The GA-map™ technology platform has been developed to demonstrate profiles of the composition of gut microbiota. The platform provides analysis of a large number of fecal samples in a rapid and cost-effective way. In a multi-center trial among patients diagnosed for IBS in Norwegian hospitals, fecal samples have been collected and compared to a population of normal subjects using GA microbiota test. In addition, a sub-cohort of IBD and non-IBD patients has been analyzed.
AIMS&METHODS: Based on peer-reviewed literature and our own research, special sets of DNA probes were designed to facilitate separation between patient groups and normal subjects based on their bacterial profile. The assay was tested in a population of 31 fecal samples from diagnosed IBS patients (confirmed by Rome III criteria and exclusion of inflammation by colonoscopy and/or calprotectin analysis) and a population of 78 normal subjects with no clinical signs of gut disorder (not confirmed by colonoscopy), in addition to 187 samples from the IBSEN II cohort, comprising treatment naïve IBD patients and symptomatic non-IBD patients, confirmed by colonoscopy (1, 2). The GA microbiota test was performed essentially as described in (3), using the BioCode-1000A system for detection and quantification of labeled DNA probes (indicative of presence of different bacteria). Classification was performed using Partial Least Squares Discriminant Analysis (PLS-DA) and the model was validated using leave-one-out validation. Further studies will be performed including independent patient populations.
RESULTS: The results from the studies are outlined in table 1. The results are preliminary and will be confirmed in further studies. Age-group of subjects ranged from 18 to 55 years.
Table 1. Results from GA microbiota PLS-DA analysis of diagnosed IBS patients vs normal subjects, and IBD vs non-IBD patients diagnosed by colonoscopy.

Cohort	N	Sensitivity*	Specificity*
IBS vs normal	31/78	87%	77%
IBD vs non-IBD	105/82	78%	70%

* Leave-one-out validation, not independent patient population
CONCLUSION: The GA microbiota test gives a unique opportunity to study specific profiles of the gut microbiota that may be associated with GI related disorders. The results suggest that the GA test may be a useful tool in differentiating between IBS and normal subjects, and IBD/non-IBD patients, and thus an aid in the diagnosis and follow up of patients with inflammatory and functional GI disorders.
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Disclosure of Interest: None Declared
Keywords: diagnostic, IBD, IBS, microbiota, non-IBD, PCR

P593 APPLICATION OF HUMAN ADULT STEM CELL BASED TISSUE ENGINEERING STRATEGY ON RECONSTRUCTION OF ORAL TISSUE

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INTRODUCTION: A defect in oral tissues is commonly affected by a number of clinical disorders in oral cavity. Studies had demonstrated that the bioengineered oral mucosa samples, such as collagen and gelatin, can develop a multilayer epithelium *in vitro* and *in vivo*. Resveratrol (RSV, trans-3, 4H, 5-trihydroxystilbene), a phytoalexin belongs to the group of compounds known as stilbenes

which has been studied for anti-oxidative, anti-proliferative activities and inhibition of nitric oxide pathway in mammalian macrophages, represents a feasible and productive approach to support dermal wound healing.

AIMS&METHODS: This study is going to combine the human adipose stem cells and resveratrol contained gelatin-collagen I (GCI) membrane for oral reconstruction and clinical application.

We evaluated the synergistic effect of human adipose tissue-derived stem cells and resveratrol contained collagen membrane as a novel substrate in oral tissue reconstruction. The physical characterization of GCI membrane and stem cells *in vitro* was done and rat *tongue defect model in vivo* was applied.

RESULTS: The scanning electron microscopic photos, RSV releasing test, immunofluorescence results, chemical staining indicated the excellent bio-characteristics of stem cells and resveratrol contained collagen biomaterials *in vitro*. The histological results *in vivo* also demonstrate some typical structures of native oral mucosa such as rete ridges and corial papillae re-growing under this model of tongue defected animals.

CONCLUSION: This study not only proved that stem cells and resveratrol contained collagen membrane can be a good bioengineering substrate for oral reconstruction but also produced a robust protocol for clinical application in the future.

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Disclosure of Interest: None Declared

Keywords: biomaterial, collagen, human adult stem cells (hASCs), oral mucosa tissue engineering, Resveratrol (RSV)

P594 EXTRACOLONIC SCREENING STRATEGIES IN HEREDITARY COLORECTAL CANCER SYNDROMES: PRELIMINARY DATA

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INTRODUCTION: The major hereditary colorectal cancer syndromes (HCCS), Lynch syndrome (LS), Familial Adenomatous polyposis (FAP) and its attenuated variant (Mutyh Polyposis, MAP) predispose apart from CRC, to early onset extracolonic malignancies (EC). A major concern for clinicians is the definition of surveillance programs for target organs. Few prospective studies are available and the optimal strategies, timing for surveillance, spectrum of EC associated remains to be defined.

AIMS&METHODS: Aims of the present study are: to define HCCS-associated EC; to evaluate the efficacy of prevention strategies in the affected.

From January 2010, patients (pts) who refer to the Cancer Family Clinic of Regina Elena National Cancer Institute, with a diagnosis of LS, FAP or MAP, are prospectively included in the study. FAP/MAP pts undergo: side viewing gastroscopy and videocapsule endoscopy (VCE) every 3 years by the age of 20; thyroid ultrasound (US) every year by the age of 15; abdominal TC or RMN every 3 years by 1 year after colectomy.

LS affected undergo by the age of 30: endoscopic upper US or abdominal TC for pancreato-biliary surveillance, urine cytology, dermatological screening, transvaginal US with endometrial sampling, breast US and mammography every year; gastroscopy and VCE every 3 years. We report an ''ad interim'' analysis of the data after 3 years of follow-up.

RESULTS: We recruited in the study 86 FAP (44M/42F), 17 MAP (11M/6F) and 71 LS (33M/38F). We did not detect any EC in MAP. In the 86 FAP pts we observed: 10 duodenal adenomas (11,6%); 3 jejunal adenomas (3,5%); 2 thyroid papillary cancer (PTC)(2,3%); 6 intrabdominal desmoid (ID) (6,9%), one of which was aggressive and required chemotherapy. In the 71 LS we detected: a cholangiocarcinoma, a ureteral carcinoma and a sebaceous skin carcinoma, These four cases carried a MSH2 gene mutation.

CONCLUSION: In our MAP series, so far we did not observe EC. In 2,3% of FAP we found PTC, vs 1-2% reported in other studies. Considering PTC detected in our series before 2010, the prevalence goes up to 4,6%. These data seem to justify US screening. Once a year appeared an adequate timing. 6,9% of FAP had ID, less than reported in FAP cancer registries studies (20%). In our LS series, we did not find any endometrial cancer, the second most common cancer of the syndrome. We observed EC only in MSH2 carriers. If these data will be confirmed on a larger series and longer surveillance, could justify a tailored and more intensive surveillance in MSH2 rather than MLH1 carriers.

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Disclosure of Interest: None Declared

Keywords: extracolonic cancer, hereditary colorectal cancer syndromes, surveillance

P595 LIVER TRANSPLANTATION IN ALCOHOLIC PATIENTS: IMPACT OF AN ALCOHOL ADDICTION UNITWITHIN A LIVER TRANSPLANT CENTER

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INTRODUCTION: Many concerns about liver transplantation in alcoholic patients are related to the riskof alcohol recidivism. Starting from 2002, an Alcohol Addiction Unit (AAU) was formed within theliver transplant center for the management of alcoholic patients affected by end-stage liver disease andincluded in the waiting list for transplantation. We evaluated retrospectively the impact of the AAU onalcohol recidivism after transplantation. The relationship between alcohol recidivism and the durationof alcohol abstinence before transplant was evaluated as well.

AIMS&METHODS: AIM: To evaluate the impact of the AAU inside the Liver Transplantation Centre on alcohol recidivism and mortality after OLT, using a retrospective design. **Methods:** Between 1995 and 2010, 92 cirrhotic alcoholic patients underwent liver transplantation. Clinical evaluation and management of alcohol use in these patients was provided by psychiatrists with expertise in addiction medicine not affiliated to the liver transplant center before 2002 (n = 37; group A), or by the clinical staff of the AAU within the liver transplant center starting from 2002 (n = 55; group B).

RESULTS: Comparing the two groups of patients, those followed by the AAU showed a significantly lower prevalence of alcohol recidivism (16.4% vs. 35.1%; p=0.038) after OLT. Patients followed by the AAU showed a significantly lower prevalence of death with respect of those patients who were not followed-up by the AAU (14.5% vs. 37.8%; p=0.01). There were no differences between the two groups regarding the mean age, mean MELD score, mean time of abstinence before OLT and mean alcohol intake. Analyzing the group of patients followed by AAU, there were no differences in term of alcohol recidivism after OLT (21.1% vs. 15.4%; p=0.623) between patients with an alcohol abstinence time pre-OLT >6 moths vs. <6 months.

CONCLUSION: The present study shows that the presence of an AAU inside a Liver Transplantation Center reduces the risk of alcohol recidivism and of mortality after OLT. Moreover, when clinical conditions do not allow a 6 months waiting time, the abstinence time before OLT could be shortened at least in selected patients managed by AAU.

Disclosure of Interest: None Declared

Keywords: Alcohol Addiction Unit, liver transplantation (LT).

P596 A SYMPTOM TRIGGERED CHLORDIAZEPOXIDE REGIMEN EMPOWERS STAFF AND SIGNIFICANTLY REDUCES ADMISSION DURATION FOR ALCOHOL WITHDRAWAL SYNDROME

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INTRODUCTION: The management of the Alcohol Withdrawal Syndrome (AWS) is often complex. At the Great Western Hospital Swindon we anecdotally noted a long length of stay for AWS and a significant number of adverse events (e.g. oversedation and aggression) relating to incorrect dosing. We hypothesised that this was due to the fixed dose regimen of withdrawal medication used within the trust, often written up by the most junior medical staff. We proposed a variable dose prescribing regimen based on the CIWA-Ad score[1] and the positive experiences of other centres in the region.

AIMS&METHODS: We undertook a retrospective casenote audit of patients with AWS presenting to the acute medical assessment unit over a 6 month period in 2011. We collected data on length of stay, length of detoxification regime, evidence of adverse events and correct prescribing of vitamin supplementation. We then undertook a programme of nursing and junior doctor education to promote the introduction of a symptom triggered chlordiazepoxide (CDP) dosing regimen in January 2012. This regimen was based on nursing staff assessing the CIWA-Ad score and administering a variable dose of CDP. A doctor was called only if the patient was not responding to treatment or excessively high doses of CDP were being administered. We reaudited the same outcomes over 3 months at the end of 2012. The patient populations in each study were broadly comparable.

RESULTS: In the initial analysis 36% of patients (n=103) had CDP prescribed at an efficacious starting dose. Mean length of stay was 15.1 days. Adverse events were reported in many cases. Prescribing of supplements was incorrect in half of patients. On reaudit (n=41) all patients had an efficacious starting dose of CDP prescribed. Mean length of stay had reduced to 10.9 days. Prescribing of supplements was correct in 80% of cases. On interviewing nursing and medical staff a significantly reduced number of patient adverse events were noted and staff felt empowered to provide individualised care to this vulnerable group of patients.

CONCLUSION: We conclude that a variable dose regimen for CDP prescribing is safe and leads to a significant reduction in admission duration at a cost saving to the NHS. We have also shown that this approach empowers staff, especially nursing colleagues, to take ownership of the management of AWS and ultimately reduces adverse events. This outcome was achieved by opportunistic education of fellow professionals and a drive to improve outcomes for this notoriously complex patient group. We propose that such a regimen be adopted as standard for the management of AWS across Europe[2].

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Disclosure of Interest: None Declared
Keywords: Alcohol, Alcohol withdrawal syndrome, Service Development

P597 POISONING MUSHROOMS INTOXICATION: EVALUATION OF LIVER TRANSPLANT SCORES

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INTRODUCTION: Intoxication by poisonous mushrooms (PM) is a potentially fatal entity and there is no consensus in the application of liver transplant (LT) scores.
AIMS&METHODS: Aims: The aim of this study was to evaluate the accuracy and precocity of the different LT scores in PM intoxication. **Methods:** Retrospective study of patients with PM intoxication diagnosis between January 1997 and December 2012. Accuracy and precocity have been assessed for the following LT criteria: King's College (KC), Clichy, Ganzert and Escudié.
RESULTS: The study focused on 22 patients (average ages: 50,8 ± 15,8 years old, extreme ages: 16 e 75 years old; 11 men), coming from 6 national districts, all of them during Autumn and 45% related among each other. The beginning of the symptoms (vomiting: 100%, diarrhea: 90% and abdominal pain: 68%) occurred, in average, 11 hours after CV ingestion, being the interval between ingestion and internment > 48h in 32% of cases. When admitted, 36% of patients already exhibited encephalopathy and 75% a V factor < 30%. There was ventilatory support need in 36% of patients and renal in 23%. 7 (58%) out of the 12 patients (55%) who fulfilled the KC criteria were transplanted. 7 patients died [mortality global rate: 32% (57% non transplanted, 43% transplanted)]. The evaluation of the different criteria on the 3rd day of evolution showed that Escudié's criteria had superior accuracy (100%) in the assessment of LT need comparing to the remaining ones (KC: 95%, Clichy: 91%, Ganzert: 86%).
CONCLUSION: 1. PM intoxication reveals a high parental and seasonal incidence (Autumn); **2.** The high mortality rate of this serie might be related with the delay in hospital admission; **3.** The combination of precocity and accuracy parameters recommends the usage of Escudié LT criteria within the PM intoxication context.
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Disclosure of Interest: None Declared
Keywords: Hepatotoxicity, Liver transplantation, Poisoning mushrooms

P598 EVALUATION OF OXIDATIVE STRESS LEVELS IN CHRONIC LIVER DISEASE

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INTRODUCTION: Evaluating oxidative stress levels is important in the diagnosis and treatment of chronic liver disease. Recently, a convenient measurement device for active oxygen and free radicals has become available, and this device is reportedly useful in various fields. In this study, we measured oxidative stress levels in chronic liver disease and compared the findings with biochemical test results.
AIMS&METHODS: Thirty-nine NAFLD patients (15 men, 24 women; mean age 51.3±14.8 years, range 24-76 years), 20 healthy subjects (10 men, 10 women; mean age 34.7±10.5 years, range 21-63 years), and 35 patients with chronic hepatitis (HCV) (15 men, 20 women; mean age 63.9±9.9 years, range 36-80 years) were included in the study. The NAFLD patients were further placed in separate SS and NASH groups based on histologic differential diagnosis. For measurement of oxidative stress levels, oxidative stress (d-ROM test; reactive oxygen metabolites, U.Carr), and antioxidant potential (biological antioxidant potential [BAP], μmol/L) were measured using an FRAS4 autoanalyzer (Wismerll, Italy).
RESULTS: d-ROM in the NAFLD (358.7±67.1), SS (354.7±55.8), NASH (360.1±58.9), and CHC (364.1±82.5) groups was significantly increased compared to that in healthy subjects (281.5±48.56) ($P<0.05$). BAP in the NAFLD (2107.7±201.4), SS (2109.5±125.3), NASH (2082.2±188.4), and CHC (2172.4±194.1) groups was not significantly different from that in healthy subjects (2109.5±125.3). The adjusted BAP/d-ROM ratio in the NAFLD (0.807±0.184), SS (0.809±0.184), NASH (0.784±0.132), and CHC (0.819±0.144) groups was significantly lower than that in healthy subjects (1.022±0.194) ($P<0.05$). d-ROM exhibited a significant correlation with γ-GTP ($r=0.499$, $P=0.0003$).
CONCLUSION: In patients with liver disease, oxidative stress levels were higher and antioxidant potential and potential antioxidant ability were lower than those in normal subjects. Oxidative stress levels did not significantly differ between SS and NASH. This finding suggests the presence of oxidative stress, similar to NASH, even at the stage of SS. Oxidative stress levels were correlated with γ-GTP. As a mechanism, γ-GTP is thought to be an enzyme involved in the conversion of oxidized glutathione (generated by oxidative stress) to reduced glutathione.
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The oxidative stress defense system can be conveniently evaluated in patients with liver disease.
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Disclosure of Interest: None Declared
Keywords: chronic liver disease, d-ROM test, oxidative stress

P599 BACLOFEN AS AN ADJUNCT PHARMACOTHERAPY FOR THE MAINTENANCE OF ABSTINENCE IN ALCOHOL DEPENDENT PATIENTS WITH ESTABLISHED LIVER DISEASE

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INTRODUCTION: It is axiomatic that effective treatment of patients with established ALD necessitates that patients achieve abstinence [1, 2] Pharmacotherapy for this indication is limited for this patients group, however Baclofen is one of a number of contemporary pharmacotherapies that have been shown to be safe, and effective in reducing craving[3] [4] and withdrawal symptoms[5]. To date, experimental research shows some promising results. However, there is a paucity of evidence for its effectiveness and tolerability in acute hospital and ambulatory settings.
AIMS&METHODS: AIM: The primary aim of this study was to measure the effectiveness of Baclofen in maintaining abstinence in patients with evidence of ALD.
An observational prospective clinical audit was performed to review the effectiveness of Baclofen. Patients with liver disease and concomitant alcohol use were commenced on Baclofen at 10mg TDS, and titrated according to tolerability and response up to 30mg TDS. The primary outcome measures were severity of physical dependence, as determined by Severity of Alcohol Dependence Questionnaire (SADQ score), days abstinent, and biochemical markers of liver function (GGT and ALT). These were compared at baseline, and 3 months.
RESULTS: Of the 75 patients commenced on Baclofen 57 (76%) remained on the treatment and returned for all follow-up sessions at 1 week, 2 weeks, 6 weeks and 3 months.
There was a significant reduction in alcohol consumption. ($P < 0.0001$ 95% CI for difference 20 to 26) with 49 of the 57 patients (93%) maintained total abstinence. There was a significant reduction in the presence of physical dependence ($Chi^2 = 0.5$ (1 DF) $P = 0.4795$) as measured by SADQ.
Data were available for 3 month post treatment GGT for 36 (63%) of the 57 patients. Paired t-tests on log transformed data identified a significant difference between GGT levels at baseline and at 3 month follow-up [$t(34)=3.625$, p.001].
CONCLUSION: Baclofen has a positive impact on alcohol consumption in this very difficult to treat, high risk patient group. Those patients who attended follow-up; adhered to the treatment regime and significantly decreased their alcohol consumption. There was also a significant improvement in liver biochemistry. These results are promising however a well-designed randomised control trial is needed to investigate the utility and efficacy of Baclofen in this patient group, and intitiate in acute hospital settings.
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Disclosure of Interest: None Declared
Keywords: Acute care, Alcohol and Liver disease, Baclofen

P600 AMINOPYRINE BREATH TEST AS A DIAGNOSTIC TOOL TO EVALUATE HEPATIC FUNCTIONAL RESERVE IN NEOPLASTIC PATIENTS RECEIVING HIGH DOSE CHEMOTHERAPY.

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INTRODUCTION: Liver toxicity is a frequent and serious complication of hematopoietic stem cell transplantation following high dose chemotherapeutic preparative regimens. Altered hepatic clearance may cause increased hepatic and non hepatic chemotherapy-induced toxicity. Common liver function tests do not reflect hepatic reserve function, therefore an additional diagnostic tool is needed. Aminopyrine breath test is a non invasive quantitative liver function test based on the hepatic clearance of a test substance. Its utility to assess liver function in patients with liver disease has been well documented.
AIMS&METHODS: We sought to determine hepatic functional reserve in patients with relapsed or refractory lymphomas and multiple myeloma undergoing high dose chemotherapeutic preparative regimens and hematopoietic stem cell transplantation.
From 2001 to 2013 we evaluated 227 consecutive patients with relapsed or refractory Hodgkin lymphoma, non-Hodgkin lymphoma and multiple myeloma who underwent aminopyrine breath test before initiation of high dose chemotherapy.

13-C aminopyrine (2 mg/kg) was administered at baseline and breath samples were collected every 15 minutes up to two hours after 13-C aminopyrine administration. Results were expressed as the cumulative percentage of administered dose of 13 C recovered at 120 min. Cut-off value of 3.5% was used for severe reduction of metabolism rate.
RESULTS: In 6 out of 227 (2.6%) patients the cumulative percentage of administered dose of 13-C recovered at 120 min was below 3.5 % showing severe reduction of metabolism rate.
CONCLUSION: We propose the aminopyrine breath test as a diagnostic tool to evaluate hepatic functional reserve in neoplastic patients undergoing high dose chemotherapy for appropriate chemotherapy regimens and dosing in order to prevent severe hepatic chemotherapy-related toxicity.
Disclosure of Interest: None Declared
Keywords: Aminopyrine breath test, Chemotherapy

P601 LOW FRUCTOSE DIET IMPROVES OUTCOME IN PATIENTS WITH SEVERE ALCOHOLIC LIVER DISEASE DURING FOLLOW UP IN AN OUTPATIENT CLINIC

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INTRODUCTION: Fructose is metabolized only in the liver. Fructose is firstly metabolized to fructose-1-P. This reaction is not regulated leading to uncontrollable degradation of fructose and severe depletion of ATP in the liver, when excess fructose is presented to the liver. Severe depletion of ATP is a characteristic finding in different types of acute liver failure.
AIMS&METHODS: We have since 2008 followed patients with severe alcoholic liver failure in an outpatient slinic after they have survived one episode of hepatic encephalopathy. They had open access to our stationary department and could be transported directly in the department day and night, if they experienced a new episode of encephalopathy. The patients were followed in the outpatient clinic with 2-8 week intervals. Different liver parameters and serum alcohol was measured at each visit and at acute admissions. The patients should abstain from alcohol. A diet low in fructose was introduced to all the patients in january 2011 both in the department and at home.
RESULTS: A total of 63 patients were included until may 2013 of which 19 died (age 35-75). Two patients were transplanted, 5 patients left the clinic, all still alive, Two patients died from cerebrovascular events and not from liver related disease. Intermittently positive serum alcohol was recorded at controls in 9patients but not in any of the patients at acute admissions.

Year	new patients	non surviving	surviving (cummulative)
2008	13	1	12
2009	10	8	14
2010	10	7	17
2011	9	0	26
2012	14	3	35
2013	7	0	42

Mortality First 3 years against 3 last years significant different p=0,001 (Fisheŕs test)
CONCLUSION: A diet low in fructose improves outcome in a group of patients with severe alcoholic liver disease during a 2,5 year period compared with a similar group of patients not treated with fructose restriction durign the preceeding 3 years.
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Disclosure of Interest: None Declared
Keywords: ALCOHOLIC LIVER DISEASE, low fructose diet

P603 PREDICTORS OF QUALITY OF LIFE IN PATIENTS WITH CHRONIC LIVER DISEASE

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INTRODUCTION: Undoubtedly proven that patients with Chronic liver disease (CLD) have impaired Health related quality of life (HRQoL). However, the relative contribution of sociodemographic, clinical and behavioral factors in the reduction of HRQoL, has not been fully elucidated.
AIMS&METHODS: The aim of our study was to evaluate the effect sociodemographic, clinical and behavioral characteristics in patients with CLD, as predictors of physical (PCS) and mental component of HRQoL (MCS).We performed a cross sectional study. As a HRQoL questionnaire was used Short Form Health Survay-36 (SF-36). For psychometric assessment we used: Hamilton depression rating scale, Hamilton anxiety rating scale and Fatigue severity scale. An individual effect of variables on the quality of life was assessed by univariate and multivariate regression analysis, adjusted for potential confounding factors. Hierarchical multiple regression analysis was conducted to identify predictors of HRQoL, separately for PCS and MCS as outcome variables.
RESULTS: The study included 103 patients with CLD, average age 53.8±12.9 years.The average values of the total SF-36 scores were 52.6±20.4. The mean score of the composite scores were 49.8±21.3 for the PCS, and 53.5±19.6 for the MCS. Sociodemographic variables (gender, age, employment) explained 16.7% of the variance ($p<.01$) of the PCS as outcome measure. Addition of the variables Depression and anxiety in the second model caused an increase of 26.7% in the variance explained ($p<.01$). After adding the Fatigue in the third block an additional 16.7% of the variance in PCS was explained ($p<.01$). The final model explained 60.1% of the variance in PCS ($p<.01$). The results in the final block have shown that employment (B=8.64±4.09, $\beta=.18$, $p<.05$), depression (B=-1.02±.27, $\beta=-.45$, $p<.01$) and fatigue (B=-4.82±.77, $\beta=.47$, $p<.01$) significantly influenced PCS. With MCS as dependent variable, sociodemographic variables explained 6.0% of the variance in the outcome variable ($p<.01$). Depression and anxiety explained additional 39.1%, while Fatigue accounted an additional 10.7% of the variance in MCS ($p<.05$). The final model explained 55.8% of the variance in MCS ($p<.01$). Among all investigated variables statistically significant impact on mental component of quality of life was observed only for depression (B=-1.04±.26, $\beta=-.49$, $p<.05$) and fatigue (B=-3.56±.75, $\beta=-.38$, $p<.01$).
CONCLUSION: Depression and fatigue are negative predictors of physical and mental components of quality of life, while employment has a positive predictive significance only for the physical components of quality of life, in patients with CLD.
Disclosure of Interest: None Declared
Keywords: chronic liver disease, quality of life

P604 ASSOCIATION BETWEEN SINGLE NUCLEOTIDE POLYMORPHISM OF INTERLEUKIN-21 GENE AND CHRONIC HEPATITIS B VIRUS INFECTION IN A CHINESE POPULATION

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INTRODUCTION: Previous studies have revealed that three SNPs (rs13143866, rs2221903 and rs907715) in IL-21 gene were associated with autoimmune disease among both Asian and non-Asian populations; however, these associations have not been evaluated in chronic HBV infection diseases yet.
AIMS&METHODS: The aim of this study was to examine the association of SNPs in IL-21 gene with susceptibility to chronic HBV infection in a Chinese population. Chronic HBV infected patients and healthy controls were from the First Affiliated Hospital of Sun Yat-sen University from Jun 2011 to October 2012. Three SNPs (rs13143866, rs2221903 and rs907715) within the IL-21 gene intronic region were genotyped by SNaPshot SNP technique.
RESULTS: (1) A total of 303 independent chronic HBV infected patients and 208 unrelated healthy controls were recruited for the case–control association study. (2) There were no significant differences in the frequencies of all alleles and genotypes (rs13143866, rs2221903 and rs907715) between chronic HBV infection group and control group (P=0.417, 0.126, 0.870 for alleles, P=0.399, 0.285, 0.120 for genotypes). (3) According to the existence of hepatocellular carcinoma (HCC), the chronic HBV infection group was divided into HCC group (n=94) and non-HCC group (n=209), unfortunately, no significant differences were found in the frequencies of all alleles and genotypes between HCC group and non-HCC group (P=0.199, 0.307, 0.979 for alleles, P=0.307, 0.571, 0.208 for genotypes). (4) In subgroup analysis, non-HCC group was classified into three clinical subsets, chronic hepatitis B (CHB) (n=76), HBV carrier (n=101), and HBV related cirrhosis (n=32). no significant differences were found in the frequencies of all alleles and genotypes among all groups (P=0.506, 0.313, 0.965 for alleles,, P=0.319, 0.097, 0.510 for genotypes). (5) When compared to the healthy controls, the effect of recessive model (AA versus GG+GA, OR (95%CI)=0.154 (0.030~0.776) was observed in HBV carrier group. (6) Distributions of allele and genotype frequencies of the SNPs rs907715 and rs2221903 showed no significant differences among all groups. (7) In haplotype analysis, although no haplotype was found to be associated with chronic HBV infection, our study found the ATA and GTA haplotypes (rs13143866, rs2221903 and rs907715) tended to be associated with HBV-related HCC (P=0.070, 0.104, respectively).
CONCLUSION: Our study demonstrate that the allele G of rs13143866 may be a protective factor for chronic HBV infection. However, further studies are needed to determine the associations and functional consequences of these polymorphisms with chronic HBV infection susceptibility.
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Disclosure of Interest: None Declared
Keywords: chronic hepatitis B virus infection, IL-21 gene, Single-nucleotide polymorphism

P605 THE RATIOS OF PRO TO ANTICOAGULANT FACTORS: INDEX OF HEMOSTATIC IMBALANCE IN CIRRHOTIC PATIENTS

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INTRODUCTION: Patients with cirrhosis are characterized by decreased levels of most of pro- and anti-coagulant factors. This state results in an unstable balance. Therefore, patients are prone to hemorrhagic or thromboembolic events particularly in advanced stages. The aim of this study was to evaluate the ratios of pro coagulant to inhibitor coagulation factors in cirrhotic patients according to disease severity
AIMS&METHODS: A case control study including cirrhotic patients and healthy subjects matched by age and sex was conducted. Patients were stratified according to Child Pugh classification. Pro coagulant factor activity (factor VII, II, V, VIII, XII) and inhibitor factor activity were determined (Protein C, protein S and ant thrombin). Mean value of pro coagulant to inhibitor coagulation factor ratios in patients were compared to those in controls and investigated in patients according to Child Pugh classification.

RESULTS: 51 cirrhotic patients and 51 controls were included. Their mean age was 56.8 years. Sex ratio (men to female) was 0.9. Patients were classified in Child Pugh A in 13 patients (25.5%), B in 23 patients (45.1%), C in 15 patients (29.4%). Among ratios, II/PC, V/PC, VII/PC, XII/PC were significantly higher in cirrhotic patients than in controls (respectively, p=0.001, p=0.002, p=0.001, p=0.001) but there wasn't any difference between Child Pugh classes. Likewise, VIII/PC, VIII/PS and VIII/AT were significantly higher in cirrhotic patients than in controls ($p<0.001$) and increased significantly from class A to C ($p<0.001$), reaching a value of 5. On the other hand, II/PS was lower in cirrhotic patients than in controls showing marginal significance (p=0.04). However, II/PS, V/PS, VII/PS decreased significantly from class A to C (p=0.006, p=0.013, p=0.002, p=0.024).
CONCLUSION: The ratios of pro- to anti-coagulant factors showed a coagulation imbalance in our patients with trend to hypercoagulabilty state. This hemostatic change was significantly correlated with severity of cirrhosis.
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Disclosure of Interest: None Declared
Keywords: CIRRHOSIS, hemostasis

P606 ROSUVASTATIN HAD THE INHIBITED EFFECT OF LIVER FIBROSIS AND PRENEOPLASTIC LESION IN RAT LIVER CIRRHOSIS MODEL

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INTRODUCTION: Non-alcoholic steatohepatitis(NASH) may progress to advanced liver fibrosis and ultimately to hepatocellular carcinoma. Hyperlipidemia is known to enhance the risk of fatty liver and carcinogenesis, which is associated with hydroxyl radical formation. The HMG-CoA reductase inhibitor(Rosuvastatin) has greater lipid-lowering efficacy than any of the other statins.
AIMS&METHODS: The aim of this study was to investigate whether Rosuvastatin has the effect of inhibiting liver fibrosis as well as the development of preneoplastic lesions.We were examined using the choline-deficient L-amino acid-defined(CDAA) diet-induced liver fibrosis model.The total study periods were 12 and 16 weeks. Rosuvastatin in powder was mixed into the CDAA diet at concentrations of 5.0% (w/w). One group was CDAA diet containing Rosuvastatin, the other group was CDAA diet without Rosuvastatin. Liver fibrosis was analyzed with Azan, Sirus–red, aSMA, TGFb expression, hydroxyproline level. The enzyme-altered lesion was analyzed with Glutathione S-transferase placental form (GST-P) expression. The change of laboratory data was analyzed. Type I procollagen, TIMP-1, 2 TGFb mRNA expression was analyzed by real time-PCR system and many gene expression in liver by DNA array. We analyzed the expression of IL-1b,2,4,6,10,MCP1,TNFa,CRP,TGFb,ACRP30,PDGFb in liver.
RESULTS: After 16 weeks, Rosuvastatin prevented fibrosis in a dose-dependent manner by Azan, Sirius Red, aSMA, TGFb expression ($p<0.05$). Hydrocyproline level in liver was decreased (mean value:CDAA+Rosuvastatin 4.4 vs CDAA only 12.1 umol/Wg $P<0.05$). Rosuvastatin reduced the area of preneoplastic lesions in the liver by GST-P stain ($p<0.01$). Administration of Rosuvastatin significantly reduced serum alanine aminotransferase (AST) (mean value: CDAA+Rosuvastatin 460.4 vs CDAA only 548.0 IU/l $P<0.05$), Albumin(mean value:CDAA+Rosuvastatin 3.80 vs CDAA only 2.52 g/dl $P<0.01$), Hyaluronic acid (mean value:CDAA+ Rosuvastatin 86.8 vs CDAA only 181.4 ng/ml $P<0.01$). Rosuvastatin significantly inhibited Type 1 procollagen, TIMP-1, 2,and TGFb mRNA expression (all of $P<0.01$). The Rosuvastatin treated groups decreased the level of IL-4,IL-6,TNFa, TGFb and increased the level of IL-10,IFNγ.
CONCLUSION: Our results show that Rosuvastatin inhibited liver fibrosis as well as preneoplastic lesions. These results suggested that Rosuvastatin will be the new drug for liver fibrosis in NASH
Disclosure of Interest: None Declared
Keywords: hepatic fibrosis, liver fibrosis, nafld, NASH

P608 ARTIFICIAL NEURONAL NETWORKS IN DIAGNOSIS AND PROGNOSIS OF LIVER CIRRHOSIS

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INTRODUCTION: The prognosis cirrhosis is determined by the presence portal hypertension (PHT) that is best evaluated by hepatic venous pressure gradient (HVPG). Recently, non-invasive methods were proposed to evaluate PHT. The aim of this study was to create a new model using artificial neural networks (ANNs) and to compare-it with other non-invasive tests and HVPG for diagnosis of clinical significant portal hypertension (CSPHT) (HVPG > 10 mmHg) and esophageal varices (EV).
AIMS&METHODS: One hundred seven cirrhotic patients were included to create and validate the ANNs: 82 patients in the ANNs training group and 25 patients for validation of this model. The ANNs training have been performed using MATALB (The MathWorks Inc., USA) software. Only the variables correlated with HVPG were included in the ANN (age, albumin, platelets count, bilirubin, prothrombin index and liver stiffness (LS)). Two ANNs were created: one for predicting CSPH and one for presence of EV. All patients underwent HVPG measurement, serological test (AST/ALT index, APRI, Lok, FIB-4, GUCI, Risk score) and LS measurement. All patients from validation group were follow-up for 2 year or until decompensation.
RESULTS: The ANN was able to predict CSPH with Se=100%, Sp=83.3%, PPV=94.7%, NPV=100% and AUROC=0.97 (p=0.001). These performances were superior to all serum scores but slightly inferior to LS. For EV presence, ANN had Se=100%, Sp=75%, PPV=95.4%, NPV=100% and AUROC=0.87 (p=0.02), inferior only to HVPG, LS and Lok score. During the follow-up, 13 patients (52%) experienced at least one clinical complication within a mean period of 403 days. The ANNs performance to predict clinical decompensation was modest, AUROC=0.605 (p=0.38). None of the non-invasive tests reached statistical significance in decompensation prediction.
CONCLUSION: ANNs may be useful in diagnosis of CSPH or EV but the prognostic relevance is modest.
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Disclosure of Interest: None Declared
Keywords: artificial neuronal networks, HVPG, liver stiffness measurement, non-invasive tests, portal hypertension

P609 COMPARISON OF RIFAXIMIN AND CONVENTIONAL ORAL THERAPY FOR THE TREATMENT OF HEPATIC ENCEPHALOPATHY: A META-ANALYSIS

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INTRODUCTION: Hepatic encephalopathy is a serious neuropsychiatric condition occurring in patients with liver disease. The efficacy of rifaximin is well documented in the treatment of acute hepatic encephalopathy, but its efficacy for prevention of the disease has not been established. This meta-analysis aims to review data concerning the efficacy and safety of Rifaximin in comparison to conventional oral therapy in the treatment of cirrhotic patients with hepatic encephalopathy.
AIMS&METHODS: We performed a systematic review and random effects meta-analysis of all eligible trials identified through electronic and manual searches. Two authors independently assessed trial quality and extracted data. Four randomized controlled trials met the inclusion criteria with a total of 236 patients. Statistical analyses were performed using the random effects model and the results expressed as weighted mean difference for continuous data with 95% confidence intervals. Heterogeneity was measured using the Chi-square and I statistic.
RESULTS: The effectiveness of Rifaximin in terms of changes in hepatic encephalopathy index was equivalent to oral disscharides and oral antibiotics [odds ratio 1.02; 95% CI: 0.48-2.18] as well as to change in mental status [odds ratio 0.91; 95% CI 0.18-4.68]. Rifaximin also showed lower serum ammonia levels [weighted mean difference= -34.93; 95%CI -39.41- -30.95; P = <.00001] and less asterixis [WMD = -0.06; 95% CI -0.22 - 0.10; P = 0.38]. Rifaximin was well tolerated with few side effects.
CONCLUSION: Rifaximin is somewhat equivalent to non-absorbable disaccharides or antibiotics for treatment of hepatic encephalopathy. Adverse effects of rifaximin were mostly minor gastrointestinal complaints. Moreover, no significant difference was found between rifaximin and oral conventional therapy in terms of their efficacies.
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5. Javier A. Adachi1,2 and Herbert L. DuPont2,3 Rifaximin: A Novel Nonabsorbed Rifamycin for Gastrointestinal Disorders 1Department of Infectious Diseases, Infection Control and Employee Health, MD Anderson Cancer Center, and 2Center for Infectious Diseases, Houston School of Public Health and Medical School, University of Texas, and 3St. Luke's Episcopal Hospital and Baylor College of Medicine, Houston, Texas
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Keywords: hepatic encephalopathy, oral antibiotics, oral dissacharides, Rifaximin

P610 NONINVASIVE PREDICTORS OF HIGH-RISK VARICES IN CHRONIC LIVER DISEASE PATIENTS

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INTRODUCTION: Esophageal varices (EV) are a major complication of portal hypertension in chronic liver disease patients. Follow-up of cirrhotics by

periodical upper GI endoscopy can be quite costly and poorly accepted by patients. In this setting we need to identify noninvasive models to predict the presence of high-risk varices (large varices and varices with red marks).
AIMS&METHODS: We retrospectively studied 104 patients with chronic liver disease (hepatitis or cirrhosis) of various etiologies (viral, ethanolic, autoimmune, drug-induced) admitted to out unit in 2012. Clinical, biological, ultrasonographic and endoscopic data were collected from their charts and used to calculate the APRI (AST to platelets ratio index), ASPRI (age-spleen-platelets ratio index) and SPRI (spleen to platelets ratio index) scores. The diagnostic performance of these scores was evaluated by the area under the receiver operating characteristic curve (AUROC).
RESULTS: Of the 104 patients (62.5% males, mean age 62 years), 83 (79.80%) were cirrhotic. On EGD, 25% were without EV, 55.77% had small varices (Paquet I-II) and 19.23% had large varices (Paquet III-IV). Portal vein, splenic vein and spleen diameter were significantly higher in patients with large varices than those with small or no varices, while platelet count was significantly lower. APRI, ASPRI and SPRI scores were good predictors for the presence of large varices on endoscopy (AUROC 0.652, 0.703 and 0.702 respectively). The three scores performed even better when predicting both large varices or small varices with red marks (AUROC 0.758, 0.806 and 0.803). They also had good accuracy for predicting gastric varices (AUROC 0.676, 0.711 and 0.719).
CONCLUSION: These simple non-invasive scores can accurately predict high-risk esophageal varices in liver disease patients, targeting those who need to undergo EGD and prophylactic treatment.
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Disclosure of Interest: None Declared
Keywords: CIRRHOSIS, non-invasive, PREDICTORS, Varices

P611 GUT MICROBIOTA PLAYS A PIVOTAL ROLE IN THE DEVELOPMENT OF SPONTANEOUS BACTERIAL PERITONITIS IN LIVER CIRRHOTIC PATIENTS

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INTRODUCTION: The impairment of gut barrier and microbial translocation are frequent in liver cirrhotic patients, predisposing to infectious complications such as spontaneous bacterial peritonitis (SBP). Little is known about the role of SIBO in SBP development.
AIMS&METHODS: To investigate the relationship between SIBO, IP and the development of SBP in liver cirrhotic patients.
31 patients were enrolled in this study (10 Child A, 10 Child B and 11 Child C; mean age 60 years, all viral etiology or previous alcohol abuse). SIBO was diagnosed by glucose-hydrogen breath test. IP was evaluated by the (51)Cr-EDTA test (Cr excreted in urine, UCr); UCr higher than 3% indicated increased IP. Statistical analysis was performed using chi-squared test, t-test, ANOVA and cluster analysis.
RESULTS: IP was increased in all patients: mean UCr was 4+3% for Child A , 4+2% for Child B and 5+3% for Child C patients (p=0.607). SIBO was diagnosed in 4/10 (40%) patients with Child A, 7/10 (70%) Child B, 9/11 (82%) Child C (p=0.123); 4/10 (40%) Child B and 8/11 (73%) Child C patients had at least one episode of SBP (p=0.130). Therefore among patients who presented with ascites, 16/21 (76%) also presented with SIBO, which was significantly associated with at least one episode of SBP (p=0.05). According to UCr, two subgroups could be identified: G1 (no SIBO, mean UCr 3+2%) and G2 (SIBO, mean UCr 5+2%). 92% of patients with at least one episode of SBP belonged to the group 2 (p=0.05). Notably no difference in IP was found between patients with and without SBP if the presence of SIBO was not considered (mean Ucr 4.5+3% and 4.5+2%, respectively).
CONCLUSION: Increased IP "per se" is not the only determinant of SBP development, which is rather more frequent in cirrhotic patients with SIBO.
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Disclosure of Interest: F. R. Ponziani : No Conflict of Interest to declare, E. Scarpellini : No Conflict of Interest to declare, A. Tortora : No Conflict of Interest to declare, M. Gabrielli : No Conflict of Interest to declare, M. E. Ainora : No Conflict of Interest to declare, F. Mangiola : No Conflict of Interest to declare, G. Gasbarrini : No Conflict of Interest to declare, V. Valenza : No Conflict of Interest to declare, C. Balsano : No Conflict of Interest to declare, A. Gasbarrini : No Conflict of Interest to declare
Keywords: intestinal permeability, liver cirrhosis, small intestinal bacterial overgrowth (SIBO), spontaneous bacterial peritonitis

P612 LIVER STIFFNESS MEASUREMENT PREDICTS THE PRESENCE OF LARGE OESOPHAGEAL VARICES IN PATIENTS WITH CHRONIC LIVER DISEASES

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INTRODUCTION: One of the most serious complications of liver cirrhosis is the variceal bleeding. The early recognition of the oesophageal varices is of primary importance in the prevention of their bleeding. Liver stiffness (LS) measured by transient elastometry (FibroScan) may associate with portal pressure and could predict the presence of oesophageal varices.
AIMS&METHODS: We studied the diagnostic accuracy of LS by FibroScan for selecting patients at risk of bearing large oesophageal varices and high risk (Paquet =>II grade) of bleeding. We performed oesohago-gastro-bulboscopy and FibroScan examination in 74 patients with chronic liver disease simultaneously. We examined the relation between the presence of oesophageal varices (Paquet grade 0-IV) and the LS (kPa) as well as the blood hematological and biochemical laboratory parameters (INR, platelet count, ALT, AST, albumin). We analysed the predictive role of LS by FibroScan for selecting patients at high risk of variceal bleeding (Paquet =>II).
RESULTS: LS values correlated to the grade of oesophageal varices (Paquet–grade) r= 0,67, p<0,0001. The LS value was highly predicitve of the presence of oesophageal varices (AUROC:0,885, 95% CI: 0,81-0,96) and allowed to predict the high grade varices (Pq=>II) (AUROC: 0,85, 95% CI: 0,754-0,94). We found high measurement sensitivity: (sens) 85 %, specificity (spec): 87%, positive predictive value (PPV): 85%, negative predictive value (NPV):87% and validity: 86% at the cutoff 19,2 kPa LS value. LS measurement value <19,2 kPa was highly predicitive of the absence of oesophageal varices grade =>II (sens.: 95%, spec.: 70%, PPV:54%, NPV: 97%), thus we verified that below LS 19,2 kPa the high grade of oesophageal varices (Pq=>II) is not probable. The laboratory parameters did not predict oesophageal varices.
CONCLUSION: The non-invasive LS measurement by FibroScan may select patients who are at high risk of bearing large oesophageal varices (Paquet =>II) and variceal bleeding and need endoscopic screening. LS above 19,2 kPa indicates an oesophageal-gastro-buboscopy for the judgement of varices.
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Disclosure of Interest: None Declared
Keywords: liver stiffness measurement, oesophageal varices

P613 NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS BY REAL-TIME SUPERSONIC SHEAR WAVE ELASTOGRAPHY (SWE™) IN PATIENTS WITH CHRONIC VIRAL HEPATITIS

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INTRODUCTION: Supersonic Shear wave elastography (SWE™) is new quantitative real-time ultrasound based elastography method for non-invasive assessment of liver fibrosis (LF) with only preliminary results on its clinical performance published so far.
AIMS&METHODS: To investigate if it was possible to distinguish between the LF stages by using SWE in pts with CVH. Naive fasting CVH pts underwent SWE of the liver (SWEL) on Aixplorer® Ultrasound system (SuperSonic Imagine), by right intercoastal approach following expiration, with 5 measurement performed per patient. Patients with ALT values >3x ULN, cholestasis and liver congestion were not included in the study. The result were expressed in kPa as the average of 5 measurements and compared to LF stage as assessed by liver biopsy (LB). The LF was classified as mild (Ishak stages F0-2), moderate (F3-4) or severe (F5-6, i.e. compensated cirrhosis). In a subgroup of patients with decompesated cirrhosis the diagnosis relied upon clinical, biochemical, ultrasound and endoscopic criteria and these pts were analysed separatelly.
RESULTS: Out of 105 pts with CVH B (N=24) and C (N=81) SWEL was succesfully performed in 82 pts (failure rate 22%). Liver stiffness (LS) as assessed by SWE was signifficantlly different between the pts with mild, moderate and severe LF: 6,3 *vs* 10,0 *vs* 16,2 kPa respectivelly (p<0,001). Cut-off values for Ishak F≥3 and F≥5 were 8,1 (sens. 95,5%, specif. 100%, AUC 0,993) and 11 kPa (sens. 87%, specif. 92,7%, AUC 0,955). LS was significantlly different between the pts with compensated (Ishak F5-6) and decompensated cirrhosis (16,2 *vs* 33,7 kPa, p<0,001; cut-off 25,2, sens. 88,9%, specif. 95,7%, AUC 0,953). In 46 pts spleen stiffness (SS) was also assessed by SWE and signifficant difference was observed between the non-cirrhotic LF stages (F0-4) and compensated cirrhosis (F5-6) (21,2 *vs* 26,7 kPa, p=0,001; cut-off 24 kPa, sens.66,7% specif. 85%, AUC 0,795) as well as compensated *vs* decompensated cirrhosis (26,7 *vs* 37,0 kPa, p=0,001; cut-off 38kPa, sens. 54,6%, specif. 100%, AUC 0,845).
CONCLUSION: The performance of Supersonic SWE™ for non-invasive assesment of LF in CVH pts was excellent especially for differentiation between the mild and more advanced stages of LF. Both LS and SS were significantly different between compensated cirrosis and non-cirrhotic stages of LF, as well as between compensated and decompensated cirrhosis with better performance of liver SWE.
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Disclosure of Interest: None Declared
Keywords: elastography, liver fibrosis

P614 DO ENDOSONOGRAPHY FINDINGS PREDICT VARICEAL RECURRENCE AFTER ENDOSCOPIC BAND LIGATION?

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INTRODUCTION: Endoscopic band ligation (EBL) has a considerable tendency of variceal recurrence.
AIMS&METHODS: The aim was to analyse the value of esophageal collateral veins (ECV) evaluated on endosonography (ES) as predictors for variceal recurrence after EBL.
31 patient with large esophageal varices and EBL indicated was enrolled in prospective study. ES was performed before EBL and ECV were classified into 3 types (peri-ECV, para-ECV and perforator) and 2 grades - mild (peri-ECV <2mm; para-ECV <5mm) and severe (peri-ECV ≥2mm and para-ECV ≥5mm). EBL was repeated every 2 weeks until varices were obliterated and

endoscopy was repeated every 3 month for 1 year period to detect recurrence - reappearance of any form of varices or red-color signs. Relationship between ES findings and variceal recurrence was analysed. Quantitative results are presented as mean±SD. Student's t-test for unpaired data was used. Qualitative data were analysed by the chi-square test. A p value <0,05 was considered significant.
RESULTS: From September 2011 to January 2013 31 patient (21 men (67,7%); average age 53,6 ±8,9 years) was enrolled in the study. To this day 31 patient was being followed for 3 months, 22 – for 6 months, 21 – for 9 months and 16 - for 1 year. Recurrence of varices was detected in 16,1% of patients within 3 months, in 36,6 % of patients within 6 months and in 75% of patients within 1 year. Patients, followed for a year, were divided into recurrent (n=12) and non-recurrent (n=4) groups. Mean diameter of peri-ECV in the recurrent group was 2,42±0,37 mm (75% severe and 25% mild) and in the non-recurrent group - 2,34±1,16 mm (50% severe and 50% mild) (p=0,8). Mean diameter of para-ECV in recurrent group was 3,76±1,75 mm (33% severe and 67% mild) and in non-recurrent group - 4,2±1,09 mm (100% mild) (p=0,5). Perforators were detected in 58% of patients in the recurrent group and in 50% of patients in the non-recurrent group (p=0,5). Further, the recurrent group was divided into early recurrent (≤ 6 months (n=8)) and late recurrent (> 6 months (n=4)) groups. No significant difference (p>0,05) regarding ECV type and grade was found between the early and the late recurrent groups. Regarding clinical characteristics only spleen diameter had a statistically significant difference between these groups (p= 0,012). Mathematical cox proportional hazards model of data found that severe peri-ECV are associated with higher and earlier recurrence risk after EBL (hazard ratio 1,57), but in our small sample size did not reach statistically significant difference.
CONCLUSION: Our study showed that ES findings do not predict variceal recurrence after EBL.
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Disclosure of Interest: None Declared
Keywords: endoscopic band ligation, endosonography, esophageal varices, variceal recurrence

P615 DIAGNOSTIC VALUE OF SECONDARY HYPERALDOSTERONISM IN DEVELOPMENT OF RESISTANCE TO NONSELECTIVE BETA-BLOCKERS(BB) PORTAL HYPERTENSION(PH) WITH CIRRHOSIS

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INTRODUCTION: Diagnostic value of secondary hyperaldosteronism in development of RESISTANCE TO NONSELECTIVE BETA-BLOCKERS(BB) PORTAL HYPERTENSION(PH) WITH CIRRHOSIS
AIMS&METHODS: Aim: To study the influence of activity RAAS on the hemodynamic response to BB of PH in patients with cirrhosis.
Methods: 32 patients with cirrhosis (mean age 56 ±3,0) were studied. All patients were divided into two groups: the 1st group (n = 18) were administered with propronolol 40 mg titrated up, the 2nd group (n = 14) were administered with propronolol +spironolactone 100 mg. There were no significant differences on a degree of Child-Pugh in both groups (mean score 6,9). Hepatic venous pressure gradient (HVPG), renin and aldosteron plasma levels were measured before and after 4 weeks of treatment.
RESULTS: Propronolol significant reduced HVPG at 10 patients 1st group (15,1±14,6 %,p=0,04). 8 patients 1st group were resistance to propronolol(mean change of HVPG−1.7 ± 2.4 mm Hg).Aldosteron and renin plasma levels a prior to the beginning of therapy was significant above (p=0,047) in the resistance BB group. There was a significant reduction in the HVPG in the propronolol + spironolactone group (−5.7 ± 3.9 mm Hg; p=0,02) as compared to the 1st group. 11 of 14 patients 2nd group significant reduced HVPG (p=0,003). 3 patients were resistance to BB and had aldosteron plasma levels exceeded norm in 2 times. At an estimation of interrelation between aldosteron plasma levels and a negative effect of therapy propronolol with method ROC- analysis, taps relative risk of a negative effect of therapy at patients with aldosteron plasma levels from 300 ng/ml and more = 1,75 (1,03-2,95; 95%DI), p=0,03 (sensitivity of 85,7 % and specificity of 55,6 % (AUCROC=0,651; p=0,1).
CONCLUSION: In the study of resistance BB of portal hypertension should be screened for the main parameters of the renin-angiotensin-aldosterone system. Patients with initially high levels of aldosterone, regardless of the presence of ascites to the treatment of portal hypertension should be added aldosterone antagonists.
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Disclosure of Interest: None Declared
Keywords: beta- Blocker, cirrhosis, aldosteron, portal hypertention

P616 BODY MASS INDEX (BMI) AND NUTRITIONAL RISK INDEX (INR): HOW USEFUL ARE FOR ASSESSING THE NUTRITIONAL STATUS IN PATIENTS WITH CHRONIC LIVER DISEASE?

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INTRODUCTION: There is no consensus regarding the parameters that we should consider for assessing the nutritional status in patients with chronic hepatitis or cirrhosis.
AIMS&METHODS: AIM: to evaluate the parameters used in general population for assessing nutritional status in patients with chronic hepatitis or cirrhosis of different ethiologies.
METHODS:
We used the data of a prospectiv study performed in our department on 98 consecutive patients with chronic liver disease, in which we evaluated the nutritional status using 2 questionnaires: Subjective Global Assessment (SGA) and Mini-Nutritional Assessment (MNA). For every patient we calculated the body mass index (BMI) and we evaluated the nutritional status using nutritional risk index (INR).
RESULTS: RESULTS:
Using the combined value of the 2 tests (SGA and MNA) we obtained the following results: 10/64 (15.6%) were malnourished, 24/64 (37.5%) had malnutrition risk and 30/64 (46.9%) had normal nutritional status. We considered these 2 tests as the standard in diagnosing malnutrition and we evaluated the other 2 parameters: BMI and INR. For BMI we obtained 88.4% sensibility, 33.3% specificity, 85.1% positive predictive value, 40% negative predictive value, with 0.781 accuracy in diagnosing malnutrition. Using INR we obtained 61.5% sensibility, 33.3% specificity, 80% positive predictive value, 16.6% negative predictive value, with 0.562 accuracy in determining the correct nutritional status.
CONCLUSION: CONCLUSIONS: Using BMI and INR we can identify the cases of malnutrition with a good sensibility (60-90%), but they have a poor negative predictive value (16-40%), especially because of the presence of ascites, edemas and hypoalbuminemia which are modifing these 2 parameters.
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Disclosure of Interest: None Declared
Keywords: cirrhosis , malnutrition

P617 PROCALCITONIN AND MACROPHAGE INFLAMMATORY PROTEIN-1 BETA (MIP-1BETA) IN SERUM AND PERITONEAL FLUID OF PATIENTS WITH DECOMPENSATED CIRRHOSIS AND SPONTANEOUS BACTERIAL PERITONITIS

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INTRODUCTION: Spontaneous bacterial peritonitis (SBP) is the most frequent infection in patients with cirrhosis causing significant mortality which requires rapid recognition for effective antibiotic therapy, whereas ascitic fluid cultures are frequently negative.
AIMS&METHODS: The aim of this study was to evaluate the SBP diagnostic efficacy of procalcitonin (PCT) and macrophage inflammatory protein-1 beta (MIP-1b) measured in serum and peritoneal fluid.
Thirty-two participants with liver cirrhosis and ascites were included into the study (11 females and 21 males, mean age 49,5 ±11,9 years). The peritoneal fluid and venous blood were collected for routine laboratory examinations and measurements of PCT and MIP-1b. Patients were divided into two groups according to the ascitic absolute polymorphonuclear leukocytes count (>250/mm^3 and <250/mm^3).
RESULTS: Ascites was sterile in 22 participants and SBP was diagnosed in 10 patients. Serum and ascitic levels of PCT and MIP-1b did not correlate with clinical and routine laboratory parameters. MIP-1b in the ascitic fluid was significantly higher in patients with SBP (213 +279 pg/ml vs 66,3 +49,8 pg/ml; p=0,01). The sensitivity and specificity for diagnosis of SBP with ascitic MIP-1b was 80% and 72,7%, respectively (cut-off value 69,4 pg/ml) with AUROC 0.77 (95%CI 0.58-0.96). Serum levels of MIP-1b showed lower diagnostic yield. Serum and ascitic PCT levels were not different in patients with and without SBP.
CONCLUSION: MIP-1b concentration in ascitic fluid may distinguish patients with and without SBP with satisfactory sensitivity and specificity. Chemokines should be further explored for diagnostic use.
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Disclosure of Interest: None Declared
Keywords: macrophage inflammatory protein, procalcitonin, spontaneous bacterial peritonitis

P618 CO-EXISTENCE OF PANCREATIC AND LIVER DISEASE IN ALCOHOLICS: A PROSPECTIVE AND RETROSPECTIVE ANALYSIS

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INTRODUCTION: On genetic basis co-existence of alcoholic pancreatitis (ALP) and alcoholic liver disease(ALD) was considered rare. Fibroscan and endoscopic ultrasound (EUS) have revolutionized fibrosis detection in liver and pancreas respectively.
AIMS&METHODS: ***AIM:*** To prospectively evaluate pattern of liver and pancreatic involvement prospectively using fibroscan and EUS and retrospectively on autopsy data in alcoholics.
MATERIALS & METHODS: Daily alcohol consumption was evaluated. Patients with BMI>40, HBV, HCV, HIV, gallstones and diabetes mellitus were excluded. In group A, 68 ALD patients (mean age 42yrs, all males) were classified as alcoholic hepatitis/cirrhosis based on signs of portal hypertension, biochemistry and imaging. Pancreatic parenchymal and ductal changes were characterized using Rosemont's classification on EUS. In group B, 70 symptomatic ALP patients with imaging features on USG/CT/EUS/ERCP were fibroscanned for liver stiffness and graded per protocol. In group |C autopsy specimens of liver and pancreas of 51 alcoholics(mean age=46yrs, all males) who died of alcohol related liver and pancreatic diseases from Jan 2008-Dec 2010 were analyzed.
RESULTS: Of 68 ALD patients (group A), 40%(27) had pancreatic involvement on EUS (chronic pancreatitis(CP)-7%, suggestive CP–12%, indeterminate CP-21%). Of 70 ALP patients (group B), 26(37%) had liver involvement on fibroscan (cirrhosis-6%, severe fibrosis-13%, significant fibrosis-19%). Altered liver function with raised bilirubin, AST, ALT, ALP and low albumin were observed in 23(30%), 39(51%), 24(32%), 27(35%) and 27(35%) patients

respectively. Of 51 autopsy patients (group C), 82%(42) had ALD and 18%(9) had ALP. Of these 42 ALD patients, 25(60%) had some form of pancreatitis (CP-31%, acute on CP-17% and acute pancreatitis-12%). Of these 9 ALP patients, 44%(4) had liver injury (fatty liver-33%, steatohepatitis-11%). There was no difference in age, type, frequency and pattern of alcohol consumption in both groups. Amount and duration of alcohol intake in ALD(211gm, 21yrs) was more than in patients with ALP(183gm, 13yrs)(p=0.038, p=0.003).

CONCLUSION: Our study shows that 37% ALP had evidence of liver disease on fibroscan and 40% ALD had evidence of pancreatic disease on EUS. High degree of co-existence of ALD and ALP (60%) was noted in our autopsy data. ALD patients consumed more alcohol and for longer periods than ALP. This is the first study of its kind.

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Disclosure of Interest: None Declared

Keywords: Alcohol, CIRRHOSIS, pancreatitis

P619 RISK FACTORS OF ARTERIAL OR VENOUS THROMBOEMBOLISM IN CIRRHOTIC PATIENTS

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INTRODUCTION: Cirrhosis results in a complex pattern of defects in haemostatic functions with reduced synthesis of pro and anticoagulant factors. As possible complication of coagulation disorders in cirrhosis, could be the development of arterial or venous thromboembolism (AVTE). The purpose of our study was to determine thrombotic risk factors in cirrhotic patients.

AIMS&METHODS: Cirrhotic patients were enrolled. The presence of personal and familial history of AVTE was investigated. Patients were divided into 2 groups. Group1 included patients who developed arterial or venous thromboembolism after cirrhosis diagnosis and group 2 cirrhotic patients without thrombotic event. White blood cells, platelet count, prothrombine time, INR, albumin, urea, pro coagulant factors (VIII, XII, VII, II, V) were determined. Level of antithrombin, protein C and protein S were measured. Search for factor V Leiden and prothrombin gene mutation (G20210A) were performed with PCR-RFLP. Anticardiolipin and antiB2glycoprotein antibodies were also investigated. Both groups of patients were compared with regard of clinical and biological findings.

RESULTS: Fifty one cirrhotic patients were included. Their mean age was 56.8 years. They were men and women. Among the 51 cirrhotic patients, 7 (13.7%) had experienced AVTE after cirrhosis diagnosis: deep venous thrombosis (n=2), pulmonary embolism (n=1), Budd Chiari syndrome (n=1), portal thrombosis (n=3). They were compared to 46 cirrhotic patients without thrombosis. No patient with AVTE had neither personal nor familial history of thrombosis. In an univariate analysis, white blood cell count and platelet count were significantly higher in patients with AVTE than other cirrhotic patients (respectively 8795 vs 5032/mm^3,p $<$ 0.018 and 91133 vs 154375/mm^3, p=0.03) However,In a multivariate analysis only the platelet count was independently predictive of VTE in cirrhotic patients (P=0.05). Moreover, prothrombin time, INR, albumin, urea, level of pro and anticoagulant factors were not statistically different in both groups. There was no link between the presence of Factor VLeiden, prothrombin gene mutation (G20210A), anticardiolipin and antiB2glycoprotein antibodies to thrombosis.

CONCLUSION: Approximately 13.7% of cirrhotic patients resulted in a thromboembolic event. Platelet count was predictive of increased risk of AVTE as it was supported by other studies. Understanding the factors predisposing to thrombosis in cirrhotic patients could play a role in identifying a subgroup of patients at high risk of thrombosis and making decisions regarding the utility of anticoagulation therapy.

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Disclosure of Interest: None Declared

Keywords: CIRRHOSIS, Thrombosis

P620 CAN TERLIPRESSIN REDUCE ACUTE KIDNEY INJURY INCIDENCE IN PATIENTS WITH PORTAL HYPERTENSION AND ACUTE UPPER GASTROINTESTINAL BLEEDING?

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INTRODUCTION: Terlipressin is currently only approved for the treatment of variceal upper gastrointestinal bleeding (VB) and Hepatorenal Syndrome type I. There are no data regarding its use in the prevention of acute kidney injury (AKI) in patients with portal hypertension, namely in the context of non-variceal upper gastrointestinal bleeding (NVB).

AIMS&METHODS: AIM: To determine if the use of terlipressin in patients with VB reduces the incidence of AKI as compared with patients with portal hypertension and NVB.

METHODS: All patients with portal hypertension and NVB admitted to a Gastrointestinal Intensive Care Unit during a 5-year period were included (NVB group). Patients with VB treated in the same unit with terlipressin in the same time frame were randomly selected for the VB group. The criteria used for AKI were a rise of serum creatinine of $>$50% compared with the value at admission or a rise of $\geq$0.3 mg/dl in less than 48 hours.

RESULTS: Seventy-five patients were recruited (NVB group: 25; VB group: 50). There were no significant differences between groups regarding sex (males: 72% vs. 68%), age (mean age: 60.8 vs. 59.0 years), severity of hepatic disease (Child-Pugh Class C: 52% vs. 32%, p = 0.094) or magnitude of bleeding (initial hemoglobin value 7.6 vs. 8.7 g/dL, p = 0.067). Patients with NVB had a significantly higher initial creatinine value than those with VB (1.42 vs 0.88 mg/dL; p $<$ 0.001).Even though AKI incidence was very low (5 patients in both groups combined), it was significantly greater in those with NVB (16% vs. 2%, p = 0.04).

CONCLUSION: The low incidence of AKI in our sample is probably related to the admission to a dedicated intensive care unit and stresses the importance of treating patients with portal hypertension and upper gastrointestinal bleeding in this setting, irrespective of its cause. The use of terlipressin in the VB group was associated with a lower incidence of AKI. However, the reduced sample size and heterogeneity between groups may have played a significant role in the results and thus a prospective validation of these findings is justified.

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Disclosure of Interest: None Declared

Keywords: acute kidney injury, cirrhosis, portal hypertension, Terlipressin, upper gastrointestinal bleeding

P621 A NEW SCORE FOR PREDICTING THE MORTALITY IN CIRRHOTIC PATIENTS WITH INFECTIONS

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INTRODUCTION: Liver cirrhosis is a disease with lots of complications, infections being common in these patients.

AIMS&METHODS: Aim: to assess the factors correlated with mortality in cirrhotic patients with infections and to obtain a new score for predicting the mortality in these patients.

Methods: Our retrospective study included 170 episodes of infection in 141 cirrhotic patients admitted in our Department between January 2011-December 2012. We performed univariant analysis to evaluate the correlation of the following parameters (obtained at admission) with mortality: age, gender, Child-Pugh score, MELD score, AST, ALT, total bilirubin, direct bilirubin, INR, blood nitrogen urea (BUN), serum creatinine, serum Na, serum K, albumin, prothrombin time, serum cholinesterase, hemoglobin, white blood count and platelet count. The factors correlated with mortality in univariant analysis were included in multiple regression analysis in order to create a new score for predicting mortality in cirrhotic patient with cirrhosis.

RESULTS: In our cohort of cirrhotic patients with infections, 20/141 (14.1%) died during hospitalization. In univariant analysis, the following factors were correlated with mortality: BUN (r=0.342, p$<$0.0001), serum creatinine (r=0.285, p=0.002), MELD score (r=0.260, p=0.001), white blood count (r=0.248, p=0.001) and INR (r=0.216, p=0.007), while the following factors were not correlated with the mortality: age (r=-0.059, p=0.43), gender (r=-0.025, p=0.76), Child-Pugh score (r=0.116, p=0.14), AST (r=0.053, p=0.45), ALT (r=0.022, p=0.77), total bilirubin (r=0.072, p=0.35), direct bilirubin (r=0.188, p=0.06), serum Na (r=0.029, p=0.70), serum K (r=0.083, p=0.28), serum albumin (r=-0.121, p=0.16), prothrombin time (r=-0.134, p=0.09), serum cholinesterase (r=0.013, p=0.87), hemoglobin (r=-0.150, p=0.06) and platelet count (r=-0.031, p=0.68).

Using multiple regression analysis the following score was obtained: **Prediction mortality in infected cirrhotic patients (PMIC)**: -0.125+0.005xcreatinine (mg/dl) + 0.02xINR+ 0.0015xwhite blood count/1000 (cells/mm^3) + 0.0005xMELD + 0.002xBUN (mg/dl).

For a cut-off value $>$0.120, PMIC score had 86.7%Se, 77.9% Sp, 30.2% PPV, 98.1% NPV and 78.8% accuracy (AUROC=0.854, p=0.0001) for predicting mortality in cirrhotic patients with infections.

CONCLUSION: PMIC score had a good accuracy and an excellent NPV for predicting mortality in cirrhotic patients with infections.

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Disclosure of Interest: None Declared

Keywords: infections, liver cirrhosis, mortality

P622 EVALUATION OF PORTAL HYPERTENSIVE DOPPLER PARAMETERS IN PATIENTS WITH PERIPORTAL BILHARZIAL HEPATIC FIBROSIS

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INTRODUCTION: Schistosomiasis is the third most devastating tropical disease in the world and is a major source of morbidity and mortality in developing countries.

AIMS&METHODS: Aim: To assess portal hypertensive Doppler parameters; using color Doppler ultrasonography, in patients with bilharzial hepatic periportal fibrosis. **Patients and Methods**: This case/ control study included 50 patients; 44 males and 6 females with their mean age 34± 9 years and 40 subjects as a control group. Diagnosis of bilharziasis was established by history, examination and investigations. Patients were classified into patients with fine and thick periportal fibrosis (PPF) by abdominal US. All included subjects underwent hepatosplenic Color Doppler Ultrasonographic examination.

RESULTS: No statistically significant differences in portal vein diameter (PVD), portal vein velocity (PVV) and portal vein flow volume (PVFV) between patients and control. Patients with thick PPF showed statistically significant higher values in PVD (P value= 0.001) and PVFV (P value= 0.05) than those with fine PPF. Congesion index of the portal vein (CI) was significantly higher in patients than

control (P value= 0.001), also in patients with thick than those with fine PPF (P value= 0.000). Statistically significant higher values of splenic vein diameter (SVD) (P value=0.026), splenic Index (SI), splenoportal index (SPI) (P value=0.000) were detected in patients than control, also in patients with thick than those with fine PPF (P value= 0.000).
CONCLUSION: Color Doppler portal hypertensive parameters are greater in patients with more advanced bilharzial hepatic periportal fibrosis.
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Disclosure of Interest: None Declared
Keywords: bilharziasis, Doppler US, Hepatic , periportal fibrosis

P623 IL-28B POLYMORPHISM IS A PREDICTIVE FACTOR FOR SUSTAINED VIRUOLOGICAL RESPONSE, INSULIN RESISTANCE AND HEPATIC STEATOSIS IN CHRONIC HEPATITIS C INFECTION

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INTRODUCTION: Sustained virologic response (SVR) in patients with chronic hepatitis C (CHC) depends on several factors. One of the most investigated was single nucleotide polymorphism (SNP) of IL-28B gene (rs12979860) important even in the new era of the triple therapy.
AIMS&METHODS: The aim of the study was to evaluate the role of IL-28B polymorphism on SVR, and the association of these polymorphisms with insulin resistance (IR) and hepatic steatosis in naive patients with CHC treated with peginterferon plus ribavirin(Peg IFN si RBV).
One hundred and three non-diabetic CHC patients with liver biopsy proven CHC genotype 1 were studied. The SNPs rs12979860(IL-28B) were investigated by RT-PCR. Insulin resistance (HOMA-IR) stages of fibrosis and degrees of steatosis were also evaluated. SVR and rate of relapse were assessed for each polymorphism of IL-28B.
RESULTS: According to IL-28B polymorphysms SVR was obtained as follows: 89.6% for genotype CC, 55.7% for genotype CT and 23,0% for genotype TT. The rates of relapse were 10.3%, 44.3%, 76.9% for before mentioned genotypes. IR was lower in CC genotype (1.81±0.88) compare to CT (3.7±2.75) and TT genotypes (4.2±2.78), $p < 0.0001$. T allele carriers had a higher frequency of IR irrespective of stages of fibrosis. Cholesterol levels in IL-28B CC genotype were higher (265.2±57.6 mg%) than in genotypes CT (187.1±43.5mg%) or TT (210±57.4 mg%), $p < 0.005$, and degree of steatosis was lower in patients with CC genotype (p=0.015). In multivariate analysis IL-28B CC genotypes and stages of fibrosis were independent predictors of SVR.
CONCLUSION: Apart from the predictive role of SVR in patients with CHC treated with PegIFN plus RBV double therapy, IL-28B CC genotype was associated with the degree of IR and hepatic steatosis. In our study, IR do not undermine the advantage of IL-28B polymorphism.
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Keywords: IL28B, insulin resistance, steatosis, sustained virologic response (SVR)

P624 INCREASED CYTOTOXIC POTENTIAL OF CD160 RECEPTOR POSITIVE NATURAL IMMUNE CELLS IN CHRONIC HCV INFECTION

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INTRODUCTION: Since innate immune cells are uniquely enriched in the inflammatory cell infiltrate of HCV infected liver, the importance of these innate cells in the pathogenesis of liver inflammation emerges. Altered natural killer (NK) cell activity in chronic HCV infection is still controversial, since both impaired and intact NK cell function have been described. Activation of CD160 receptor causes strong cytotoxic activity and Th1 type pro-inflammatory cytokine production in NK cells. Very little information is currently available about the expression pattern and function of CD160 receptor in innate immune cells during chronic HCV infection.
AIMS&METHODS: In our study we analyzed cytotoxic characters of different CD160 receptor positive (CD160+) natural immune cells during chronic HCV infection.We investigated the expression of Fas molecule (a marker of susceptibility to apoptosis), TIM3 (a marker of Th1 phenotype) and intracellular cytotoxic granule content (perforin, granzyme) of peripheral blood CD160+ gamma/delta T cells, NK cells and invariant NKT (iNKT) cells by Flow Cytometry in 10 patients with chronic HCV hepatitis and in 12 healthy controls.
RESULTS: TIM3 expression and cytolytic granule content of CD160+ gamma/delta T cells were significantly enhanced in chronic HCV infection compared to controls. The CD160+ iNKT cells had also increased TIM3 expression but did not show elevated cytotoxic potential. The perforin expression of the CD160+ NK cells was also significantly higher in chronic HCV hepatitis compared to healthy controls. HCV infection was associated with elevated expression of Fas molecule on CD160+ iNKT lymphocytes, but the susceptibility to apoptosis of CD160+ gamma/delta T cells and CD160+ NK cells did not differ from control.
CONCLUSION: Our results suggest that chronic HCV hepatitis is associated with increased cytotoxic granule content of CD160+ NK, CD160+ gamma/delta T cells and Th1 phenotype of CD160+iNKT cells. These innate immune cells infiltrating the liver might induce inflammatory cytotoxic response and contribute to the pathogenesis of chronic HCV hepatitis. Therapeutic strategies modifying innate immune cell function may be of benefit for limiting intrahepatic inflammatory process and liver injury.
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Disclosure of Interest: None Declared
Keywords: CD160, chronic HCV hepatitis, NK, NKT, gd cells

P625 NUCLEOTIDE SUBSTITUTIONS IN THE HEPATITIS E VIRUS GENOME: A PRIME AGENT IN ACUTE LIVER FAILURE

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INTRODUCTION: Previous studies suggest that the genotype of Hepatitis E virus influences the severity of hepatitis E. Viral capsid proteins play extensive role in interacting cellular proteins during capsid assembly and virus entry. Studies at the molecular level of the capsid protein of the HEV genome are hence warranted.
AIMS&METHODS: We aimed to scrutinize the molecular alterations in the HEV genome in patients with acute liver failure and acute viral hepatitis.A total of 28 patients with acute liver failure and 155 patients with acute viral hepatitis were screened for the study during the years 2010-2012. HEV IgM was detected by anti HEV IgM ELISA. HEV RNA was detected using Viral RNA extraction kit. The Open Reading Frame 2(ORF 2) region of the HEV genome was amplified using Reverse Transcriptase PCR. Representative samples were directly sequenced. Full length nucleotide sequences of HEV isolates were retrieved from the Gen Bank /EMBL/DDBJ databases and compared with the strains. Sequences were aligned by CLUSTAL W software.
RESULTS: The mean age of the AVH and ALF patients were 23.9 ± 3.71 years and 24.6±3.33 years respectively. HEV RNA was detected in 84 (54.19%) AVH and 22 (78.57%) ALF patients respectively. A total of 15 nucleotide substitutions at various positions of the ORF 2 were observed after aligning the obtained sequence of 5 ALF patient with the other reference sequences. The nucleotide substitutions obtained were mainly silent substitutions with some conserved substitutions with only one amino acid change from Lysine to Cysteine
CONCLUSION: The single amino acid substitution and the silent substitutions may be associated with the poor outcome in ALF patients. Substitutions covering these regions may play crucial role in enhancing HEV replication through interactions with other proteins thus leading to disease severity.
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Disclosure of Interest: None Declared
Keywords: ACUTE LIVER FAILURE, Hepatitis E virus, Nucleotide substitution

P626 EXPRESSION OF IL-21 IN CHRONIC HEPATITIS B VIRUS INFECTION

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INTRODUCTION: Interleukin-21, as a multifunctional immunoregulator playing a role in control of chronic viral infections, is prospective in the antiviral therapy and vaccine preparation. The role of IL-21 in hepatitis B virus (HBV) infection is not understood.
AIMS&METHODS: The main purport of this study is to confirm the relationship between IL-21 and chronic HBV infection. Serum IL-21 levels collected from chronic HBV-infected patients and healthy controls were measured by Cytometric Bead Array (CBA). IL-21 mRNA and IL-21 receptor mRNA was measured by real-time PCR. Meanwhile, HBV-DNA and liver function were tested.
RESULTS: (1) A total of 79 chronic HBV-infected patients, including 34 patients with chronic hepatitis B (CHB), 19 HBV carriers and 24 patients with HBV related cirrhosis, and 25 healthy controls were involved, with no obvious difference of age or gender. (2) Serum IL-21 level in chronic HBV-infected patients was higher than in healthy controls (57.80±31.23 pg/ml *vs*. 31.90±12.48 pg/ml, $P < 0.001$). (3) Serum IL-21 level in the group of CHB (70.67±28.41 pg/ml) was also higher than in the groups of HBV carriers (26.52±10.13 pg/ml) and healthy controls (31.90±12.48 pg/ml) (both $P < 0.001$), but not higher than group of HBV related cirrhosis (63.83±29.93 pg/ml) (P=0.425). Serum IL-21 level in the group of HBV related cirrhosis was higher than in the groups of HBV carriers and healthy controls (both $P < 0.001$). Meanwhile, there were no significant differences between group of HBV carriers and healthy controls (P=0.138). (4) Considering the different statements of CHB, the group of CHB was divided into three subgroups, mild-CHB, moderate-CHB and severe-CHB, including 16, 12, 6 patients respectively, yet there was no difference of serum IL-21 levels among the three subgroups (P=0.204). (5) A total of 79 chronic HBV-infected patients were divided into to two groups according to HBeAg, HBeAg-positive group and HBeAg-negative group, 25 and 53 patients for each, yet there was no difference of serum IL-21 levels among the two subgroups (P=0.756). (6) mRNA of IL-21 in the group of HBV related cirrhosis was higher than in the groups of HBV carriers and healthy controls (both $P < 0.001$), and mRNA of IL-21 in the group of CHB was higher than the groups of HBV carriers (P=0.041). (7) mRNA of IL-21 receptor in the group of CHB was higher than in the groups of HBV related cirrhosis, HBV carriers and healthy controls (P=0.032, P=0.001, $P < 0.001$, respectively). (8) Serum IL-21 levels had no association with gender, age, HBV-DNA level and other clinical characteristics.
CONCLUSION: The up-regulation of serum IL-21 levels may related to chronic HBV infection, and the mechanisms have to be studied further.
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Disclosure of Interest: None Declared
Keywords: chronic hepatitis B virus infection, Interleukin-21

P627 RS2230201 POLYMORPHISM MAY DICTATE COMPLEMENT C3 LEVELS AND RESPONSE TO TREATMENT IN CHRONIC HEPATITIS C PATIENTS

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INTRODUCTION: Complement is a group of serum proteins which participate in antigen antibody reactions leading to irreversible cell damage and eventually lysis. The serum concentration of C3 closely reflects the total complement activity. Individuals affected by C3 deficiency, often manifestation of SNP, suffer from recurrent pyogenic infections.
AIMS&METHODS: This study aims to find out if there is any relation between chronic hepatitis C infection and levels of C3 in serum.The study included 132 chronic hepatitis C (CHC) patients out of which 48 obtained conventional IFN+Ribavirin. Control groups comprised of 81 healthy blood donors who did not have any history of liver disorders. C3 levels in serum were determined utilizing commercially available kit. Genotyping of SNP was done by Allele-specific PCR.
RESULTS: Out of 132 chronic hepatitis C patients included 81 were males (61.36%) and 51 were females (38.63%) with mean age±S.D. of 35.11±11.40 years. Out of 81 healthy controls included in the study 48 were males (59.26%) and 33 were females (40.74%) with mean age±S.D. of (37.34±15.2). C3 Level of the healthy group was 88.5±19 mg/dl whereas that of the CHC group was 56±18 mg/dl ($p<0.01$) indicating lowering of C3 during CHC. 9 out of 12 non-responders were CT-genotypes and 33 out of 36 responders were CC genotype. It was observed that patients carrying rs2230201 heterozygous CT allele had an increased risk of not attaining sustained virological response after being administered conventional interferon + Ribavirin (p=0.00041). It was observed that before initiation of treatment there was no significant difference between the mean viral loads of CT and non CT allele carrying patients (p=0.25) but significant variation was observed after treatment (p=0.0011). The CT genotype of rs2230201 was found to be associated with decreased C3 levels when compared to other allele in CHC group (CT=**48±14** mg/dl, CC=59±15 mg/dl, TT=61±10.4 g/dl; P=**0.00046**, F=8.14).
CONCLUSION: This is the first study that attempts to co-relate the C3 levels and the single nucleotide polymorphism that influences its expression in chronic hepatits C infection and also its relation to treatment.The significant difference between the chronic hepatitis C patient and healthy control C3 level indicates that there is reduction in C3 levels during CHC and the rs2230201 CT allele is associated with lowered C3 expression during infection and subsequently resulting in significantly increased fraction of SVR failures in therapy group. Hence C3 levels should be included as one of the factor monitored during hepatitis C infection and its SNP rs2230201 included as predictor of treatment response.
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Disclosure of Interest: None Declared
Keywords: Chronic hepatitis C, Complement C3, Interferon, polymorphism, rs2230201

P628 ALCOHOLIC LIVER DISEASE: THE PRESENTATION FEATURES AND CLINICAL SIGNIFICANCE OF VIRUS B INFECTION IN HOSPITALIZED PATIENTS WITH ALCOHOLIC CIRRHOSIS

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INTRODUCTION: Alcoholic liver disease(ALD)remains one of the major causes of morbidity and mortality in the world. In Western countries alcohol is responsible for approximately 40-80% of the alcoholic cirrhosis. In fact 25% of the alcoholics people develop ALD. Patients with liver cirrhosis, are often infected with B or C virus, which can change the clinical course of the disease.
AIMS&METHODS: To evaluate the epidemiological, clinical and laboratoric patterns of ALD, also seroprevalence of B and C virus and their impact over the clinical profile of the hospitalized patients with alcoholic liver cirrhosis. A descriptive study was performed in 170 patients with confirmed diagnosis of alcoholic liver disease, age 51.56 ± 8.15 (range 28 – 72),The data collected for each patients were: Use frequency of alcoholic drinks, kind of the drink, daily amount and the time of use. For all the patients were done: serological markers of hepatitis B and C, Child-Pugh classification. All the patients were devided in two groups according to the etiology, (with or without the viral infection) and according to the clinical forms (liver cirrhosis, alcoholic hepatitis and steatosis of the liver).
RESULTS: Virus B infection was found in 17.14% of the cases and all these cases were liver cirrhosis. It was found significant change between liver cirrhosis and alcoholic hepatitis related to the diagnostic time (p=0.05) and the age (p=0.008). In clinical examination we found jaundice more in alcoholic and viral forms (p=0.037), haemorrhagic diatesis (p=0.04) and ascites (p=0.02). We don't found significant change related to the Child-Pugh classification. For the etiological forms, with and without virus B infection there were significant changes related to the total bilirubin ($p< 0.05$), AST(p=0.013), ALT (p=0.045), total protein (p=0.001), albumin (p= 0.01), globulin (p=0.04), kreatinine (p=0.01). In total was found significant correlation through use of alcoholic drinks and ALD forms : for daily use r= -0.09, time of use r= - 0.06, frequency r= -0.09 and Child-Pugh. (daily use r= 0.06, time of use r= 0.18 and frequency r= -0.33). At the group with liver cirrhosis, 96.6 % had used alcoholic drinks over a 5 years period, in steatosis 66.7% and alcoholic hepatitis 80% (p=0.01).
CONCLUSION: The virus B infection is frequently found in patients with ALD. This infection may agravate the clinical course of the patients with ALD and jaundice, increase of ALT/AST, also significant changes of the total protein, albumin and creatinine are most common in the patients with Virus B superinfection.
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Disclosure of Interest: None Declared
Keywords: Alcoholic cirrhosis, Alcoholic liver disease, Virus B infection

P629 A MATHEMATICAL MODEL FOR CLASSIFYING CHRONIC HEPATITIS C EGYPTIAN PATIENTS AS EASY AND DIFFICULT TO TREAT

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INTRODUCTION:
Egypt has the largest burden of HCV infection in the world. Current therapy is associated with adverse events in addition to the high cost and sub-optimal response. Data mining can explore tremendous volumes of data to discover hidden patterns and relationships in highly complex dataset and thus can enable the development of predictive models.
AIMS&METHODS: To develop a mathematical model for prediction of therapeutic outcome in chronic HCV genotype-4 patients using routine pretreatment data.
This cross sectional nationwide study included retrospective data of 3719 chronic HCV patients who had received PEG-IFN/RBV therapy at Cairo-Fatemia Hospital, Egypt. Factors predictive of SVR were explored using data mining analysis. Weka implementation C4.5, classification and regression tree (CART), Fast decision tree learner (FDTL) were constructed using the pretreatment patients' data (19 attributes).
RESULTS: The estimated SVR was 52.5%. Out of 19 attributes, the applied decision-tree models showed that serum AFP ≥4.7 ng/ml (most decisive), alanine transferase (ALT) >1.74 folds upper limit of normal (ULN), serum albumin level <4g/L, body mass index (BMI) >25.5kg/cm^2, and female gender were associated with unfavorable response. This was further confirmed using multivariate logistic regression analysis. A model including these five variables was significantly associated with failure of response ***(Table 1)*** with sensitivity 0.66, specificity 0.71, PPV 0.62 and NPV 0.75($P<0.01$).
Table(1): Scoring system to predict response to interferon/ribavirin according to number of unfavourable variables.

Number of unfavorable factors	Response	Non response	Total	P value
0-2	1097(75.2%)	361(24.8%)	1458 (100%)	<0.01 (S)
3	591(64.5%)	257 (30.3%)	848 (100%)	
4-5	182 (54.5%)	318 (45.5%)	500 (100%)	

CONCLUSION: The proposed model involving female gender, BMI>25.5kg/cm2, AFP≥4.7ng/ml, ALT>1.74 folds ULN, and serum albumin<4g/L was significantly related to unfavorable response and thus could identify difficult to treat among chronic HCV Egyptian population. This model has the prospective to support clinical decisions regarding the proper selection of patients for therapy (based on a possibility of response), without imposing extra costs.
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Disclosure of Interest: None Declared
Keywords: virological response prediction, Chronic hepatitis C, data mining, decision tree, Egypt, pegylated interferon

P630 DIFFERENT PRACTICE IN THE PATIENTS MANAGEMENT OF HEPATITIS B VIRUS (HBV) IN EGYPT

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INTRODUCTION: Hepatitis B virus (HBV) infects more than 300 million people worldwide and is a common cause of liver disease and liver cancer. HBV infection leads to a wide spectrum of liver disease ranging from acute (including fulminant hepatic failure) to chronic hepatitis, cirrhosis, and hepatocellular carcinoma.
AIMS&METHODS: To assess the different patterns of Egyptian physicians practices in management of patients with HBV infection, and evaluate their knowledge about the disease from different aspects including; epidemiology, knowledge to screening and treatment guidelines. The study included 350 physicians of different age groups, specialties and from different hospitals which distributed all over Egypt that treat patients with HBV infection. All physicians have filled a questionnaire this questionnaire was specially prepared for Egyptian physicians to evaluate their practice and knowledge about management of patients with HBV.
RESULTS: ***Awareness to epidemiology of the disease***: There are significant difference with hospital type and knowledge of physicians in these hospitals about epidemiology of HBV ($P>0.05$). ***Availability of educational resources***

and awareness to national guidelines: There is a significant difference with physician specialty and availability of local guidelines for management of HBV infection, local records or registries of HBV cases under care of doctors and also, significant difference with specialty as regard awareness to national HBV treatment guidelines ($P<0.05$). ***Knowledge about HBV screening and coinfection:*** As regard physician specialty there are no significant differences between all groups (Internal medicine, Tropical& Gastroenterology and Family medicine, GP& others), there is no significant difference in testing the spouse for infection and screening for HBV infection. As regard hospitals type, there are no significant differences between all groups in testing the spouse for infection and screening for HBV infection. ***Investigations have been done before starting therapy:*** As regard physician specialty and Hospital types, there are no significant differences between groups in investigations done before starting therapy. ***Knowledge about treatment:*** There is a significant difference in routes of management of patient with decompnsated liver disease according to the type of hospital which doctor work in.

CONCLUSION: There is an accepted percent of knowledge to the epidemiology of the disease, national guidelines, with better knowledge to doctors who work in university hospitals. Most of the Egyptian physicians don't have local guidelines in their hospitals.

Disclosure of Interest: None Declared

Keywords: Different Practice , Hepatitis B Virus , The Patients' Management

P631 CLINICAL SIGNIFICANCE OF CO-INFECTION WITH HEPATITIS B.VIRUS AND HUMAN T-CELL LYMPHOTROPIC VIRUS TYPE 1

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INTRODUCTION: Little information is available on the co-infection with hepatitis B virus (HBV) and human T-cell lymphotropic virus type1 (HTLV-1).

AIMS&METHODS: The purpose of this study was to determine the clinical significance of co-infection with HBV and HTLV-1. Data of 9838 patients screened for both HBV and HTLV-1 were extracted from a database at a hospital in South-West Japan, where both HBV and HTLV-1 are prevalent. Screening of HBV and HTLV-1 was performed with hepatitis B surface antigen and anti-HLTV-1, respectively. Laboratory data of patients in relation to these viral markers, especially data of patients co-infected with HBV and HTLV-1 and those infected with only HBV, were studied. Data were shown as median and range (min-max). This study was conducted respectively.

RESULTS: Among 9838 patients, 44 (0.4%) were positive for both viruses (group A). 305 (3.1%) were positive for HBV alone (group B), 833 (8.4%) were positive for HTLV-1 alone (group C), and 8656 (88.0%) were negative for both (group D). Group C included patients with a higher age than in the other groups, however, no significant age difference was found between group A (median age, 60 years; range, 37-93 years) and B (median age, 60 years; range 19-94 years). No difference in the aspartate aminotransferase (AST; IU/L) and alanine aminotransferase (ALT; IU/L) levels were found between groups A and group B (AST: 25, 6-208 vs. 24, 9-2966; ALT: 20, 9-391 vs. 23, 4-4079, respectively). The albumin, white blood cells, and platelet count did not differ between groups A and B. Among the 44 patients in group A, 5 patients died of diseases not associated with HBV or HLTV-1 infection. Hepatitis B e antigen (HBeAg), HBV-DNA, and HBV genotype were tested in small numbers of patients. In groups A and B, the number of patients positive for HBeAg (1/18 vs. 0/13) and HBV-DNA levels (2.6 log copies/mL, 0-8.1 log copies/mL, and 2.7 log copies/mL, 0-7.3 log copies/mL) did not differ significantly. The HBV genotype was similar between groups A and B (genotype A:B:C = 0:1:9 and 1:1:11, respectively).

CONCLUSION: No significant differences were found in the laboratory data between patients co-infected with HBV and HTLV-1 and those with HBV infection alone. A limited clinical significance of co-infection with HBV and HTLV-1 was found.

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Disclosure of Interest: None Declared

Keywords: hepatitis B virus, human T-cell lymphotropic virus type1

P632 ANTIHBS TITERS AFTER HEPATITIS B VIRUS VACCINATION DETERMINES THE DURATION OF THE IMMUNIZATION IN CHRONIC KIDNEY DISEASE PATIENTS

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INTRODUCTION: The response to vaccination against the hepatitis B virus (HBV) is poor in chronic kidney disease (CKD) patients.

AIMS&METHODS: The aim of this study was to evaluate the response to vaccination against HBV and the duration of the immunization in CKD patients after two cycles of 40 mcg doses of conventional vaccine and a cycle of 20 mcg doses of adjuvanted vaccine in non-responders at 0, 1, 2 and 6 months. AntiHBs titers were analyzed one month after each dose and at 3, 6 and 12 months of the end of each cycle.

RESULTS: We recruited 301 patients (221 patients in predialysis and 80 on hemodialysis). The 56.7% of patients responded to the first vaccination cycle, rising to 78.8% to 97.6% after the second and the third. Age and CKD were significantly associated with the response to vaccination. Immunization remained in 96.3% at 3 months, 87.9% at 6 months and 66% at 12 months after the first cycle; after the second cycle, it remained at 100% at 3 and 6 months and at 50% at 12 months; and at 100% at 12 months after the third cycle. Correlation was found between antiHBs titers and the immunization achieved and maintained at 3, 6 and 12 months. Only patients reaching antiHBs titers of 500-600 mIU/ml maintained immunization at 3 and 6 months; patients with antiHBs greater than 800 mIU ml were immunized at 12 months.

CONCLUSION: HBV vaccination with two cycles of four double doses of conventional vaccine and a cycle of four doses of adjuvanted vaccine achieves immunization for most CKD patients. Higher antiHBs titers after vaccination determines a more durable immunization.

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Disclosure of Interest: None Declared

Keywords: chronic kidney disease, hepatitis B virus, vaccination

P633 THE HLA-G 14-BASE PAIR DELETION ALLELE AND THE DELETION/DELETION GENOTYPE ARE ASSOCIATED WITH DIFFERENT FORMS OF EVOLUTION OF CHRONIC HEPATITIS B INFECTION

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INTRODUCTION: *HLA-G* has well-recognized immunomodulatory properties, and the molecule is frequently expressed in the liver of hepatitis B virus (HBV) infected patients.

AIMS&METHODS: Since the *HLA-G* 14 bp-insertion/deletion polymorphism has been associated with the magnitude of *HLA-G* expression we evaluated the association between this polymorphism and different forms of evolution of chronic HBV infection and susceptibility to chronic HBV infection**.** We studied 196 chronic HBV infected patients (118 HBeAg-negative, 53 HBeAg-positive and 25 inactive carriers) followed at the University Hospital, Faculty of Medicine of Ribeirão Preto, University of São Paulo, Brazil, and 201 healthy controls from the same geographic area. *HLA-G* typing was performed using PCR-amplified DNA hybridized with specific primers. It was considered as inactive carriers those patients showing low levels of serum HBVDNA (<2000 UI/ml, b-DNA, Bayer) and persistently normal ALT levels.

RESULTS: The frequencies of I/D and I/I genotypes were not different comparing HBV patients to healthy controls ($P> 0.05$). On the other hand the frequency of allele D was significantly higher in HBeAg-positive chronic hepatitis compared to HBeAg-negative chronic hepatitis; [P=0.0460; OR=1.26; 95%CI=1.01-1.45]. Similarly the frequency of genotype DD was significantly higher in HBeAg-positive chronic hepatitis compared to HBeAg-negative chronic hepatitis; [P=0.0356; OR=2.08; 95%CI=1.05-4.09]. No differences were observed when HBV inactive carriers were compared to HBeAg-negative chronic hepatitis.

CONCLUSION: We showed an association between the presence of allele D and genotype DD of 14 bp of the*HLA-G* and HBeAg-positive chronic hepatitis B. The 14bp deletion allele has been associated with increased HLA-G production and in this way may influence the host immune response to the viral infection and the natural history of the infection.

Disclosure of Interest: None Declared

Keywords: 14 bp-insertion/deletion (I/D) , chronic hepatitis B, HBeAg-positive, HLA-G

P634 A META-ANALYSIS ON THE EFFICACY OF TENOFOVIR IN THE TREATMENT OF HEPATITIS B IN HIV CO-INFECTED PATIENTS

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INTRODUCTION: *Patients with Hepatitis B coinfected with HIV have significantly more elevated serum HBV DNA levels with accelerated fibrogenesis and decompensation, giving them poorer prognosis. Studies on the efficacy of Tenofovir in Hepatitis B and HIV coinfection are mostly retrospective and observational, while existing randomized controlled studies are few with small sample size. This meta-analysis aims to study the efficacy of Tenofovir in the treatment of HIV-HBV coinfection by consolidating the results of the small trials.*

AIMS&METHODS: *This meta-analysis aims to study the efficacy of Tenofovir in the treatment of HIV-HBV coinfection by consolidating the results of the small trials.We selected randomized controlled studies comparing efficacy of Tenofovir versus control in the treatment of Hepatitis B-HIV coinfection, measuring the following outcomes: mean change in the HBV DNA level, number of patients with undetectable HBV DNA level, normalization of ALT and HBeAg seroconversion at the end of 48 weeks. The quality of each study included was assessed by two independent reviewers and data was analyzed using Review Manager version 5.*

RESULTS: *Fifteen studies from the search were collected. Three studies, with a total of 79 patients, met the inclusion and exclusion criteria, as well as the quality scale assessment. The studies included were homogenous. The results show a trend favoring the use of Tenofovir in the treatment of Hepatitis B-HIV coinfection, with a mean difference of -1.74 log_{10} copies/ml (CI 1.30 - 2.18, p-value < 0.00001) from baseline in the HBV DNA level. HBV DNA levels were found to be undetectable in*

42 (53%) patients using Tenofovir [RR 3.19 (CI 1.42 – 7.2, p-value = 0.005)]. Normal ALT levels were found in 15 patients after 48 weeks [RR 1.85 (CI 0.66 – 5.15, p-value = 0.52)], while no difference was observed in the HBeAg seroconversion.

CONCLUSION: *The use of Tenofovir as treatment of Hepatitis B infection among subjects coinfected with HIV showed a trend towards better efficacy compared to control in decreasing the mean HBV DNA and ALT levels.*

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Disclosure of Interest: None Declared

Keywords: Hepatitis B - HIV co-infection, Tenofovir

P635 EFFECTS OF THE CHEMOKINE RECEPTOR 5 (CCR5)-DELTA32 MUTATION ON HEPATITIS C VIRUS-SPECIFIC IMMUNE RESPONSES AND LIVER TISSUE PATHOLOGY IN HCV INFECTED PATIENTS

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INTRODUCTION: The specific antiviral T cells provide CC chemokine receptor 5 (CCR5) for the immune response during the hepatitis C virus (HCV) infection. Heterogenous and/or homozygous 32 base pair deletion in CCR5 gene(CCR5Δ32 bpdel) leads to reduced protein expression. In the current case control study, we aimed to compare the histopathological findings of liver to the CCR5Δ32bpdel mutation profiles, expression and some other clinical findings in patients with chronic HCV infection.

AIMS&METHODS: Multiple StripAssay reverse hybridisation and Real Time PCR techniques were used to determine the germline CCR5 mutations and immunohistochemical technique was used to evaluate the gene expression in targer tissue biopsies.

RESULTS: Target CCR5 WT/WT, WT/Δ32, and Δ32/Δ32 genotypes were observed in 91.4%, 8.6%, and 0.0% for HCV positive patients and 98.3%, 1.7%, and 0.0% for control group respectively. The histologic activity indices (HAI) was significantly lower (4.0±1.0) in the mutated group than the non-mutated group (5.7±1.0). Decreased fibrosis levels were detected in HCV positive mutated group.

CONCLUSION: Results showed that CCR5 polymorphism was more frequent in HCV positive patients than in healthy population in Turkish population. Current resuls also showed that mutated CCR5 signalling pathway due to CCR5-Delta32 may potentially result in subtle reduction of HCV specifity to the drug responses due to the positive impact on liver inflammation, fibrosis levels and liver destruction in HCV infection.

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Disclosure of Interest: None Declared

Keywords: chemokines, Chronic HCV

P636 ADHERENCE AND LIFE IMPACT OF TRIPLE THERAPY IN PATIENTS WITH CHRONIC HEPATITIS C

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INTRODUCTION: Triple therapy with Peg-IFNs, Ribavirin and protease inhibitors is the new gold-standard treatment for hepatitis C in relapsers or nonresponder patients raising the treatment success up to 83%. In front of a new treatment challenge is now the low adherence, the new combination regimens bringing together with the significantly higher rates of sustained virologic response (SVR) more side effects interfering with patient's quality of life and work productivity.

AIMS&METHODS: This study aimed to analyze the adherence and life impact of triple therapy using Peg-IFNs, Ribavirin and protease inhibitors (Telaprevir vs. Boceprevir) in 50 patients from different counties from Romania diagnosed with chronic hepatitis C with failure to first line therapy. Multivariate Cox proportional hazards regression was used to analyse determinants of re-treatment initiation and compliance during treatment according to patient features.

RESULTS: This observational study identified as major drivers of retreatment initiation in patients with chronic infection with C virus the young age (2-3 medical visits vs. 4-8 visits, p=0.031), the female gender (28 vs. 22), the urban provenience and the high income (p=0.0337, 95% CI 4.66-44.56), the psychiatric and the alcohol or drugs abuse history (p=0.0351, CI 11.98-44.51). The adherence and the life impact of therapy during the retreatment were similar despite the regimen used and obvious lower in patients with history of previous abandon (p=0.0228 95% CI 2.47-39.01), drugs and alcohol abuse (p=0.0283, CI 95% 12-45, respectively p=0.0117 CI 95% 1-38), hematologic and psychiatric decompensation (p=0.0447, 95% CI 9.66-34.86). The bad capacity of work and temporary drop of job to continue the therapy was seen in 12.5% of patients (2pts) taking Telaprevir and 8.82% of patients (3pts) taking Boceprevir. Abandon of therapy without any known reason was more frequent in males (p=0.0345), with alcohol and drugs intake history (p=0.0221), from rural region and with low income (p=0.0119, respectively, p=0.0371), with psychiatric disturbances in personal history(p=0.0290).

CONCLUSION: Having as the principal end-point the sustain viral response (SVR), our study results, next to other similar literature information, should focus the researchers and physicians to discover molecules with fewer side effects or to improve the medical strategies in order to raise the quality of life in chronic hepatitis C patients following triple therapy.

Disclosure of Interest: None Declared

Keywords: adherence, life impact, triple therapy

P637 BUPRENORPHINE MAINTENANCE ACHIEVES A HIGHER COMPLIANCE RATE THAN METHADONE IN PATIENTS CHRONICALLY INFECTED WITH HCV TREATED WITH PEGYLATED INTERFERON AND RIBAVIRIN COMBINATION

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INTRODUCTION: Chronic HCV infection (HCV) is the most common infectious disease among intravenous drug users.

AIMS&METHODS: To determine and compare compliance rates between two groups of chronic HCV patients from the National Greek Organization Against Drugs (OKANA) in substitution programs with buprnorphine or methadone, treated with pegylated interferon plus ribavirin during 24 or 48 weeks of therapy and 24 weeks of follow up. Also, to evaluate the efficacy of treatment in each group. 97 consecutive chronic HCV infected patients, members of the OKANA program, were treated with pegylated interferon α-2α (180 μg/wk administered subcutaneous) in combination with oral ribavirin (1000 or 1200 mg/day depending on baseline body weight $\leq$ or $>$ 85 Kg, respectively, divided in two doses), for 24 or 48 weeks according to their genotype. 45 were in buprnorphine maintenance (Group A, 36 males, 9 females) and 65 in methadone maintenance (Group B, 52 males, 13 females). During the study, all patients were followed up periodically by hepatologists, internists and psychiatrists.

RESULTS: Baseline characteristics were similar between the two groups. 34/45 patients (75,6%) from group A and 31/65 (47,7%) from group B completed therapy (p=0.006). Thirty-two (71,1%) patients from group A and 27 (41,5%) from group B were followed up until the end of the follow-up period (p=0.004). At the end of the follow-up, sustained virologic response (SVR) was achieved in 23/45 (51.1%) patients from group A and 21/65 (32.3%) from group B (p= 0.075).

CONCLUSION: Buprenorphine maintenance achieves a significantly higher compliance rate than methadone in patients with chronic HCV infection treated with pegylated interferon and ribavirin. After 24 weeks of follow-up, response rates were similar for patients who were compliant to treatment for both groups.

Disclosure of Interest: None Declared

Keywords: buprenorphine, drug users, hepatis c virus, methadone

P638 EVALUATION OF PREDICTORS OF SUSTAINED VIROLOGICAL RESPONSE (SVR) TO INTERFERON THERAPY AND HEPATIC PROGENITOR CELLS (HPCS) IN CHRONIC HEPATITIS C VIRUS (HCV) INFECTED PATIENTS

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INTRODUCTION: Studying the predictors of SVR to pegylated interferon (PEG-INF) alfa-2a and ribavirin (RBV) therapy in chronic HCV infected patients is crucial for selecting those who would benefit most from therapy. Increased HPCs in HCV-infected patients were shown to be correlated with increasing fibrosis and response to treatment. HPCs could be detected in the liver by immunohistochemical expressions of cytokeratin (CK) 7 and CK19.

AIMS&METHODS: a. Evaluate the response rate to interferon based treatment in chronic HCV patients. b. Detect the predictors of SVR to treatment. c. Study the correlations between CK7 and CK19 expressions and treatment response.
This study included 483 chronic HCV infected patients who fulfilled the study criteria who underwent clinical, biochemical and virological assessments before treatment and at 12, 24, 48 and 72 weeks post-treatment. Only 330 patients; 193 male and 137 completed the course and were included in the statistical analysis. Only 50 specimens were examined for CK7 and CK19 expression using avidin, biotin, peroxidase technique.

RESULTS: End of treatment virologic response (ETVR) was achieved in 70% of patients, while 30% were non responders. SVR was higher in females whereas most of male patients didn't achieve SVR ($P < 0.01$). Patients with SVR were significantly younger ($P < 0.004$) and had lower body weight ($P < 0.001$). There was significant inverse relation between SVR and aspartate aminotransferase (AST) and alpha feto-protein (AFP); $P < 0.000$ for each. The independent predictors of SVR were younger age and lower AST ($P < 0.02$ for each). There was significantly positive correlation between the grade of necro-inflammatory activity, AST and AFP and the stage of hepatic fibrosis ($P < 0.003$, $P < 0.000$ & $P <$

0.000 respectively). There was significant association between CK7 and/or CK19 expressions and grade of necro-inflammation ($P<0.033$, 0.026 respectively), and/or advanced stage of fibrosis ($P<0.001$, 0.000 respectively). There were significant inverse relations between SVR and stage of hepatic fibrosis ($P<0.001$), and CK19 expression ($P<0.000$).

CONCLUSION: Forty % of patients with chronic HCV who completed the course of combination therapy achieve SVR. Younger age and lower pre-treatment AST are independent predictors of SVR. HPCs as assessed by CK7 and CK19 expressions may be incorporated in assessment of treatment response of these patients.

Disclosure of Interest: None Declared

Keywords: hepatic progenitor cells (HPCs), Hepatitis C virus (HCV), sustained virologic response (SVR)

P639 ABT-267 COMBINED WITH PEGYLATED INTERFERON ALPHA-2A/RIBAVIRIN IN GENOTYPE 1 HCV-INFECTED TREATMENT-NAÏVE PATIENTS: EFFICACY AND SAFETY UPDATE

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INTRODUCTION: ABT-267 is a novel hepatitis C virus (HCV) NS5A inhibitor being developed for use in combination with other anti-HCV agents. This double-blind, randomized study evaluated ABT-267 combined with pegylated interferon+ribavirin (P/R) in genotype 1 (GT1) HCV-infected treatment-naïve patients.

AIMS&METHODS: Non-cirrhotic patients with HCV RNA >50,000 IU/mL received ABT-267 (5, 50 or 200mg once-daily) or matching placebo (PBO) in combination with P/R (pegylated interferon alpha-2a 180μg/week + weight-based ribavirin 1000-1200mg/day) for 12 weeks. After week 12, patients received P/R for 36 weeks and were followed post-treatment for 48 weeks. RVR, cEVR, SVR_{12} and SVR_{24} were assessed in the intent-to-treat population (flanking imputation and non-completer=failure to handle missing data). Adverse events (AE) and laboratory abnormalities were recorded.

RESULTS: 37 patients received ABT-267+P/R (n=28) or PBO+P/R (n=9): 60% male, 16% black, 30% Latino, 73% GT1a infection, 33% IL28B CC genotype, mean age 48 years, BMI 27 kg/m^2, baseline HCV RNA 6.6 $\log_{10}$ IU/ml. Virologic efficacy is shown in the table. There were no serious AEs during ABT-267/PBO + P/R treatment; AEs and laboratory abnormalities were similar for the PBO and ABT-267 groups and were consistent with the safety profile of P/R. Two patients discontinued ABT-267 prematurely (1 withdrew consent, 5mg group; 1 had virologic failure, 200mg group.) No patient discontinued ABT-267 due to an adverse event.

	PBO	ABT-267 5mg	ABT-267 50mg	ABT-267 200mg	ABT-267 Total
N	9	9	9	10	28
RVR, n (%)	2 (22)	7 (78)	7 (78)	8 (80)	22 (79)
cEVR, n (%)	6 (67)	9 (100)	8 (89)	8 (80)	25 (89)
SVR_{12}, n (%)	3 (33)	6 (67)	6 (67)	6 (60)	18 (64)
SVR_{24}, n (%)	2 (22)	5 (56)	4 (44)	5 (50)	14 (50)
Reasons for non-response (SVR_{24}):					
On-treatment virologic failure*	1	0	2	2	4
Relapse	4	3	0	0	3
Lost to follow-up	2	1	3	3	7

*HCV RNA value at the end of P/R treatment was ≥ LLOQ.

CONCLUSION: The proportion of patients achieving SVR_{12} and SVR_{24} was greater among patients who received ABT-267+P/R compared with P/R alone (64% and 50% versus 33% and 22%, respectively). ABT-267 was well tolerated in this study. These findings support exploring the combination of ABT-267 with other direct acting antiviral agents for interferon-free treatment of chronic HCV GT1 infection.

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Keywords: clilnical trial, direct-acting agents, HCV

P640 THE SUBGROUP GENOTYPE AND RAPID VIRAL RESPONSE PREDICT SUSTAINED VIRAL RESPONSE IN PATIENTS WITH MIXED GENOTYPE CHRONIC HEPATITIS C

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INTRODUCTION: It is unclear whether the rapid virological response (RVR) influences the probability of achieving a sustained virological response (SVR) in patients with mixed genotype (mix-GT) infection of chronic hepatitis C.

AIMS&METHODS: The aim of this study is to clarify the influence of genotypes and other factors in mix-GT patients on RVR and SVR. Data were retrospectively analyzed from treatment-naive patients who received peginterferon alfa-2a (180μg/week) or 2b (15 mg/kg/wk) plus ribavirin 15 mg/day for 24 or 48 weeks according to RVR response. Sixty-nine mixed genotype(GT) 1 and 2 or mix-GT 1a+1b patients with evaluable HCV RNA at baseline and week 4 were grouped according to RVR status: RVR (HCV RNA <14 IU/ml) or no RVR. The proportion of patients with undetectable HCV RNA at week 12 (EVR) and the proportion with an SVR was calculated.

RESULTS: Overall, 78.2% achieved SVR and 95.7% had EVR. All patients in RVR group and 76.9% non-RVR group had EVR. There are 85.7 % (48/56) of RVR and 46.2 % (6/13) of non-RVR patients achieved SVR ($p<0.0001$). Among non-RVR patients, only twenty percent (1/5) achieved SVR when 1a including in their GT population (e.g. 1a+1b, 1a+2a, or 1a+2b). High viral load and elder patients are significantly more in non-RVR patients. The type and dosage of interferon, dosage of rivabirin, adherence of medication and clinical manifestations are no difference between non-RVR and RVR patients.

CONCLUSION: The probability of achieving SVR is depending on subgroup of genotype, viral load, and age in patients with mix-GT chronic hepatitis C. When the patients can get RVR, the SVR rate is equal to mono-GT infection patients.

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Disclosure of Interest: None Declared

Keywords: Chronic hepatitis C, Mixed genotype, Rapid viral response, Sustained viral response

P641 CLINICAL IMPACT OF OCCULT HBV INFECTION IN PATIENTS WITH CHRONIC HEPATITIS C

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INTRODUCTION: Occult HBV infection is more frequently found in HCV–positive subjects than in healthy subjects, but its clinical impact remains still controversial.

AIMS&METHODS: The aim of this study is to determine clinical impact of occult HBV infection in subjects with chronic hepatitis C.

From March 2004 to January 2013 the study prospectively included 152 subjects with chronic hepatitis C, all HbsAg-negative (mean age 45±8,1 years), 95 males/57 females. Sera of all subjects were tested for the presence of HBV DNA by real-time PCR Cobas TaqMan ® Test with detection limit of 6 IU/ml (35 copies/ml) (Roche Molecular Systems, Inc.). Liver biopsy was performed in all patients. Two consecutive liver biopsies were preformed in 77 subjects and the rate of fibrosis progression was calculated. 85 subjects received antiviral treatment.

RESULTS: Occult HBV infection, defined in this study as positive serum HBV DNA, was found in 15% (23/152) of the subjects with chronic hepatitis C. Positive HBV DNA significantly associates with positive antiHBc Ab ($P<0.0001$). Positive HBV DNA associates with more severe grade of necro-inflammation changes in the liver (P=0,001). No association was found between positive HBV DNA and stage of liver fibrosis (P=0,570). Positive HBV DNA was found in 32% of subjects with progression of fibrosis and in 6,7% of the patients without fibrosis progression (P=0.010). Occult HBV infection didn't affect efficacy of antiviral treatment (P=1,000). No association between positive HBV DNA gender (P=0,116), age (P= 0,248), HCV genotype (P=0,501) and serum HCV RNA (P=0,641) was found.

CONCLUSION: Occult HBV infection is found in 15 % of the patients with chronic hepatitis C and associates with more severe necro-inflammatory changes in the liver and more rapid progression of liver fibrosis

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Disclosure of Interest: None Declared
Keywords: Anti HBcore Ab, Chronic hepatitis C, Fibrosis progression, Occult HBV infection

P642 PEGYLATED THERAPY IN ELDERLY PATIENTS WITH CHRONIC HEPATITIS C : WHAT'S THE RESULTS?

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INTRODUCTION: Chronic hepatitic C (CHC) is particular in elderly patients by the infection itself and the physiological state
AIMS&METHODS: The aims are to compare CHC patients treated by Pegylated therapy younger and older than 65 years concerning their virological, histological and to compare also their early virological response (EVR) and the sustained virological response (SVR).All cases of CHC treated with combination therapy were recruited from 2005 to 2012. All clinical, biological, virological and histological data were collected and analyzed. Patients were divided in 2 groups according to their age, Group 1: Patients younger than 65 years, Group 2: Patients older than 65 years. We compared the groups regarding their epidemiological, virological and histological characteristic as well as the EVR and the SVR. Statistical analysis was performed by chi 2 test
RESULTS: 200 patients were included, 130 patients (52%) in group 1 and 70 patients (48%) in group 2. The mean age was 50 years in Group1 and 67.4 years (range 65-83) in Group 2 with female predominance (77%) in Group 2. Genotype 1 was predominant in both groups: 53% in Group 1 and 67% in Group 2. The viral load was $\geq$ 600 000 IU/ml in 65% in Group 2 and 55% in Group 1. Severe fibrosis and cirrhosis were frequent (58%) in Group 2 ($p = ns$). Concerning the virological response, EVR was 80% in Group 1 and 65% in Group 2 ($p = ns$) and SVR was 84% in Group 1 and 52.7% in Group 2 ($p = ns$).
CONCLUSION: The most prevalent profile in CHC-patients older than 65 years was women infected by HCV-Genotype 1 and high viral load. EVR was achieved in most of cases (65%) and SVR in 52.7% without significant difference of these results in CHC-patients younger than 65 years.
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Disclosure of Interest: None Declared
Keywords: chronic HCV hepatitis, Peg IFN/Ribavirin

P643 HIV PREVALENCE AMONG HCV EGYPTIAN INFECTED PATIENTS AND ITS IMPACT ON THE RESULT OF HCV TREATMENT

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INTRODUCTION: HCV infection is the most common co-infection in HIV patients so we aimed to determine the prevalence of HIV infection in chronic HCV patients and its impact on chronic HCV patients treatment response.
AIMS&METHODS: A retrospective study performed on 1852 chronic HCV patients subjected to anti HCV treatment with alpha 2a, alpha 2b or standard interferon and Ribavirin and tested and confirmed for HIV co infection by ELISA twice. Upon HIV testing, two groups were generated, **Group1**: 1840 HCV patients, positive for HCV RNA and **Group 2**: 12 HIV positive patients and positive also for HCV. Informed consents were obtained from patients. Proper hematological biochemical investigations and other causes of hepatitis rather than HCV were carried out and excluded.
RESULTS: The prevalence of HIV among HCV infected Egyptian patients was 0.64%. We found male gender predominance; the hematological and biochemical parameters were similar in both groups with mild elevations in liver enzymes in group II. High rates of failure to treatment (77.8%) with lower SVR (22.2%) were in group II compared to group I (59.9%) as SVR was 22.1% in group II vs. 34.1% in group I, however with no statistical significance.
CONCLUSION: Despite the lower prevalence of HIV in Egyptian patients with HCV infection, still it affects their response to treatment .Therefore; we must screen HIV in all HCV patients and recommend its test to routine investigations before starting HCV therapy.
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Disclosure of Interest: None Declared
Keywords: HCV/HIV coinfection, Peg IFN/Ribavirin, Treatment response

P644 SHOULD WE INVESTIGATE RETINOPATHY IN CHRONIC HEPATITIS C PATIENTS RECEIVING TREATMENT WITH INTERFERON?

S. Aoufi Rabih[1,*], L. B. Alfaya Muñoz[2], A. Fidalgo Broncano[2], R. Villanueva Hernández[1], P. González Carro[1], F. Pérez Roldán[1]. [1]*Gastroenterology and Hepatology, [2]Ophthalmology, Complejo Hospitalario La Mancha Centro, Alcázar de San Juan, Spain*

INTRODUCTION: Retinopathy secondary to interferon (IFN) was described in 1990. Its incidence is uncertain. Published studies include short series of patients. There seems to be a direct relationship between the dose of IFN and the duration of treatment. It may appear from week 8 of treatment initiation. It is usually asymptomatic and doesn't associate loss of visual acuity. It disappears completely in most patients after the discontinuation of treatment. There have also been some cases caused by hepatitis C virus with the formation of a variety of thrombogenic antibodies, causing retinal damage.
AIMS&METHODS: The aim of this study was to determine the prevalence of retinopathy in a cohort of chronic hepatitis C patients receiving or not antiviral treatment with IFN and ribavirin. We consecutively enrolled chronic hepatitis C patients from the Hepatology Consultation. We excluded patients with ocular pathology caused by other diseases (arterial hypertension, diabetes, etc.). Patients underwent a fundus of the eye performed by a single ophthalmologist.
RESULTS: We recruited 219 chronic hepatitis C patients of all genotypes, of which 81 were excluded due to concomitant eye diseases. We performed a fundus of the eye to 138 patients, 18 were receiving treatment with pegylated IFN and ribavirin for at least three months before the test. The 63.4% of patients were male, with a mean age of 54 years (18-74). None of the patients studied showed visual symptoms. Pathological eye changes were found in a patient treated with IFN (5.5%); the characteristics of the lesions were attributed to antiviral treatment by the ophthalmologist.
CONCLUSION: The prevalence of ophthalmic disorders in patients with chronic hepatitis C is very low and especially present in those receiving antiviral treatment with IFN. As the fundus of the eye is an inexpensive, noninvasive, easy to perform and accessible test at all sites, it seems advisable to indicate it in patients undergoing treatment with IFN. This retinopathy screening study contains the largest series of patients with chronic hepatitis C and interferon therapy.
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Disclosure of Interest: None Declared
Keywords: Hepatitis C, Interferon

TUESDAY, OCTOBER 15, 2013 9:00-17:00
PANCREAS II - Poster Area

P645 VALIDATION OF THE ORIGINAL ULTRASOUND SCALE FOR STRATIFICATION OF SEVERITY OF ACUTE PANCREATITIS

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INTRODUCTION: An increasing number of cases and severity of acute pancreatitis (AP) guides the necessity of early identification of cases that require an intensive care and/or operation. There exist different complex scoring systems that are used for stratification of severity of AP, i.e. Balthazar–Ranson (B-R) & SOFA, but they have some limitations. According to the classification that was proposed by M.S. Petrov & J.A. Windsor [1] we devised a new scale for stratification of severity of AP that is based on the ultrasound (US) signs of inflammation or destruction processes in pancreas.
AIMS&METHODS: To compare the value of original scale with well-known B-R & SOFA scales in stratification of severity of AP. For US scale we analyzed the following parameters in points: US signs of oedema of pancreas (1), dilatation of Virsung (1), infiltration of parapancreas adipose tissue (2), parapancreatic abscess (3), fluid in parapancreatic adipose tissue and/or upper level of the abdominal cavity (3), fluid in the other parts of abdominal cavity (4); necrosis of pancreas: $<$ 30% (2), 30-50% (5), $>$ 50% (8); dilatation of choledochus (1); enlargement of gallbladder or cholelythiasis (1), dilatation of intrahepatic bile ducts (1).
RESULTS: There were 158 patients with AP (mean age 50.2±17.8, 72.4% male), of which 31.6% were classified as mild, 20.3% as moderate, 30.4% as severe & 17.7% as critical AP. The comparison of the scales depending on the severity of AP is shown in the table.

	Categories of acute pancreatitis (Petrov & Windsor)				P value		
Scales (points)	Mild	Moderate	Severe	Critical	mild vs moderate	moderate vs severe	severe vs critical
SOFA	3.89±0.10	9.12±1.16	9.71±1.92	12.29±1.73	<0.001	0.28	<0.001
B-R	1.22±0.42	2.43±1.05	7.31±1.83	9.71±1.78	<0.001	<0.001	<0.001
US scale	4.32±1.13	12.20±2.25	16.48±5.48	21.32±3.87	<0.001	<0.001	<0.001

We received well-known correlations between SOFA scale & B-R scale (Rs=0.69; $p<0.001$). US scale correlated also with SOFA scale (Rs=0.79; $p<0.001$) & B-R scale (Rs=0.88; $p<0.001$).
One of the prognostic factors of the severe AP is more than 14 points according to US scale (sensitivity 73%, specificity 87%, positive predictive value 65%, negative predictive value 90%).

CONCLUSION: Prognostic value of a new US scale is high for stratification of severity of AP. The best efficiency in the early prediction of severe AP could be achieved with the measurements of the B-R & US scales.

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Disclosure of Interest: None Declared

Keywords: Acute Pancreatitis, Baltazar-Ranson, SOFA, Ultrasound scale

P646 CLINICAL CHARACTERIZATION OF HYPERTRIGLYCERIDEMIC SEVERE ACUTE PANCREATITIS: OUR EXPERIENCE DURING THE LAST DECADE

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INTRODUCTION: Hypertriglyceridemia is the third most common non iatrogenic cause of Acute Pancreatitis (AP), accounting for 1 to 38% of cases. This entity is defined by the presence of high triglyceride levels (> 1000mg/dL) in the absence of other etiological factors for acute pancreatitis.

AIMS&METHODS: Clinical characterization of inpatients with Hypertriglyceridemic Severe Acute Pancreatitis (HTG SAP) in a Gastroenterology Intensive Care Unit.

Retrospective analysis between 2002 and 2012; 185 cases of Severe Acute Pancreatitis (SAP); 13 patients with SAP and Triglycerids (TG) ≥ 1000mg/dL (7,3%). Other etiologies were excluded. We considered demographic and clinical variables with diagnostic and prognostic value. Medical and surgical management was reviewed.

RESULTS: Male: 92,3%; Mean age: 42,8 years (23-68); Time of evolution: 27 hours (3-72); Known dyslipidemia: 84,6%; Diabetes mellitus: 42,9%; Body Mass Index > 30Kg/m 2: 46,2%; Chronic alcoholism: 69,2%; Mean TG level at admission: 4805mg/dL (1011-11442); Ranson score at admission ≥ 3: 57,1%; C reactive protein level at 48 hours > 15mg/dL: 85,7%; Shock 7,7%; Renal failure 15,4%; Respiratory failure 84,6%; Pancreatic necrosis 30,8%; Infected pancreatic necrosis 7,7%; Fluid collections 38,5%; Plasmapheresis: 61,5%; mean TG level for these patients: 4926mg/dL; mean number of sessions: 1,9; mean reduction of TG level after first plasmapheresis session: 5496mg/dL (1194-11056); mean duration of stay: 7 days; mortality: 7,7%; statistically significant difference between HTG SAP mortality ans lithiasic SAP (p=0.042).

CONCLUSION: HTG is a rare cause of SAP, mainly affecting young adult male patients, most of which with a known past history of dyslipidemia. In about half of the cases it is associated with Diabetes mellitus and in two thirds with chronic alcoholism. The most frequent complications in this setting are respiratory failure and pancreatic necrosis. Plasmapheresis is an effective tool for rapid reduction of TG level. HTG SAP has a favourable outcome when compared with more frequent lithiasic aetiology.

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Disclosure of Interest: None Declared

Keywords: Acute Pancreatitis, Hypertriglyceridemia, Intensive care unit

P648 INCIDENCE, RISK FACTORS AND CLINICAL COURSE OF PANCREATIC FLUID COLLECTIONS IN ACUTE PANCREATITIS

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INTRODUCTION: Acute pancreatic fluid collection and pseudocyst formation are the most frequent complications of acute pancreatitis.

AIMS&METHODS: The aims of this study were to evaluate the incidence, risk factors, and clinical course of pancreatic fluid collections and pseudocyst formation following acute pancreatitis. A prospective multicenter study was conducted with five participating centers from January 2011 to July 2012. A total of 302 patients diagnosed with acute pancreatitis were collected.

RESULTS: The incidence of pancreatic fluid collections and pseudocyst was 42.7% and 6.3%, respectively. Patients with fluid collection were significantly younger, compared to those without fluid collection (51.5±15.9 vs. 60.4±16.5 years, p = 0.000). Alcohol showed a higher proportion (54.3%) of etiology in patients with fluid collection, compared to other etiologies. CRP (48 hr) was significantly higher in patients with fluid collection, compared to patients without fluid collection (39.2±77.4 vs 15.1±36.2 mg/dL, p=0.016). LDH (48 hr) was significantly higher in patients with pseudocyst formation, compared to patients with complete resolution (1317.6±706.4 vs 478.7±190.5 IU/L, p=0.000). Pancreatic fluid collection showed spontaneous resolution in 69.8% (90/129) and 84% of the pseudocysts disappeared or decreased in size during follow up.

CONCLUSION: Age, CRP (48 hr), and alcohol etiology are risk factors for pancreatic fluid collection. LDH (48 hr) appears to be a risk factor for pseudocyst formation. Most pseudocysts showed a decrease in size or spontaneous resolution.

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Keywords: Acute pancreatitis, Fluid collection, Pseudocyst

P649 LOW PLASMA CALCIUM LEVELS PREDICT SEVERE ACUTE PANCREATITIS AT ADMISSION WITH EQUAL ACCURACY AS SOPHISTICATED ORGAN FAILURE SCORES

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INTRODUCTION: Acute pancreatitis is one of the leading causes of hospitalization for gastrointestinal disorders. While 80% of patients develop mild acute pancreatitis, the remaining 20% develop severe acute pancreatitis (SAP) associated with significant morbidity and mortality. To ensure adequate clinical management and distribution of resources early prediction of the disease course is essential.

AIMS&METHODS: The objective of this study was to evaluate the use of several organ dysfunction scores (APACHE II, SAPS II, SOFA, LODS, MODS) and the pancreatitis specific scores (Ranson, Glasgow) for the prediction of SAP in patients admitted to the university hospital of Greifswald. 114 patients were prospectively enrolled in this study during 2004 and 2010, of which 22 developed SAP. Data for the calculation of the organ dysfunction scores was obtained at admission, data for calculating Ranson and Glasgow score during the following 48 hours. Subsequently, receiver operator curves were generated for each score. Area under the curve (AUC) estimates were interpreted as a comparative measure of the potential usefulness and test accuracy was compared at visually optimal thresholds.

RESULTS: The organ dysfunction scores showed a similar performance in predicting SAP at admission (AUC for: APACHE II 0.75 (95% confidence interval, 0.62-0.87); SAPS II 0.66 (0.54-0.79), SOFA 0.71 (0.57-0.85), LODS 0.77 (0.68-0.86), MODS 0.72 (0.58-0.86)), but none of these was adequate accurate to be used for clinical decision making. Ranson score performed better and Glasgow

score similar (AUC for: Ranson 0.89 (0.57-0.85), Glasgow 0.74 (0.67-0.85)) compared to the organ dysfunction scores, however these scores are only available 48 hours after admission. Hypocalcemia seemed to correlate well with SAP and prompted us to analyse its potential as a single predictive parameter. The predictive value of low plasma calcium levels for SAP was at least equivalent to that of the sophisticated organ dysfunction scores and to the pancreatitis specific scores (AUC for plasma calcium: at admission 0.78 (0.67-0.9); at 48 hours 0.92 (0.84-0.99)).
CONCLUSION: This study showed that several organ dysfunction scores are only of limited value for predicting SAP. The pancreatitis specific scores partially showed better performance, but their use is limited because of their delayed availability. Surprisingly, evaluation of hypocalcemia as predictor for SAP was at least equivalent to organ dysfunction scores and to the pancreatitis specific scores and thus could be a simple alternative for predicting SAP in clinical routine.
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Keywords: Severe acute pancreatitis, Severity prediction

P650 ACUTE PANCREATITIS IN THE ELDERLY: ETIOLOGY AND CLINICAL FEATURES

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INTRODUCTION: The incidence of acute pancreatitis has increased in recent years. With prolonged life expectancy the number of elderly patients affected by this pathology has consequently risen, becoming an important concern in this group of patients. The influence of age in the severity and clinical course of acute pancreatitis has been a subject of debate.
AIMS&METHODS: The purpose of our study was to evaluate the clinical features and the outcome of elderly patients with acute pancreatitis. We studied retrospectively all patients admitted with the diagnosis of acute pancreatitis at our Service between January 2010 and December 2010. Demographic data and clinical characteristics of elderly (≥65 years-old) and non-elderly (<65 years-old) were registered. The severity of pancreatitis was stratified according to the BISAP score (Bedside Index for Severity in Acute Pancreatitis).
RESULTS: 114 patients were included, being 67 elderly and 47 non-elderly. The former presented a higher Charlson co-morbidity index (mean of 1,96 *versus* 0,87, p=0,003). Biliary etiology was more common in the elderly group (82% *versus* 55%, p=0,000) and alcoholic etiology was more frequent in the younger group (30% *versus* 6%; p= 0,000). The BISAP score was significantly higher in the elderly (p=0,000). In regards to systemic complications related to this disease, they were more common in the elderly (58,21% *versus* 29,79%, p=0,003) namely renal insufficiency (29,85% *versus* 6,38%, p= 0,002) and hypocalcemia (32,8% *versus* 12,8%, p= 0,014). Nevertheless, the presence of local complications (10,4% *versus* 14,9%, p=0,477), medium hospital stay (10,97 ± 9,282 days *versus* 8,77 ± 9,418 days, p=0,108) and hospital mortality (7,5% *versus* 2,1%, p= 0,209) did not differ between groups.
CONCLUSION: Although clinically more severe and more frequently associated with concomitant diseases, acute pancreatitis in the elderly patients did not determine a higher mortality rate in our study.
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Disclosure of Interest: None Declared
Keywords: Acute Pancreatitis, clinical characteristics, elderly patients, outcome

P651 THE ROLE OF PSMAD2,3L-THREONINE IN THE MURINE PANCREATITIS MODEL

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INTRODUCTION: Pancreatic exocrine acinar cells have regenerative ability from acute pancreatitis in mice and increase expression of several genes associated with undifferentiated pancreatic progenitor cells. In our previous report, we showed that, in small intestines,colons and Helicobacter-associated gastritis, pSmad2/3L-Threonine (pSmad2/3L-Thr) immunostaining-positive cells were detected in specific epithelial cells where the respective putative stem cells are thought to exist. We observed pSmad2,3L-Thr expression in pancreas to elucidate the location of progenitor cells in the pancreas after caerulein-induced pancreatitis.
AIMS&METHODS: The aims of this study are to characterize cell proliferation and differentiation during regeneration after caerulein-induced pancreatitis and to evaluate the role of pSmad2,3L-thr positive cells. Male C57BL/6 mice received 7times hourly intraperitoneal injections of caerulein, each consisting of 50μg/kg of body weight, and were analized on the day 1,2,4,7 after induced pancreatitis. Tissue sections were immunostained for pSmad2,3L-Thr with Ki67, amylase and CK-19 to determine the functions of pancreatic progenitor cells.
RESULTS: Immunohistochemical analysis revealed pSmad2/3L-Thr immunostaining-positive cells increased in acinar cells(co-localization with amylase), duct-like tubular complexes and duct cells(co-localization with CK-19) in the process of the pancreatitis, this phenomenon was observed during acinar-to-ductal metaplasia (ADM). Furthermore, pSmad2/3L-Thr positive cells significantly increased on the day2 simultaneously with Ki67 positive actively proliferating cells. However, immunohistochemical co-localization of pSmad2/3L-Thr with Ki67 was never observed at any points. These results suggest that pSmad2/3L-Thr positive cells within the proliferating lesions may remain in the quiescent and undifferentiated state.
CONCLUSION: pSmad2,3L-Thr expression occurs during acinar-to-ductal metaplasia(ADM) following induced caerulein pancreatitis and may contribute to the differentiation of the pancreatic progenitor cells.
Disclosure of Interest: None Declared
Keywords: pancreatitis, pSmad2,3L-Thr, regeneration

P652 EFFECT OF CIGARETTE SMOKING ON THE PRODUCTION OF ADVANCED OXIDATION PROTEIN PRODUCTS (AOPP) IN PLASMA OF PATIENTS WITH ACUTE PANCREATITIS

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INTRODUCTION: Cigarette smoking is one of the many factors inducing oxidative stress. As a result of oxidation modifications may be formed advanced oxidation protein products (AOPP) in the blood - different forms of proteins in terms of structure, function and physicochemical properties.
AIMS&METHODS: The study was aimed to determine the relationship between cigarette smoking and AOPP production in patients with acute pancreatitis (AP). Materials were plasma and serum obtained from 30 patients with AP and 39 persons from control group. The study population was divided into subgroups of smokers and non-smokers based on the serum cotinine determination (ELISA method). AOPP concentration was determined by spectrophotometric method developed by Witko-Sarsat et al. (1996r.) and based on the reaction of plasma AOPP and potassium iodide in an acidic medium. In order to express the amount of AOPP production for 1 gram of albumin, the plasma albumin concentration by colorimetric method using bromocresol purple (BCP) was determinated.
RESULTS: It was shown a reduced albumin concentration in the group of non-smoking patients with AP (35.53±8.14 g/l) and smoking (38.69±8.98 g/l) compared to non-smoking control group (44.94±10.52 g/l) (p=0.0123 and p=0.0294). The difference in albumin concentration between the smoking control group (51.63±9.37 g/l) and smoking patients was demonstrated (p=0.0307). It was noted a higher AOPP concentration in the group of non-smoking patients (39.71±14.71 umol/l) compared to non-smoking control group (33.18±5.64 umol/l) (p=0.0385). A difference between the group of smoking patients (45.25±9.52 umol/l) compared to non-smoking (p<0.0001) and smoking control group (33.04±5.52 umol/l) (p=0.0434) was shown. It was observed an increased AOPP/albumin coefficient in the group of patients: non-smokers (1.14±0.45 umol/g) and smokers (1.20±0.53 umol/g) compared to non-smoking control group (0.74±0.21 umol/g) (p=0.0003 and p<0.0001).
CONCLUSION: Acute pancreatitis is an important factor causing a decrease in albumin concentration and an increase in AOPP formation and cigarette smoking can intensify this process.
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Disclosure of Interest: None Declared
Keywords: acute pancreatitis, cigarette smoking

P653 IMPACT OF CLINICAL PATHWAY ON TREATMENT OUTCOME IN PATIENTS WITH ACUTE PANCREATITIS

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INTRODUCTION: Acute pancreatitis (AP) is one of the most common reasons for hospitalization among all gastrointestinal diseases, and is associated with high mortality and costs of treatment.
AIMS&METHODS: To determine the impact of clinical pathway (CP) and control of indicators of quality (IOQ) on the outcome of treatment in patients with AP. All medical records after the introduction of CP are analyzed monthly and are discussed at the departmental meeting with emphasis on the most common deficiencies of the treatment. A retrospective analysis of medical records was performed and the following data were analyzed: demographic features of patients, etiology of AP, severity of acute pancreatitis, diagnostic procedures performed during hospitalization, antibiotic therapy prescribed, outcome of AP. We compared results of two periods in our centre: before (2006-2007) and after (2010-2012) implementation of CP.
RESULTS: There were 139 patients treated in the three-year period after introduction of CP: 81(58.3%) male and 58 (41.7%) female, mean age 59.6±17.3 years. The most common etiologies were alcoholism and gallstones (38.8% each), followed by unexplained (11.5%), drug-induced, hypertriglyceridemia, post ERCP (2.9% each) and tumors (2.2%). Antibiotic therapy was prescribed in 72 (51.8%) of patients.
The most frequent morphological condition was interstitial edematous pancreatitis in 60.4% of patients, followed by acute peripancreatic fluid collection (25.9%), necrotizing pancreatitis (12.2%) and pancreatic pseudocysts (1.4%). Abdominal US was performed in all patients in the first 24 hours. CE CT was performed in 57 (41%) of patients. Thirty-two (23.0%) patients were treated in ICU. Four patients died (2.9%). We found an increase in the number of alcoholic and gallstone pancreatitis on the account of a decrease in unexplained etiology in 2010-12, compared to 2006-7. The differences in the structure are statistically significant (Chi-square =39.398, df= 3, p=0.000). The use of antibiotics significantly decreased after implementation of CP (from 70.3% to 51.8%; p=0.003). There was no statistically significant difference in mortality (1.8% vs. 2.9%). Length of stay in Slovenj Gradec General Hospital is significantly shorter compared to Slovenian average (p=0.018).

CONCLUSION: Introduction of CP and control of IOQ has improved the treatment of patients with AP in all observed parameters: reduced length of stay,reduced percentage of unexplained cases, reduced use of antibiotic therapy (without changes in total mortality)
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Keywords: Acute Pancreatitis, outcome

P654 EVALUATION OF NGAL AS A BIOMARKER IN PREDICTING PERSISTENT AKI AND SEVERE ACUTE PANCREATITIS(SAP)

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INTRODUCTION: Acute kidney injury (AKI) in severe acute pancreatitis (SAP) causes high mortality and serum creatinine is an insensitive biomarker for these acute changes. Neutrophil gelatinase-associated lipocalin (NGAL), is a glycoprotein secreted by activated neutrophils, and has been used to predict AKI.
AIMS&METHODS: To study the role of plasma and urinary NGAL in predicting acute kidney injury (AKI) and severity (classified as per Atlanta criteria) in patients with acute pancreatitis (AP).
Fifty consecutive patients with AP within 3 days of symptom onset and age matched healthy controls were studied. Patients were treated as per a uniform protocol. Patients were tested for urinary and serum NGAL levels (ELISA) within 24 hours of admission and after 72 hours. Serum and urine NGAL were tested once in controls. Urine and serum NGAL levels were correlated with severity of AP and development of AKI.
RESULTS: Pancreatitis patients were aged 13-85 yrs (males 60%), with 31 age and sex matched controls. The mean serum-NGAL levels (587.66±251.5ng/ml [day1], 573.98±259.86ng/ml[day3]) and mean urine-NGAL levels (252.84±165.89ng/ml [day1], 202.36±132.46ng/ml[day3]) were significantly higher in patients with AKI ($p<0.05$). Mean serum and urine NGAL levels in controls were 15.10±6.29 and 4.26±4.57 ng/ml respectively. Both serum NGAL (cut off day1-705ng/ml & day3-650 ng/ml, AUC-0.77) and urine NGAL (cut off day1-293ng/ml&day3-205ng/ml, AUC-0.89) predicted persistent AKI with good sensitivity and specificity (p=0.000). Serum and urine NGAL levels at admission correlated with severity (4-tier and Atlanta classification), APACHE and BISAP score and mortality ($p<0.05$). Patients who had high urine-NGAL on day1(n=36) had significantly higher mortality(11 patients had persistent AKI(5 expired) while 7 patients had transient AKI(4 expired); this was statistically significant (p=0.001)).Of the patients who had lower urine-NGAL on day1(n=14), none had persistent AKI and 3 had transient AKI . Day1 urine-NGAL had a high probability to predict persistent AKI as well as mortality. At a cut off of 221ng/ml, urine-NGAL had a sensitivity and specificity of 65% in predicting severe pancreatitis (AUC=0.755,p=0.013). NGAL levels were significantly higher in AP than in controls both in serum and urine on both days(p=0.00).
CONCLUSION: NGAL(both serum and urinary) predicts AKI and severity in acute pancreatitis. Day1 urine-NGAL can be used to predict AKI, both its occurrence and persistence and can be used to monitor renal failure in patients with AP.
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Disclosure of Interest: None Declared
Keywords: Acute Pancreatitis, AKI, NGAL

P655 CIRCULATING LEVELS OF FGF21 ARE ELEVATED DURING THE COURSE OF ACUTE PANCREATITIS IN PATIENTS

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INTRODUCTION: Fibroblast Growth Factor 21 (FGF21) is a stress-induced hepatokine that affects glucose and lipid homeostasis via effects on white adipose tissue and possibly other tissues. Moreover, FGF21 reduces severity of cerulein-induced acute pancreatitis (cAP) in mice. Pancreatic expression of FGF21 is transiently induced in the early phase of cAP, and may evoke autocrine signalling in acinar cells that express the relevant (co)receptors for FGF21. It is currently unknown how FGF21 limits pancreatic damage during cAP, and if a similar protective effect exists in humans. As an initial step to address the role of FGF21 in human AP, we determined FGF21 serum levels during the course of AP and studied the contribution of genetic variation in the FGF21 locus.
AIMS&METHODS: FGF21 levels were determined by ELISA in a total of 219 sera from AP patients at 0-9 days after onset of symptoms, and in 61 healthy controls. In addition, over 400 patients with AP and 1080 healthy controls were genotyped for three SNPs with predicted loss of FGF21 function and for one promoter variant with predicted impairment of stress-induction of FGF21.
RESULTS: Relative to healthy controls (median 0.11 ng/mL, range 0.02-0.49 ng/mL), circulating FGF21 levels increased from the first day after onset of AP symptoms, becoming significantly elevated after 3 (median: 0.23 ng/mL, range 0.018-18.0 ng/mL, $P<0.01$) and 4 days (median 0.29ng/mL, range 0.02-1.3 ng/mL, $P<0.01$) before levelling off. Drastic elevation (>2.5 ng/mL, *i.e.* >5 times higher than the maximum level in healthy controls) of serum FGF21 levels was noted in several patients, mostly after 1-3 days of symptom onset. Genetic analysis failed to detect minor alleles of three of the studied SNPs in both patients and controls. The fourth SNP did not show association to acute pancreatitis.
CONCLUSION: Serum FGF21 levels become elevated during the course of AP. The stimulus for this elevation and the source of FGF21 are unknown. Elevated FGF21 levels may counteract inflammation-induced lipolysis in white adipose tissue, and prevent lipotoxicity in the already compromised pancreas in AP patients. The large interindividual variation of FGF21 levels in AP patients, and a possible pancreatoprotective action of FGF21 require further study.
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Keywords: FGF21, genetic polymorphism, pancreas, pancreatitis

P656 FACTORS ASSOCIATED WITH SEVERE OUTCOME OF ACUTE PANCREATITIS – LARGE MONOCENTRIC EXPERIENCE

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INTRODUCTION: Acute pancreatitis (AP) is an acute inflammation of the pancreas with an unpredictable evolution. There are several scales and markers which try to predict its evolution.
AIMS&METHODS: Aim: to retrospectively assess the factors associated with severe evolution of AP.
Material and method: Between January 2006 and December 2012, 822 patients with AP were admitted in our Department. According to the Atlanta criteria we classified AP as mild or severe. We performed univariant and multivariate analysis to evaluate the correlation of the following parameters with a severe outcome of AP: age, body mass index (BMI), gender, etiology of AP, serum lipase, hematocrit, white blood count, serum creatinine, aspartat-aminotransferase (AST), alanine-aminotransferase (ALT), total bilirubin, alkaline phosphatase, gamma-glutamyl transpeptidase (GGT) and C reactive protein (CRP). All biological tests were performed at admission, excepting CRP which was collected 48-72 hours from the onset of AP symptoms.
RESULTS: From the entire cohort of patients, 62.5% had mild AP and 37.5% severe AP, while the mortality rate was 4.2%. The etiology of AP was: alcoholic - 31.9%, biliary – 46.5% and non-alcoholic, non-biliary-21.6%.
In univariant analysis, the following factors were correlated with severe evolution of AP: CRP (r=0.458; $p<0.0001$), white blood count (r=0.291; $p<0.001$), creatinine (r=0.279; $p<0.001$), age (r=0.219; $p<0.0001$), AST (r=0.102, p=0.01), ALT (r=0.098, p=0.01), BMI (r=0.096; p=0.007), alkaline phosphatase (r=0.085; p=0.04), serum lipase (r=r=0.076, p=0.007); and the following factors were not correlated with severe AP: etiology (r=0.005, p=0.88), gender (r=0.024, p=0.48), hematocrit (r =-0.021, p=0.54), total bilirubin (r=0.044, p=0.27), GGT (r=0.083, p=0.06).
In multivariate analysis only the following factors were associated with severe outcome of AP: white blood count ($p<0.0001$), age (p=0.001), serum creatinine (p=0.002) and CRP (r=0.002).
CONCLUSION: In univariant analysis, CRP was the factor best correlated with a severe outcome of AP, while in multivariate analysis, besides CRP, serum creatinine, age and white blood count were the only parameters correlated with a severe outcome of AP.
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Disclosure of Interest: None Declared
Keywords: Acute Pancreatitis, mortality, severity

P657 MYRIADS OF MARKERS AND SCORING SYSTEMS FOR MULTIPLE EVENTS IN ACUTE PANCREATITIS . . .. WHICH DO WE MIX AND WHEN DO WE MATCH . . .

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INTRODUCTION: Pancreatitis includes a plethora of events and markers for risk stratification.
AIMS&METHODS: *AIMS*
To prospectively evaluate the role of serum biochemical parameters, clinical scoring systems and computerized tomography(CT) severity scoring systems in determination of severity & hospital course of acute pancreatitis at different time frames during hospitalization.
MATERIALS AND METHODS Patients with acute pancreatitis from January2009-June2011 were stratified into mild & severe pancreatitis as per Atlanta criteria. CT scan was done in all patients after & was graded as per CT severity index(CTSI) and Mortele's modifiedCTSI(mCTSI). RANSON, Acute Physiology and Chronic Health Evaluation II(APACHE) score,Bedside Index for Severity in Acute Pancreatitis score (BISAP), Modified Organ Failure Score(MOFS)were calculated along with C – ReactiveProtein(CRP), coagulation

parameters, renal functions, liver functions and blood gases. All of them were repeated as required &correlated with clinical course and outcome.
RESULTS: 250 consecutive patients with acute pancreatitis (66%males, age13–84yrs) were analyzed. CRP($p<0.001$), urea ($p<0.001$), creatinine ($p=0.002$), arterial pH($p=0.004$), bicarbonate ($HCO3^-$) ($p<0.001$), D-Dimer ($p<0.001$) were found to correlate with severity of pancreatitis on multivariate analysis along with all scoring systems.When analyzed on ROC, D-Dimer (AUC=0.970, $p<0.001$)& BISAP scores (AUC=0.976, $p<0.001$) ranked best in predicting severe pancreatitis. Need for intervention was best assessed by CTSI (AUC=0.910, $p<0.001$)& mCTSI(AUC=0.890, $p<0.001$). APACHE and MOFS were repeated weekly in hospital and the highest score amongst them correlated along with initial score in predicting organ failure (AUC=0.989,0.966, $p<0.001$), infected necrosis (AUC=0.950,0.966, $p<0.001$) & final outcome (AUC=0.886,0.905, $p<0.001$).
CONCLUSION: Different parameters are required at different time frames.Emergency teams need not concentrate on complex scores & multiple markers which can be used if the patient requires prolonged hospitalization.
At admission simple parameters like BISAP and serum D-Dimer could be valuable in stratifying pancreatitis**. Need for interventions** could be predicted better with CTSI either at onset or during hospital course**. For clinical follo-wup**in patients with prolonged hospital stay, scoring systems APACHE and MOFS are useful to predict organ failure, infected necrosis and final outcome.
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Disclosure of Interest: None Declared
Keywords: Acute Fluid Collection, pancreatitis

P658 ARTERIAL BLOOD GAS ABNORMALITIES IN ACUTE PANCREATITIS

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INTRODUCTION: Blood gas anomalies are common in patients with acute pancreatitis and its multifactorial in origin
AIMS&METHODS: *AIMS*
To study arterial blood gas abnormalities(ABG) at admission in acute pancreatitis and correlate them with various outcome.
MATERIALS AND METHODS
Patients with acute pancreatitis from January 2009-June 2012 were included into study after informed consent. They were stratified into mild & severe pancreatitis as per Atlanta criteria. ABG was obtained at admission prior to oxygen supplementation. Relevant biochemical and radiological investigations were done and institutional protocol for management of pancreatitis was followed. Outcome measures included occurrence of organ failure, infected necrosis, hospital course and mortality.
RESULTS: 450 consecutive acute pancreatitis patients(67% males, mean age-42.8±12.4yrs) were analyzed. There was no difference in arterial pH, pAo2, pCO2, $HCO3^-$ and SaO2 amongst males and females and various etiologies of acute pancreatitis. ArterialpH($p<0.001$), pAO2($p<0.001$), pCO2($p=0.007$) and SAO2($p=0.001$) correlated with severity of pancreatitis at admission. pAO2($p=0.004$) and pCO2($p=0.009$) correlated with incidence of necrosis while pH($p<0.001$) correlated with infected necrosis. Mortality correlated significantly with pH ($p<0.001$), pAO2($p<0.001$), $HCO3^-$($p=0.041$) and SpO2($p=0.043$). Arterial pH($p<0.001$), pAO2($p=0.035$), $HCO3^-$($p=0.016$) and SAO2($p=0.004$) correlated with occurrence of cardiovascular failure and hypotension. The mean pH and pCO2 in patients with respiratory failure (7.27±0.12, 33.75±5.7) were significantly lower than those without (7.35±0.06, 40.24±5.6, $p<0.001$) signifying the presence of mixed acid base disorder contributed by metabolic acidosis and alkalosis. Arterial pH correlated with all these parameters with significance even after excluding renal failure ($p<0.001$).
CONCLUSION: Arterial pH at admission is an important predictor of severity, mortality, organ failure and necrosis. Mixed acid base disorders exist in acute pancreatitis which need keen observation and correction.
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Disclosure of Interest: None Declared
Keywords: arterial blood gases, pancreatitis, respiratory failure

P659 EFFICACY OF RECOMBINANT HUMAN SOLUBLE THROMBOMODULIN ON THE TREATMENT OF SEVERE ACUTE PANCREATITIS

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INTRODUCTION: Severe acute pancreatitis (SAP) is a subgroup of acute pancreatitis with poor prognosis which is characterized by systemic inflammatory responses. The pathogenesis of SAP remains unclear, but recent studies revealed that inflammatory cytokines in SAP triggered the development of systemic inflammatory responses, including disseminated intravascular coagulation (DIC). Thus, a therapeutic agent with anti-inflammatory and anti-coagulatory effect seems to be practical for the treatment of SAP. Recombinant human soluble thrombomodulin (rTM) is an anti-coagulatory agent which was recently approve for the treatment of DIC in Japan. Furthermore, increasing numbers of reports revealed its anti-inflammatory effect through binding to cleave high mobility group box 1 (HMGB1).
AIMS&METHODS: To investigate the efficacy of rTM on the treatment of SAP. We reviewed the medical records of 12 patients who were treated with rTM for SAP in our department between 2009 and 2012. All of them were accompanied by DIC and 380U/kg of rTM was administrated once daily until resolution of DIC in addition to the other therapeutic agents, such as anti-bacterial agents and protease inhibitors (rTM group). The efficacy of rTM was evaluated by comparing the clinical outcome with that of 12 patients who were treated without rTM for SAP (Control group). Diagnosis of SAP was based on the Japanese severity scoring for acute pancreatitis.
RESULTS: As expected, SAP was more severe in rTM group than Control group at day 0 (day 0 is just before initiation therapy) (average age: 73.7 *v.s* 57.5, APACH II score: 13.6 *v.s* 7.3, CRP level: 21.9mg/dL *v.s* 15.0mg/dL, $P<0.05$). And, the ratio of patients with infected pancreatic necrosis was 50% for rTM group and 25% for Control group. In rTM group, the resolution of DIC was observed in 100% of cases. And the average level of CRP at day 7 was 8.31mg/dl, which was significantly lower than CRP level at day 0 ($P<0.05$). Negative conversion days in CRP were 20.7 days, and oral intake period were 9.9 days, and hospitalization days were 40.8 days. In addition, HMGB1 level was a tendency to decrease from 22.8ng/mL (at day 0) to 15.3ng/mL (at day 7). In Control group, there were no patients accompanied by DIC at day 0. And, the average level of CRP at day 7 was 4.51mg/dL, Negative conversion days in CRP were 18.5 days, oral intake period was 9.5 days, and hospitalization days were 30.6 days. Of note the clinical outcome of rTM group was not inferior to that of Control group. Moreover, HMGB1 level at day 7 in Control group (25.6ng/mL) was not decreased as compared with 20.2ng/mL at day 0.
CONCLUSION: rTM might be a novel therapeutic agent for the treatment of SAP.
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Disclosure of Interest: None Declared
Keywords: Acute Pancreatitis, disseminated intravascular coagulation, thrombomodulin

P660 CLINICAL COURSE OF HEREDITARY PANCREATITIS IN CHILDREN.

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INTRODUCTION: Hereditary Pancreatitis (HP) is a rare inherited condition. The reported pediatric experience with HP is small. We reviewed our experience over the last 20 years.
AIMS&METHODS: The aim of our study was to evaluate the clinical course of HP in children.
209 children with chronic pancreatitis, hospitalized since 1988 to 2012, were enrolled into the study. The medical records of these patients were reviewed for data on the presentation, diagnostic findings and endoscopic treatment. All children were screened for the PRSS1 gene mutations.
RESULTS: Hereditary pancreatitis was diagnosed in 28 patients (13.4%) (20 girls and 8 boys). PRSS1 gene mutations were found in 24 patients. We detected R122H/- in 13, R122C/- in 5, N29I/- in 5 and E79K/- in 1 patient. Family history was positive in all children with HP except one. In 4 patients without mutations diagnosis of HP was made when the patients satisfied the requirements of the family history. In one patient we found SPINK1 mutation (N34S/-). In 2 children CFTR mutation (IVS8-5T(TG)11/-) was present. There was no difference in age of the disease onset between HP group and non-HP group (7,4 vs. 9.08 years; NS). In children with PRSS1 mutation ERCP had mean 2,5° Cambridge grade, vs. 1.6°, $p<0.05$. 19 patients with HP had calcifications in the imagine studies (68% vs. 31%, $p<0.05$). Therapeutic intervention, including both surgical and endoscopic intervention, was more frequent in the HP group (75% vs. 35%; $p<0.05$). Pancreatic duct stenting was done in 16 children with HP (58% vs. 26%; $p<0.05$). ESWL was performed more frequent in HP group (20% vs. 3%; $p<0.05$). Endocrine pancreatic insufficiency was observed in 7 patients (25% vs. 17,6%, NS).
CONCLUSION: Hereditary pancreatitis in children has worse clinical course than CP in children without PRSS1 mutations.
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Disclosure of Interest: None Declared
Keywords: children, GENE MUTATIONS, hereditary pancreatitis

P661 REVIEW OF PANCREATITIS IN CHILDREN - A TERTIARY CENTRE EXPERIENCE OVER 6 YEARS

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INTRODUCTION: Paediatric pancreatitis is relatively uncommon & the aetiology is diverse compared to adults. Due to heterogeneous symptoms in children it is often misdiagnosed.
AIMS&METHODS: To evaluate clinical presentation, aetiology, management & outcome of pancreatitis in children. This study reports a tertiary centre cohort of 60 children aged 0 yrs to 18 yrs with pancreatitis in the last 6 years. Diagnosis was made on clinical information with biochemical and/or radiological evidence. Demographic & clinical data were collected.
RESULTS: Sixty cohort (males 30) - Median age (yrs) was 10.5 (range: 2 to 17). Abdominal pain was the predominant symptom (86%) & in one third it was the only symptom. Thirty eight (63%) had acute pancreatitis **(AP)** of which 5 had recurrent acute pancreatitis. Twenty two (37%) had chronic pancreatitis **(CP).** In AP the predominant aetiology was Biliary disease in 36.8% half of them had associated Pancreato-biliary anatomic (PBA) anomalies and trauma in 23.7%. In CP the predominant aetiology was hereditary (27.3%) and idiopathic (27.3%). In hereditary group: PRSS1 & SPINK1 gene mutations in 86% & 14% respectively. Table 1: Aetiology (Top five) of AP and CP

	AP		CP	
	Aetiology	% Of AP	Aetiology	% Of CP
1	Biliary	36.8	Hereditary	27.3
2	Trauma	23.7	Idiopathic	27.3
3	Idiopathic	10.5	Biliary	13.6
4	Multisystem including infections	7.9	Autoimmune	13.6
5	Metabolic	7.9	PBA Anomalies	9.0

Other causes: AP - Isolated PBA anomalies in 5.4% and 2.6% each of autoimmune, hereditary & drug induced. CP - Multisystem & metabolic in 4.6% each. MRCP & ERCP were done in 73% and 65% respectively. In the entire cohort - PBA anomalies were identified in 11/60 (18.3%) and aetiology was idiopathic in 10/60 (16.6%).
One-third (36.7%) was medically managed, 26.6% had therapeutic ERCP (stent insertion), 25% had surgical intervention (cystogastrostomy -2, hepaticojejunostomy - 9, distal pancreatectomy -2 & Puestow procedure - 2) and 11.7% had ERCP & surgery. Mean number of inpatient admissions - 4.6 (range 1 to 14). Mean cumulative hospital stay for each patient - 21.5 days (range 1 to 81 days). Complications (25%) of which Pseudocyst in 9 (15%). One (1.6%) died due to systemic illness.
CONCLUSION: In our centre acute pancreatitis in children is predominantly associated with Biliary disease and trauma. One-fourth of chronic pancreatitis was hereditary. Extensive investigation including genetic testing is required to determine aetiology, as the outcome is dependent on it. Paediatric Pancreatitis has significant morbidity. Children with pancreatitis need to be referred to a tertiary centre where paediatric ERCP facility is available.
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Disclosure of Interest: None Declared
Keywords: Acute Pancreatitis, Children, Chronic Pancreatitis

P662 MANAGING CYSTIC PANCREATIC LESIONS. THE EXPERIENCE AT A REGIONAL CANCER CENTRE IN THE UK

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INTRODUCTION: Cystic pancreatic lesions are increasingly recognised due to higher detection rate afforded by current CT technology. Concerns about malignant transformation have led to many attempts at stratifying this risk. Our regional protocol involves CT followed by EUS and fluid analysis. High risk lesions are resected if patients tolerate surgery, medium risk lesions are followed with CT and patients with low risk lesions are reassured and discharged.
AIMS&METHODS: To review the success of the risk stratification strategy and to assess the predictive capability of the various indicators.
All cases of pancreatic cysts that underwent EUS at our referral centre between August 2009 and February 2013 were included. All patients underwent CT with a pancreatic protocol and EUS with FNA. Amylase, CEA and CA 19-9 were estimated in the fluid at a single laboratory. Cyst characterisation was done at EUS by a single operator. An experienced cytopathologist reported on all smears. Surgery was performed at the Pancreatic-biliary Cancer unit at King's College Hospital, London.
RESULTS: We included 99 patients with average age of 68 years (53.5 % female and 46.46 % male). All patients had EUS within 2.65 months of the index CT. 59 % of the cysts were in the head, 17 % in the body and the rest were in the neck, uncinate and tail. The average cyst area was 6.59 cm^2 [0.27-100]. The EUS diagnosis was of mucinous cystadenoma in 24 %, pseudocysts in 19 %, serous cystadenoma in 12 % and IPMN in 14 %. Of these, 11 were branch IPMN, the rest were main duct IPMNs. Three patients had an associated mass. Although cytology was productive in 83 cases, diagnostic information was obtained in 49 (50%) with positive mucin stain, 4 with atypical cells (2 were malignant), 3 with papillary and 1 with neuroendocrine. A sample adequate for fluid biochemical analysis was obtained in 48 cases. Positive cytology or suspicious CT influenced the decision to operate. Nine patients underwent surgery. Of these 3 had mucinous cystadenoma, 1 IPMN, 3 pseudocysts, 1 papillary neoplasia and one neuroendocrine tumor. Another patient had an adenocarcinoma with cyst degeneration, not candidate for surgery. None of the cases surveyed developed malignancy during the surveillance period. None of the patients discharged developed malignancy but information on this group is not universally available.
CONCLUSION: The risk stratification protocol for pancreatic cysts reliably detects individuals with high risk lesions. CT and cytology are most useful in identifying high risk lesions and EUS and cyst fluid analysis identify low risk lesions. Overall, the risk of malignancy in this group is low and an expectant approach as practiced in the majority appears appropriate.
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Disclosure of Interest: None Declared
Keywords: Endoscopic Ultrasound, Intraductal papillary mucinous neoplasm, mucinous cystadenoma, Pancreatic cystic neoplasms, serous cystadenoma

P663 DIAGNOSTIC ACCURACY OF CONTRAST-ENHANCED COMPUTED TOMOGRAPHY IN ASSESSING EXTRA-REGIONAL LYMPHADENOPATHY IN PANCREATIC CANCER: A SYSTEMATIC REVIEW

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INTRODUCTION: Pancreatoduodenectomy is the only potentially curative option for patients with pancreatic cancer. One of the contra-indications for curative resection is extra-regional lymph node (ELN) metastases. Although computed tomography (CT) quality improved over the last decade, pre-operative evaluation of ELN may be difficult. This is the first systematic review that focuses on the CT in assessing ELN metastases in pancreatic or peri-ampullary cancer.
AIMS&METHODS: The aim of this study was to determine the diagnostic accuracy of CT in assessing ELN metastases in pancreatic cancer.
We performed a systematic review in PubMed/Embase/Cochrane according to the PRISMA guidelines of studies published up to March 22nd 2013. Studies reporting on the CT assessment of ELN in patients undergoing pancreatoduodenectomy were included. We excluded studies that did not report the number of suspected ELN on CT and number of ELN metastases during histopathological investigations; i.e. if it was not possible to construct a 2×2 contingency table. Data on baseline characteristics, CT-investigations and histopathological outcomes were extracted. Diagnostic accuracy, positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity were calculated for individual studies and pooled data.
RESULTS: After screening 4.030 studies, 4 cohort studies reporting on CT-findings and histopathological outcome in 157 patients with pancreatic cancer were included. Histopathologically proven ELN metastases were present in 28/157 (18%) patients, which had been diagnosed pre-operatively on CT in 7 (25%) patients. Of the remaining 129 patients without ELN metastases, CT falsely suggested presence of ELN metastases in 18 patients. Overall diagnostic accuracy varied from 63-81% and specificity, PPV and NPV ranged from 80-100%, 0-100% and 67-90% respectively. However, sensitivity was poor with ranges from 0-38%. Pooled accuracy, sensitivity, specificity, PPV and NPV were 75%, 25%, 86%, 28% and 84% respectively.
CONCLUSION: CT has a low diagnostic accuracy in assessing ELN metastases in patient suspected of pancreatic cancer. We therefore propose that – in absence of other signs of irresectability, e.g. liver metastases, arterial encasement – the suspicion of ELN metastases on CT should not be a contra-indication for explorative laparotomy and, when possible, pancreatoduodenectomy.
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Disclosure of Interest: None Declared
Keywords: Computed tomography, diagnostic accuracy, lymph node metastases, Pancreatic Cancer, systematic review

P664 RESECTION MARGIN CLEARANCE IN PANCREATIC CANCER AFTER IMPLEMENTATION OF THE LEEDS PATHOLOGY PROTOCOL (LEEPP): CLINICALLY RELEVANT OR JUST ACADEMIC?

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INTRODUCTION: Applying rigorous standardized histopathological protocols in the examination of resection specimens of PDAC of the pancreatic head reveals microscopic incomplete (R1) resection rates of up to and greater than 80%. Aim of this study was to assess oncological outcome in patients after R0/R1 resections in a homogenous cohort suffering from ductal adenocarcinoma (PDAC) of the pancreatic head.
AIMS&METHODS: Between January 2007 and May 2011, 125 consecutive patients underwent surgical pancreaticoduodenectomy (PD) or pylorus-preserving PD because of PDAC of the pancreatic head. These patients were histopathologically examined according to a standardized protocol (Leeds Pathology Protocol *LEEPP*). The oncological outcome and clinicopathological data were compared to a matched patient group before implementing the abovementioned protocol (n = 108).
RESULTS: The R1 rate increased significantly after implementing the LEEPP from 13 to 52%. A difference in overall survival (OS) could not be detected between R0 and R1 resections. The median OS in patients with a tumor clearance

of less than 2 mm from the resection margin was 15.1 months (12.1 to 18.1 months) vs. 22.2 months (7.8 - 36.7 months) (P = .046). Multivariate analysis revealed a margin clearance or 2mm and more as independent prognosticator for OS.
CONCLUSION: With applying a standardized histopathological protocol, there was still no correlation between the R-status and OS in patients with PDAC. However, since a margin clearance of 2 mm or more is a predictive factor for OS the R1 definition might have to be changed in PAC.
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Disclosure of Interest: None Declared
Keywords: Pancreatic Cancer, Pathology, Prognosis, Resection margins, Survival Rate

P665 EFFICACY OF EUS-IMPLANTED FIDUCIAL MARKERS TO DIMINISH MARGINS IN RADIATION OF PANCREATIC CANCER

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INTRODUCTION: Radiation treatment of pancreatic tumors uses target volume margins to correct for the substantial day-to-day position variation of the pancreas. Modern linear accelerators (linacs) are equipped with Cone-Beam CT (CBCT), a CT device with reasonable image quality enabling imaging during treatment. Fiducial markers in the pancreas are well visible on CBCT. These markers can help diminish the error in daily patient treatment, thereby reducing the large margins. Consequently the radiation exposure of surrounding healthy tissue can be reduced. The aim of our study is to study the feasibility of EUS-guided placement of fiducial markers and to quantify interfractional position variation using these markers.
AIMS&METHODS: Eleven consecutive patients with borderline-resectable pancreatic cancer were included in our study. Each patient had 2 or 3 flexible gold fiducials (Visicoil; 10–20 mm, 0.35mm diameter; 27 in total) implanted under EUS-guidance using a 22-gauge needle. Daily CBCTs were obtained before each of 25 radiation fractions and registered with the reference CT on bony anatomy and on each of the fiducials. From this, the position variation of the fiducials relative to the vertebrae was measured as well as the distance between the markers.
RESULTS: In 10 out of 11 patients fiducial markers could be detected on the treatment planning CT, 0 to 5 (average 3.4) days after implantation, as well as on all 242 CBCTs obtained during treatment. A clear shift in the distance between markers that would indicate marker migration was not seen for any of the 20 pairs. Position variations (displacements) were largest in the cranio-caudal direction. For 51/242 (21%) of fractions, the variation in at least one direction was >10mm.
CONCLUSION: The large position variation and its range between patients strongly supports the benefit and
necessity of EUS-implanted fiducial markers for better focusing the radiation to the pancreas tumor, enabling
smaller safety margins
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Disclosure of Interest: None Declared
Keywords: fiducial markers, EUS-guided, Pancreatic Cancer, radiotherapy

P666 DAXX/ATRX AND MEN1 GENES ARE STRONG PROGNOSTIC MARKERS IN PANCREATIC NEUROENDOCRINE TUMOR

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INTRODUCTION: The incidence and prevalence of pancreatic neuroendocrine tumors (PNET) are increasing; these tumors represent approximately 1.3% of all cases of pancreatic cancer in incidence and 10% of cases in prevalence. PNET has usually better prognosis compared to that of pancreatic ductal adenocarcinoma, however, some of PNETs are diagnosed as in advanced stage with distant metastasis. Accurate prediction of its prognosis and the proper treatment may be very important in patients with PNETs.
AIMS&METHODS: The aim of this study was to explore prognostic markers based on genetic basis of PNETs and they were known as the most frequently mutated genes MEN1, DAXX/ATRX. The pathologically confirmed 111 patients with PNETs were enrolled and the following clinical and pathologic factors were evaluated; AJCC stage, treatment modalities, differentiation and mitosis. Also, immunohistochemical staining of MEN1, DAXX/ATRX genes, Ki-57, chromogranin, synaptophysin, CD56, somatostatin, insulin and glucagon were done.
RESULTS: The median age of study patients was 55 yrs and AJCC staging of the patients were as follows: IA; 41 patients, IB; 30 patients, IIA; 13 patients, IIB; 8 patients, IV; 19 patients. The median OS was 55.5 months and 81 patients underwent R0 resection. There were 23 patients (27%), 17 patients (20%) and 27 patients (31%) were positive for MENIN, ATRX and DAXX respectively. In addition, DAXX and ATRX are known to be mutually exclusive genes. Mutations in the MEN1 and DAXX/ATRX genes were resulted in negative immunohistochemical staining and it was significantly associated with longer DFS () and OS (33 mo. vs. 65 mo., $p < 0.01$; 63 mo. vs. 124 mo., $p < 0.001$ respectively). AJCC staging and grade of differentiation were the statistically significant prognostic factors among other clinical variables.
CONCLUSION: Mutations in the MEN1 and DAXX/ATRX genes (negative immunohistochemical staining results) were associated with better clinical prognosis. This study was the first one to investigate prognostic markers based on genetic basis of PNETs.
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Disclosure of Interest: None Declared
Keywords: DAXX/ATRX gene, MEN gene, neuroendocrine tumour

P667 POSTOPERATIVE RECURRENCE IN PATIENTS OPERATED ON FOR BENIGN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMN)

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INTRODUCTION: Risk of postoperative recurrence in patients operated on for benign IPMN has not been extensively studied. Benign and malignant IPMN were often considered together, and recurrence not always distinguished from lesions not resected at time of surgery.
AIMS&METHODS: To evaluate the recurrence rate of IPMN and the occurrence of non IPMN-related pancreatic adenocarcinoma after partial pancreatectomy for benign IPMN; to assess the need for reoperation; to look for predictive factors of relapse. Clinical, imaging and pathological data were collected for all consecutive patients operated on in a single centre between 1998 and 2008. Recurrence of IPMN was evaluated on MRI performed at intervals depending on the stage of resected lesions. Recurrence was defined as new cystic lesions communicating with main pancreatic duct. The evolution of IPMN cysts not resected during surgery was documented but not considered as a recurrence. A minimal 2-yearpostoperative follow-up was necessary.
RESULTS: The data for 125 patients (63 males, median age at surgery 60 (20-77) yrs, low (LGD), moderate (MGD), high (HGD) grade dysplasia in 47, 43 and 35 pts, respectively) were analysed. IPMN involved branch ducts (BD, n=69), main pancreatic duct (MPD, n=5) or mixed-type, n=51. Examination of pancreatic section showed no IMPN lesion in 83 pts, LGD in 42 pts, MGD or HGD in no pts. Median postoperative follow-up was 4(2-13) years. 83 pts had no residual lesion after surgery (group 1, median F/U: 4yrs (2-13)), while 42 had some lesions deliberately not resected in order to avoid extensive pancreatectomy (group 2, median F/U: 4 yrs (2-8)). 3 recurrences were observed in Group 1 pts, all of them were invasive recurrence leading to total pancreactectomy. In group 2 pts, no new lesion occurred in any pt but 1 or more changes in existing lesions were observed in 5 pts (increase in size, mural nodule, MPD involvement, occurrence of symptoms in 3, 1, 2 and 1 pts, respectively, leading to total pancreatectomy in 4 pts (LGD and MGD in 2 and 2 pts respectively, 1 inoperable pt).
CONCLUSION: Postoperative relapse rate of benign IPMN is low (3.6%) after a 4-year follow-up. Detection of invasive recurrence prompts to carefully follow all operable patients. Residual lesions should be followed like de novo IPMN
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Disclosure of Interest: None Declared
Keywords: IPMN, recurrence

P668 PROGNOSTIC SIGNIFICANCE OF QUALITY OF LIFE IN PANCREATIC CANCER

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INTRODUCTION: We only use tumor marker (CA19-9) and imaging method for evaluating chemotherapy response. But, there might be several factors for predicting chemotherapy response. We evaluated quality of life (QoL) as the factor for predicting chemotherapy response.
AIMS&METHODS: Between November 2005 and April 2013, 243 patients with locally advanced or metastatic pancreatic adenocarcinoma who had favorable response at the time of first follow-up were enrolled. We defined 5 categories of QoL as ECOG, pain scale, ascites, jaundice, weight loss. We evaluate whether worsening of QoL influence to predictability for chemotherapy response.
RESULTS: 55 of 243 patients had worsening of QoL which is related to cancer. We defined these patients as group B, while rest of them defined as group A. When we accessed chemotherapy response evaluation second time, in group A, 49 (26.2%) of 188 patients had disease progression, but, in group B, 47 (85.5%) of 55 patients had disease progression ($p < 0.001$). There also be significant difference in overall survival between group A and B patients (median OS; group A : 14.3 months vs. group B : 8.8 months, $p < 0.001$). If we divided groups according to increment of CA19-9, the group who had increment of CA 19-9 at the first follow-up had poor survival outcome compared to the group who had decrease of CA 19-9 (median OS; 11.3 months vs. 13.9 months, $p = 0.012$). But, it seemed that QoL was more powerful factor for predicting chemotherapy response compared to CA19-9 (HR (hazard ratio) = 2.483 for QoL, $p < 0.001$ vs 1.277 for CA19-9, $p = 0.243$).
Table 1. Comparison of disease progression rate at the time of second follow-up and survival outcome according to worsening of QoL

	Group A*	Group B*	Total	p-value
Total, n	188	55	243	
Disease progression at the time of second follow-up, n (%)	49 (26.2%)	47 (85.5%)	96 (39.5%)	<0.001
Overall Survival (months)	14.3	8.8	13.2	<0.001
Progression-free survival (months)	7.9	4.9	6.9	<0.001

CONCLUSION: We suggest that worsening of QoL should be considered as important factor for predicting chemotherapy response. Objective measurement system for evaluating QoL will be needed for validation of QoL as the factor for predicting chemotherapy response.
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Disclosure of Interest: None Declared
Keywords: Pancreatic cancer, prognosis, quality of life

P669 EVALUATION OF THE ROLE OF SURGERY FOR METASTATIC PANCREATIC CANCER: A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Metastasectomy has become standard treatment for some malignancies. However, the role of surgery for metastatic pancreatic cancer remains unclear because these tumors are uncommon.
AIMS&METHODS: A retrospective study during the period between April 2000 to March 2013 was designed to evaluated the surgical treatmetn and prognosis of metastatic pancreatic cancer in our institution.
RESULTS: Nine patients with metastatic pancreatic cancer were identified. Of these 9 patients, 4 were men and 5 were women with a mean age was 62 (49-76) year-old. Primary cancer were renal cell carcinoma (RCC) in 7 and lung cancer (LC) in 2. The tumor was located in the head in 2, in the body in 2, in the tail in 2, and the other 3 cases were multiple metastasis. Surgical method included pancreaticoduodenectomy in 2, distal pancreatectomy in 2, total pancreatectomy in 2, pancreaticoduodenectomy with partial resection in 1, partial resection in 1, and laparoscopic distal pancreatectomy in 1. Median desease free survival after metastasectomy of RCC was 2.8 years. All patients of RCC except 2 cases (died of other illness) were alive at follow up period and 5-year survival rate was 75.0%. All the recurrent cases of RCC were treated molecular target therapy such as sorafenib or sunitinib. In the LC group, one patinet who was diagnosed pleomorphic carcinoma died of local recurrence only 3 months after metastasectomy. In contrast, the other patinent who underwent laparoscopic surgery is alive more than 1 year after metastasectomy without any recurrence.
CONCLUSION: An aggressive surgical resection combined with molecular target therapy contributes long-term survival of the patients of pancreatic metastasis from RCC. However, usefulness of the pancreatic metastasectomy of LC is still unclear and their prognosis may depend on pathological diagnosis. Laparoscopic surgery should be considered in the cases of isolated pancreatic metastasis with neither local invasion nor lymph node metastasis.
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Disclosure of Interest: None Declared
Keywords: metastasectomy, metastasis, pancreas, pancreatectomy

P670 TREATMENT STRATEGIES AFTER CURATIVE RESECTION OF PANCREATIC ADENOCARCINOMA: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

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INTRODUCTION: Major adjuvant therapies for pancreatic cancer include 5-fluorouracil, gemcitabine, chemoradiation, and chemoradiation plus 5- fluorouracil or gemcitabine. The optimal therapy remains elusive, and opinions on chemoradiation are divisive.
AIMS&METHODS: We conducted a random-effects Bayesian network meta-analysis to compare observation and these adjuvant therapies in terms of overall survival. We systematically reviewed randomised controlled trials comparing the above 6 treatment strategies. For meta-analysis of overall survival, hazard ratios (HRs) and survival durations were combined in a single network meta-analysis, and the influences of prognostic factors on effects of adjuvant therapies were evaluated with meta-regression.
RESULTS: Compared with observation, the HR (95% credible interval) for death was 0.62 (0.42-0.88) with 5-fluorouracil, 0.68 (0.44-1.07) with gemcitabine, 0.91 (0.55-1.46) with chemoradiation, 0.54 (0.15-1.80) with chemoradiation plus 5-fluorouracil, and 0.44 (0.10-1.81) with chemoradiation plus gemcitabine. The HR for death of adjuvant therapies vs observation increased by 2.5% (95% credible interval 0% to 5.3%) per 1% increase in the percentage of patients with positive lymph nodes. After adjustment for this factor, 5-FU and gemcitabine provided a significant survival benefit over observation alone [HR 0.65 (0.49-0.84) and 0.59 (0.41-0.83), respectively], whereas chemoradiation was associated with worse overall survival compared with 5-FU [HR 1.69 (1.12-2.54)] and gemcitabine [HR 1.86 (1.04-3.23)].

Table 1. Included randomised controlled trials

Author, year	Trial	Treatment arms
Kalser, 1985	GITSG	ChemoRT plus 5-FU/observation
Neoptolemos, 2001	ESPAC-1	Observation/5-FU/chemoRT
Neoptolemos, 2004	ESPAC-1	Observation/5-FU/chemoRT/ chemoRT plus 5-FU
Oettle, 2007	CONKO-001	Observation/gemcitabine
Smeenk, 2007	EORTC 40891	Observation/chemoRT
Regine, 2008	RTOG 9704	ChemoRT plus 5-FU/chemoRT plus gemcitabine
Ueno, 2009	JSAP-02	Observation/gemcitabine
Neoptolemos, 2009	ESPAC-1+/3 (v1)	Observation/5-FU
Neoptolemos, 2010	ESPAC-3 (v2)	5-FU/gemcitabine

ChemoRT: chemoradiation.
CONCLUSION: Compared with observation and chemoradiation, adjuvant 5-FU and gemcitabine prolonged overall survival after resection. Adding chemoradiation to 5-FU or gemcitabine did not provide significant additional survival benefit. Lymph node positivity adversely affected the overall survival advantage of adjuvant therapy over observation.
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Disclosure of Interest: None Declared
Keywords: adjuvant chemothrapy, chemoradiotherapy, Meta-analysis, Pancreatic Cancer

P671 OBJECTIVE ASSESSMENT OF SURGICAL RESTAGING AFTER CONCURRENT CHEMORADIATION FOR LOCALLY ADVANCED PANCREATIC CANCER

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INTRODUCTION: The role of neoadjuvant chemoradiation therapy in locally advanced pancreatic cancer (LAPC) is still controversial, and previous studies did not provide objective improvements after neoadjuvant treatment.
AIMS&METHODS: The aim of this study was to evaluate surgical downstaging after concurrent chemoradiation therapy (CCRT) for LAPC by measuring the objective changes after treatment. From January 2003 through July 2011, 54 patients with LAPC underwent neoadjuvant CCRT. CT findings about tumor size, major vessel invasion before and after CCRT were analyzed.
RESULTS: Fourteen patients had borderline resectable and 40 patients had unresectable disease before CCRT. After CCRT, partial response was achieved in 4 patients. Stable disease and progressive disease were noticed in 36 and 14 patients, respectively. Tumor size showed no significant difference before and after CCRT (3.6 ± 1.1 vs. 3.6 ± 1.0 cm, $P = 0.61$). Vessel invasion was improved in 2 patients, while aggravated in 13 patients. Thirty-nine patients with unresectable and 11 patients with borderline resectable state at initial diagnosis still had unresectable and borderline resectable state after CCRT, respectively. Four borderline pancreatic cancers were aggravated to unresectable pancreatic cancer, whereas 1 unresectable pancreatic cancer was improved to borderline resectable after CCRT. Only 1 patient with borderline resectable disease underwent operation after CCRT, however curative resection was failed due to CA invasion and peritoneal seeding. The adverse events associated with CCRT were tolerable.
CONCLUSION: Preoperative CCRT in LAPC rarely leads to surgical downstaging, and it could make resectability rate become lower.
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Disclosure of Interest: None Declared
Keywords: chemotherapy, locally advanced pancreatic cancer, Neoadjuvant therapy, Pancreatic neoplasm, radiation therapy

P672 CUX1 – A MARKER OF INVASIVE PHENOTYPE IN NEUROENDOCRINE TUMORS OF THE PANCREAS

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INTRODUCTION: Previously, we identified the transcription factor CUX1 as a mediator of proliferation, resistance to apoptosis, invasiveness and angiogenesis

in neuroendocrine tumor cells. However, the molecular signaling pathways driving CUX1 effects in neuroendocrine neoplasias (NEN) remain to be elucidated.
AIMS&METHODS: The aim of this study is to characterize CUX-dependent signaling pathways mediating its tumor-promoting effect in-vitro and in-vivo.
We used an RNA profiler comprising 84 key genes involved in neoplastic transformation, invasion and angiogenesis. The target genes were validated on protein level via Western Blot. In addition, CUX1 was also evaluated in-vivo by xenograft experiments of CUX1 overexpressing Bon1 cells in nude mice. Furthermore CUX1 expression was assessed in a human micro tissue array (MTA) of 63 human insulinomas.
RESULTS: Several target genes mediating tumor invasion and metastasis were upregulated by CUX1 on mRNA level, among them MMP2, MMP9, TGFß, HIF-1α and integrin-α-5. CUX1-dependent regulation of MMP9 and HIF-1α was further validated on protein level. In vivo, CUX1 overexpression led to an increased tumor volume which was accompanied by a significantly higher proliferation index and increased microvessel density, as assessed by Ki-67 and CD31 immunostaining. Under hypoxic cell culture conditions, CUX1-expressing tumor cells showed increased HIF-1α levels, suggesting a role of CUX1 in mediating HIF-dependent escape mechanisms in tumor hypoxia. Immunohistochemically, CUX1 expression was evaluated in 63 human insulinomas using a multiple tissue array: In this series, malignant insulinomas expressed higher CUX1 levels compared to those with benign behavior, with a trend towards higher expression in metastatic versus primary tumors.
CONCLUSION: These data identify CUX1 as important mediator of an invasive proangiogenic phenotype in malignant pancreatic neuroendocrine tumors in-vivo and suggest a role for CUX1 in mediating HIF-1α-dependent escape mechanisms to antiangiogenic strategies.
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Disclosure of Interest: None Declared
Keywords: angiogenesis, CUX1, neuroendocrine tumour

TUESDAY, OCTOBER 15, 2013 9:00–17:00
ENDOSCOPY AND IMAGING II – Poster Area

P673 PNEUMATIC BALLOON DILATATION IN ACHALASIA: A COMPARISON STUDY OF SAFETY AND EFFICACY WITH WITZEL DILATOR AND RIGIFLEX BALLONN

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INTRODUCTION: Several studies have shown that the use of the Witzel dilator or Rigiflex balloon is an effective and safe treatment for achalasia. But there is no consensus on the optimal method for performing pneumatic dilation (PD) and there is no comparison between these dilators.
AIMS&METHODS: to compare efficacy and safety in untreated patients with achalasia of graded PD with Witzel dilator and Rigiflex balloon. Between 1999 and 2012, two operators treated 192 patients with achalasia. They were 103 (54%) females and 87 (46%) males; mean age: 40 ± 18, 7 years (10-86), mean symptoms duration: 38±28 months (6 -190). Achalasia was diagnosed according to manomertric criteria. The dilatation was performed in the group A (n: 94) with Witzel balloon (diameter: 40 with an initial inflation pressure of 150 mm Hg during the first session. In case of relapse, dilatation was repeated with an incremental pressure (200 and 300 mm Hg) during the second and the third session. In the group B (n:96), we used the graded method with Rigiflex balloon (balloon 30 mm diameter inflated with 5 PSI pressure during 30 minutes at first session, 35 mm at the second and 40 mm at the third session). In two groups, PD was performed ambulatory, under endoscopic control, after simple premedication by diazepam. The PD was carried out every week until remission (1-3 sessions). Clinical results were evaluated according to Eckardt score.
RESULTS: The mean oesophageal diameter was 5 cm in group A vs 4.6 cm in group B , the mean lower oesophageal sphincter pressure was 33±10 mm Hg VS 33.5+/-11 mmHg and mean lower oesophageal relaxation was 49±23 VS 46.5±20. A total of 276 dilatation (152 sessions in Group A vs 124 Group B) were performed (mean: 2±1 per patient). Pneumatic dilatation was effective (immediate success) in 81 of 94 patients in group A (87%) and in 89 of the 96 in group B (93%). The difference was not statistically significant ($p < 0,3$). No perforations occurred in Witzel group and none in Rigiflex group. The rate of gastro-oesophageal reflux with esophagitis was 6% in group A vs 17% in group B, the difference was statistically significant ($p < 0.025$)
CONCLUSION: Pneumatic dilatation performed with Witzel dilator or Rigiflex balloon is an effective and safe treatment of achalasia. In the short term, the therapeutic results with both dilators are identical. Reflux is more common with Rigiflex.
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Disclosure of Interest: None Declared
Keywords: Achalasia, Rigiflex balloon, Witzel dilator

P674 PNEUMATIC DILATATION FOR THE TREATMENT OF ACHALASIA IN PATIENTS YOUNGER THAN 20 YEARS : ABOUT 90 PATIENTS

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INTRODUCTION: achalasia is a rare motor disease, seen in all ages but rarely reported before age of 20 years. Pneumatic dilation (PD) efficacy and safety in large series has not been assessed.
AIMS&METHODS: to study the profile of achalasia in this slice of age and to assess efficacy and safety of pneumatic dilatation in a large series. over a period of 10 years, from January 2000 to December 2009, all symptomatic achalasia patients younger than 20 years who referred to our centre were enrolled consecutively. They were 49 females and 41 males; mean age: 14.57 ± 4.88 years (5 months- 20 years). All patients underwent a standardized symptoms questionnaire, a barium esophagogram, an upper endoscopy and an esophageal manometry. Achalasia was diagnosed according to manomertric criteria. The dilatation was performed with a Witzel balloon or Rigiflex balloon, ambulatory, under endoscopic control, after simple premedication by diazepam (10 mg IM) . The PD was carried out every week until remission (1-3 sessions). After complete dilatation, patients were controlled at 6 month and 12 month. Clinical results were evaluated according to Vantrappen classification.
RESULTS: Achalasia was associated with Allgrove syndrome in 23 cases. A total of 252 dilatations were performed (mean: 2.8 ± 1.5 per patient). Only one session was performed in 19 patients, two in 16 patients, three in 15 patients and more than three sessions in 28 ones. Immediate success was obtained in 63 (70%) patients whereas it declined to 39% at 12 months. The final rate of failure at 12 months was 61%. 25 patients took isosrbid dinitrate, 15 (60%) of them improved. No perforation occurred in this study.
CONCLUSION: Allgrove syndrome is frequently observed in patients with achalasia before age of twenty. At short term, pneumatic dilatation is effective and safety. However, the long term success rate is rather low, resulting in permanent successful treatment of achalasia in only 39% of patients after the first sessions of dilatation.
Disclosure of Interest: None Declared
Keywords: achalasia,, manometry, pneumatic dilatation

P675 ASSESSMENT OF DUODENAL VILLOUS MORPHOLOGY USING MAGNIFICATION NARROW BAND IMAGING: A PROMISING TECHNIQUE FOR OPTIMISING DUODENAL BIOPSY PROCEDURE

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INTRODUCTION: Narrow band imaging (NBI) with magnification enables detailed assessment of the duodenal villi and may be useful in predicting the presence of villous atrophy or normal villi.
AIMS&METHODS: We aimed to assess the morphology of duodenal villi using magnification narrow band imaging and correlate it with the histology findings in patients with clinically suspected malabsorption syndrome. Patients were prospectively recruited and underwent upper gastrointestinal endoscopy using white light followed by magnification narrow band imaging. The mucosa in second part of duodenum was carefully assessed initially using white light without magnification for presence of features like scalloped mucosal folds, mucosal nodularity, atrophic mucosal folds and mosaic pattern. On NBI, presence of numerous finger or leaf shaped villi denoted a normal pattern while shortened or stubbed villi, villi in gyriform configuration or complete absence of villi suggested villous atrophy. The villous morphology on NBI in the second part of duodenum was assessed independently by two endoscopists and the presence of normal or atrophic villi was recorded. Biopsy specimen was obtained from the same area and was examined by two pathologists together. The sensitivity and specificity of magnification narrow band imaging in detecting the presence of duodenal villous atrophy was calculated compared to the histology.
RESULTS: The study included 100 patients with clinically suspected malabsorption. Their mean age was 37.5+12.4 years and 42% were females. Sixteen patients had histologically confirmed villous atrophy. The sensitivity and specificity of narrow band imaging in predicting villous atrophy was 87.5% and 95.2% respectively for one endoscopist. The corresponding figures for the second endoscopist were 81.3% and 92.9% respectively. The inter-observer agreement was very good with a kappa value of 0.87. The duodenal white light examination showed abnormal features in only two patients and hence had a very poor sensitivity of 12.5%. The final diagnosis in the sixteen patients with villous atrophy was celiac disease in 7, tropical sprue in 3, giardiasis in 2, strongyloidosis in 1, AIDS enteropathy in 1, Crohn's disease in 1 while the diagnosis could not be established in one patient with villous atrophy.
CONCLUSION: Magnification narrow band imaging performed very well in predicting duodenal villous morphology. This may help in performing targeted biopsies and avoiding unnecessary biopsies in patients with suspected malabsorption.
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Disclosure of Interest: None Declared
Keywords: duodenum, malabsorption, narrow band imaging

P676 DETECTION OF GASTRIC CANCER BY HYPERSPECTRAL IMAGING

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INTRODUCTION: Esophagogastroduodenoscopy is widely used for the screening of gastric cancer, however, skill is required to detect small gastric cancer. Image enhancement endoscopy developed in recent years, but the modality which is useful for the detection of gastric cancer has not been established yet. The hyperspectral imaging (HSI) is the new technology that obtains spectroscopic information and renders it in image form. This study examines the difference of the spectral reflectance (SR) in the gastric tumor and the normal mucosa recorded by hyperspectral camera (HSC) equipped with HSI technology and tries the specifying of the wavelength, which is useful for the diagnosis of gastric cancer.

AIMS&METHODS: A total of 104 gastric tumors removed by endoscopic submucosal resection from 96 patients at Yamaguchi University Hospital, were recorded using a HSC1701. SR was obtained from 10 samples of tumors and 10 samples of normal mucosa for each case. Because the SR varied in each case, corrected SR which was defined as subtracting mean SR of normal samples from mean SR of tumor samples was used. 104 cases are randomly divided into 54 training cases and 50 test cases. To determinate the optimal wavelength and the cutoff point for differentiating tumors from normal mucosa, we established a diagnostic algorithm with training samples and evaluated it with test samples. And we tried highlighting tumors by image processing using HSC analysis software at the optimal wavelength and the cutoff point. Also we examined correlation between the SR at the optimal wavelength and the clinicopathological characteristic of tumors.
RESULTS: Especially in the range of 600 to 800 nm, the SR in the tumors tended to be higher than that in normal mucosae. The diagnostic algorithm used the 770-nm wavelength, with a cutoff point established from training samples. The sensitivity, specificity, and accuracy rates of the algorithm's diagnostic capability in the test samples were 70%, 99%, and 84% respectively. It was possible to enhance tumors by image processing using HSC analysis software at 770-nm wavelength. The tumor-emphasized areas and the histopathologically determined tumorous areas are almost identical. And also the SR at 770-nm wavelength admitted correlation with the microvessel density of tumors.
CONCLUSION: The result of recording the removal specimen of gastric tumors by HSC, the wavelength to identify tumors and normal mucosa could be specified. Differences in SR between tumors and normal mucosa suggested that tumors can be clearly distinguished from background mucosa with HSI technology.
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Disclosure of Interest: None Declared
Keywords: gastric cancer, hyperspectral camera, hyperspectral imaging

P677 PROSPECTIVE LONG TERM ASSESSMENT OF SEDATION-RELATED ADVERSE EVENTS AND PATIENT SATISFACTION FOR GASTROINTESTINAL ENDOSCOPY

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INTRODUCTION: Fear and sedation-related adverse events are supposed barriers for patients to attend endoscopic screening or surveillance programs.
AIMS&METHODS: In this prospective, double-blind controlled trial we investigated the long term effect of different sedation protocols in patients undergoing upper gastrointestinal endoscopy and colonoscopy. Therefore, consecutive patients undergoing screening or surveillance endoscopy were included. Before and after the endoscopic procedure patient satisfaction was assessed with a standardized clinical interview by using a visual analogue scale (VAS). In addition, sedation recovery times, recall of pain and clinical parameters including blood pressure, pulse rate and oxygen saturation were evaluated. Two weeks after the procedure, the patient was contacted again, to either repeat the clinical interview and to assess any potential adverse events which may have occurred after the endoscopic procedure.
RESULTS: 102 patients were prospectively included (44% female, mean age 51 years; mean BMI 25). Fear and concerns regarding the endoscopic procedure were not different between patient groups. Upon full recovery, patient satisfaction was highest if propofol sedation or a combination of propofol and pethidine was used. Combination of benzodiazepines and pethidine yielded high satisfaction rates while combination of propofol and benzodiazepines resulted in poorest patient satisfaction rates. Blood pressure and pulse rate were significantly reduced if propofol sedation was used while mean oxygen saturation levels were lowest for combination of propofol and pethidine. On follow up, patient satisfaction was highest if propofol monosedation was used. Major side effects occurred in no cases. Minor side effects including nausea, vomiting and pain at the injection side occurred in 15% of patients and were mostly due to propofol sedation.
CONCLUSION: Monotherapy with propofol has the best long term outcome regarding patient satisfaction for upper endoscopy and colonoscopy and should therefore preferable be used for sedation in order to increase acceptance rates for endoscopic procedures.
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Disclosure of Interest: None Declared
Keywords: adverse events, Propofol sedation, sedation, surveillance colonoscopy

P678 THE INCIDENCE AND COST OF UNEXPECTED HOSPITAL ATTENDANCE FOLLOWING ELECTIVE OUTPATIENT OESOPHAGO-GASTRO-DUODENOSCOPY

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INTRODUCTION: Elective outpatient Oesophago-gastro-duodenoscopy (OGD) is an increasingly common diagnostic and therapeutic procedure, with 10% annual growth in the UK. It is considered a safe procedure, with an overall complication rate traditionally quoted at 0.13% (1). However, a recent American study has suggested almost a 10 fold higher rate of hospital attendances post-procedure (2).
AIMS&METHODS: The aim of this study was to identify the true morbidity and related healthcare costs following elective outpatient OGD within a UK population. We conducted a retrospective observational study to identify all Accident & Emergency (A&E) attendances and hospital admissions within 14 days of all outpatient OGDs performed at West Middlesex University Hospital London in 2011. Of these, post-OGD related attendances were identified and associated healthcare costs calculated. Attendance data were collated from the hospital's electronic records system, enterpriseCAMIS®.
RESULTS:
Of the 1,977 outpatient OGDs performed, 44 patients (2.26%) presented to A&E within 14 days post OGD. However, only 6 re-attendances were procedure-related (0.3%), most commonly for pain. 4 patients required hospital admission, all of whom had undergone therapeutic interventions. 1 patient required a 3 day admission for vomiting post stent insertion. 1 patient required a 16 day admission following bleeding post variceal banding. 1 patient required a 5 day admission due to pain following stent removal. The final 5 day admission was precipitated by haematemesis following stent insertion. The total cost of hospital admissions and A&E attendances was £10,075, equating to £5.10 per endoscopy.

	A&E Attendances (cost)	Hospital Admissions (cost)
Related to Procedure	6, 0.3% (£870)	4, 0.2% (£9,205)
Unrelated to Procedure	38	5

CONCLUSION:
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The rate of procedure related hospital reattendance demonstrated by this study was substantially less than that recently identified in America (1.07%) (2). However it is still significantly in excess of that traditionally quoted. All patients within our cohort who experienced substantial morbidity had undergone therapeutic interventions; the likelihood of therapeutic intervention should be considered when estimating morbidity and budgeting for post procedure costs.
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Disclosure of Interest: None Declared
Keywords: healthcare costs, Oesophago-gastro-duodenoscopy

P679 EVALUATION OF WHITE OPAQUE SUBSTANCE WITHIN GASTRIC NEOPLASIA AS VISUALIZED BY NONMAGNIFYING AND MAGNIFYING ENDOSCOPY WITH NARROW-BAND IMAGING

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INTRODUCTION: White opaque substance (WOS) within gastric neoplasia is a unique finding visualized in magnifying endoscopy with narrow-band imaging (M-NBI) and represents intramucosal accumulation of lipid droplets. The clinical features of WOS within gastric neoplasia are not well known.
AIMS&METHODS: Our aim was to study whether the presence and morphology of WOS can be used to discriminate between adenoma and early carcinoma. One hundred fifty-six patients with 164 gastric neoplasias (17 adenomas and 147 early carcinomas) who underwent nonmagnifying endoscopy with NBI (N-NBI) and M-NBI before endoscopic resection in our hospital between January 2010 and December 2012, were retrospectively investigated. We studied the frequency of the presence of WOS within gastric neoplasia and the clinicopathological findings of WOS-positive gastric neoplasias. We also studied the morphology of WOS and the presence of WOS on narrow-band imaging with or without magnifying endoscopy.
RESULTS: WOS was more frequently seen in adenomas (6/17: 35.3%) than in early carcinomas (31/147: 21.1%). Among the 6 WOS-positive adenomas, 4 cases (66.7%) were clearly visualized by N-NBI and 2 cases (33.3%) by M-NBI. Among the 31 WOS-positive carcinomas, 19 cases (61.3%) were visualized by only M-NBI and 12 cases (38.7%) by N-NBI. Regarding the morphology of WOS, WOS within adenoma demonstrated a symmetrical distribution with a regular reticular pattern because the intervening part between the crypts is wide and has no severe structural abnormalities; in contrast, WOS within carcinoma demonstrated an asymmetrical distribution with an irregularly dotted, speckled, or reticular pattern because the intervening part between the crypts is narrow and has severe structural abnormalities. WOS-positive gastric neoplasias tended to locate in the middle to lower third of the stomach [35/37 (94.6%): U2/M14/L21], represent superficial elevated type [25/37 (67.6%): 0-I:1/0-IIa:25/0-IIb:2/0-IIc:9] macroscopically, and indicate well differentiated adenocarcinoma [29/37 (78.4%): adenoma:6/pap:1/tub1:29/tub2:1/por:0/sig:0] histologically.
CONCLUSION: In cases in which the WOS is observed, WOS within adenoma tends to be clearly visualized by N-NBI and has a regular pattern, whereas WOS within carcinoma tends to be visualized by M-NBI and has an irregular pattern. The presence of WOS on N-NBI or M-NBI and the morphology of WOS may be useful to discriminate between adenoma and early carcinoma.
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Disclosure of Interest: None Declared
Keywords: gastric neoplasia, narrow-band imaging, white opaque substance

P680 THE SENSITIVITY AND SPECIFICITY OF CONVENTIONAL ENDOSCOPY FOR THE DIAGNOSIS OF GASTRIC ATROPHY IN PATIENTS WITH DECREASED PEPSINOGEN TESTS.

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INTRODUCTION: The aim of the study was to assess the sensitivity and specificity of conventional endoscopy for the diagnosis of gastric atrophy in patients with decreased pepsinogen tests (high risk group) based compared to histological diagnosis of atrophy.
AIMS&METHODS: The study was a subanalysis of a larger randomly selected cross-sectional sample of the general population in Latvia recruited from November 2008 to July 2009 with the primary objective of exploring cardiovascular risk factors. The selected individuals underwent a structured interview and blood sample collection. From the total number of 6000 invitees, in 3807 cases pepsinogen I (PgI) and pepsinogen II (PgII) was measured in plasma by Eiken (Eiken Chemical Co., Tokyo, Japan) pepsinogen test systems and PgI/PgII ratio was calculated. Patients with PgI level <70 ng/ml and PgI/PgII ratio <3 (indicating any degree of gastric mucosal atrophy) were invited for upper gastrointestinal conventional white light endoscopy from January 2012 to July 2012. For adequate staging and grading of gastric mucosa atrophy, at least four non-targeted biopsies of two topographic sites (at the lesser and greater curvature, from both the antrum and the corpus) were taken and clearly labelled in separate vials; additional target biopsies of lesions were also taken.
RESULTS: 100 patients (39 male, mean age 61) with changed pepsinogen tests, showing gastric mucosa atrophy underwent conventional white light gastroscopy (Olympus GIF-Q165 gastroscope). In 17/19(90%) patients endoscopic signs of atrophy were confirmed by histology: 14/17 patients (74 %) had mild (OLGA stage I) and 3/17 (16%) patients - moderate (OLGA II) atrophy. However, among 81 endoscopically negative patients (without endoscopic signs of atrophy) gastric mucosa atrophy by histology was diagnosed in 54/81 (67%) patients: 47/54 (87%) had OLGA stage I, 6/54 (11%) - OLGA stage II and 1/54 (2%) patient had OLGA stage III gastritis. The overall sensitivity and specificity of conventional endoscopy for the diagnosis of atrophy based on histological diagnosis of atrophy were **56.7%** and **93.3%,** respectively. The accuaracy was higher in patients with atrophy in both corpus and antrum: sensitivity - **60.9%**, specificity - **95.2%**. The negative predictive value (NPV) of conventional gastroscopy was 34%; positive predictive value (PPV) - 97%.
CONCLUSION: Conventional white light endoscopy cannot accurately diagnose atrophic gastritis in patients with changed serum pepsinogen tests (high risk group).
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Disclosure of Interest: None Declared
Keywords: conventional gastroscopy, gastric atrophy, serum pepsinogens

P681 ENDOSCOPIC REMOVAL OF PARTIALLY MIGRATED INTRA-GASTRIC BANDS FOLLOWING SURGICAL GASTROPLASTY: A PROSPECTIVE CASE SERIES DEMONSTRATING SAFETY AND EFFICACY

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INTRODUCTION: Introduction: Laparoscopic gastric banding is a popular surgical technique for morbid obesity. However, the intra-gastric partial migration of bands is a well-recognized complication. Intra-gastric band partial migration usually necessitates repeat surgery. Endoscopic band removal is reported to be effective, yet reports are sporadic and scarce. We report on the efficacy and safety of endoscopic removal of partially migrated intra-gastric bands in a prospective case series.
AIMS&METHODS: Methods: From 1/1/2011 to 15/11/2012, we prospectively collected data on patients referred to a tertiary-care university hospital for endoscopic removal of migrated intra-gastric bands. Under endoscopic visualization, using a standard gastroscope, the partially migrated band was visually identified within the gastric lumen; a Jagwire was introduced, looped through the band and withdrawn to the mouth using a grasper. A mechanical lithotriptor was then threaded over the Jagwire and under fluoroscopic guidance slowly advanced. By twisting the handle of the lithotripter, the band was readily cut by strangulation. The cut edge of the band was then grasped using a snare and with gentle traction extracted from the gastric wall and then removed per os.
RESULTS: Results: There were n=7 patients (4F/3M, mean age 38.4 years). Mean time from laparoscopic gastric band placement to endoscopic intra-gastric band removal was 6.2 years. The migrated intra-gastric bands were all successfully removed in a mean of 1.3 sessions. No patient required subsequent surgical intervention. There were no immediate or delayed adverse events.
CONCLUSION: Conclusion: Endoscopic removal of partially migrated intra-gastric bands appears feasible, effective, safe, and may prevent repeat surgery.
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Disclosure of Interest: None Declared
Keywords: Endoscopic Removal, Gastroplasty, Intra-Gastric Bands, migration

P682 ENDOSCOPIC MANAGEMENT OF FISTULAE AFTER SLEEVE GASTRECTOMY

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INTRODUCTION: Background: Treatment of gastric fistulas after sleeve gastrectomy is difficult, and is often associated with additional surgery, sepsis, and prolonged non-oral feeding.
Objective: To assess an endoscopic strategy for management of gastric fistulas.
Design: Observational study.
AIMS&METHODS: Patients: All consecutive patients from July 2007 to December 2011.
Intervention: Endoscopic management involved successive procedures for endoscopic diversion of the fistula with a stent and/or closure of the residual orifice with surgical clips or sealant.
Main Outcome Measurements: Technical success, fistula closure, mortality and morbidity, stent migration.
RESULTS: Results: twenty patients (12 males, mean-age 36.5 years, range 18-60 years) with gastric fistulas after sleeve gastrectomy underwent multiple endoscopic procedures (1-6) for the fistula treatment. Most fistulas (90%) were located just distal to gastro-esophageal junction. Two patients (10%) had distal sleeve fistula. Sixteen patients (80%) were managed successfully with endoscopic treatment. Two patients were re-operated. Two patients were treated by over-the-scope-clips (OTSC), 9 patients- by stent insertion (one or more), 7 patients-by stents and OTSC combination and 2 patients- by OTSC and glue application. Two patients still have a minor draining fistula. Stent migration occurred in 88% of patients. The mean time to fistula closure from the start of endoscopic management was 6.6 weeks (range 1-16 weeks) with a mean of 3 endoscopic procedures per patient.
CONCLUSION: Conclusion: An endoscopic approach to the management of gastric fistulas that develop after sleeve gastrectomy using sequential stent insertion and closure of the residual orifice achieved resolution of the fistulas with minimal morbidity in the majority of patients.
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Disclosure of Interest: None Declared
Keywords: endoscopic management, gastric fistulas, sleeve gastrectomy

P683 IS IT POSSIBLE TO PERFORM GASTRIC ESD ONLY AFTER SEEING EXPERT'S TECHNIQUES?

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has become established as a minimally invasive treatment for gastric neoplasms in Japan. We reported the validity of our training system for gastric neoplasms at DDW 2012. As you know, gastric ESD is considered difficult compared with endoscopic mucosal resection (EMR). Although high en bloc resection rate has been reported and a few papers were known about the training for gastric ESD under the mentorship of the specialist in Japan. Experience in Europe, however, is still limited and ESD is only performed in a few selected centers with low volumes of cases. This study examines if only seeing an expert's technique is effective for trainee to perform gastric ESD or not.
AIMS&METHODS: Between April 2012 and March 2013, a total of 152 ESD procedures in 140 patients (104 gastric ESD, 30 colorectal ESD and 16 esophageal ESD) were seen by one trainee who is not specialist in endoscopy. He graduated from medical school six years ago and his major was hepatology. He performed 1200 cases of gastroscopy and 700 cases of total colonscopy examinations during 6 years.
RESULTS: Fifteen cases treated with gastric ESD from April 2013 to May 2013 were investigated. They consist of 8 lesions in the antrum; 5 lesions in the angle or the lesser curvature in the body; 2 lesions in other locations. The En block R0 Resection rate was 100% (n=15) and the perforation rate was 0%. Delayed hemorrhage was seen in one case which was controlled by endoscopic treatment. The mean procedure time was 102.5min and the mean tumor size was 14.5mm. The trainee could complete the whole ESD procedures in 15 cases.
CONCLUSION: This study suggested that only seeing expert's ESD procedure enabled ESD trainees to perform gastric ESD without decline the treatment outcome.
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Disclosure of Interest: None Declared
Keywords: gastric ESD, training

P684 AETIOLOGY OF ANAEMIA IN HOSPITALIZED PATIENTS: A PROSPECTIVE SINGLE-CENTRE CROSS-SECTIONAL STUDY

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INTRODUCTION: Anaemia is a common finding in patients admitted to hospital, resulting in a number of gastroenterology referrals for consideration of endoscopy. Various studies have evaluated the aetiology of anaemia in the elderly population and its burden on the endoscopy service, however very few studied this across all adult age groups.
AIMS&METHODS: To evaluate the aetiology of anaemia in adult patients of all age groups admitted to hospital.
Methods
Adult ($\geq$15 years) patients, with incidental/ symptomatic anaemia, admitted unselectedly between May 2010 and May 2011, under a gastroenterology firm, forming part of the unselected medical take rota in a secondary care hospital, were prospectively studied. Anaemia was defined as below the lower limit of normal of our laboratory's reference range ($<$13g/dl males, $<$11.5g/dl females). History and physical examination, together with a complete blood count, iron studies, vitamin B12/folate levels and renal profile were carried out in all patients. Additional blood tests, imaging and GI endoscopy were requested at the physician's discretion, guided by the mean corpuscular volume. Causes of anaemia were classified as anaemia of inflammation, iron-deficiency anaemia, overt blood loss, other causes and unexplained.

RESULTS: A total of 505 patients were admitted during the study period, of which 132 (26.1%) had anaemia. 14 were excluded as had incomplete data. 118 patients were included for analysis (mean age 69.9 ±16.1 years, males n=73 (61.9%)). The mean haemoglobin was 10.0 ±1.8g/dl (normocytic 64.5%, microcytic 28.8%, macrocytic 5.9%, pancytopenia 0.8%). 16.9% (n=20) had 2 or more causes for anaemia. The frequency of the different diagnosis can be seen in Table 1. Age, gender or mean corpuscular volume did not show statistical significance in predicting malignant or non-malignant GI lesions (*p value* 0.61, 0.92, 0.11 respectively).

Table 1: Frequency of the different diagnoses obtained following appropriate investigations

	n	%
Anaemia of inflammation	**49**	**41.5**
- sepsis	25	51
- non-haematological/non-GI malignancy	15	30.6
- haematological malignancy	8	16.4
- autoimmune disease	1	2
Fe-deficiency anaemia	**22**	**18.7**
- GI malignancy	7	31.8
- non-malignant GI lesion	6	27.3
- undetermined	4	18.2
- menstruation	3	13.6
- non-GI malignancy	2	9.1
Overt blood loss	**10**	**8.5**
- upper GI	6	60
- lower GI	2	20
- respiratory	1	10
- urinary	1	10
Other causes	**25**	**21.2**
- renal disease	17	68
- liver disease	3	12
- thalassaemia	3	12
- thyroid disease	1	4
- folate deficiency	1	4
Unexplained	**12**	**10.2**

CONCLUSION: Sepsis, non-GI malignancy and GI lesions (malignant and non-malignant) were the primary causes of anaemia in this cohort of patients, each comprising about 20% of the cases. Gastrointestinal endoscopy is thus only required in one fifth of adult patients with anaemia.

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Disclosure of Interest: None Declared

Keywords: Anaemia, gastrointestinal malignancy, iron deficiency

P685 A LARGE-SCALE MULTICENTER PROSPECTIVE STUDY VALIDATING THE CRITERIA FOR PERIENDOSCOPIC ANTITHROMBOTIC THERAPY CESSATION: THE SAPPORO CONSENSUS

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INTRODUCTION: It is common practice to shorten the duration of anticoagulant (AC) and antiplatelet (AP) therapy cessation during endoscopic procedures to minimize the risk for thrombosis. In its guidelines for periendoscopic AC/AP therapy published in 2006, the Japan Gastroenterological Endoscopy Society (JGES) recommended a longer duration of AC/AP cessation than that recommended in Europe.

AIMS&METHODS: This multicenter prospective study aimed at determining and validating an optimal duration of periendoscopic AC/AP cessation. Endoscopists and various specialists prescribing AC/AP therapy participated to develop a consensus on the criteria for AC/AP cessation (Sapporo consensus) based on the JGES guidelines with the risk for thrombosis in mind, and followed up all institutions that had jointed in the consensus for adherence to the consensus practice as well as for post-procedural events. All but except for emergency endoscopic procedures performed during follow-up were included for analysis. All procedural events were analyzed, based not only on reports from participating institutions but also on patient questionnaires.

RESULTS: A total of 5,331 patients (mean age:72.3 years; male:female=13:7) were enrolled from 16 participating institutions. Of these, 202 patients (3.8%) had a longer duration of AC/AP cessation than that defined in the consensus. Questionnaires on post-procedural events were collected from 77.3% of patients and all procedural events were reported from all participating institutions. Post-procedural events included thrombosis in 2 patients (0.04%) and post-procedural hemorrhage in 42 patients (0.8%), which was significantly higher in incidence in those receiving 2 or more AC/AP (1.3%), those receiving clopidogrel (1.7%), high-risk patients with AC/AP cessation (3.5%), those receiving therapeutic endoscopy (4.9%), and those undergoing heparin-bridging (14%). Of those undergoing therapeutic endoscopy, high-risk patients with AC/AP cessation and those undergoing heparin-bridging were associated with a significantly higher incidence of hemorrhage.

CONCLUSION: Data showed generally high adherence to the consensus practice, with no marked increase in post-procedural events compared to those reported in previous studies. The consensus practice calls for further examination to identify and manage those potentially at risk of hemorrhage with the approach.

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Disclosure of Interest: None Declared

Keywords: antithrombotics, Bleeding, Complication, endosopy, managment

P686 DEVELOPMENT OF NEW ANESTHESIA PROCEDURE USING PROPOFOL FOR THERAPEUTIC ENDOSCOPY

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INTRODUCTION: In recent years, the use of Propofol has been attracting attention to use as a sedative medicine during endoscopic therapeutic procedure, but its complications and cumbersome administration method have become problems. However, there is no standard protocol for Propofol so far. To use Propofol safe and effective, standardized protocol should be necessary.

AIMS&METHODS: Our aim was to establish a simple and safe way of using Propofol during therapeutic endoscopic procedures. Patients who were scheduled to undergo endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR) were recruited and after obtain the informed consent, following anesthesia induction procedure were performed. At the time of anesthesia induction, we injected Propofol 0.05 ml/kg for 10 seconds by power injector after pethidine hydrochloride 0.5mg/kg iv. After that, 1.0ml of Propofol was added every minute until sedation was achieved. As a maintenance dose, 0.25ml/kg/hr of Propofol was continuously administered. If patient getting awake, 1.0ml additional injection was repeated for every minute until sedation was obtained and added 5ml/hr to maintenance dose. SpO2 and blood pressure were monitored. Anesthesia depth was monitored by BIS monitor and maintained as Ramsay anesthetics depths scores 6 (it does not awake in an irritation). Propofol was stopped temporally under these patients' conditions, that is, SpO2 < 90, BP < 80mmHg or BIS under 60 (5 seconds or more). After recovered, Propofol was resumed. We evaluated the number of doses of Propofol at the time of anesthesia induction and maintenance phase, and the number of patients who need to stop temporarily.

RESULTS: There were 31 patients (mean age70.9yr, men/women; 24/7) with upper gastrointestinal neoplasms. ESD was 29cases and EMR was 2 cases. Mean procedure time was 109.7min (range; 30-410). All patients achieved sufficient anesthesia and underwent successful endoscopic procedure. Average number of doses at anesthesia induction was 3.0 times (range; 0-11). Average number of doses at maintenance phase was 1.9 times (range; 0-4). The number of patients who need to stop temporarily were 2 cases (3.2%) because of hypotension. However, there was no case of cessation of Propofol due to decreased SpO2 or low BIS score.

CONCLUSION: This newly developed Propofol anesthesia protocol is effective and well tolerated for longtime therapeutic endoscopy. Therefore, this protocol could be used as standard protocol for various kind of therapeutic endoscopic procedures.

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Disclosure of Interest: None Declared

Keywords: endoscopic mucosal resection, endoscopic submucosal dissection, endoscopic therapeutic procedure, Propofol

P687 A PROSPECTIVE, RANDOMIZED CONTROLLED TRIAL OF SOFT-COAGULATION VERSUS HEATER PROBE THERMAL COAGULATION FOR ENDOSCOPIC HEMOSTASIS OF BLEEDING PEPTIC ULCERS

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INTRODUCTION: Thermal coagulation is the most common method in endoscopic hemostasis for bleeding peptic ulcer. Recently, the efficacy and safety of soft-coagulation for treatment of bleeding peptic ulcer has been reported.

AIMS&METHODS: The aim of this study was to compare the efficacy of soft-coagulation with that of thermal coagulation in patients with bleeding peptic ulcers. Patients who visited our hospital with hematemesis or melena were considered for the study and randomized to receive soft coagulation or heater probe thermal coagulation. Soft-coagulation was performed with a 70 W current. Heater probe unit was used with a pulses of 20 to 30 J. Initial hemostasis was declared when the hemostasis was obtained by the single allocated method. When the second-look endoscopy revealed hemostasis, primary hemostasis was declared to be achieved. Specialists were defined as endoscopists who had over 5 year experience with special endoscopic qualification in Japan. Primary endpoint was the primary hemostasis rate and secondary endpoints were the procedure time, rebleeding rate, and complications. The factors associated with primary hemostasis was analyzed with regard to clinical characteristics.

RESULTS: Between May 2010 and February 2012, there were 111 patients enrolled in the study, 56 patients in the soft coagulation group (group S) and 55 patients in the heater probe group (group H). Primary hemostasis were achieved in 54 patients (96%) in the S group and in 37 patients (67%) in the

H group ($p < 0.001$). The duration of endoscopic therapy was less in the S group than in the H group, but not significant ($p = 0.10$). Rebleeding occurred in 7 patients (13%) in group H and none in group S ($p < 0.01$). Minor perforation occurred in two patients in group H. In the subanalysis, primary hemostasis rate achieved by trainee was 96% in the group S, and 60% in the group H ($p < 0.001$), while primary hemostasis rate achieved by specialist was 100% in both groups ($p = 1.00$). When the diameter of exposed vessel on ulcer bed was over 1 mm, primary hemostasis rate was significantly higher in the S group than in the H group (96% vs. 64%, $p < 0.001$).
CONCLUSION: Soft-coagulation was more useful than heater probe thermal coagulation on endoscopic hemostasis for bleeding peptic ulcer. It may provide a promising hemostasis irrespective of endoscopic experience or diameter of exposed vessel on ulcer bed.
Disclosure of Interest: None Declared
Keywords: Bleeding Peptic Ulcers, Soft-coagulation, Thermal Coagulation

P688 PREDICTIVE FACTORS OF MORTALITY AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY PLACEMENT

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INTRODUCTION: Percutaneous endoscopic gastrostomy (PEG) is considered one of the preferred routes for long-term enteral feeding.
AIMS&METHODS: To determine predictive factors of an increased mortality risk after PEG insertion. Retrospective study which included patients who underwent PEG placement between May 2007 and January 2013. Variables analyzed: sex, age, Charlsońs co-morbidity index, previous aspiration pneumonia, indication for PEG, follow-up period, 30-, 90-, 180-day mortality rates after PEG insertion and analytic variables: hemogram, ionogram, urea, creatinine, albumin and C-reactive protein. Exclusion criteria: absence of follow-up. Statistical significance was established at $p<0.05$.
RESULTS: One-hundred ninety patients were evaluated, 135 were included: 69 women, mean age of 73 years-old, Charlsońs index of 4 (mode and median), 71% with past history of aspiration pneumonia. Indications for PEG: cerebrovascular disease (50%), dementia (18%), cancer (10%) and others (22%). The mean follow-up time was 320 days, the overall mortality rate was 62% and previous aspiration pneumonia (p=0.006), higher levels of C-reactive protein (p=0.002) and leucocytosis (p=0.005) are among the predictive factors of mortality found. The 30-day mortality rate was 19% and the only predictive factor of mortality found was higher urea levels (p=0.046). Ninety-six percent of patients had a follow-up period superior to 90-days and 91% superior to 180-days: mortality rates were 30% and 43%, respectively, and the predictive factors of mortality observed were: diabetes mellitus (90-days:p=0.013;180-days:p=0.040) and higher levels of C-reactive protein (90-days:p=0.002; 180-days:p=0.008).
CONCLUSION: The mortality rate after PEG placement is high. Past history of aspiration pneumonia, presence of diabetes mellitus and higher levels of C-reactive protein significantly influenced the prognosis of these patients. These factors should be considered in the decision making of PEG insertion.
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Disclosure of Interest: None Declared
Keywords: PERCUTANEOUS ENDOSCOPIC GASTROSTOMY , PREDICTIVE FACTORS OF MORTALITY

P689 FEASIBILITY, EFFICACY AND SAFETY OF A PURE NATURAL ORIFICE TRANSLUMENAL ENDOSCOPIC GASTROJEJUNAL BYPASS IN A GASTRIC OUTLET OBSTRUCTION SURVIVAL ANIMAL MODEL

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INTRODUCTION: Natural orifice translumenal endoscopic surgery (NOTES) gastrojejunal anastomosis (GJA) may be a less invasive surgical technique for creating a gastrojejunal bypass without incisions. This approach may be useful for bariatric procedures and for the treatment of gastric outlet obstruction.
AIMS&METHODS: The aim is to determine feasibility, efficacy and safety of a pure NOTES gastrojejunal bypass using a simulated gastric outlet obstruction in a porcine survival animal model.This prospective animal study was performed on nine 20 to 30 kg domestic pigs, with a double-channel gastroscope (Karl Storz GmbH). The procedure steps were: 1) gastric incision with a needle-knife, 2) transgastric peritoneal access, 3) jejunal loop selection and mobilization into the stomach, 4) incision of the jejunum and creation of a stoma within the stomach wall, 5) full thickness suturing using an endoscopic T-tag suturing prototype (Brace Bar, Olympus, Japan). To create a gastric outlet obstruction model, we closed the pylorus with T-tag sutures. The animals were assessed clinically during the three weeks survival period. Weight gain was assessed by comparison of baseline and final weight at the end of the study. Patency of GJA was assessed at the post-mortem examination.
RESULTS: We successfully performed nine pure NOTES gastrojejunal bypass procedures with a mean operative time was 108 ± 26 minutes [65-142]. Each GJA was endoscopically sutured using four to seven T-tag sutures (mean of 5.55 ± 1.30). Two T-tags were used for the pyloric closure. There were no intra-operative complications. Five out of nine pigs were survived for three weeks. The mean weight was 29.5 kg at baseline versus 27.7 kg at three weeks follow-up. By comparing our series with a control group, we found a significant difference in the weight curves: a loss of 3.2 kg in the study group in comparison to 5.2 kg in the control group. We observed an incomplete closure of the pylorus in two animals. On post-mortem examination, the diameter of the GJA was about 20 mm [8-250 mm]. Four pigs died from anastomotic dehiscence complicated with septic peritonitis.
CONCLUSION: Gastrojejunal bypass with pyloric closure is technically feasible using a pure NOTES approach. This procedure is techlinically efficient resulting in a patent anastomosis and a weight loss in surviving animals. Anastomotic dehiscence is a major a concern since it carries a high mortality rate. Further improvements for this model for reducing the risk of anastomotic dehiscence may be creation of a two-step procedure in separate occasions.
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Keywords: Gastric by-pass, Gastrojejunal anastomosis, NOTES, Obesity surgery, Surgical endoscopy

P690 USEFULNESS OF OVER-THE-SCOPE (OTSC) CLIPS FOR CLOSING DIGESTIVE FISTULAS

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INTRODUCTION: Therapeutic endoscopy has recently evolved into treatment of complex gastrointestinal (GI) postoperative leakages. New endoluminal devices such as Over-The-Scope (OTSC) clips may facilitate the closure of large defects. The aim of this study was to describe our 3-year experience on 28 patients treated for digestive fistulas using this OTSC clipping device.

AIMS&METHODS: This is a retrospective study conducted on patients referred for GI fistulas in two French teaching hospitals. Technical aspects, clinical outcomes and closure rate were recorded.

RESULTS: Twenty-eight patients were treated for GI leaks: eighteen (60%) had a gastric fistula after laparoscopic sleeve gastrectomy (LSG), the others where distributed into recto-vaginal, urethro-rectal, recto-vesical, gastro-gastric, gastro-cutaneous, esophago-jejunal fistulas and colo-rectal anastomotic leak. The average follow up was 10.4 months. Out of the 28 patients treated, eighteen (64.2%) had undergone a previous endoscopical or surgical treatment. The orifice size was 3 mm to 20 mm (average 7.2 mm). Successful OTSC clip placement was achieved in 30 out of 34 attempts. There were four intraoperative undesired events (14.2%) but successfully managed and without any clinical consequences. Overall success rate was 71.4% and fourteen patients (50%) recovered with primary efficacy. Six patients (21.4%) required a subsequent endoscopic treatment. Eight patients (28,5%) required surgery for endoscopic treatment failure. In nine cases, we used one or more additional endoscopic procedures concomitantly with the OTSC combining SEMS, standard clips and glue injection. Healing rate after LSG fistula was 88.9% was and significantly higher than overall rate (p=0.01).

CONCLUSION: OTSC placement seems to be safe and effective for treatment of GI fistulas, as primary or as adjuvant endoscopic therapy. Better results were seen in early fistulas, and leaks after LSG rather than chronic fistulas.

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Keywords: Anastomotic leak, Digestive perforations, fistula, Interventionnal endoscopy, OTSC (over-the-scope clip)

P691 CLINICAL IMPACT OF WHITENESS OF GASTRIC MUCOSAL CRYPT OPENING OBSERVED BY MAGNIFYING ENDOSCOPY

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INTRODUCTION: Several studies have reported a relationship between the micromucosal structure observed by magnifying endoscopy (ME) and *Helicobacter pylori*-induced gastritis. However, there has been no report on the relationship between *H. pylori* gastritis and whiteness of gastric mucosal crypt opening (CO) observed by ME.
AIMS&METHODS: One hundred and seventy-five consecutive patients (including 86 patients with gastric cancer) were enrolled. We observed mucosal microsurface at the lesser and greater curvature in the gastric corpus by ME. Whiteness of CO was subclassified as "white-edged dark spot (WED)" type, consisting of a dark spot bordered by white color; "white" type, consisting of no dark spot and only white color; and "dense white pit (DWP)" type, consisting of a dense white color with the appearance of a snow-ball. Histological gastritis was also evaluated according to the updated Sydney System.
RESULTS: In a total 249 areas with round CO observed by ME, histological findings showed mononuclear cell and neutrophil infiltration were significantly higher in "white" and "DWP" type than in "WED" type CO ($P<0.0001$). Whiteness of CO were significantly differences between *H.pylori*-positive (n=139) and -negative (n=36) patients (WED, 16.7% *vs* 77.8%; White, 60.7% *vs* 22.2%; DWP, 22.6% *vs* 0%). There were significant differences between whiteness of CO in patients with gastric cancer and patients with no gastric cancer (WED, 19.8% *vs* 36.2%; White, 53.8% *vs* 46.3%; DWP, 26.4% *vs* 17.5%). DWP were frequently observed in patients with undifferentiated-type gastric cancer (45.7%).
CONCLUSION: ME observation of CO whiteness was associated with histological gastritis and may identify patients at high-risk of *H. pylori*-associated gastric diseases.
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Disclosure of Interest: None Declared
Keywords: Helicobacter pylori, magnification endoscopy

P692 THE UTILITY OF ULTRATHIN ENDOSCOPY AS A DIAGNOSTIC TOOL FOR BARRETT'S OESOPHAGUS (BO). SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Screening for BO in patients with multiple risk factors is increasingly recommended by gastrointestinal (GI) societies. Standard Endoscopy (SE) is not suitable for population screening. Unsedated Ultrathin Endoscopy (UE) has been proposed as a more cost-effective alternative. However, reports on the performance characteristics of this tool vary among different studies.
AIMS&METHODS: The aim of this study was to estimate the pooled diagnostic accuracy, technical success rate and tolerability of UE (via trans-nasal or trans-oral insertion route) for the diagnosis of BO in adult patients with upper GI symptoms.
A systematic literature search and meta-analysis was performed of all primary studies evaluating UE (index test). We only included studies which used SE as the gold standard. Studies were excluded if data on accuracy or BO presence were not extractable; or if they used fibreoptic endoscopy as this technology is obsolete in current practice.
Data extraction was undertaken by three reviewers independently of each other and who then cross-checked the consistency of their findings. The quality of included studies was assessed using a validated tool (QUADAS-2). Data analysis was performed using the Meta-DiSc (version 1.4) software.
RESULTS: Five studies including 439 patients met the inclusion criteria. The pooled sensitivity, specificity, diagnostic odds ratio (DOR), and area under the curve (AUC) for the diagnosis of BO were 0.91 (95% confidence interval [CI] 0.84-0.96), 0.96 (95% CI 0.94-0.98), 353.9 (95% CI 56.8-2204.7) and 0.97 (Standard error [SE] 0.03) on a per-protocol analysis.
Success rate for both UE and SE was 0.86 in the smallest study using unsedated trans-oral route, while all the other studies reported success rates ranging from 0.95 to 1.0 for UE (including unsedated trans-nasal route) and from 0.98 to 1.0 for SE. The majority (0.57-0.71) of patients preferred UE compared to SE and said they were willing to have UE again in the future if necessary. The mean tolerability scores for unsedated UE were significantly better in two studies, similar in one study and not reported in the rest of the studies.
CONCLUSION: These data suggest that UE in general and unsedated trans-nasal UE in particular is accurate in detecting BO and more acceptable to patients compared to SE. However, the current available UE devices require a dedicated endoscopy suite and decontamination facilities adding to the cost and complexity as well as limiting their access to the general population. There is a clear need for more simple, portable and disposable device to screen for BO in the community setting.
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Keywords: Barrett's oesophagus, Endoscopy, Ultrathin

P693 ANALYSIS OF 25,000 CASES INVOLVING TRANSNASAL ENDOSCOPIC SCREENINGS IN THE WORLD'S FIRST DEDICATED VEHICLE FOR TRANSNASAL ENDOSCOPY AND OUR HOSPITAL FOR 7 YEARS.

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INTRODUCTION: Transnasal endoscopy (TNE) has been widely available as less painful and more easy and safe method than peroral endoscopy (POE) in gastrointestinal (GI) tract screening, especially a checkup of the upper GI tract in Japan. In our hospital, we have started to use TNE systems since 2005, and performed approximately 4,000 tests a year for cases that asymptomatic subjects who mainly underwent health screenings and checkups. Furthermore, we introduced the world's first dedicated vehicle for TNE to conduct checkups for employees on company property in 2008 as reported at 2011 UEGW Stockholm. Subsequently, 4,500 tests (about 1,300 cases per year) were performed for employees in the vehicle on company property. We report the increasing importance of TNE for the upper GI tract in a hospital and on company property.
AIMS&METHODS: The results, characteristics of detected cancer and optical images from TNE were compared with POE in 25,000 cases that asymptomatic subjects who underwent screenings for 7 years since the introduction of TNE.
RESULTS: In the 25,000 cases, we pointed out that a total of 35 subjects had malignant lesions, of which 1, 5, 27 and 2 were hypopharyngeal, esophageal, gastric and duodenal cancer, respectively. Subjects with early gastric, esophageal and duodenal cancer were treated by endoscopic submucosal dissection. Epistaxis was seen in 1% or less of 25,000 cases, and any severe procedural accidents did not occur. Cases that subjects who underwent POE switched from TNE because of inability to insert the endoscopes for TNE was 0.3%. There was no significant difference between TNE and POE, and the optical images were similarly clear.
CONCLUSION: We have recommended and performed endoscopic screenings for workaholic employees without enough time to visit a hospital in the world's first dedicated vehicle for transnasal endoscopy on company property. Radiation exposure and discomfort from gag reflex are issues in barium contrast x-ray and POE as a screening, respectively. With TNE, the detection accuracy of lesion seems to be higher than barium contrast x-ray, and it is less painful and more easy and safe than POE. Moreover, TNE has not only a good compliance, but also allows better risk management of sedation.
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Disclosure of Interest: None Declared
Keywords: transnasal endoscopy, endoscopic screening, vehicle for transnasal endoscopy

P694 THERAPEUTIC STRATEGY FOR RESIDUAL/RECURRENT LESIONS AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION: PREVENTION AND SALVAGE BY ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Several years have passed since the development of Endoscopic Submucosal Dissection (ESD), and its spread has enabled therapies with a higher R0 rate and lower local recurrence rate. However, the fact that ESD is now also carried out for more difficult lesions has caused the new, though infrequent, problem of post-ESD local residual/recurrence. With repeat ESD for a post-ESD recurrent lesion, because far more severe and extensive fibrosis is present in the submucosa, the technical difficulty of submucosal dissection is very high, and both safety and radical curability must be assessed. On the other hand, it is important to prevent post-ESD residual/recurrent tumor that would be difficult to treat by ESD.
AIMS&METHODS: The aims of this study were to clarify the clinical features of the post-ESD residual/recurrent lesion and compare the outcomes between early additional ESD (addESD) and repeat ESD (reESD) after initial ESD to establish the treatment strategy for cases of the LM+ that causes post-ESD residual/recurrence. The short-term results (tumor size, resection size, treatment time, complete en bloc resection rate, complication rate) and long-term results (local recurrence rate, distant metastasis) were retrospectively studied in addESD and reESD for 2,042 lesions subjected to ESD between April 2005 and March 2013.
RESULTS: 53 lesions were determined to be post-ESD LM+ with suspected regional residue of the tumors. Of the 53 LM+ lesions, 11 underwent addESD immediately after initial ESD, 15 lesions had additional surgery, and 38.5% (10/26) had regional residual lesions. A total of 27 lesions did not undergo addESD or additional surgery; in follow-up, 29.6% (8/27) had local recurrence (mean time to recurrence, 806 days) and most recurrences were discovered within three years after initial ESD. A total of 15 lesions with post-ESD local recurrence underwent reESD, including the 5 recurrent lesions and 10 lesions referred from another hospital. Of the reESDs, 73.3% (13/15) involved curative resections and also

have not shown local recurrence or distant metastasis. AddESD showed significantly higher performance in dissection speed than reESD.
CONCLUSION: Both sESD and reESD had favorable short-term and long-term results. About 32% of cases that consequently tested LM+ after ESD developed local residual/recurrent disease, so implementing addESD as soon as possible, before complete scarring of the ulcer makes reESD difficult, is useful for preventing residual/recurrent disease. If a residual/recurrent lesion occurs, reESD is useful.
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Disclosure of Interest: None Declared
Keywords: endoscopic submucosal dissection (ESD), gastric tumor, local residual/recurrent tumor, post-ESD

P695 COMPARISON OF TWO DOSES OF INTRAVENOUS PROTON PUMP INHIBITOR FOR THE PREVENTION OF BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Intravenous bolus loading followed by continuous infusion of proton pump inhibitor (PPI) is the standard treatment of choice for the prevention of gastric ulcer rebleeding. But the optimal dose of proton pump inhibitor (PPI) for the prevention of bleeding after endoscopic submucosal dissection (ESD) is unclear.
AIMS&METHODS: Our aim is to compare the effects of continuous infusion and bolus injection of PPI for the prevention of recent bleeding after ESD.
273 patients with gastric epithelial neoplasm were enrolled. All patients who underwent ESD were randomly assigned to either the continuous infusion (n=136) or bolus group (n=137). For both groups, initial pantoprazole 80mg bolus loading infusion for 30 min before ESD. In continuous infusion group, 8mg/hr continuous infusion for 72 hours, totally 576mg is done after initial loading. For bolus group, pantoprazole 40mg is injected twice a day for 72 hours, totally 240mg. Follow-up endoscopy is performed the next day after ESD routinely. Indication of additional EGD is melena, hematemesis, Hb loss $>$ 2g/dL. Primary outcome measure is the bleeding related to ESD. Secondary outcome is risk factors of the bleeding after ESD.
RESULTS: Clinical characteristics were not different between the two groups. The bleeding rate of the continuous infusion group was not significantly lower compared with the bolus group (6.6 % vs 5.8 %, p = 0.79). No significant difference of bleeding incidence was found for the factors of tumor location, gross type, invasion depth, histology, ulcer or fibrosis presence. On multivariate analysis, the specimen size (relative hazard : 1.855, 95% CI : 1.083 – 3.179, p = 0.24) was independent factors predictive of bleeding after ESD. Subgroup analysis according to tumor size, there was no significant difference of bleeding rate between two group.
CONCLUSION: A continuous infusion of high-dose pantoprazole does not show the superiority compared to pantoprazole bolus in the prevention of bleeding after ESD. So bolus of PPI (pantoprazole 40mg twice a day) is more cost-effective dose for the prevention of bleeding after ESD.
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Disclosure of Interest: None Declared
Keywords: ESD (endoscopic submucosal dossection), PPI

P696 EFFICACY OF FAMOTIDINE OR PANTOPRAZOLE FOR THE HEALING OF ENDOSCOPIC SUBMUCOSAL DISSECTION-INDUCED ULCER: A PROSPECTIVE RANDOMIZED TRIAL

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INTRODUCTION: Currently acid suppressing agents are routinely prescribed to heal the iatrogenic ulcer, however, it is still controversial that which treatment of proton pump inhibitor or H2 receptor antagonist is more effective regimen. Although several reports showing similar efficacy in the bleeding prevention and healing of EMR induced ulcer, to date there have been no controlled study in patient with ESD induced ulcer which had larger ulcer size. Therefore, we prospectively compared famotidine and pantoprazole for the healing of relatively larger ESD-induced ulcers.
AIMS&METHODS: Following ESD, all patients were given intravenous infusion of pantoprazole 40 mg once daily for two consecutive days, starting from the day of ESD. From the third day after ESD, all patients were allocated to famotidine (40 mg/day) or pantoprazole (40 mg/day) group for 8 week and instructed not to take other antisecretory drugs or possible ulcerogenic drugs. At 4 weeks, all enrolled subjects underwent follow-up endoscopy to compare the degree of healing including ulcer size and stage, and ulcer related symptoms between the two groups.
RESULTS: A total of 85 patients were randomized to each group according to the category of initial ulcer size; group 1 (ulcer size $<$ 3cm), group 2 (3 $\leq$ ulcer size $<$ 4), group 3 (ulcer size $\geq$ 4). Four patients were excluded following reasons; follow-up loss (two) and follow-up endoscopy at 5 weeks after ESD (two).
Finally, forty one patients in famotidine group and forty patients in pantoprazole group were compared. The two groups were comparable in terms of baseline characteristics such as age, sex, comorbidity, history of previous peptic ulcer, history of NSAID medications, social history including smoking and alcohol, final diagnosis, *H. pylori* status, location of lesion, injection materials, immediate complications and initial ulcer size. Four weeks after ESD, the two groups were not different with respect to ulcer stages (P = 0.35) or ulcer related symptoms (P = 0.38). The ulcer reduction ratios were no significant difference between the famotidine and pantoprazole group (0.274 ± 0.253 vs. 0.24 ± 0.187, $P = 0.72$). In subgroup analysis for patients according to the category of initial ulcer size, the three groups were comparable with the baseline characteristics. In comparing ulcer stages, ulcer related symptoms and ulcer reduction ratios were not significantly different among the three groups.
CONCLUSION: Our results demonstrate that the effects between the famotidine and pantoprazole therapy are similar in terms of the ulcer healing for the iatrogenic following ESD.
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Disclosure of Interest: None Declared
Keywords: endoscopic submucosal dissection (ESD) , ulcer healing

P697 EX VIVO PILOT STUDY FOR CONFOCAL ENDOMICROSCOPIC IMAGING OF GASTROINTESTINAL STROMAL TUMORS.

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INTRODUCTION: Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal (GI) tract arising from the deeper layers hidden by the overlying normal mucosa, and therefore it is difficult to sample tissues for histologic analysis and even endoscopically observe the tumors. Probe based confocal laser endomicroscopy (pCLE) is a newly established endoscopic method providing in vivo histology at a subcellular resoloution. Our preceding animal experiments demonstrated that the muscularis propria could be visualized with pCLE within an artificial submucosal space.
AIMS&METHODS: Aims of this study was to evaluate the technical feasibility of visualization of GIST tumor cells with pCLE after topical application of neuronal stains. Surgically removed full-thickness wall of 4 stomachs and 1 duodenum containing GISTs were studied. First, the overlying normal mucosa and the submucosa was removed approximately 5mm^2 until the tumor surface was exposed. A neuronal fluorescent molecular probe (NeuroTrace500/525, Invitrogen) was topically sprayed onto the exposed submucosal tumor and pCLE (Cellvizio, Mauna Kea Technologies, Paris) observation of the exposed portion of the GIST were performed. Cresyl violet was additionally sprayed for 3 gastric tumors. Standard histologic analysis was then performed after formalin fixation and the recorded pCLE images were capered with the corresponding histology.
RESULTS: pCLE succeeded to visualize the morphology of GIST tumor cells demonstrating each spindle shaped cell with image quality identical to bench microscopic images. NeuroTrace visualized the cell body and the nuclei of tumor cells. Meanwhile, the Cresyl violet selectively stained cell body and cytoplasm including a gastric GIST that NeuroTrace failed to visualize.
CONCLUSION: The results of this pilot ex vivo study showed the technical feasibility of the morphology based histologic analysis of GISTs using pCLE following topical application of the neuronal stains successfully visualized tumor cells. We believe that this minimally invasive endoscopic histology would overcome existing technical limitations currently associated with needle or forceps based biopsies.
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Disclosure of Interest: None Declared
Keywords: confocal endomicroscopy , gastrointestinal stromal tumor, histology, pCLE

P698 USEFULNESS AND SAFETY OF A COMBINED USE OF SB KNIFE AND IT KNIFE NANO IN ENDOSCOPIC SUBMUCOSAL DISSECTION FOR ESOPHAGEAL SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Endoscopic submucosal dissection (ESD) for esophageal squamous cell carcinoma (SCC) has been developed in Japan as a standard endoscopic resection technique. Recently, we have used a combination of an IT knife nano for peripheral incision and a SB knife for submucosal dissection. The aim of this study is to examine the usefulness and safety of the combined use of the SB knife and IT knife nano in ESD for esophageal SCC.
AIMS&METHODS: Esophageal ESD was performed on 414 lesions of 338 patients at Hiroshima University Hospital between April 2006 and March 2013. Lesions were divided into 3 groups: Group A, 235 lesions in 186 patients dissected with only a Hook knife between April 2006 and October 2010; Group B, 131 lesions in 110 patients dissected with the Hook knife and SB knife between November 2010 and June 2012; and Group C, 48 lesions in 42 patients dissected with the IT knife nano and SB knife between July 2012 and March 2013. We retrospectively examined mean procedure time, procedure time per unit area, rate of en bloc resection, and rate of complications (perforation, delayed bleeding) between the 3 groups.

RESULTS: There were no significant differences in tumor location, macroscopic type, invasion depth, or degree of fibrosis among the 3 groups. Tumor size was significantly larger in Group C than in Group A ($P < 0.05$). Mean procedure time was 68.5 ± 46.8 min (15–300 min) in Group A, 92.9 ± 48.3 min (20-300 min) in Group B, and 103.0 ± 42.1 min (35–180 min) in Group C. Procedure time per unit area in Group C was significantly shorter than that in Group A (7.8 ± 3.7 min in Group C vs. 11.7 ± 8.0 min in Group A, $P < 0.05$). The rate of en bloc resection was 93.2% (219/235) in Group A, 97.7% (128/131) in Group B, and 100% (48/48) in Group C. The rate of perforation was 6.0% (14/235) in Group A, 6.1% (8/131) in Group B, and 2.1% (1/48) in Group C. The rate of delayed bleeding was 1.7% (4/235) in Group A and 0.8% (1/131) in Group B; no delayed bleeding occurred in Group C.
CONCLUSION: The combination use of SB knife and IT knife nano showed possible potential for shortening of procedure time and increasing the safety of ESD for patients with esophageal SCC.
Disclosure of Interest: None Declared
Keywords: endoscopic submucosal dissection (ESD), esophageal cancer

P699 PRELIMINARY STUDY ON USE OF CARBON DIOXIDE SUBMUCOSAL INJECTION CUSHION IN ESOPHAGEAL AND GASTRIC TUMOUR ENDOSCOPIC SUBMUCOSAL DISSECTIONS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) can be used for the successful *en bloc* resection of early stage gastrointestinal tumours including large lesions, but requires a satisfactory facilitative submucosal (sm) injection agent for safety and efficacy. We previously reported on the effectiveness of carbon dioxide (CO_2) as an sm injection agent using isolated and live pig models (*Dig Endosc* 2011), but this novel technique had not previously been assessed clinically.
AIMS&METHODS: The aim of this preliminary clinical study was to assess the safety and feasibility of this technique in esophageal and gastric ESDs.
Nine consecutive patients with 9 lesions including for 4 superficial esophageal and 5 early gastric cancers were enrolled for outcome analysis. The study protocol was approved by the ethics committee of our institution and informed consent was obtained from each patient. A gastroscope with a distal attachment was used along with a syringe filled to 50ml with CO_2 and connected to a 23-gauge injection needle catheter. CO_2 was then injected by hand into the sm layer followed by a circumferential incision and sm dissection using an electrosurgical knife. Standard sm injection with a glycerin solution (glycerol) was allowed for case of insufficient sm cushion. All resected specimens were examined histopathologically.
RESULTS: Mean resected specimen and tumour sizes were 35.0±13.0mm and 10.4±8.0mm, respectively. Median procedure time was 40 minutes (range, 20-70). Partial physical sm layer dissections were observed in all cases from the pressure of the CO_2 sm injections resulting in easier dissection of the sm layer using the electrosurgical knife with current and the distal attachment manually. Additional injections of glycerol were required in each case because of rapid CO_2 absorption. All tumours were successfully resected *en bloc* endoscopically and histologically without any complication enabling for precise histopathological assessment. Eight patients could be followed up for more than 22 months with no recurrences in any of those cases.
CONCLUSION: This study demonstrated the safety and efficacy of using CO_2 sm injections during esophageal and gastric ESDs despite the need for additional glycerol injection although further investigation of the technique will be needed prior to extensive clinical use.
Disclosure of Interest: None Declared
Keywords: carbon dioxide, Endoscopy, ESD, endoscopic submucosal dissection, esophageal cancer, gastric cancer, submucosal injection

P700 USEFULNESS OF ENDOSCOPIC EXAMINATION UNDER GENERAL ANESTHESIA IN THE DETECTION OF SUPERFICIAL CANCERS OF THE OROPHARYNX AND HYPOPHARYNX

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INTRODUCTION: The concept of field cancerization indicates that the possibility of multicentric cancer should be considered when superficial squamous cell carcinomas (SCCs) of the oro- and hypopharynx are detected. However the complex structure and the gag reflex make it difficult to adequately examine.
AIMS&METHODS: In this study, we compared the ability to detect superficial pharyngeal SCCs endoscopically with and without general anesthesia (GA). The subjects were 22 patients (male:female = 21:1, average age 68.1 years) who underwent endoscopic resection (ER) of 33 superficial SCCs of the oro- and hypopharynx at our Department between January 2005 and February 2013. Both preoperative endoscopies and endoscopies under GA were performed using non-magnifying white light imaging (WLI), narrow-band imaging (NBI) and magnifying NBI. Endoscopies under GA were performed just before ER. We exposed the larynx with the assistance of a curved laryngopharyngoscope (Sato-style, Nagashima Medical Instruments) in 14 cases. We determined the number of newly detected lesions under GA and compared the clinicopathological findings in the lesions detected preoperatively (A group) and the newly detected lesions under GA (B group).
RESULTS: The numbers of detected lesions by preoperative endoscopies and endoscopies under GA were 26 and 33, respectively (P=0.016, binomial test). Accordingly, 7 lesions were newly detected. As shown in Table 1, examination under GA was useful in the detection of small lesions white in color or the same color as the background mucosa. There is no significant difference in macroscopic appearance and depth of invasion between A group and B group.
Table 1. The size and endoscopic appearance

	A group (n=26)	B group (n=7)	P value
Mean diameter (SD) mm	17.9 (10.8)	7.7 (4.2)	0.02*
Coloration			0.04**
Red	20	1	
White / same as sorrounds	6	6	

*: Student's t-test, **: Fisher's exact test
CONCLUSION: WLI + NBI examination under GA markedly improves the detection rate for multicentric cancers of the oro- and hypopharynx, and is essential for endoscopic treatment.
Disclosure of Interest: None Declared
Keywords: detection, endoscopy, hypopharynx, oropharynx, superficial squamous cell carcinoma

P701 THE STUDY REGARDING FEASIBILITY OF REPEATED ENDOSCOPIC RESECTION FOR METACHRONOUSLY MULTIPLE SUPERFICIAL HEAD AND NECK SQUAMOUS CELL CARCINOMA

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INTRODUCTION: Progress of endoscopic instrument has led to early detection of superficial cancer and has allowed for endoscopic resection (ER) in head and neck (HN) region. In contrast, metachronously superficial cancers often occur in patients with head and neck squamous cell carcinoma (HNSCC) during followed up periods. Although it is reported that ER as an initial treatment is safe and effective, the feasibility of repeated ER (R-ER) for metachronously superficial cancers has not been clarified.
AIMS&METHODS: The aim of this retrospective study was to analyze the feasibility of R-ER for superficial HNSCC. Between June 2002 and December 2010, a total of 151 consecutive patient received initial ER (I-ER) for naive superficial HNSCC in our Hospital. Endoscopic mucosal resection using the cap (EMR-C) or endoscopic subepithelial dissection (ESD) was performed in all patients under general anesthesia. We have comparatively evaluated fasting period, hospital staying and early (within a week after ER) and late (1 week to 3 months) complications in same patients.
RESULTS: I-ER was performed for 196 lesions in 151 patients. Of 151, 48 (32%) had metachronously multiple HNSCC with median follow up period of 43 months (range: 2-124) from I-ER. R-ER was performed for 122 lesions in 48 patients. Patient characteristics of 48 patients included median age of 64 years (45-82), male/female: 46/2, 44 (92%) had history of synchronous or previous esophageal cancer. Median times of R-ER were twice (2-7 times). Median tumor size was 15 mm in diameter (2-50) of 196 lesions for I-ER, and 10 mm (2-43) of 122 lesions for R-ER. While local recurrence developed in 8 (5.2%) of 151 patients with median follow up period of 43 months (2-124), no local recurrence was found in 48 patients received R-ER with median follow up period 40 months (3-95), respectively. Fasting period during hospital staying was 3 days (1-14) of 7 (4-23) for R-ER, and 3 (1-20) of 8 (3-58) for I-ER. Early complication rates of R-ER and I-ER were 9.8% and 7.9%, respectively (bleeding: 1.6%vs1.3%, subcutaneous emphysema: 3.3%vs2.6%, mediastinal emphysema: 0.8%vs0%, pneumonia: 1.6%vs 2.6%, laryngeal edema requiring tracheostomy: 2.5%vs1.3%). Late complication rates of R-ER and I-ER were 1.6% and 2.6%, respectively (delayed bleeding: 1.6%vs1.3%, percutaneous endoscopic gastrostomy with dysphagia: 0%vs1.3%). Overall complication rates were 11.5% in R-ER and 10.6% in I-ER. There was no significant difference at any events.
CONCLUSION: These results indicate that R-ER may be almost same the feasibility compared with I-ER.
Disclosure of Interest: None Declared
Keywords: Endoscopic resection, head and neck cancer

P702 SHORT-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR SUPERFICIAL ESOPHAGEAL NEOPLASMS: A MULTICENTER SURVEY

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INTRODUCTION: Endoscopic submucosal dissection (ESD) for superficial esophageal neoplasms (SENs) is a promising procedure that enables en bloc resection regardless of the tumor size. Despite of its technical difficulties, recently good outcomes have been reported from high-volume centers as a single-center study, but safety and efficacy have not been evaluated in a multicenter survey including municipal hospitals.
AIMS&METHODS: This is a multicenter retrospective study from May 2005 to October 2012 in 11 hospitals attending the Osaka Gut Forum. Of 295 consecutive patients with 354 esophageal lesions treated by ESD, a total of 349 SENs in 290 patients (239 male, median age 69 yrs) were analyzed. The incidence of complications was estimated. In addition, we compared the results between before and after December 2009, or between 4 high-volume centers (HVC) that experienced more than 30 cases and 7 low-volume centers (LVC) that experienced less than 30 cases.
RESULTS: Mean tumor size was 20.9mm. Over half SENs were located in the middle thoracic esophagus (60%) and depressed type (54%). The pathological diagnoses were as follows; dysplasia/intraepithelial neoplasia 100 (29%); SCC 230 (66%); adenocarcinoma 10 (3%); undetermined 9 (3%). The invasion depth of SCC was EP 73; LPM 79; MM 45; SM1 11; SM2 ($>200\mu$m) or deeper 22. Two hundred and ninety five lesions (85%) were completely resected with negative margins and 259 lesions (76%) were curatively resected. Procedure times were 100±66 mins. Perforation including mediastinal emphysema, postoperative pneumonia, bleeding, and esophageal stricture occurred in 22 (6.5%), 6 (1.8%), 0 (0%), and 23 (6.8%), respectively. Outcome survey showed that the rates of perforation and long procedure time (≧2 hrs) were significantly decreased in the later period compared with the prior period [10.3% vs. 4.0%, p=0.025, 48.5% vs. 25.7%, $p<0.001$, respectively]. There were, however, no significant differences of short-term outcomes between HVC and LVC.
CONCLUSION: This multicenter survey indicated that esophageal ESD had a high risk of perforation and required long procedure time at first, but was becoming more feasible as a standard treatment with acceptable complication risks.
Disclosure of Interest: None Declared
Keywords: endoscopic submucosal dissection (ESD), esophageal cancer, short-term outcomes

P703 PRETREATMENT FACTORS CONTRIBUTING TO NON-CURATIVE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is established as a curative treatment for early gastric cancer (EGC). Although the expansion of the criteria for ESD permits an increase in the number of patients who benefit from ESD, it may also increase the number of cases wherein ESD results in non-curative resection.
AIMS&METHODS: We conducted this study to clarify pretreatment factors for non-curative ESD. Between January 2008 and December 2012, 364 patients (276 males and 88 females; median age, 71 years) with 401 EGC lesions underwent ESD. In case of EGC lesions with suspected submucosal invasion, endosonography was performed before treatment. Curative ESD was defined as complete ESD meeting the criteria described in the Japanese gastric cancer treatment guidelines or the expanded criteria proposed by Gotoda et al. Pretreatment factors for non-curative ESD were examined using multiple logistic regression analysis. Variables included age (>70 years vs. <=70 years), gender, tumor size (>20 mm vs. <=20 mm), tumor location (upper vs. middle and lower), morphological classification (superficial elevated and depressed type vs. others), ulceration, and histological differentiation (differentiated type vs. undifferentiated type).
RESULTS: Non-curative ESD was observed in 63 (15.7%) lesions. The reasons for non-curative ESD were positive horizontal/vertical margins for 15 lesions, lymphatic and/or venous invasion for 23 lesions, sm2 invasion for 12 lesions, and others for 13 lesions. Multivariate analysis revealed that tumor size >20 mm [odds ratio (OR), 3.6; p = <0.0001], superficial elevated and depressed type (OR, 5.2; p = 0.0002), ulceration (OR, 5.3; p = 0.0007), and undifferentiated type (OR, 8.2; p = 0.0001) were significant factors for non-curative ESD. The reasons for non-curative ESD in superficial elevated and depressed lesions were sm2 invasion for 9 lesions, lymphatic and/or venous invasion for 3 lesions, and another for 1 lesion.
CONCLUSION: This study suggested that EGC lesions with large sizes, ulceration, or undifferentiated type have an increased risk for non-curative ESD, even if they satisfy the eligibility criteria for ESD. Furthermore, superficial elevated and depressed type was found to be an important factor influencing the curability of ESD.
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Disclosure of Interest: None Declared
Keywords: early gastric cancer, endoscopic submucosal dissection, non-curative, pretreatment factors

P704 RISK FACTORS OF DELAYED HEALING OF IATROGENIC GASTRIC ULCER AFTER ENDOSCOPIC RESECTION

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INTRODUCTION: Endoscopic resection is safe, and applicable to a wide variety of clinical situations. However, endoscopic submucosal dissection (ESD) may cause large and deep defects after the procedure. Iatrogenic ulcers after endoscopic resection were thought to heal faster and to recur less often than peptic ulcers. About 10% of iatrogenic gastric ulcers after ESD were still remained as incomplete healing state at 8 weeks. So, we conducted a retrospective cohort analysis to clarify the contributing factors of delaying gastric ulcer healing after endoscopic resection and review the optimal duration of proton pump inhibitor (PPI) after endoscopic resection.
AIMS&METHODS: We analyzed retrospectively total 629 lesions in 533 patients who performed endoscopic resection due to gastric adenoma or early gastric cancer (EGC) between January, 2007, and December, 2011, at Kyung Hee University Hospital in Seoul, Korea. First post-ESD follow-up endoscopy was performed at the 8 weeks after ESD/EMR in the *Helicobacter pylori* (*H. pylori*) negative group and at the 12 weeks after ESD/EMR in the *H. pylori* positive group. Standard dose of PPI were administered for the treatments of iatrogenic ulcers after ESD/EMR in all patients.
RESULTS: After ESD/EMR, 77 in 629 lesions (12%) were healed incompletely at the first follow-up endoscopy. In univariate logistic regression analysis, the following factors were significantly associated with incomplete healing of iatrogenic ulcers: (1) the presence of depression [hazard ratio, 2.322 (95% CI, 1.270-4.245)], (2) the presence of ulcer or erosion [hazard ratio, 2.926 (95% CI, 1.531-5.590)], (3) the histologic type (high grade dysplasia or EGC) [hazard ratio, 2.661 (95% CI, 1.501-4.719)], and (4) the removed specimen size after ESD [hazard ratio, 3.066 (95% CI, 1.425-6.341)]. And, the use of antiplatelet agents showed borderline significance [hazard ratio, 1.844 (95% CI, 0.921-3.693)]. In multivariate logistic regression analysis, three factors were significantly associated with incomplete healing of iatrogenic ulcers: the presence of ulcer or erosion [hazard ratio, 2.210 (95% CI, 1.115-4.381)], the histologically high grade dysplasia or early gastric cancer [hazard ratio, 2.157(95% CI, 1.115-4.381)], and the removed specimen size (≥ 3.0 cm) [hazard ratio, 2.285 (95% CI, 1.042-5.011)].
CONCLUSION: Delayed healing of iatrogenic ulcers in ESD/EMR was associated with the presence of ulcer or erosion before ESD/EMR, the histologic type (high grade dysplasia or EGC) and the removed specimen size.
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Disclosure of Interest: None Declared
Keywords: Endoscopic resection, Gastric cancer, Healing, Iatrogenic ulcer

P705 LONG DECOMPRESSION TUBE PLACED BY TRANSNASAL ULTRATHIN ENDOSCOPY WITH HYDROPHILIC GUIDEWIRE FOR SMALL BOWEL OBSTRUCTION: SAFE METHOD AND RAPID INSERTION

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INTRODUCTION: Placement of a long intestinal decompression tube is a common option for the nonoperative management of small bowel obstruction (SBO). However, there is sometimes a great difficulty in intubating small bowel with conventional technique using fluoroscopy and guidewire manipulation, which could cause prolonged procedure time and severe patient distress.
There have been some reports regarding the usefulness of long tube intubation method assisted with endoscopy, however still some problems remain. A novel technique was developed using a combination of transnasal endoscopy and hydrophilic guidewire.
With this method, the tube can easily advance through the jejunum benefit by the stiffness of the guidewire, and hydrophilic guidewire can be easily controlled through the tube thanks to the minimal striction.
We performed a retrospective study in patients with SBO treated by long decompression tube to compare the new method with conventional method.
AIMS&METHODS: The aim of this study is to evaluate the safety and efficacy of this new technique.
We analyzed a total of 141 patients with long tube intubation performed in our institution from October 2010 to March 2013. Tubes were inserted either with our new method or with conventional method, and patients were categorized in 2 groups accordingly; endoscopy group and conventional group.
We evaluated the cause of the obstruction, success rate of the placement, the total procedure time, and adverse events.
We used transnasal gastrointestinal videoscopes with diameter of 5.0 mm at the distal end (GIF-XP260N, Olympus Medical Systems, Japan). Hydrophilic guidewires and hydrophilic long tubes with 16 Fr diameter and 300 cm length were used in both groups.
RESULTS: Subjects comprised 80 men and 61 women, and median age was 68 years. There were no significant differences in background characteristics between the 2 groups. The most common cause of SBO was postoperative adhesion followed by malignancy and herniation.
The success rate was significantly higher in endoscopy group (99.1%) as compared to 85.1% in conventional group ($p = 0.01$). The mean procedure time was significantly shorter in endoscopy group (42 minutes) compared with 68 minutes in conventional group ($p < 0.01$)
In endoscopy group, 63.6% of the patients could avoid surgery during hospitalization and 73.3% in conventional group respectively, though there was no significant difference between them. No major adverse events such as perforation were observed in either group.
CONCLUSION: Using a combination of transnasal ultrathin endoscopy and hydrophilic guidewire is a safe and efficient method for patients with SBO to place long decompression tubes, and is superior to conventional intubation methods.
Disclosure of Interest: None Declared
Keywords: long decompression tube, new technique, small bowel obstruction, transnasal endoscopy

P706 CONFOCAL LASER MICROSCOPY FOR THE EVALUATION OF NEW MORPHOMETRIC PARAMETERS OF NEOANGIOGENESIS AND TARGETED PANENDOTHELIAL MARKERS IN HUMAN COLORECTAL CANCER

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INTRODUCTION: Tumor microcirculation is characterized by an abnormal vascular network with dilated, tortuous, saccular vessels. Imaging the tumor vasculature and determining its morphometric characteristics represent a critical goal for optimizing the development of antiangiogenic therapy.
AIMS&METHODS: In this study we evaluated vascular morphometric parameters in colorectal cancer by using a minimally-invasive imaging technique, confocal laser endomicroscopy (CLE). Fresh biopsies from tumor and normal tissue were collected during colonoscopy from five patients with T3 colorectal carcinoma without metastasis, and were marked with fluorescently labeled anti-CD31 antibody. The imaging was performed using a dedicated endomicroscopy system (Pentax Inc). ImageJ NIH software was used for image processing. To account for directional variability, the parameters of vascular segments from two equal perpendicular rectangles (50 microns wide in the horizontal and vertical direction) were averaged for each sample. Vessel diameters, vessel density, vessel lenght, tortuosity index and daughter/mother ratio were expressed as the average±standard deviation. Statistical differences were calculated using the Student's t-test, considering p-values $\leq$0.05 significant.
RESULTS: The average diameter of vessels in the normal sample was 7.6±0.3μm, the vessel density was 988.8±51.4vessels/mm^2, whereas in the tumor sample the vessel diameter was 9.4±0.4μm and the vessel density 1511.1±69.3vessels/mm^2 ($p<0.05$). The tortuosity index (ratio of segmented and straight line lengths) and vessel length were 1.06±0.02 and 28.7±3.2μm in normal tissue, 1.07±0.01 and 24.6±3.1μm in tumor tissue respectively. The daughter/mother ratio (ratio of the sum of the squares of daugther vessel radia over the square of the mother vessel radius, considerind the mother as the largest vessel at a branching point) was 1.11±0.09 in normal tissue, while in tumor tissue we obtained a similar average value of 1.10±0.08 ($p>0.05$).
CONCLUSION: Our study found no significant difference in the tortuosity index and daughter/mother ratios between normal and tumor microvasculature in contrast to the conventional perception that the blood vessels are more tortuous in colorectal cancer. Provided new contrast agents will be clinically available, future *in vivo* use of CLE could lead to identification of novel biomarkers based on the morphometric characteristics of tumor vasculature.
Disclosure of Interest: None Declared
Keywords: colorectal cancer, confocal laser endomicroscopy, morphometric parameters, neoangiogenesis, panendothelial markers

P707 POLYP RESECTION RATE AND POLYPECTOMY SUCCESS RATE – TWO NEW COLONOSCOPY QUALITY ASSURANCE PARAMETERS. – POLYPECTOMY IS A YOUNG MANS' GAME!

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INTRODUCTION: One of the core purposes of colonoscopy is to detect and remove polyps. Incomplete resection of polyps is associated with an increased risk of subsequent cancer. In spite of this, no Quality Assurance (QA) benchmarks have been developed to assess the ability of endoscopists to competently deal with polyps.
AIMS&METHODS: We retrospectively analysed the colonoscopy database from 3 British endoscopy units over a 5 year period (2008-2012 inclusive). Colonoscopies carried out with therapeutic intent were excluded. Screening and surveillance examinations were included.
RESULTS: Data from 4393 polyps (average size 6.3mm) found during 17060 colonoscopies carried out by 15 colonoscopists was analysed. Removal of 4121 polyps was attempted (1981 by snare polypectomy and 938 by EMR, the remainder removed by hot biopsy or cold snare). In 559 cases the polypectomy "failed", either due to incomplete resection (121 polyps) or failure of retrieval of the polyp (438 polyps). Most failures were in removing larger sessile lesions (avg size 14.7mm) found in the rectum, sigmoid or caecum.
By dividing the unsuccessful procedures with the total number of polypectomies, a "Polypectomy Success Rate" (PSR) was calculated. The median PSR was 82% (std 11.5%). Two endoscopists had Polypectomy Success Rates (PSR) 2 standard deviations below median at (51% and 62%, minimum standard Polypectomy Success Rate: 62%). There was no significant association between the PSR and the caecal intubation rate (P=0.83), the total number of polyps removed (P=0.25) or the total number of colonoscopies carried out (P=0.37). However, there was a significant association with the age of the endoscopist (P=0.002, $r^2 = 0.53$)!
1946 polyps were in the size range for removal at the initial examination (up to 2cm on the left side and 1cm on the right). However, 475 eligible polyps were not removed, giving a median Polyp Resection Rate (PRR) of 71%. Reasons for not removing a polyp included finding a more significant nearby lesion (26%), comorbidities (20%), patient uncomfortable (12%), inadequate bowel prep (11%), difficult polyp position requiring deferral to a dedicated session (8%) and lesion not found on extubation (5%). One endoscopist was 2 STD below the median at 35% (STD 11.6% giving a minimum quality standard of 48%).
CONCLUSION: We propose two new, important QA benchmarks and propose minimal standards for Polyp Resection Rate (62%) and Polypectomy Success Rates (48%).
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Disclosure of Interest: None Declared
Keywords: polyp removal, quality assurance

P708 30 DAYS HOSPITALIZATION RATE AFTER SCREENING COLONOSCOPY – CASE-CONTROL STUDY NESTED IN PROSPECTIVE RANDOMIZED CONTROLLED STUDY

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INTRODUCTION: In the past few years it have been proven that screening, including primary colonoscopy, reduces colorectal cancer incidence and mortality. Few studies have addressed the risk of 30 day hospitalization rates following screening colonoscopy.
AIMS&METHODS: The aim of our study was to compare the 30 day hospitalization rates after screening colonoscopy with the age and sex matched control groups and then to identify definite and possible serious adverse events leading to these hospitalizations.
The study was approved by the institutional ethical committee.
Methods: This study was nested in a randomized controlled trial in which 55-64 year old individuals living in one geographical area between 2009-2011 were drawn from population registries and randomly assigned in a 1:2 ratio to either colonoscopy group (COL; offered screening colonoscopy via mail invitation) or control group (CON; not contacted). Each subject randomized to the screening group was matched to two subjects from the control group with the same sex and birth year and assigned an identical screening and virtual screening dates. We have followed screening participants and their matched controls for deaths and causes (ICD 10 coding) of hospitalizations within 30 days from the date of actual or virtual screening, using the Ministry of Interior and National Health Service databases (covering over 98% of all insured population), respectively.
Adverse events leading to hospitalization in both groups were divided for definitely related (bleeding, post-polypectomy syndrome, perforation) and possibly related (cardiovascular (CVS), central nervous system (CNS), other gastrointestinal, infectious and deaths) to colonoscopy. Any other causes were assessed as unrelated.
RESULTS: 12,033 participants were included, 4,011 to the COL group and 8,022 to the CON group; hospitalization for any reason within 30 days occurred in 93 (2.32%) and 183 (2.28%), respectively ($p>0.1$). We identified 3 definitely and 13 possibly (9 CVS, 1 CNS, 2 infectious and 1 death) related complications in the COL group. There were 21 possibly (15 CVS, 3 CNS, 1 infectious and 2 deaths) related hospitalizations in the CON group ($p>0.1$). In the COL group there were no statistically significant differences in the rates of sedations, total exams, bowel preps, tolerance, polypectomies and diverticulosis between patients with and without possibly related adverse events.
CONCLUSION: The study shows no difference in the 30 day hospitalization rates between both groups. Serious adverse events were uncommon (4/1000) and no risk factors of hospitalizations were identified. Screening colonoscopy carries no additional risk for hospitalization.
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Disclosure of Interest: None Declared
Keywords: Complications, Hospitalization, Screening colonoscopy

P709 RANDOMIZED CONTROLLED TRIAL OF ULTRA-THIN VERSUS PEDIATRIC INSTRUMENTS FOR COLONOSCOPY IN OLDER FEMALE PATIENTS

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INTRODUCTION: Pediatric colonoscopes with 11 mm diameter are often used to negotiate the female colon. Gastroscopes, which are thinner than pediatric colonoscopies, are occasionally required to negotiate angulated sigmoid colons. However, the use of ultra-thin colonoscopes (6.8 mm diameter, standard length) for such difficult cases has not been studied.
AIMS&METHODS: Study aims: To compare the use of ultra-thin instrument with a pediatric instrument for colonoscopy in older female patients.
Methods: Following approval from Institutional Review Board, we commenced a randomized controlled study in August 2012. Female patients aged 70 years or older were enrolled and randomly allocated to colonoscopy with an ultra-thin scope (UTS) or a pediatric scope (PDS). Patients with a history of colonic resection were excluded from the study. Three board-certified endoscopists performed colonoscopy with carbon dioxide insufflation and no fluoroscopic guidance. Patients did not receive any sedation. Conventional insertion techniques, including clockwise torque shortening technique, were used with position change and abdominal pressure when necessary. We measured cecal intubation rate, ileal intubation rate, time to cecum and adenoma detection rate and degree of pain experienced (using a numerical rating scale, NRS). Patients were blinded to the instrument used until after measurement of the NRS. We used the Fischer's exact test or Mann-Whitney test to compare outcomes between groups.
RESULTS: Seventy-three patients enrolled into the study and 3 patients withdrew after randomization: 38 patients were allocated to the UTS group and 35 patients to the PDS group. The median age was 77 years (range 70 to 92 years). Cecal intubation rates were 97% in UTS and 94% in PDS (p=0.60). Ileal intubation rates were 81% in UTS and 88% in PDS (p=0.52). Median times to cecum

were 15.2 minutes (range 4.3 to 44.1) in UTS and 9.8 minutes (range 4.6 to 30.0) in PDS. There was a significant difference in insertion time (p=0.0085). Adenoma detection rates were 32% in UTS and 26% in PDS (p=0.62). There was a significant difference in pain experienced during colonoscopy ($p<0.0001$) between UTS (NRS 1/11, range 0 to 9) and PDS (NRS 4/11, range 1 to 8).
CONCLUSION: In older female patients undergoing unsedated colonoscopy, use of an ultra-thin instrument was associated with significantly less pain although insertion time was longer, compared with a pediatric instrument.
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Disclosure of Interest: None Declared
Keywords: Colonoscopy, randomized controlled trial, Ultra-thin endoscope

P710 INCIDENCE, TREATMENT AND OUTCOME OF ADVERSE EVENTS OF 100.000 SCREENING COLONOSCOPIES PERFORMED BY QUALITY CERTIFIED ENDOSCOPISTS IN AUSTRIA

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INTRODUCTION: In Austria screening colonoscopy is part of the preventive health checkup since 2005. Since screening colonoscopy is an invasive examination performed on a potentially healthy population, it is essential that adverse events occur as seldom as possible. In this study we evaluated incidence, treatment and outcome of adverse events in screening colonoscopies.
AIMS&METHODS: This retrospective cohort study included all patients who underwent screening colonoscopy by one of 204 quality certified endoscopists in Austria between November 2007 and March 2013.
RESULTS: In total 102.328 patients were included in this study. 53.286 (51.1%) women and 50.042 men (48.9%). The mean age in women was 61.2 years, in men it was 61.1 years. 86.8% received sedation. Cecal intubation rate was 95.5%. In 0.3% (n=264) of all colonoscopies adverse events were reported. 39% of them were cardiopulmonary events, 62% in women and 38% in men; followed by bleeding (46.2%; 30.3% vs 69.6%), perforation (4.5%; 42% vs 58%) and others (10.2%). 58.3% of perforations and 97.5% of bleedings occurred in colonoscopies with polypectomy. Colon perforation rate was 1:8527, post-polypectomy bleeding rate was 1:328. Further risk factors are polypectomy of multiple (>4; 0.04%), big (>2cm; 0.23%) and pedunculated polyps (0.04%) using snare (0.07%). 62.1% of all adverse events were treated conservatively, 19.3% in an ambulant setting, 13.6% were hospitalized and 4.5% required operative intervention. Out of the 12 perforations, 9 were treated in an operative setting, 2 as inpatients, 1 conservatively. 11 patients reached institution ad integrum, in one case we had no information about the outcome.
CONCLUSION: Colon perforation and postpolypectomy bleeding rates of 1:8527 and 1:328 were rarer than recommended in current guidelines (perforation rate should not exceed 1:1000 and bleeding rate 1:200). The results of our study show an internationally comparable adverse event rate in colonoscopies, performed within the ''Quality certificate screening colonoscopy''. Screening colonoscopy in Austria corresponds to highest requirements in regard to safety and quality.
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Disclosure of Interest: None Declared
Keywords: adverse events, quality assurance, Screening colonoscopy

P711 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR SUPERFICIAL RECTAL TUMORS: PROSPECTIVE EVALUATION IN FRANCE

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INTRODUCTION: Endoscopic Submucosal Dissection (ESD) allows monobloc and complete resections of digestive superficial tumors with high rate. The aim of this study was to evaluate the feasibility of ESD and the complete resection rate at 1 year. Preliminary results were available.
AIMS&METHODS: Patients with superficial medium or distal rectal tumors, more than 1 cm in size, were prospectively included in 9 expert French centres between February 2010 and June 2012.Follow-up was one year. The study was temporary stopped from September 2010 to June 2011 because of the high complications rate. Inclusions have resumed after remedial action.
RESULTS: 45 patients were retained for analysis (67 years, 24 males). Median procedure time was 110 [30, 280] minutes and median diameter was 35 [10-100] mm. Perforations rate was 17% (n=8), immediately detected with none salvage surgery. 6 (13%) patients had immediate bleeding treated during ESD and 6 (13%) had late bleeding treaded endoscopically for 5 and surgically for 1 patient who needed red blood transfusion. Mortality was zero. Total monobloc resection rate was 29 (65%) with 5 (11%) monobloc ESD finalised by a snare. Macroscopic complete resection rate was 95% and curative R0 resection rate was 54%. 3 (6%) patients had an invasive tumour (2 sm1: 1 with curative criteria and 1 requiring surgery, 1 T2 requiring surgery). At 3 months, there was 93% compliance to endoscopic control and complete resection rate was 86%. 1 patient needed a complementary mucosectomie. At 1 year, 33 (73%) patients had an endoscopic control and complete resection rate was 31 (69 %). Monobloc resection was significantly associated with less tumour diameter (37 +/- 21 cm monobloc versus 52 +/- 27 piecemeal, p=0 .04) and RO resection was significantly associated with less than 3cm diameter (84% R0 versus 60% R1, p=0.05). At the end of the study, after the remedial action, there was more monobloc resection (74% vs 52%), less procedure duration/tumour size (2.2 vs 4.1) and less perforations (0% vs 34%).
CONCLUSION: Superficial rectal tumours can be treated safely and effectively by ESD with a high complete resection rate. Experience in ESD is low in Europe and curative RO resection should increase and complications rate decrease with experience and corrective actions.
Disclosure of Interest: None Declared
Keywords: endoscopic submucosal dissection (ESD), superficial rectal tumour

P712 HIGH-DEFINITION ENDOSCOPY WITH VIRTUAL CHROMOENDOSCOPY ALLOWS ACCURATE PREDICTION OF FOOD ALLERGY IN REAL-TIME – AN OBSERVATIONAL STUDY

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INTRODUCTION: Food allergy is an adverse immune response to food antigens involving the immune system via IgE and non-IgE mediated mechanisms. Previously it was shown that standard white-light endoscopy may reveal discrete mucosal alterations in patients with severe food allergy. Of note, these findings were mostly unspecific for the underlying disease.
AIMS&METHODS: Study objective was to access the value of high-definition colonoscopy with virtual chromoendoscopy (i-scan) for prediction of mucosal changes in patients with suspected food allergy. Therefore, consecutive patients suffering from recurrent abdominal pain and diarrhea were included. First, the patients underwent a clinical interview in order to contain the diagnosis. Afterwards, ileocolonoscopy was performed using high-definition endoscopy with i-scan. The mucosa of the terminal ileum, caecum and at the rectosigmoid junction was carefully inspected with i-scan. Than a diagnostic lavage was performed at these locations and analyzed by measuring 13 different allergic markers, including TNF-alpha and IgE. Subsequently, biopsies were obtained for additional histopathological analysis.
RESULTS: 26 patients (19 female, mean 46 age years; Range 50-68 years) were prospectively included. Based on the clinical presentation and the lavage diagnosis intestinal food allergy was diagnosed in 60% of patients. High-definition endoscopy with i-scan visualized lymphoid hyperplasia, slight mucosal edema and blurred mucosal vascular pattern. Based on these findings i-scan could predict food allergy with a sensitivity, specificity and accuracy of 85%, 89%, and 86%, respectively. Positive and negative predictive value of i-scan for prediction of food allergy was 92% and 80%, respectively.
CONCLUSION: High-definition endoscopy with virtual chromoendoscopy could mimic slight mucosal changes in patients with intestinal food allergy which were highly predictive for the disease.
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Disclosure of Interest: None Declared
Keywords: chromoendoscopy, food allergy, i-scan, predictive factors

P713 DEVELOPMENT OF A NEW CLASSIFICATION SYSTEM FOR CONFOCAL LASER ENDOMICROSCOPY IN INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Probe-based confocal laser endomicroscopy (pCLE) allows in vivo histology during ongoing colonoscopy and assessment of mucosal and submucosal alterations in real time. Here, an international collaboration of five experts proposed a new and unique pCLE classification for the use in patients with inflammatory bowel disease (IBD).
AIMS&METHODS: Main study objective was to establish a pCLE classification for IBD. Second study objective was to assess accuracy, interobserver and intraobserver agreement of the new classification. Therefore, consecutive patients with known IBD underwent screening or surveillance colonoscopy and were evaluated using pCLE. First, a post hoc review of 25 pCLE video sequences was performed in order to accomplish the new classification system which is based on different vessel and crypt categories. Accordingly, all observers scored an additional set of 100 pCLE video sequences, using the new classification. In all cases, histopathology served as the reference standard.
RESULTS: Based on different vessel and crypt categories a new pCLE classification for IBD was developed. Interobserver agreements for vessel and crypt architecture were substantial with kappa values of 0.77 (95% confidence interval: 0.65-0.90) and 0.63 (95% confidence interval: 0.48-0.79), respectively. Intraobserver agreements for vessel and crypt architecture were substantial with kappa values of 0.75 (95% confidence interval: 0.49-1) and 0.68 (95% confidence interval: 0.38-0.97), respectively. Overall, sensitivity, specificity and accuracy for predicting histological inflammation in macroscopically non-inflamed mucosa were 94%, 81%, and 87%, respectively. Positive and negative predictive values were 82% and 94%, respectively.
CONCLUSION: Here, a panel of international experts developed and validated a new and unique classification for pCLE in IBD. The classification allows

prediction of microscopic inflammation even in macroscopically non-inflamed mucosa. Final results will be reported at UEGW.
Disclosure of Interest: None Declared
Keywords: classification, endomicroscopy, IBD

P714 I-SCAN IMPROVES THE DETECTION OF RIGHT SIDED COLON ADENOMAS IN COMPARISON TO HIGH-DEFINITION WHITE LIGHT ENDOSCOPY

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INTRODUCTION: Colonoscopy remains the gold standard for colorectal cancer surveillance. Nevertheless, population based studies have shown, that 20-50% of colorectal lesions may be missed during colonoscopy and that colonoscopy has only limited effects on the occurrence of proximal colon neoplasms. i-scan is a newly introduced virtual staining technique that provides an improved tissue contrast.
AIMS&METHODS: Main study objective was to assess if i-scan improves the detection of proximal colon adenomas in comparison to high-definition white light endoscopy (HD-WL). Therefore, consecutive patients undergoing surveillance colonoscopy were prospectively included. The right colon was first investigated with HD-WL followed by a repeat examination with i-scan.
RESULTS: Overall, 300 patients (40% female; mean age 61 years) were prospectively included. In the HD-WL group 76 polyps (mean diameter 9.2mm, range 2-40mm) were detected within the right colon. i-scan detected 62 additional polyps (mean diameter 3.7mm, range 2-10mm) within the right colon. Histopathological analysis revealed 22 hyperplastic lesions and 54 adenomas in the HD-WL group. Additionally, 12 carcinomas were found. i-scan detected additional 12 hyperplastic lesions, 48 adenomas and 1 tumor (schwannoma of 2mm in the caecum). Overall, i-scan detected significantly more colorectal lesions and more adenomas (both $p < 0.001$). The median additional time exposure for i-scan was 157 seconds.
CONCLUSION: Additional investigation of the right colon with i-scan requires less than 3 minutes and yields in an increased adenoma detection rate. Therefore, i-scan has the potential to significantly enhance the quality of screening and surveillance colonoscopy.
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Disclosure of Interest: None Declared
Keywords: advanced imaging, chromoendoscopy, i-scan, PIVI, polyps, sessile serrated adenoma/polyp

P715 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL NEOPLASIA DURING THE CLINICAL LEARNING CURVE

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INTRODUCTION: The efficacy of endoscopic submucosal dissection (ESD) for en bloc resection of colorectal neoplasia has been reported. However, even in Japan, colorectal ESD has not yet been widely spread because of the technical difficulty and higher risk of complications, especially for novices of colorectal ESD who have little experience in gastric ESD. The same is also true of skilled endoscopists in western countries that have smaller number of early gastric neoplasia. We report here the results of colorectal ESD during the clinical learning curve. We also discuss ways to reduce the difficulties of colorectal ESD, especially for novices.
AIMS&METHODS: Colorectal ESD was performed at Tohoku University Hospital between July 2009 and April 2013 by 4 endoscopists with experience in fewer than 5 cases of gastric ESD. The first 20 cases of each endoscopist were investigated. The dual knife (standard tip-type knife; Olympus Optical Co., Tokyo, Japan) or the SB knife junior (small scissors-type knife; Sumitomo Bakelite Co., Tokyo, Japan) was used as a knife for mucosal incision and submucosal dissection. From among the clinicopathological factors (location, macroscopic types, tumor size, histological types and knife types), the factors that affected the co-primary outcomes (the procedural time, the en bloc resection rate and the complication rate) were identified.
RESULTS: (Clinicopathological characteristics) A total of 80 cases (54 males, 26 females; 56 colonic and 24 rectal lesions; 29 IIa, 30 IIa+Is, 9 IIa+IIc and 12 Is) were included in this study. The mean age of the patients was 68.1 (30-87) years. The mean tumor diameter was 35.2 (20-95) mm. The histological analysis showed 39 adenocarcinomas (48.8%) and 41 adenomas (51.2%). (Outcomes) The mean procedural time was 108.8 (37-329) minutes. The en bloc resection rate with tumor-free margins was 75.0% (60/80). Perforation occurred in 6 patients (7.5%) who were managed by conservative medical treatment after the endoscopic closure. Postoperative hemorrhage occurred in 3 patients (3.8%) who were treated by endoscopic hemostasis. Multivariate analyses revealed that colonic lesions and larger lesions (40mm or more) were significantly associated with longer procedural time (90min or more). The use of SB knife junior was significantly associated with higher en bloc resection rate. Colonic lesions were also associated with perforations.
CONCLUSION: Colorectal ESD is technically challenging for novices. The use of the SB knife junior may increase the en bloc resection rate. It may be better to begin from rectal and smaller lesions (less than 40mm) in order to reduce complications.
Disclosure of Interest: None Declared
Keywords: colorectal neoplasia, Complication, en bloc resection, endoscopic submucosal dissection (ESD), learning curve

P716 EFFICACY AND SAFETY OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECTAL NEOPLASIA CLOSE TO THE DENTATE LINE

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INTRODUCTION: Although colonic endoscopic submucosal dissection (ESD) is difficult and has a higher risk of perforation, rectal ESD is relatively easy and has lower risk of perforation. However, the ESD procedure for rectal lesions close to the dentate line may be difficult, because such lesions have a higher risk of bleeding from rectal venous plexus. Moreover, the working space in the anal canal is very narrow. We report here the results of ESD for rectal neoplasia close to the dentate line.
AIMS&METHODS: ESD was performed at Tohoku University Hospital between January 2011 and April 2013 by an endoscopist with experience in more than 50 cases of colorectal ESD. Because of sensory nerves, the ESD procedure for squamous epithelium is usually accompanied by pain. Therefore, local lidocaine injection was used on the occasion of incision of the dentate line. Clinicopathological characteristics (tumor size, macroscopic types, histological types and existence of hemorrhoids) were investigated. Co-primary outcomes were the procedural time, the rate of en bloc resection and the rate of complications.
RESULTS: (Clinicopathological characteristics) A total of 15 cases (7 males, 7 females; 1 female with 2 lesions close to the dentate line) were included in this study. The mean age of the patients was 63.2 (40-83) years. The mean tumor diameter was 59.8 (21-122) mm. Among the 15 cases, 11 were laterally spreading tumors of the granular type, and 4 were large protruding tumors. Twelve cases (80.0 %) had hemorrhoids. The histological analysis showed 8 cases (53.3 %) of adenocarcinomas and 7 cases (46.7 %) of adenomas. (Outcomes) The mean procedural time was 121.1 (38-224) minutes. The en bloc resection rate was 100.0% (15/15) and the en bloc resection rate with tumor-free margins was 80.0% (12/15). Two cases required another knife, a hook knife. No case required a snare. Postoperative hemorrhage occurred in two cases (13.3%), which were treated by endoscopic hemostasis. Two cases complained of anal pain for about a week after ESD, which were treated by oral loxoprofen. One case (6.7%) had low grade fever for several days after ESD, which may be due to sepsis and was treated by antibiotics. Anal-stenosis occurred in one patient (6.7%) who was treated by endoscopic balloon dilation.
CONCLUSION: The procedure of ESD for rectal lesions close to the dentate line is feasible and safe, only if it is performed by endoscopists with sufficient experience. The pain can be well-controlled using local lidocaine injection. However, in order to reduce complications, further devices are required.
Disclosure of Interest: None Declared
Keywords: Complication, dentate line, en bloc resection, endoscopic submucosal dissection (ESD), rectal neoplasia

P717 A NOVEL BALLOON-COLONOSCOPE IS SAFE & EFFECTIVE IN ADENOMA DETECTION - A PROSPECTIVE HUMAN STUDY

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INTRODUCTION: Colonoscopy is the "criterion standard" for detecting colorectal adenomas & cancers. However, multiple studies show adenomas (20% > 30%) are missed. This is primarily due to inadequate visualization of the proximal aspect of colonic folds and flexures. The NaviAid™ G-EYE™ (SMART Medical Systems Ltd, Ra'anana, Israel) is a novel, balloon-colonoscope comprising a standard colonoscope with a reprocessable, permanently integrated, inflatable balloon at the colonoscope tip. The balloon is inflated (endoscopist controlled) through the endoscope internally, without external accessories. The balloon-colonoscope is advanced by the endoscopist with the balloon deflated. At the cecum, the balloon is inflated to engage the colon walls and the balloon-colonoscope is then withdrawn by the endoscopist. Withdrawal of the inflated balloon-colonoscope causes mechanical straightening of colonic folds & flexures.
AIMS&METHODS: To establish the feasibility of use and safety of a novel balloon-colonoscope. This was a prospective cohort study in human subjects (ages 40-75 years) referred for CRC screening, polyp surveillance or diagnostic evaluation. The primary study endpoint was cecal intubation, additional endpoints included: time to cecal intubation, withdrawal time, total procedure time, polyp detection rate (PDR), adenoma detection rate (ADR), success of polypectomies, and adverse events. Telephone follow up with subjects was performed 24-72 hours post-colonoscopy. This study was Helsinki committee approved.
RESULTS: From 15/11/12 - 30/1/13, n=50 consecutive subjects (mean age 59.0 years, range 40-74 years, 27 female) were enrolled. Three subjects were excluded due to inadequate colon prep, technical problem, and hernia, thus 47 subjects analyzed. A 47/47 (100%) cecal intubation rate was achieved. Mean time to cecum was 4.3 mins, withdrawal time 7.4 mins, and total procedure time 16.5 mins. We identified a total of 44 polyps in 25/47 subjects, a 53.2% PDR. There were 36 (81.8%) polyps (1-5mm), 4 (9.1%) polyps (6-9mm) and 4 (9.1%) polyps (≥10mm) in size. We found that 36/44 (81.8%) polyps were "adenomas", and 21/47 subjects had at least one adenoma, yielding an ADR=44.7%. All polyps were removed by cold / hot snare polypectomy. There were 2 subjects with minor adverse events: diarrhea & abdominal pain.
CONCLUSION: The NaviAid™ G-EYE™ balloon-colonoscope appears feasible, usable, and safe. There was 100% cecal intubation, a 53% PDR, a 45% ADR, and no serious adverse events. Comparative human studies are now in progress.
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Keywords: colonoscopy, colorectal cancer screening, endoscopic imaging, endoscopic technology

P718 THE INCIDENCE AND COST OF UNEXPECTED HOSPITAL ATTENDANCE FOLLOWING ELECTIVE OUTPATIENT FLEXIBLE SIGMOIDOSCOPY

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INTRODUCTION: Outpatient flexible sigmoidoscopy is an increasingly utilised investigation shown to be effective in the detection and prevention of bowel cancer. The procedure is thought to entail a low risk of complications. However, recent literature suggests the complication rate of other endoscopic procedures may be up to 10 fold that traditionally quoted (1). The true complication rate of flexible sigmoidoscopy is of particular importance as the UK is introducing the Bowel Cancer Screening Programme (BCSP) by which all citizens will be offered the procedure at age 55.
AIMS&METHODS: The aim of this study was to identify the morbidity and related healthcare costs of unexpected hospital attendance following outpatient flexible sigmoidoscopy. An observational study of A&E attendances and admissions occurring within 14 days of all outpatient flexible sigmoidoscopies which took place in 2011 was conducted. All procedures took place at West Middlesex University Hospital, London. Data was collected using the hospital's electronic records system, enterpriseCAMIS®. Cases were analysed to assess whether reattendance could be attributed to the procedure, and healthcare costs were determined.
RESULTS: Of the 1137 outpatient flexible sigmoidoscopies performed, 18 patients (1.58%) presented to A&E within 14 days. Only 2 of these attendances were thought to be related to the procedure (0.18%). 1 case resulted in a 5 day admission due to bleeding post polypectomy. The second A&E attendance was also due to bleeding. The cost of the above admission was £4,682. Including the related A&E attendance, the total financial burden of related reattendance following flexible sigmoidoscopy was approximately £4,827 in 2011. This equates to an additional cost of £4.25 per procedure.
CONCLUSION: This study suggests outpatient sigmoidoscopy is relatively safe, with complications necessitating reattendance occurring following 0.18% procedures. The financial burden of hospital reattendance within our UK based study population was minimal, supporting the cost effectiveness of extending services for National bowel cancer screening programs.
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Disclosure of Interest: None Declared
Keywords: Complications, costs, outpatient endoscopy

P719 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY COLORECTAL NEOPLASM WITH SEVERE FIBROSIS

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INTRODUCTION: Colorectal endoscopic submucosal dissection(ESD), has not been widely spread because of technical difficulty and high incidence of perforation. The first aim of study is to evaluate clinical outcome of colorectal ESD. Of colorectal ESD cases, submucosal severe fibrosis is the most difficult situation. To overcome severe fibrosis is so important to improve clinical outcome. Secondary aim was to evaluate the feasibility of ESD for severe fibrotic lesions in comparison with non-severe fibrotic lesions.
AIMS&METHODS: 250 colorectal consecutive lesions were enrolled in this study. Flush knife was used in all cases. We defined that submucosal layer like screen was not lifted by injection liquid even with sodium hyaluronate use. In dissecting severe fibrosis, we minutely dissected the expected line just above the muscle layer after dissection of both sides horizontally. The comparison was done in the two groups for operative time, en bloc resection rate, curative resection rate, the rate of ancillary device use, the delayed bleeding rate, and perforation rate. A P value $< .05$ was considered statistically significant.
RESULTS: The average diameter of lesions was 34.0mm. Sixty-eight lesions were located in the rectum, 61 in left colon, and 121 in the right colon. For morphological type, 113 lesions were LST-NG, 86 LST-G, 32 protruded, 13 depressed and 6 recurrent lesions. By histological examination, 161 intramucosal cancers, 45 slightly invasive submucosal cancers, 17 massively submucosal invasive cancers, and 27 tubular adenomas. The average operative time was 85.4 minutes, and the en bloc resection rate was 97.6% (244/250). With regard to complications, postoperative bleeding was observed 1.2% (3/250). Microperforation which occurred in only 1 case was conservatively repaired with endoscopic clipping. Severe fibrotic lesions were detected in 19 including 6 recurrent lesions. The tumor size was significantly larger for the severe fibrotic lesions (45.3mm) than non-severe fibrotic lesions (33.1mm). Operative time was significantly longer for the severe fibrotic lesions (180min) than non-severe fibrotic lesions (77.6min). En bloc resection (100%:97.4%) and curative resection rates (89.5%:91.3%) were respectively similar between two groups. The rate of ancillary device use tended to be higher for the severe fibrotic lesions (10.5%) than non-severe (7.4%). The perforation (0%:0.4%) and delayed bleeding (0%:1.3%) rates were also similar between two groups.
CONCLUSION: Our study showed ESD with severe fibrosis was much more time-consuming and difficult than non-severe fibrosis. However, we managed to obtain equivalent safety and curability for severe fibrotic lesions compared to non-severe.
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Disclosure of Interest: None Declared
Keywords: early colorectal cancer, endoscopic submucosal dissection, fibrosis

P720 ENDOCYTOSCOPY CAN PREDICT THE VENOUS AND LYMPHATIC VESSEL INVASION: A RETROSPECTIVE STUDY

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INTRODUCTION: Endocytoscopy (EC) , which enables observation of *in vivo* cells and nuclei at about 400-fold magnification, provides more detailed information about the lesions.
AIMS&METHODS: The aim of our study is to evaluate the possibility of EC with regard to prediction of venous and lymphatic vessel permeation.The subjects were 86 colorectal tubular adenocarcinomas (36 Tis, 27 T1 carcinomas, 13 T2 carcinomas, nine T3 carcinoma and one T4 carcinomas) from 86 patients treated by endoscopic or surgical resection after observation with EC at Showa University Northern Yokohama Hospital from February 2009 to March 2013. In observing EC images, we defined the average scale of four vessels as ''vessel diameter'' and proportion between maximum portion and minimum portion of the vessel as ''vessel caliber variation''. We analyzed the correlationship between these parameters (''vessel diameter'' and ''vessel caliber variation'') and venous or lymphatic vessel permeation. Then, we predict the cutoff value from ROC curve with consideration of tumor invasion depth.
RESULTS: In confirming the association between vessel diameter and venous permeation, ROC curve (AUC 0.776) suggested that 47μm could be a cutoff value of vessel diameter correlated to venous permeation (sensitivity 64.0%, specificity 85.2%). And in confirming the association between vessel caliber variation and lymphatic vessel permeation, ROC curve (AUC 0.689) suggested that 50% vessel caliber variation could be cutoff value correlated to lymphatic vessel permeation (sensitivity 61.5%, specificity 68.4%). Odds ratio of venous permeation was 5.30 in T1 carcinoma, 8.00 in T2 carcinoma and 1.00 in T3 and T4 carcinoma, while that of lymphatic vessel permeation was 1.18 in T1 carcinoma, 1.11 in T2 carcinoma and 5.00 in T3 and T4 carcinoma.
CONCLUSION: EC could evaluate the venous and lymphatic vessel invasion by measuring the vessel formation.
Disclosure of Interest: None Declared
Keywords: Colorectal cancer, endocytoscopy, vessel invasion

P721 MANDATED ENDOSCOPY SAFETY CHECKLISTS: A TICK-BOX EXERCISE OR A USEFUL CLINICAL INTERVENTION?

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INTRODUCTION: Errors in endoscopy are common but often inconsequential, and therefore go uncorrected. A series of minor errors however, may culminate in a significant adverse event. This is un-surprising given the volume and complexity of cases and shift-working patterns.
Surgical safety checklists (SSC) can prevent errors thus reducing morbidity and mortality[1]. Consequently, SSC are now mandatory. Many UK hospitals are mandating use of the World Health Organisation (WHO) SSC for endoscopy without an evidence base. It is unknown if checklists are applicable to Endoscopy.
AIMS&METHODS: - Develop, implement and provide training for an endoscopy specific safety checklist
- Evaluate compliance with the checklist
A checklist was developed to address common and significant patient safety issues in endoscopy. Sequential multidisciplinary expert focus groups were convened to draft the initial checklist and revise subsequent versions following feedback from team-members. The checklist was designed to be concise, practical and used by the endoscopist and assisting nurses just prior to the procedure.
A training programme including workshops and video examples of appropriate and poor checklist usage was delivered to endoscopists and nurses. Hands-on training and in-room support was provided by a clinical researcher during the first week of checklist implementation.
Errors prevented by the checklist were prospectively recorded. Factors affecting compliance were assessed 11 months post implementation. Prospective data collection for a 7-day period included:
1. Degree of checklist completion
2. Time of procedure
3. Endoscopist grade
4. Case mix: Routine / Emergency / Bowel Cancer Screening (BCS).

RESULTS: Provisional data shows the checklist identified 8 potential errors in the first 32 procedures. When errors were reported, the checklist was incomplete. 106 (53%) checklists were fully completed, 73 (37%) partially completed and 20 (10%) not completed. Compliance was greatest for morning than afternoon lists (60%) vs. (43%) $p=<0.05$. Registrars were least likely to complete the checklist (35%) compared to consultants (64%) and nurse endoscopists (62%) $p=<0.001$). BCS cases were most likely to have a checklist completed (82%) compared to routine (45%) and emergency (63%) cases $p=<0.01$.

CONCLUSION: Checklists avert errors by sharing vital information and enhanced teamwork. For checklists to have a meaningful impact on patient safety, considerable investment in effective implementation and compliance is required. This can be achieved by a multi-disciplinary education programme and strong clinical leadership. Further studies to establish if errors are reduced by use of an endoscopy checklist are underway.

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Disclosure of Interest: None Declared

Keywords: Checklist, Medical error, Patient safety

P722 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 aim of this study was to clarify the clinicopathological features of colorectal serrated lesions. We reviewed clinical charts and surgical pathology files of 1874 polypectomy specimens performed during January 2007 and December 2011 at our institution. A total of 131 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.

RESULTS: Of these 131 lesions, a total of 70 (53.4%) were HP, 28 (21.4%) SSA/P, and 33 (25.2%) TSA. Mean age of patients with each polyp was 62.0 years old for HP, 64.1 for SSA/P, and 59.9 for TSA. Male to female ratio (M/F) was 1.92 for HP, 1.0 for SSA/P, and 1.75 for TSA. Mean size of SSA/P (10.2mm) and TSA (9.6mm) were significantly larger than that of HP (6.7mm). SSA/Ps were located predominantly in the proximal colon, whereas HP and TSA were mainly located in the sigmoid colon and rectum. 75% 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. Incidences of concomitant carcinomas in HP, SSA/P, and TSA were 0% (0 out of 70), 7.1% (2 out of 28), and 6.1% (2 out of 33), respectively.

CONCLUSION: Though SSA/P and TSA have distinct clinical features, both are premalignant lesions of colorectum and we should detect these lesions and completely remove endoscopically.

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Disclosure of Interest: None Declared

Keywords: colorectal, serrated lesion

P723 LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION FOR RECTAL CARCINOID TUMORS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) was developed for en bloc resection of mucosal tumors of the gastrointestinal tract. In addition, recently, rectal carcinoid tumors have been treated using ESD[1]. However, only a small number of patients with rectal carcinoid tumors have been treated using ESD, and long-term outcomes have not been reported to date.

AIMS&METHODS: We investigated the efficacy, safety, and long-term outcomes of ESD for the resection of rectal carcinoid tumors. From September 2005 to March 2013, 45 patients (30 males, 15 females, age range, 31-81 years) were included in the study, and 47 rectal carcinoid tumors were treated using ESD. All the tumors were limited to the submucosal layer on endosonography. We retrospectively evaluated the size of the tumors and the resected specimens, the rate of en bloc resection, the rate of pathological free margin resection, the procedural time, and the complications (bleeding and perforation). Colonoscopy and computed tomography were performed every year after ESD. Informed written consent for ESD was obtained from all the patients.

RESULTS:

Median size of the tumors (range) (mm)	5 (1.5-11)
Median size of the resected specimens (range) (mm)	19 (7-33)
Median procedural time (range) (min)	31 (12-117)
Rate of en bloc resection (%)	100 (47/47)
Rate of pathological free margin resection (%)	100 (47/47)
Lymph vascular involvement (%)	9 (4/47)
Postoperative bleeding (%)	4 (2/47)
Perforation (%)	0 (0/47)
Recurrence (%)	0 (0/47)

The results of ESD for the tumors were presented in Table. All the tumors were resected en bloc, and free pathological margins were confirmed. Although lymph vascular involvement was histopathologically demonstrated in 4 patients (9%), additional surgery was not performed at the patients' request. Postoperative bleeding occurred in 2 patients (4%), and both these patients were successfully managed by endoscopic hemostasis with hemoclips; no recurrence was observed during the median follow-up period of 31 (range, 1-80) months.

CONCLUSION: ESD was time consuming but effective for rectal carcinoid tumors and led to favorable long-term outcomes.

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Disclosure of Interest: None Declared

Keywords: endoscopic submucosal dissection (ESD), rectal carcinoid tumors

P724 EFFECT OF CHROMOENDOSCOPY ON ADENOMA DETECTION IN THE COLON: A META-ANALYSIS

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INTRODUCTION: Early adenoma detection reduces mortality from colorectal cancers. Advances in endoscopy are aimed at improving adenoma detection. Contrast enhancement using dye spray is reported to improve the detection of subtle mucosal changes.

AIMS&METHODS: We aim to perform a meta-analysis to look at the effect of chromoendoscopy on adenoma detection in the colon.

Various electronic databases were searched for articles reporting on detection of polyps comparing conventional colonoscopy and chromoendoscopy. The pooled mean difference in total number of adenomatous polyps, number of right and left sided polyps, advanced and flat adenomas, total number of polyps and number of <5mm polyps detected was calculated. A fixed effects model was used unless there was significant heterogeneity. Publication bias was assessed using Funnel plots and Egger's test and heterogeneity was assessed using Cochran's Q and the I^2 test.

RESULTS: 3714 number of patients from 14 studies were included in the analysis. 7 studies were randomized controlled trials and 7 had tandem study design. Chromoendoscopy detected significantly higher number of adenomas, advanced adenomas, right and left sided adenomas (Table 1). A significantly higher number for hyperplastic and small ($<$ 5mm) polyps were detected by chromoendoscopy but no differences were noted for detection of flat adenomas. A random effects model was used due to significant heterogeneity between the studies mainly because of differences in patients included in the study and the study design. Sensitivity analysis for publication bias using the trim and fill method which conservatively imputes hypothetical negative unpublished studies to mirror the positive studies in the funnel plot did not change the statistical significance of the pooled analysis.Table 1

Variable	Pooled mean difference	P value
Adenoma detection	0.139 (95% CI 0.082 to 0.195)	0.0001
Right sided adenomas	0.137 (95% CI 0.048 to 0.226)	0.003
Left sided adenomas	0.117 (95% CI 0.007 to 0.227)	0.036
Advanced adenomas	0.105 (95% CI 0.017 to 0.194)	0.019
Flat adenomas	0.154 (95% CI -0.084 to 0.393)	0.205
Hyperplastic polyps	0.364 (95% CI 0.281 to 0.447)	0.001
$<$ 5mm polyps	0.271 (95% CI 0.172 to 0.369)	0.001

CONCLUSION: Chromoendoscopy improves detection rate of adenomatous polyps compared to conventional colonoscopy. This seems greater for advanced as well as right sided adenomas, but significantly higher number of hyperplastic and small ($<$5mm) polyps were detected by chromoendoscopy. Future work needs to focus on the cost effectiveness of chromoendoscopy taking into account the increased time and cost of chromoendoscopy and long term outcomes like reduction in colorectal cancer rates between chromoendoscopic and conventional colonoscopy surveillance.

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Disclosure of Interest: None Declared

Keywords: adenoma detection rate, chromoendoscopy, Colonoscopy

P725 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTROINTESTINAL NEOPLASMS: INITIAL CLINICAL EXPERIENCE IN A TERTIARY MEDICAL CENTER IN BRAZIL.

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INTRODUCTION: The endoscopic submucosal dissection (ESD) is a technique developed in Japan for *en bloc* resection of early gastrointestinal epithelial neoplasms. It is considered technically challenging and only performed in a few specialized centers. Although ESD has been popular in Japan, clinical experience has been rarely reported in Brazil.

AIMS&METHODS: For the esophageal lesions, the indications by Higuchi *et al.* and Makuuchi *et al.* were adopted; the guidelines of the Japanese Association of Gastric Cancer were used as criteria for gastric lesions; for the colorectal lesions, the recommended standards by Uraoka *et al.* and Saito *et al.* were employed. The feasibility of the method, complications and histological analysis of the specimens were evaluated at the Endoscopic Unit of the Gastrocentro at the State University of Campinas.

RESULTS: Fifty-two patients were submitted to ESD from June 2010 to April 2013: five esophageal, twenty-three gastric and twenty-four colorectal lesions. Regarding the esophageal neoplasms, the average diameter was of 27mm,

mean duration of resection was 91min and all specimens presented free-margins. There was one esophageal perforation, managed by endoscopic clips. In regard to the gastric lesions, the mean size was 30 mm and the average procedure time was 126min. There was one case of bleeding after eight days of the procedure, managed endoscopically. There was one single case with focal positive margins. Finally, for the colorectal lesions, the mean size was 29.8mm, average time of procedure was 151min. One procedure in the transverse colon was interrupted for technical difficulties. Two complications occurred in the rectal resections: a perforation managed with endoscopic clips and a bleeding during the procedure, also controlled endoscopically. Three patients presented positive margins, one of them was adenocarcinoma. All depth margins were negative.

CONCLUSION: In our service, the initial experience with endoscopic submucosal dissection achieved high success with few complications, allowing appropriate staging of lesions.

Disclosure of Interest: None Declared

Keywords: colon cancer, endoscopic submucosal dissection (ESD), esophageal cancer, Gastric cancer, Interventionnal endoscopy

P726 PROPOFOL SEDATION DURING COLONOSCOPY: BACK TO THE FUTURE!

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INTRODUCTION: Midazolam plus Meperidine (M+M) is the most common recipe for endoscopy sedation utilized in Europe. Propofol has some advantages over narcotics and benzodiazepines, but it is generally limited to anesthesiologists using manual titration.

AIMS&METHODS: To demonstrate that propofol infusion via target-controlled infusion(TCI) pump is just as safe and effective as M+M for sedation during colonoscopy. Four types of sedation were utilized in this trial: Propofol TCI(PTCI), M+M, Midazolam alone,Propofol titration(PT). Propofol was administered by non-anesthesiologists using a TCI pump(Syramed®µSP6000, Arcomed) and by anesthesiologists in the titration model. Blood pressure was measured during colonscopy at least every 5 minutes,and continuous oximetry, electrocardiography and capnography were performed.No exclusion criteria were stipulated.All the pts were evaluated at the end of the procedure using the Observer's Assessment of Altertness/Sedation(OAA/S) scale, their satisfaction was established by Numeric Visual Scale(NVS), and they were discharged when the ALDRETE score was >8.

RESULTS: 439 consecutive pts were included in the study. 200 pts(45.6%) received PTCI at an average drug dosage(ADD) of 156.8±69.6 mg; 184 pt received M+M(41.9%) at an ADD,respectively,of 4.18±1.3 mg and 47.5±5.5 mg; 40 pt(9.1 %) received PT at an ADD of 212.50±85.70 mg; 15 pt(3.4%) received Midazolam alone.All four groups were clinically homogeneus. Adverse events were: hypoxemia(So2$<$90%):PTCI 0 pt, M+M 7 pt, PT 2 pt ($p<0.05$); apnea: PTCI 0 pts, M+M 8 pts PT 16 pts($p<0.001$); hypotension (SBP$<$90mmHg): PTCI 20 pts, M+M 21 pts PT 4 pts(p=ns); bradycardia ($<$40 bpm) PTCI 2 pts, M+M 5 pts, PT 1 pts (p=ns).Apnea was treated successfully with neck extension. Pts outcome and satisfaction: mean ALDRETE score: PTCI 9.98±0.12 vs M+M 9.77±0.4 ($p<0.001$) vs PT 9.97±0.15(p=ns). Mean NVS(pain) PTCI 0.61±1.62 vs M+M 1.33±2,22 ($p<0.001$). Mean Procedure length: mean cecal intubation time (intubation rate was 98.4%) PTCI 6.38±3.59 min vs M+M 7.92±5.29 min($p<0.05$) vs PT 7.47±4.43(p=ns). Mean time for the entire procedure: PTCI 39.43±16.2 min vs M+M 53.82±15.31 min($p<0.001$) vs PT 52.10±16.9 min($p<0.001$). Mean post sedation recovery time PTCI 16,5±12,3 min vs M+M 26.5±9,4 min(P=0,0001) vs PT 24,8±9,1 min($p<0,0001$). At univariate analysis less total propofol(adjusted for BMI, Sex, Age, Endoscopist, Abdominal surgery) was administered using TCI than the titration method: 156.85±69.63 vs 212.50±85.70($p<0.0001$).

CONCLUSION: Propofol sedation using TCI pump will be the future standard of care during colonoscopy: less pain, less adverse events, faster discharge

Disclosure of Interest: None Declared

Keywords: colonoscopy, Propofol sedation, target-controlled infusion

P727 LARGE COHORT STUDY EVALUATING THE ROLE OF HYBRID ESD (H-ESD) AND CONVENTIONAL PIECEMEAL EMR TECHNIQUE IN THE RESECTION OF LARGE AND CHALLENGING COLONIC POLYPS DEMONSTRATES NO OUTCOME BENEFIT OF H-ESD OVER EMR.

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INTRODUCTION: The learning curve for ESD in the west is very long, so a hybrid technique has been proposed. The impact of Hybrid ESD (H-ESD) technique on clinical outcome is unclear. We aim to compare the outcome benefits of Multi-piece EMR and H-ESD in the resection of challenging colonic polyps.

AIMS&METHODS: A Prospective cohort study of endoscopic resection of difficult colonic polyps. Patients were tertiary referrals from experienced endoscopists. EMR was defined as submucosal injection followed by piecemeal snare resection. H-ESD involved submucosal injection before mucosal incision with an ESD knife followed by snare resection. Endoscopic follow up was arranged. Multiple linear regression analysis was performed.

RESULTS: 347 flat/sessile polyps >20 mm were resected between 2007-12. Mean follow-up was 1004 days. ***H-ESD Cohort:*** N= 110/347(32%). Mean size 45mm(range 10-170). 25/110(23%) were salvage procedures for scarred lesions due to failed EMR attempts by other endoscopists. Endoscopic clearance was achieved in 95.5%. Need for surgery (n=4): 1 for perforation and 3 for unexpected cancer. 98.6% had no recurrence at endoscopic follow up.

EMR cohort: N=237/347(68%). Mean size 42mm(range 20-150). 11/237(4.6%) were salvage procedures for scarred polyps. Endoscopic clearance was achieved in 93%. Need for surgery(n=21): 1 patient for incomplete resection & 20 for suspicion of cancer in EMR specimen. At endoscopic follow up 98% had achieved complete clearance.

Recurrence risk was higher with lesion size >50mm & scarring due to previous EMR attempts. This was unaffected by technique (EMR or H-ESD). Perforation/microperforation was more likely in the H-ESD Cohort, but the overall complication rates were similar for both cohorts.

	SIZE		TECHNIQUE		PREV EMR		SITE	
COMPLICATIONS (25)	≤50mm 15/271 (5.5%)	>50mm 8/76 (10.5%)	ESD 11/110 (10%)	EMR 12/237 (5%)	Yes 3/36 (8%)	No 20/311 (6%)	LC 20/250 (8%)	RC 3/97 (3%)
	P=0.016		P=0.11		P=0.521		P=0.201	
RECURRENCE (35)	≤50mm 19/271 (7%)	>50mm 16/76 (21%)	ESD 12/110 (11%)	EMR 23/237 (10%)	Yes 10/36 (28%)	No 25/311 (8%)	LC 31/250 (12%)	RC 4/97 (4%)
	P=0.0001		P=0.156		P=0.0001		P=0.105	

CONCLUSION: Both techniques achieved an excellent overall cure rate for large & challenging polyps. This is the first large series comparing the two techniques and demonstrates that polyp cure rate was equally good with both techniques. H-ESD technique was used more commonly for polyps with significant scarring & was associated with slightly higher perforation rates. Our data does not demonstrate any significant outcome benefit of H-ESD technique over the conventional EMR technique.

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Disclosure of Interest: None Declared

Keywords: COLONIC POLYPS, EMR, ESD (endoscopic submucosal dossection), Hybrid therapy

P728 THE CHALLENGES OF IMPLEMENTING EVIDENCE INTO ENDOSCOPIC PRACTICE: A QUALITATIVE STUDY

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INTRODUCTION: The Quality Improvement in Colonoscopy (QIC) study was a region wide service improvement study that aimed to improve adenoma detection rate (ADR) by implementation of measures into routine colonoscopy practice. They were: withdrawal time of $\geq$ 6 minutes; hyoscine butylbromide use; supine position for examination of the transverse colon; rectal retroflexion. Each has been shown to improve lesion detection. The implementation of evidence into clinical practice can be challenging.

AIMS&METHODS: We aimed to evaluate factors influencing implementation of the 'bundle' in the QIC study. Twelve endoscopy units participtaed who are members of the Northern Region Endoscopy Group (NREG), a clinical research network in England. The study team held training sessions at each unit to introduce the "bundle", supported by a nominated local lead colonoscopist and nurse. Posters were supplied for each endoscopy room to aid promotion. Following study completion, units and individuals were purposively sampled for the qualitative study to ensure a range of units (by size, bundle uptake) were included. Semi-structured interviews were conducted until saturation was reached. Data were evaluated using thematic analysis to code and categorise interviews.

RESULTS: 118 colonoscopists participated in the QIC study. Interviews were conducted with 11, 8 lead colonoscopists, 1 lead nurse and 3 non-lead colonoscopists. Increased emphasis on examination time, increased awareness of ADR as a quality marker and empowerment of endoscopy nurses to encourage use of quality measures were seen as positive outcomes of the study. The simple, highly visible posters were also reported as useful in aiding study promotion. Challenges included difficulty in arranging set up meetings and engaging certain speciality groups.

CONCLUSION: Implementation of evidence into clinical practice can be challenging. During the QIC study, challenges included arranging staff meetings and engaging all team members. Positive outcomes included increased awareness of colonoscopy quality, particularly slower withdrawal times, and empowerment of endoscopy nurses to promote quality measures. We demonstrate that emphasis on timing of meetings and strategies to engage speciality groups should be given consideration when planning implementation of evidence or guidelines into clinical practice.

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Disclosure of Interest: None Declared

Keywords: Implementation, Quality of colonoscopy

P729 PIT PATTERN ANALYSIS WITH HIGH DEFINITION CHROMO-ENDOSCOPY AND NBI IN ULCERATIVE COLITIS: CAN WE RULE OUT DYSPLASIA ?

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INTRODUCTION: Chromo-endoscopy (CE) increases the detection of neoplasia longstanding ulcerative colitis (UC). Kudo pit pattern (KPP) I/II have been suggested to be predictive of benign polyps in UC, however its' accuracy in non-magnified high definition (HD) CE or if it can be applied to HD Narrow Band Imaging (NBI) is unknown.
AIMS&METHODS: We aimed to assess inter- and intraobserver agreement and diagnostic accuracy of KPP in UC surveillance endoscopy with CE or NBI. 50 images of lesions (13 neoplastic)identified in 27 UC patients either with classical CE (methylene blue 0.1%) (n=24) or NBI (n=26), were selected and mounted in a Powerpoint file in a standardized way in two different sets. 10 endoscopists with experience in NBI/CE had to indicate the KPP, the neoplastic nature and how sure they were about the diagnosis. The interval between set 1 and 2 was at least 10 weeks to minimize recall bias. Kappa statistics were performed (SPSS Statistics 20.0). Kappa results are expressed as median ± range. Mann Whitney U test was performed to assess differences in interobserver agreement between different techniques.
RESULTS: Median sensitivity, specificity, negative predictive value and positive predictive value for diagnosing neoplasia based on the presence of KPP I/II was 77% (54-85%), 68% (51-84%), 88% (84-94%) and 46% (36-61%) resp. Similarly, based on the overall endoscopic appearance, this was 77% (31-100%) 69% (43-92%), 90% (79-100%) and 48% (37-67%) resp. The overall agreement for any KPP was only fair (Kappe = 0.291) , with CE being significantly better than NBI (0.339 vs 0.246 $p < 0.001$). Agreement for differentiation between non-neoplastic KPP (I,II) and neoplastic KPP (III l, IIIs, IV, V) was moderate (kappa= 0.584) and even substantial and significantly better for NBI (kappa= 0.683 , 0.497 resp $p < 0.001$). Similar kappa-values were found for the overall assessment for the neoplastic nature of a lesion. Intra-observer agreement was moderate for KPP assessment (0.517) and substantial to differentiate neoplastic from non-neoplastic lesions (0.665).
CONCLUSION: Among experts, assessment of KPP I or II with non-magnified HD CE or NBI has a good NPV to rule out neoplasia. Differentiation between non-neoplastic and neoplastic KPP shows a moderate to substantial agreement and is significantly better for NBI.
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Disclosure of Interest: None Declared
Keywords: chromoendoscopy, DALM, interobserver agreement, narrow band imaging, ulcerative colitis

P730 IN VITRO EVALUATION OF DNA DAMAGE IN HUMAN COLONIC EPITHELIAL CELL LINES EXPOSED TO METHYLENE BLUE AND WHITE LIGHT

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INTRODUCTION: Methylene Blue (MB) is a vital dye commonly used during chromoendoscopy. Although this procedure is generally considered safe, some concerns have been raised about its potential genotoxicity. However, the results of tests with mouse micronuclei exposed to high concentration of injected MB suggest that genotoxic effects should not occur *in vivo*.*
AIMS&METHODS: To support the clinical use of Methylene Blue-MMX® tablets as a diagnostic tool during endoscopic examinations, experiments were conducted *in vitro*, using HT-29 cell line to ascertain the level of DNA damage in cells exposed to white light for different time periods, in order to determine if photoexcited methylene blue damages DNA.
To simulate chromoendoscopy *in vitro*, a monolayer of cultured HT-29 cells was incubated with 1 mL of 0.5% MB. Thereafter, the cells were exposed to white light of the same wavelength to different durations of light exposure (from 5 to 60 minutes) and conditions (presence or absence of oxidative conditions). MB-induced DNA breaks were evaluated on histone H2A variant (H2AX) that is phosphorylated (H2AX) in response to DNA double strand damage. In additional tests, the same exposure times were repeated with and without a redox protective factor (N-acetyl cysteine). H2AX determination required fixation and permeabilization of cells, followed by incubation with a fluorescent labeled antibody to H2AX. Fluorescence intensity was quantified by flow cytometry.
RESULTS: HT-29 cells treated with MB and continuously exposed to white light for 5 and 10 minutes did not show statistically significant levels of DNA damage. Prolonged exposure to light from 15 to 60 minutes led to a proportional increase of DNA damage. We also demonstrated that the presence of a redox agent (N-acetyl cysteine) completely prevented the DNA damage
CONCLUSION: These tests show that the potential genotoxic effect of MB on HT-29 cells is closely related to the duration of the light exposure, with a cut-off time of at least 10 minutes of continuous exposure. Such exposure times i.e. continuous white light for >10 minutes on gastrointestinal mucosa is not typically reached during a normal colonoscopy procedure. Moreover, in cases of longer exposure times, the presence of a reducing agent was able to prevent completely the DNA damage.
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Keywords: chromoendoscopy, DNA damage , Methylene Blue

P731 INTESTINAL BARRIER DYSFUNCTION IDENTIFIED BY CONFOCAL ENDOMICROSCOPY IN MACROSCOPICALLY NORMAL TERMINAL ILEUM PREDICTS REQUIREMENT FOR TREATMENT ESCALATION IN INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Intestinal mucosal epithelial barrier dysfunction (IMEBD) is increasingly recognised as the antecedent event in inflammatory bowel diseases (IBD) because microbial antigen entry into the lamina propria may incite a chronic inflammatory response. Confocal endomicroscopy (CEM), which images *in vivo histology* under real time, may identify and quantitate IMEBD and predict IBD course.
AIMS&METHODS: This study evaluated IMEBD using CEM (EC-3870FK, Pentax) and correlated its severity with IBD course defined by the need for treatment escalation (TE). TE included drug dose increase, class step-up or surgery.
IBD subjects and controls were prospectively recruited for CEM using IV fluorescein contrast given dynamically. Blinded assessment of the uninflamed terminal ileum was performed. A composite 'confocal leak score' (CLS) of IMEBD was calculated from the summation of individual validated CEM features of 'fluorescein leak' (FL), 'cell junction enhancement' (CJE) and 'cell drop out' (CDO). Area under the curve (AUC) of receiver operating characteristic (ROC) analysis was used to define thresholds separating IBD from controls and for TE requirement. Primary endpoint was time (in days) to TE from date of CEM. Kaplan Meier survival, categorical and non-parametric statistics were performed.
RESULTS: A total of 63 consecutive subjects underwent prospective CEM (59% F, 34 CD, 13 UC, 16 controls) yielding 18,280 images. Sex, age and follow up time were not different (all $P > 0.05$). Median follow up was 50 days (1-1,120). There were 13 TEs (3 ASA, 2 steroid, 2 immunomodulator, 5 biological, 1 surgery). Median CLS for CD, UC and controls were 15.3, 8.2 and 5.3 respectively ($P=0.006$) and predicted for TE for both CD ($P=0.024$) and UC ($P=0.035$). On ROC, CLS of 8.8 differentiated IBD from controls (AUC=0.76, sens 70%, spec 81%; OR 10.2 [95% CI: 2.5-42]) and CLS of 14.7 predicted for TE (AUC=0.76, sens 92%, spec 59%; OR 17.1 [95% CI: 2.0-147]). The composite CLS ($P=0.004$) and its 3 components (all $P < 0.030$) all predicted for TE. Nine patients had repeat CEM after a median of 546 days of whom 56% needed TE. TE significantly decreased CLS ($P=0.043$) at follow up CEM.
CONCLUSION: Confocal endomicroscopy can identify and quantitate IMEBD in IBD. IMEBD predicts for need for treatment escalation and significantly improves following treatment escalation indicating reversibility of mucosal barrier dysfunction.
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Disclosure of Interest: None Declared
Keywords: colitis, confocal endomicroscopy, crohn disease, Inflammatory bowel disease (IBD)

P732 COLONOSCOPY FOR CHRONIC CONSTIPATION SHOULD NOT BE UNDERTAKEN AS THE YIELD IS POOR!

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INTRODUCTION: Colonoscopy is accepted as the gold standard imaging modality for colonic symptoms of altered bowel habit, anaemia, rectal bleeding and for the detection of colorectal cancer. Chronic constipation is a common condition seen within secondary care. The role of colonoscopy in chronic constipation, however, remains controversial. The ASGE guidelines recommend colonoscopy in those over 50 years of age who have not undergone prior colorectal cancer screening if they present with chronic constipation as it is thought that chronic constipation is associated with an increased risk of colon cancer. Others believe that the yield of colonoscopy in chronic constipation is low and comparable with asymptomatic patients who undergo colonoscopy for cancer screening.
AIMS&METHODS: The aim of the study was to clarify the yield of colonoscopy in patients with chronic constipation. A single centre, retrospective analysis of patients undergoing colonoscopy for chronic constipation in a district general hospital from north London was performed. The patients were identified using the Unisoft Endoscopy reporting software over a period between June 2006 and April 2013. Data obtained during the study period was scrutinized for findings of procedure and if abnormal for assessment of additional symptoms.
RESULTS: During the study period 242 patients had a colonoscopy for chronic constipation, age range 17- 96 years, Male : Female 65: 177. The findings at colonoscopy included: normal in 130 (54%), divertculosis in 52 (21%),

diverticulitis in 2, haemorroids in 31 (13%), adenomatous polyps in 16 (7%), lipoma in 1, anterior rectal prolapse 2, indeterminent colitis in 1.
There were no patients with colorectal cancer. The 16 patients with adenomatous polyps were scrutinized further: 11 had rectal bleeding in addition to constipation, 1 had left iliac fossa mass, 4 patients had adenomatous polyps and chronic constipation as the sole presenting symptom.
CONCLUSION: No patients undergoing colonoscopy for chronic constipation had colorectal cancer. In this study, adenomatous polyp was detected in 7% and is comparable to detection in asymptomatic individuals. The finds from this study do not advocate colonoscopy in patients presenting with chronic constipation alone as the yield of pathology detection is poor.
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Disclosure of Interest: None Declared
Keywords: colonoscopy, constipation

P733 ENDOSCOPIC SUBMUCOSAL DISSECTION OF RECTAL CARCINOID TUMORS USING THE CLUTCH CUTTER

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INTRODUCTION: ESD shows high tumor eradication rates in early colorectal tumor but substantial risks during the procedure. To reduce the risk of complications related to ESD using conventional knives, we developed the Clutch Cutter (CC), which can grasp and incise the targeted tissue using electrosurgical current.
AIMS&METHODS: The aim of this study was to evaluate the efficacy and safety of ESD using CC for the removal of rectal carcinoid tumors. Between June 2008 and December 2012, we prospectively enrolled consective 12 patients (Seven men, five women; mean age 65 years) with rectal carcinoid tumors less than 10mm in diameter and within the submucosal layer without lymph node involvement shown by EUS. We performed single device ESD using CC for all lesions. The CC can grasp and cut a piece of tissue with electrosurgical current. It has a thin serrated cutting edge to facilitate grasping the tissue. The outer side of the forceps is insulated so that electrosurgical current energy is concentrated at the blade to avoid burning the surrounding tissue. Furthermore, the forceps can be rotated to the desired orientation. After marking and injection of a solution into the submucosa, each lesion in our study was separated from the surrounding normal mucosa by complete incision around the lesion using the CC. A piece of submucosal tissue was grasped and cut with the CC using electrosurgical current to achieve submucosal exfoliation.
The therapeutic efficacy and safety were assessed.
RESULTS: All lesions were treated simply without unintentional incision. The mean size of the tumors and resected specimens was 7.5±2.1mm (range: 5-11) and 25±8.3mm (range: 12-40), respectively. The en-bloc resection rate was 100%. The histologically complete resection rate was 100% (12 of 12) in the horizontal margin and 92% (11 of 12) in the vertical margin. The mean operating time was 68.2±32.5 minutes (range: 20-124). No delayed hemorrhage and perforation occurred.
CONCLUSION: ESD using CC appears to be an easy, safe, and technically efficient method for resecting rectal carcinoid tumors.
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Disclosure of Interest: None Declared
Keywords: Clutch Cutter, Endoscopic submucosal dissection, rectal carcinoid tumors

P734 LOCAL RECURRENCE AFTER EMR FOR NON-PEDUNCULATED COLORECTAL LESIONS: SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Endoscopic mucosal resection (EMR) is a safe and effective technique for removal of non-pedunculated colorectal adenomas and minimally invasive carcinomas. However, local recurrence is sometimes observed after EMR. It is currently unclear in which cases follow-up colonoscopy is necessary and what the optimal time interval is for this re-examination.
AIMS&METHODS: We aimed to perform a systematic review on the risk of local recurrence after EMR, to identify risk factors for recurrence and to provide a recommendation for the interval of follow-up colonoscopy.
A literature search was performed in Pubmed, Embase and Cochrane. EMR was defined as endoscopic snare resection after submucosal fluid injection for removal of non-pedunculated adenomas and mucosal or superficial submucosal (Sm1) carcinomas. Local recurrence, as defined by the Higaki criteria,[1] was subdivided into early recurrence, found at the first follow-up colonoscopy, and late recurrence, found after at least one previous normal colonoscopy. To calculate the pooled estimate of the recurrence risk after EMR, a random effects meta-analysis was performed. Paris classification, size, localization, histopathology, piecemeal resection and additional use of argon plasma coagulation (APC) were assessed for a possible association with recurrence.
RESULTS: Our search yielded 1833 unique articles, of which 33 were ultimately selected. Overall mean recurrence risk after EMR was 15% (95% confidence interval (CI) 12% - 19%). Recurrence risk was higher after piecemeal resections (20%, CI 16% - 25%) than after en-bloc resections (3%, CI 2% - 5%; $p<0.0001$). In fifteen studies differentiating between early and late recurrences, 152/173 recurrences (88%) were found during first follow-up colonoscopy and 21 (12%) after at least one previous normal colonoscopy. In only four studies patients underwent follow-up at 3, 6 and ≥12 months. Nineteen (76%) of 25 recurrences were detected at three months, increasing to 24 (96%) at six months. Size, piecemeal resection and non-tumorfree resection margins were found to be associated with local recurrence in a majority of the studies performing univariable analysis. In multivariable analysis, only piecemeal resection remained associated with recurrence (in 3 of 3 studies).
CONCLUSION: Local recurrence after EMR for non-pedunculated colorectal adenomas and early carcinomas occurs in 3% of en-bloc resected lesions and in 20% of piecemeal resected lesions. Piecemeal resection is the only independent risk factor for recurrence. Most recurrences are found during first follow-up colonoscopy. As more than 90% of recurrences are detected within 6 months after EMR, we propose that 6 months is the optimal follow-up interval.
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Disclosure of Interest: None Declared
Keywords: Colorectal neoplasia, EMR, Local recurrence

P735 ENDOSCOPIC PIT PATTERN FOR DIFFERENTIAL DIAGNOSIS OF COLORECTAL SERRATED POLYPS: CAN IT DISTINGUISH SESSILE SERRATED ADENOMA FROM HYPERPLASTIC POLYP?

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INTRODUCTION: Sessile serrated adenomas (SSAs) have been thought to be the precursors of colorectal cancers. However, a low diagnostic accuracy of the endoscopic techniques for differentiating and conventional hyperplastic polyp (HP) has been reported. Recently, Kimura, *et al.* (Am J Gastroenterol 2012; 107:460) have identified a novel mucosal crypt pattern, type II open-shape pit pattern (Type II-O), that is specific to SSAs The aim of this study is to clarify the ability to distinguish between SSA and HP by the mucosal crypt patterns.
AIMS&METHODS: We examined 134 serrated polyps (SPs), which were histologically diagnosed at the Showa University Hospital from June 2010 to May 2012. Three experienced colonoscopists reviewed the chromoendoscopic pictures using magnifying colonoscopy. Type II-O crypt patterns were determined according to the definition previously described by Kimura, *et al.* Briefly, this crypt pattern was similar to hyperplastic (stellar or papillary pits), but the pits were wider and more rounded in shape, reflecting dilatation of the crypts. The shapes of the Type II-O pits also differed from those of normal mucosa, in that they were larger in size with serrations surrounding the pit.
RESULTS: Although 134 SPs were enrolled in this study, 15 SPs were excluded from this study because the quality of endoscopic images was insufficient. A total of 119 SPs (73 SSAs and 46 HPs) were evaluated the mucosal crypt patterns. Of 119 SPs, 52 lesions (45 SSAs and 7 HPs) were identified Type II-O. Our data of the Type II-O showed that the interobserver and intraobserver agreement of three colonoscopists was $k = 0.61$ (range, 0.57 to 0.65) and $k = 0.68$ (range, 0.52 to 0.94) The positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of Type II-O for differentiating between SSA and HP were 87% (45/52), 58% (39/67), 62% (45/73) and 85% (39/46), respectively.
CONCLUSION: Our results indicate that the Type II-O mucosal crypt pattern may be useful for differential diagnosis of serrated polyps. However, there is a need to identify more specific features of SSA.
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Disclosure of Interest: None Declared
Keywords: endoscopic diagnosis, pit pattern, sessile serrated adenoma/polyp

P736 NEW HIGH DEFINITION NARROW BAND IMAGING VERSUS CONVENTIONAL WHITE LIGHT COLONOSCOPY FOR DETECTION OF COLORECTAL ADENOMAS IN SYMPTOMATIC PATIENTS: A RANDOMIZED CONTROLLED TRIAL WITH TANDEM COLONOSCOPY

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INTRODUCTION: It remains unclear whether the narrow band imaging colonoscopy (NBI-C) is superior to white light colonoscopy (WLC) for detection of colorectal adenoma. The recently available new high definition (HD) NBI system provides more than two-time brighter images than the previous version. We tested whether the new NBI-C would improve detection of colorectal adenoma as compared to WLC in a randomized study with tandem colonoscopy.
AIMS&METHODS: We recruited patients who were scheduled to have colonoscopy for bowel symptoms or surveillance purpose. Patients were aged ≥40 years and without history of inflammatory bowel disease, previous colonic resection or familial colorectal cancer syndrome. Eligible patients were randomized to receive either the new NBI-C (CF-HQ 190; Olympus, Tokyo, Japan) or conventional HD WLC (CF-H260). NBI was used on withdrawal of colonoscope in the NBI-C and WL was used on withdrawal for the WLC. Tandem colonoscopy was immediately performed after the first examination in all patients by using the same assigned colonoscope and withdrawal method. Lesions detected on second-pass examination were considered to be missed lesions. The primary endpoint was the proportion of patients with at least one adenoma detected.

RESULTS: 272 patients (136 in each group) were available for this interim analysis, including 133 (48.9%) men with a mean age of 62 years. The proportion of patients with adenomas was 55.9% in the NBI-C and 42.7% in the WLC (Difference = 13.2%; 95% CI = 1.4 to 24.6%; P = 0.039). There was no significant difference in the proportions of patients with adenoma ≥1cm (NBI-C 8.1 vs WLC 8.8%; P = 1.0) and serrated/hyperplastic polyps (NBI-C 24.3% vs WLC 21.3%; P= 0.67). The mean number of adenomas detected per patient was 1.27 (SD = 1.81) in NBI-C and 1.06 (SD = 1.93) in WLC (P = 0.35). The missed rate for adenoma ≥ 5mm found on tandem colonoscopy was 2.9% in NBI-C and 5.1% in WLC (P = 0.38). There was a significant association between the quality of bowel preparation and missed adenoma rates (poor preparation 38.5%, fair 22.6%, good 17.7% and excellent 7.4%; P = 0.03). The mean withdrawal time between both groups was comparable (NBI-C 10.3 min vs WLC 10.1 min; P = 0.72).
CONCLUSION: Our data suggested that the new NBI-C was superior to the conventional HD WLC in detecting colorectal adenoma. Missed adenoma rate however correlated with the quality of bowel preparation rather than the imaging methods.
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Disclosure of Interest: None Declared
Keywords: adenoma detection rate, COLONIC POLYPS, narrow band imaging

P737 OUTCOMES OF ENDOSCOPIC MUCOSAL RESECTION (EMR) OF LARGE POLYPS (≥ 20 MM) DETECTED IN A COLORECTAL CANCER SCREENING PROGRAM.

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INTRODUCTION: Large polypoid lesions have a higher risk of malignancy, and a complete resection followed by an adequate surveillance is required.
AIMS&METHODS: Aim: To evaluate the treatment and outcomes of large polyps detected in an average-risk population undergoing colorectal cancer screening programm.
Methods: All polyps ≥ 20 mm detected in the first round of a CRC screening program (50 to 69 years) were evaluated retrospectively. We collected data about clinical and endoscopic characteristics (size [20-29 vs >30 mm], location [rectal, left and right colon], morphology [sessile or flat vs pedunculated] and lateral extension), histopathology, resection technique (en bloc vs piecemeal), and presence of residual/recurrent neoplasia at follow-up.
RESULTS: 483 polyps ≥ 20 mm (444 adenomas, 8 hyperplastic, 10 serrated polyps and 21 adenocarcinomas [9 in situ and 13 invasive tumors]) were diagnosed. Regarding non-invasive (n=470) polyps, globally 444 (95%) polyps were treated endoscopically (77.8% en bloc / 22.2% piecemeal) and 26 (5.5%) polyps were surgically resected (15 [57.7%] after a first endoscopic resection, in all cases fragmented). Piecemeal resected polyps were significantly larger, sessile or flat and with lateral extension. A surveillance colonoscopy was performed (median time: 5.4 months) in 154 (34.6%) of the endoscopically resected polyps. Residual/recurrent neoplastic tissue was identified in 30 (6.8%) of the resected polyps at the polypectomy site, and specifically in 22 (31%) out of the 71 piecemeal resected polyps . Regarding those sessile-flat polyps (n=139) submitted to EMR, 113 (81.3%) polyps were treated endoscopically (43.4% en bloc /56.6 % piecemeal) and 26 (18.7%) polyps were surgically resected (15 [57.7%] after a first endoscopic resection, in all cases fragmented). Residual adenoma was detected in 15.7% and significantly in the piecemeal resected polyps (34% vs. 4%, p <0.004).
CONCLUSION: Most large polyps can be successfully eradicated endoscopically. A relatively high rate of residual/recurrent neoplasia, specifically in piecemeal-resected polyps, confirms the importance of follow-up colonoscopy.
Disclosure of Interest: None Declared
Keywords: Colonoscopy surveillance, Polypectomy, polyps

P738 IMPACT OF THE INTERNATIONAL SERRATED POLYPS GUIDELINES IN THE SURVEILLANCE STRATEGIES OF A POPULATION SCREENING PROGRAM

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INTRODUCTION: Recently, it has been published the first international guideline for surveillance of patients with serrated polyps (Gastroenterology 2012, 143:844-857).
AIMS&METHODS: Aim: To evaluate the impact of the surveillance protocol of serrated polyps in the surveillance of colorectal adenomas in a population screening program
Methods: Individuals belonging to the Colonprev study undergoing screening with colonoscopy. Clinical guidelines evaluated for colorectal adenomas: European Union 2011, British Society Gastroenterology 2010 and Spanish Gastroenterological Association (AEG)/AGA 2009. Definitions: Serrated polyp (SP) : hyperplasic, sessile serrated polyp and traditional serrated adenoma. Advanced SP (ASP): proximal to splenic flexure, size >= 10 mm or dysplasia. Surveillance at three years for individuals with advanced adenomas (AA) or >= 3 non-advanced adenoma (NAA) for adenomatous lesions and for those patients with ASP.
RESULTS: After excluding 27 individuals with CRC, 5,032 individuals were included. A total of 493 (9.8%) had AA and 182 (3.6%) had >= 3 NAA. A total of 1048 (20.8%) individuals had SP, 374 (7.4%) of these, ASP. In 274 out of the 5032 individuals (5.4%) with ASP, no simultaneously AA or >= 3 NAA coexists. Of these 274 ASP, 43 (0.8% of all individuals) and 218 (4.3% of all individuals) corresponded to hyperplasic polyps >= 10 mm or proximal to the splenic flexure, respectively, while 34 (0.7% of all individuals) were a non-hyperplasic proximal SP. The additional absolute percentage of patients, who should have been included in the monitoring group of three years or less, was 5.4%.
CONCLUSION: The implementation of the monitoring protocol of SP, mainly at the expense of monitoring advanced hyperplasic polyps (proximal or size >= 10 mm), determines a moderate increase in the number of individuals requiring an endoscopic follow-up at three years or less, and therefore, needs should resize endoscopic screening programs.
Disclosure of Interest: None Declared
Keywords: Adenoma, serrated polyps, surveillance colonoscopy

P739 A RANDOMIZED, CONTROLLED, LARGE SCALE STUDY OF THE WATER-INJECTION COLONOSCOPY WITHOUT SEDATION IN BEGINNERS AND ENDOSCOPISTS

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INTRODUCTION: Water-injection colonoscopy is now recognized by endoscopists in training the beginners.
AIMS&METHODS: To investigate the advantage of the water injection colonoscopy, we conducted a large-scale study.1960 patients were randomized into the air insufflation and water injection colonoscopy group. 600 colonoscopies were performed by 6 experienced endoscopists(100each).1360 colonoscopies were performed by 4 beginners(340each). All the patients were examined without any sedatives or analgesics. The cecal intubation time, the abdominal pain (evaluated by VAS pain score) were observed. The success standard:the cecal intubation time was within 15min.
RESULTS: 1355 and 599 cases performed by beginners and experienced endoscopists respectively were in the statistics.682 were in the water group and 673 in the air group of beginners, the success rate of the cecal intubation was 91.35% vs 74.15%(P<0.05), the cecal intubation time was 9.0±5.0 vs 12.0±4.0min, (P<0.001), the abdominal VAS pain score was 2.0±2.0 vs 4.0±2.0(P<0.001) in the water and air group respectively. For experienced endoscopists, 297 were in the water group and 303 in the air group, the cecal intubation time was 6.0±3.0 vs 4.0±3.0, (P<0.001), the abdominal VAS pain score was 1.0±2.0 vs 3.0±2.0 (P<0.001) respectively.
Table Comparison of the water and air colonoscopies

Beginners	Water group (n=623)	Air group (n=499)	Z value	P value
Cecal intubation time(min)	9.00±5.00	12.00±4.00	12.05	<0.0001
Abdominal VAS pain score	2.00±2.00	4.00±2.00	15.68	<0.0001
Experienced endoscopists	Water group (n=297)	Air group (n=302)	Z value	P value
Cecal intubation time(min)	6.00±3.00	4.00±3.00	10.39	<0.0001
Abdominal VAS pain score	1.00±2.00	3.00±2.00	-10.27	<0.0001

CONCLUSION: The water method could relieve the patients' abdominal pain obviously for both beginners and endoscopists, and it could shorten the cecal intubation time and increase the success rate for beginners. Why the intubation time for experienced colonoscopists was longer with the water method than the air method was worth further investigation.
Disclosure of Interest: None Declared
Keywords: beginners, endoscopists, water injection colonoscopy, without sedation

P740 WATER-INJECTION COLONOSCOPY IS A MORE EFFECTIVE METHOD FOR TRAINING THE BEGINNERS

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INTRODUCTION: Robert concluded a Mininal Competency Criteria(MCC) assessed by Mayo Colonoscopy Skill Assessment Tool(MCSAT) in his study of beginners performing the air colonoscopy.

AIMS&METHODS: We developed a water-injection colonoscopy for training the beginners to compare with the air colonoscopy in Robert's study.800 water-injection colonoscopy procedures without any sedatives and analgesics were performed by 2 beginners (400 each). Cecal intubation times and independent cecal intubation rates were recorded. The average score of the motor and cognitive skills were assessed by using a 4-point grading scale (1, novice; 2, intermediate; 3, advanced; 4, superior).These data were grouped based on the order of performance. An average of the beginners' parameter was calculated at each step of training to establish the learning curves.
RESULTS: Compared with the MCC that the average scores of 3.5, independent cecal intubation rates of 85% and cecal intubation times of 16 minutes or less were achieved at 275 procedures with the air method in Robert's study, in our study, the average cecal intubation times were 8.8min and 10.9min, the independent cecal intubation rates reached 100% and 85% at 275 procedures of the two beginners respectively. And the average scores of the two parameters were obviously better than those in each corresponding stage in Robert's study. The average score of the motor and cognitive skills reached 3.5 at less than 275 procedures in all the items except loop reduction
CONCLUSION: The water injection colonoscopy is superior than the air colonoscopy in reaching the MCC concluded by Robert when training the beginners.
Disclosure of Interest: None Declared
Keywords: Mayo Colonoscopy Skill Assessment Tool , Minimal Competency Criteria, , Training, , Water colonoscopy

P741 PREDICTION OF DIMINUTIVE POLYP HISTOLOGY AND THE NEXT SURVEILLANCE INTERVALS USING NARROW-BAND IMAGING DURING SCREENING COLONOSCOPY

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INTRODUCTION: The American Society for Gastrointestinal Endoscopy (ASGE) recently developed a preservation and incorporation of valuable endoscopic innovations (PIVI) statement for the real-time endoscopic assessment of the histology of diminutive colorectal polyps.
AIMS&METHODS: The aim of this study was to assess performance of Narrow-Band Imaging (NBI) without magnification predicting diminutive polyp histology during real time screening colonoscopy, and whether NBI is able to predict colonoscopy surveillance intervals.
Consecutive asymptomatic subjects undergoing screening colonoscopy were enrolled. Histology of polyps was predicted at NBI and assigned a designation of high or low confidence by 6 board-certified staff endoscopists without prior experience with NBI. The predicted next surveillance interval using NBI was compared with those that would be recommended using pathologic findings according to ASGE criteria.
RESULTS: A total of 445 polyps $\leq$ 10 mm (351 polyps $\leq$ 5 mm, 218 adenoma $\leq$ 5mm) in 212 subjects were analyzed. Sensitivity, specificity, positive and negative predictive values, and accuracy of high confidence NBI predictions for adenoma $\leq$ 5 mm were 82.1%, 82.7%, 88.6%, 73.8%, and 82.3%, respectively. High confidence characterization of polyps $\leq$ 5 mm predicted the correct surveillance interval in 75% of cases. NPV of high confidence NBI for adenoma for the rectosigmoid colon lesions $\leq$ 5 mm was 87%.
CONCLUSION: Both the surveillance interval agreement and the negative predictive value for identifying adenoma by non-experts in NBI did not meet the ASGE recommended thresholds for optical biopsy. Better results should be achieved to use NBI as a real-time optical biopsy of diminutive colorectal polyps in colorectal screening of the general population.
Disclosure of Interest: None Declared
Keywords: Diminutive Polyp, Narrow-Band Imaging , Screening colonoscopy

P742 DIAGNOSTIC ABILITIES OF THREE ENDOSCOPIC MODALITIES FOR SMALL COLORECTAL POLYPS: WHITE-LIGHT ENDOSCOPY VS MAGNIFYING NBI VS ENDOCYTOSCOPY

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INTRODUCTION: Narrow band imaging (NBI) system is a technology that enchances the visualization of surface mucosal and vascular patterns on the polyp1. Endocytoscopy (EC) enables observation of in vivo cells and nuclei with 450x ultra-magnification2. Both systems may allow acute optical diagnosis of small (1-10mm) polyps without histopathology.
AIMS&METHODS: This study assesses the diagnostic ability of white light endoscopy (WL), magnifying NBI , and EC for prediction of histopathology of small colorectal polyps for experienced and novice endoscopists.
94 small colorectal polyps (77 neoplastic lesions and 17 non-neoplasticones) were observed with both NBI with magnification and EC after performing conventional WL with the use of an integrated type EC scope (CF-Y0001 and CF-Y0020, Olympus, Tokyo). For each lesion, images of three endoscopic modalities (WL, NBI, and EC) were separately stored. By computer-based randomization, three types of test files of 94 subject lesions were created to evaluate each endoscopic modality; (1) WL alone, (2) WL + NBI, and (3) WL+EC. Three blinded experienced endoscopists (KW , MM and YM ; colonoscopy $>$ 3000 cases) and three blinded novice endoscopists (YS, KK and SK ; colonoscopy $<$ 500 cases) made the diagnosis (neoplastic or non-neoplastic) of them in each file. The diagnostic abilities for three test files were calculated with reference to the final histopathological diagnoses.
RESULTS: Of the 94 polyps, 77 were neoplastic and 17 were non-neoplastic. The average of sensitivities are experienced: (1) 91.3%, (2) 93.5%, (3) 96.1%, novice: (1) 87.0%, (2) 88.7%, (3) 88.3%. The average of specificities are experienced: (1) 74.5%, (2) 88.2%, (3) 86.3%, novice: (1) 62.7%, (2) 72.5%, (3) 62.7% . The average of accuracies are experienced: (1) 88.7%, (2) 92.6%, (3) 94.3%, novice: (1) 82.6%, (2) 85.8%, (3) 83.3%. For experienced endscopists, WL+NBI and WL+EC showed significantly higher specificity and accuracy than WL alone ($P < 0.05$).
CONCLUSION: Diagnostic ability of experienced endoscopists was superior to that of novice endoscopists in any tests. Using NBI or EC in addition to WL helped experienced endoscopists to predict the histopathology of small polyps, however they provided no additional diagnostic value for trainee endoscopists.
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Disclosure of Interest: None Declared
Keywords: endocytoscopy, NBI

P743 CAN DESMOPLASTIC REACTION OF INVASIVE COLORECTAL CARCINOMAS BE INDICATED IN VIVO BY ENDOCYTOSCOPY?

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INTRODUCTION: Background:In magnifying diagnosis during colonoscopy, the detection of desmoplastic reaction(DR) on the superficial layer is useful for predicting massively-invasive submucosal carcinomas. Although endocytoscopy, using an ultra-high magnification system, can observe cellular images in living colorectal lesions, there is no data concerning the diagnostic findings of DR with endocytoscopy.
AIMS&METHODS: Aims:The aim is to clarify the feature of endocytoscopic image of DR on the superficial layer in invasive colorectal carcinomas
Methods:From Apr. 2005 to Apr. 2013, a total of 19186 colorectal neoplasms, excluding advanced cancers, were resected endoscopically or surgically at our center. Using magnifying endoscopy and endocytoscopy, 502 lesions were observed and diagnosed according to Kudo's pit pattern classification and EC classification. Of these lesions, 53 lesions showed EC3b (defined as unclear gland formation and agglomeration of distorted nuclei strongly stained with methylene blue) by endoctyoscopy. According to the pathological findings, these lesions were divided into two groups: DR positive (DR+) group and DR negative (DR-) group, and investigated the distinctive feature of endocytoscopic image of DR.
RESULTS: Results:Of these 61 lesions showing EC3b, 30 lesions were included in DR+ group and 31 lesions in DR- group. In endocytoscopic images, 'fine granular structure' was found in 23(26.5%) of 61 lesions. There was significant difference in the observation rate of fine granular structure between DR+ group and DR- group (23/30(76.6%) vs 0/31(0%): $p < 0.01$). The sensitivity and specificity that the presence of fine granular structure predicted DR on the superficial layer was 76% and 100% respectively. And other features of endocytoscopic image had not significant difference.
CONCLUSION: Conclusions:Endocytoscopic image of ''fine granular structure'' have possibility to relate with DR on the superficial layer. Detection of DR by endocytoscopy would be useful for the diagnosis and treatment of massively-invasive colorectal cancers.
Disclosure of Interest: None Declared
Keywords: colon cancer, desmoplastic reaction, endocytoscopy

P744 RISK FACTORS AND ENDOSCOPIC TREATMENT OF RECCURENT CHOLELITHIASIS - DATA FROM A HIGHLY EXPERIENCED CENTER IN ERCP

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INTRODUCTION: Endoscopic sphincterotomy and stone extraction are standard procedures for the removal of bile duct stones. Reccurence of common bile duct (CBD) stones can occur in these patients. Risk factors have been partly defined, some of them being related to bile stasis .
AIMS&METHODS: We aimed to explore the risk factors contributing to the recurrence of CBD stones after successful endoscopic stone clearance, focused on the anatomical factors of CBD.
Between 2002 and 2011, 2986 patients were evaluated in our department for a suspicion of CBD lithiasis. Of these patients, after excluding patients without sphincterotomy and those with remnant lithiasis, 2086 were followed up for the recurrence of CBD stones. Univariate and multivariate analyses for the risk factors including stone size, CBD dilation, choledocoduodenoanastomosis, gastric surgery with different types of anastomosys and the presence of diverticula were performed.
RESULTS: The recurrence of CBD stones was found in 92 (4.7%) patients. On univariate analysis, the presence of choledocoduodenoanastomosis (p=0.05), enlarged infundibulum (p=0.019), periampullary diveticulum (p=0.003) and stone size (p=0.006) were significant contributors for the recurrence of CBD stones. On multivariate analysis, the presence of periampullary diverticulum (p=0.004, OR=0.28), choledocoduodenoanastomosis (p=0.01, OR=2.86), and previous small size lithiasis (1-4mm) (p=0.002, OR=0.38) were independent risk factors for reccurent stones. Gender, age, dilated CBD, Billroth I and II anastomosis did not influence the recurrence rate.
CONCLUSION: The recurrence of CBD stones might be influenced by the presence of periampullary diverticulum, choledocoduodenoanastomosis and previous small size lithiasis. Patients with these risk factors could benefit from a regular follow-up of the lithiasic pathology.

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Disclosure of Interest: A. Tantau : none, V. Mercea : none, D. Crisan : none, M. Tantau : none
Keywords: cholelithiasis, recurrence, risk factors

P745 RESULTS OF REPEAT ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP) AFTER INITIAL BILIARY CANNULATION FAILURE

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INTRODUCTION: The failure of biliary cannulation during endoscopic retrograde cholangiopancreatography (ERCP) can occur in 5-20% of cases. After this failure, ERCP can be repeated in clinically stable patients
AIMS&METHODS: Our aim was to report the results and determine the value of repeat ERCP after the first failure. Materials and methods: We reported results and success rate of repeat ERCP in a retrospective study including all patients who underwent repeated ERCP for the same purpose after the first failure.
RESULTS: During the study period, 1036 patients underwent ERCP with a primary success rate approaching 88%.One hundred and twenty-five patients [96 female (77%); mean age: 52 years; age range: 24-80 years] with previously unsuccessful biliary cannulation at previous ERCP. The main indications for biliary cannulation and therapeutic intervention (table1) were choledocholithiasis (70.4%), cholangitis in 12.8% of which 25% was severe cholangitis, and pancreatic malignancy (12.8%). The average time of the repetition of the procedure was 10 days (1 - 25j). No reason for the initial failed biliary cannulation was identified in 40% of cases. Unstable position (16%), periampullary diverticulum (32%).The papilla could not be identified at the initial procedure in12% of cases. Biliary cannulation was successful in 79 patients (63.2%) in a single procedure. The failure of the second ERCP was mainly due to an impassable biliary stricture in 33.2% of cases. The post-ERCP complications were repeated with minimal bleeding stopped spontaneously in 11% of cases, PEP in 4% of cases.
CONCLUSION: In our experience, the repetition of the ERCP after the first failure of procedure was associated with an acceptable success leading the overall success rate of this examination to 95.6%, without increasing the incidence of post-ERCP complications, and avoiding use another alternative to access the bile duct.
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Disclosure of Interest: None Declared
Keywords: catheterization, common bile duct, endoscopic retrograde cholangiopancreatography, treatment failure

P746 SAFETY PROFILE OF ENDOSCOPIC RETROGADE CHOLANGIOPANCREATOGRAPHY IN VERY OLD PEOPLE

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INTRODUCTION: The performance of Endoscopic Retrogade Cholangiopancreatography (ERCP) in the elderly population is particularly indicated for lithiasic or neoplastic disease. With longer life expectancy, invasive and therapeutic procedures are increasingly being performed on patients of advanced ages.
AIMS&METHODS: The aim of our study is analyse the results of ERCP in very old patients (aged ≥80 years) for lithiasic or neoplastic disease. Between 1st July 2011 and 30th June 2012, we evaluated patients of ≥60 years who underwent ERCP at a single center. Two groups of patients were compared: group I (GI) aged 60-79 years old and group II (GII) aged ≥80 years. We recorded demographic data, indications, comorbidities, blood analysis before the procedure, success of ERCP, complications, mortality and length of hospitalization. Statistical analysis: chi-quare and t-Student tests.
RESULTS: 154 ERCPs were performed in 132 patients (66 in each group). The procedure was successful in 97.4% of patients in GI and in 94.7% of patients of the GII. The most frequent indications in the GI were cholangitis and malignant obstructive jaundice (59.2%) and in the GII were cholangitis and choledocholithiasis (70.8%). Malignant strictures were more common in GI (40.8%). There were 5 complications (2.7%) - 2 severe pancreatitis in GI, 1 major bleeding in GII, 2 cholangitis (1 of moderate severity in GII and 1 of mild severity in GI). During the firsts 30 days, there were 6 deaths in the GI and 5 deaths in the GII, mainly related to the underlying pathology.
CONCLUSION: Our study shows that ERCP is safe in the very old. The decision to perform an ERCP should be taken based on clinical need. The age itself should not be a contraindication for endoscopic intervention, because even for the elderly patient population the benefits outweigh the risks.
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Disclosure of Interest: None Declared
Keywords: ERCP, Safety, Very old people

P747 TEMPORARY PLACEMENT OF A FULLY COVERED SELF-EXPANDABLE METAL STENT IN THE PANCREATIC DUCT FOR AIDING EXTRACTION OF LARGE PANCREATIC DUCT STONES WITH PANCREATIC DUCT STRICTURES: PRELIMINARY DATA

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INTRODUCTION: Placement of fully covered self-expandable metal stents (FCSEMSs) has not been reported to aid extraction of large pancreatic duct (PD) stones.
AIMS&METHODS: To evaluate the technical success and safety of temporary placement of a FCSEMS in the PD to aid extraction of large PD stones.
Four symptomatic patients with large (>10 mm) pancreatic duct stones, who could not be cleared of stones using a balloon catheter and basket using ERCP alone, were selected for FCSEMS placement. After placement of FCSEMS (10-mm diameter) in the pancreatic duct for 1 week to 5 months (mean duration: 77 days), standard endoscopic maneuvers cleared large pancreatic duct stones.Technical success and safety of temporary placement of a FCSEMS in the PD for aiding extraction of large PD stones. Technical success was defined as successful placement of stents and the ability to achieve PD clearance in two endoscopic encounters. Complications were assessed according to consensus criteria.
RESULTS: The procedure was technically successful in all 4 patients. At 6-month follow-up, no residual stones were seen on pancreatography, and all patients were doing well without any symptom recurrence.
CONCLUSION: Temporary placement of a FSCEMS in the PD for aiding extraction of large PD stones is a safe technique that facilitates the removal of large stones.
Disclosure of Interest: None Declared
Keywords: fully covered self-expandable metal stent, pancreatic duct stones, pancreatic duct strictures

P748 SELECTIVE BILIARY CANNULATION USING THE DOUBLE GUIDE WIRE TECHNIQUE. SUCCESS RATE AND COMPLICATIONS.

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INTRODUCTION: Difficult selective biliary cannulation during ERCP accounts for up to 10% of cases with naïve Vater papilla. Several techniques have been introduced like needle knife papillotomy or insertion of a guide wire or a pancreatic plastic stent into the main pancreatic duct to facilitate the selective bile duct cannulation described as double guide wire technique.
AIMS&METHODS: To retrospectively investigate the frequency use and complication rate of the double guide wire technique. This technique was compared to the standard selective cannulation technique. Difficult cannulation was defined if more than 15 minutes were necessary for selective cannulation or if the quide wire was inerted more than 5 times into the main pancreatic duct. Over a period of 57 months, 701 ERCPs were performed by a single operator, 523 (74.6%) of whom were performed on a naïve Vater papilla.
RESULTS: The overall selective cannulation rate was achieved in 512 patients (97.9%). Difficult cannulation requiring an alternative technique was required in 103 (20, 1%) patients. Double guide wire technique was successful in 48 out of 56 patients (85.7%), needle knife in 49 out of 50 patients (98%) and Rendezvous technique in 5 out of the 7 patients (71.4%). Overall complications occurred in 20 patients (3.8%), with 7 (1.34%) pancreatitis (2 severe, 5 mild), 1 (0.2%) bleeding, 2 (0.4%) perforation and 10 (1.95%) cholangitis. In the conventinal cannulation group 5 cases of pancreatitis (1 severe and 4 mild), 2 cases of perforation, 1 case of bleeding and 8 cases os cholangitis were observed. Two cases of cholangitis but no pancreatitis were observed in the double guide wire technique group. One mild and one severe pancreatitis were observed in the needle knife technique group.
CONCLUSION: Insertion of a guide wire into the pancreatic duct to facilitate the selective cannulation of the difficult bile duct is feasible in high rate and can be a safer alternative than other techniques.
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Disclosure of Interest: None Declared
Keywords: biliary cannulation, double guide wire technique

P749 ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION ALONE USING SHORT DOUBLE-BALLOON ENTEROSCOPE FOR THE TREATMENT OF DIFFICULT CHOLEDOCHOLITHIASIS IN PATIENTS WITH ROUX-EN-Y GASTRECTOMY

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INTRODUCTION: Endoscopic treatment of difficult common bile duct (CBD) stones in patients who have undergone Roux-en-Y gastrectomy can be challenging.
AIMS&METHODS: We evaluated the efficacy and safety of endoscopic papillary large balloon dilation (EPLBD) using short double-balloon enteroscope (DBE) for the treatment of difficult CBD stones in patients with Roux-en-Y gastrectomy. Between April 2006 and March 2013, we performed short DBE-assisted ERCP in 30 choledocholithiasis patients with Roux-en-Y gastrectomy (m/f: 27/3, mean age 77 years). The mean stone size was 11 mm (3–25 mm). Multiple (≥4) stones were found in 13 patients (43%). The size of balloon for papillary dilation was determined according to the size of stones, not exceeding the diameter of the distal CBD.

RESULTS: Access to the papilla was successful in 29 patients (94%). The mean time required to reach the papilla was 28 min (5–82 min). Successful biliary cannulation was achieved in 28 patients (93%), 5 of which required PTBD rendezvous technique. Finally, 25 patients underwent stone removal. EPLBD without EST (10–18 mm) and EPBD (8 mm) were performed in 23 and 2 patients, respectively. The overall complete stone removal rate was 96%. Mechanical lithotripsy and extracorporeal shock wave lithotripsy were required in 4 (16%) and 5 (20%) patients, respectively. Complications occurred in 4 (13%) patients, including retroperitoneal air (n = 1) and hyperamylasemia (n = 3), but all were asymptomatic.
CONCLUSION: EPLBD using short DBE appears to be an effective and safe treatment for difficult CBD stones in patients with Roux-en-Y gastrectomy.
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Disclosure of Interest: None Declared
Keywords: Choledocholithiasis, Double-balloon enteroscopy, EPLBD

P750 ERCP-RELATED PERFORATIONS: RESULTS FROM SINGLE CENTRE EXPERIENCE AT A DISTRICT GENERAL HOSPITAL IN JAPAN

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INTRODUCTION: Endoscopic retrograde cholangiopancreatography (ERCP) has become a common procedure worldwide for various pancreticobiliary diseases. It is available in most acute hospitals in Japan. Perforation after ERCP is rare but one of the most dreaded complications. The reported incidence of perforation is 0.08 to 2.2%, and the mortality rate is 12 to 25%. These data stems mainly from older studies or retrospective databases of tertiary referral centres, however, there are few reports about the incidence and the outcomes at a district general hospital.
AIMS&METHODS: The aim of this study was to assess the incidence of ERCP-related perforation and the clinical outcomes in the district general hospital setting. A review of all patients undergoing ERCP at our institution from April 1996 and April 2013 was performed to assess the ERCP-related perforations. Perforation following ERCP was divided, according to Stapfer classification, as follows: remote from the papilla (type I, lateral or medial wall), periampullary (type II), at the level of the distal bile duct (type III, related to wire or basket instrument) or retroperitoneal air alone (type IV).
RESULTS: Out of 5732 ERCPs that were performed (71.2% therapeutic interventions), a total of 15 perforations occurred, yielding an incidence of 0.26%. Of a total of 15 patients, males were predominant (11/15, 73%) and the mean age of the patients was 70.7 (range 50-87) years. The indications for ERCP were choledocolithiasis in 7 patients (47%), malignant biliary strictures in 4 (27%), cholecystitis in two (13%), intrahepatic bile duct stricture in one (7%) and gallbladder polyp in one. We identified 5 type I, 6 type II, and 4 type III perforations. In all patients, perforation was recognised during ERCP. Type II perforations were related to sphincterotomy or procedures following sphincterotomy. Three patients with Billroth II anatomy suffered from perforation of the afferent limb. Nine out of 15 (60%) were managed medically with endoscopic biliary drainage or percutaneous transhepatic biliary drainage. The remaining 6 patients (type I in all 5 patients and type III in one) underwent surgery. Endoscopic closure of the perforation site was not performed in any patients as most of them were not amenable to endoscopic intervention. There were two mortality cases with unstable general conditions (type I in one and type III in one).
CONCLUSION: Although most patients fully recovered from perforation after ERCP, however, some patients experienced life-threatening outcomes, including mortality. Scope-related perforation is a serious complication requiring surgery. Early recognition and appropriate management is crucial for optimal results.
Disclosure of Interest: None Declared
Keywords: Complication, district general hospital, ERCP, outcome, perforation

P751 ASSESSMENT OF THE EFFECTIVENESS OF ERCP MECHANICAL SIMULATOR (EMS) EXERCISE ON TRAINEES' ERCP PERFORMANCE IN THE INITIAL LEARNING PERIOD: MULTICENTER RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: The ERCP computer-based simulator (ECS) is thought to be useful for teaching the endoscopic technique of side-viewing duodenoscopy. We have previously demonstrated that ECS can differentiate between endoscopists with lack or high level of ERCP competence. Furthermore, it has been suggested that simulator practice improves clinical performance of trainees in the initial learning period, however limited clinical information is available in terms of ECS practice.
AIMS&METHODS: The study aimed to evaluate the effect of ECS practice on trainees' clinical ERCP performance. Fifteen trainees who performed regularly esophago-gastroduodenoscopy and colonoscopy but were naive to side-viewing duodenoscopy and ERCP underwent clinical training in three different high volume endoscopy unit supervised by three ERCP experts. Trainees were randomized into two groups after a 2 hours long didactic seminar of ERCP teaching about basic duodenoscopy techniques and methods of Vater papilla cannulation. Study group (SG; n=6) participated first in ECS practice using the AccuTouch Endoscopy Simulator before starting on patients; control group (CG; n=9) did not undergo ECS practice. 59 patients were involved into the study (~3.93/trainee). ECS practice was made on 7 different computer simulated ERCP cases with 10 repetitions. The clinical performance of all participants was monitored and analyzed with different variables. Statistical analysis with Student's t-test and non-parametric Mann-Whitney test was performed.
RESULTS: Trainees who underwent ECS training intubated the pylorus and reached the papilla in significantly shorter period of time as compared to trainees without such practice (88.6 vs. 130.2 sec; $p<0.03$ and 129.4 vs. 179.4 sec; $p=0.03$, respectively). There was no statistical difference in pylorus intubation technique, proper orientation and positioning of the papilla as well as lack of unnecessary motions between the two study groups, however proper papillary cannulation control was superior in SG compared to CG (score 2.84 vs. 2.36; $p=0.04$). Additionally, reddening of the visual field was also significantly decreased in SG compared to CG (22.2 vs. 31.2 sec; $p<0.05$).
CONCLUSION: In our randomized, multicenter trial the ECS practice significantly enhanced trainees' clinical ERCP performance in the initial learning period. In conclusion, ECS has definite training potential in trainees' who are naive to side-viewing duodenoscopy and thus can be extremely useful in future ERCP training.
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Disclosure of Interest: None Declared
Keywords: computer, ERCP, randomized controlled trial, simulator, training

P752 PATIENTS RADIATION DURING INERVENTIONAL ERCP IS RELATED TO THE COMPLEXITY AND TECHNICAL DIFFICULTY OF THE PROCEDURES

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INTRODUCTION: Interventional ERCP is a well-established endoscopic procedure either for treatment or palliation for a great variety of hepatobiliary and pancreatic diseases. However, patients and endoscopy staff radiation during these procedures consists an important, although not extensively studied, not to say neglected, issue.
AIMS&METHODS: To assess and correlate patients radiation dose according to the complexity and technical difficulty (and thus fluoroscopy time) of several interventional ERCP procedures. Data of 650 patients-procedures performed in a 42 months period in a single center were retrospectively recorded and analyzed. All procedures were categorized according to a validated (Cotton scale) three degree (1 to 3) technical difficulty and complexity grading scale as follows: 1. Simple and uncomplicated common bile duct (CBD) stones (1-2 stones <1 cm in diameter) and plastic stent placement for post-operative bile duct leaks and low CBD strictures. 2. Complex CBD stones (>2 stones and/or >10mm in diameter) or when large balloon papillary dilatation was performed, treatment of hilary or more proximal strictures, benign post-operative biliary strictures. 3.Pancreatic duct procedures, procedures in patients with Billroth II operation and procedures for intra-hepatic bile ducts stones. All procedures were performed by one senior endoscopist with more than 10 years of experience. Fluoroscopy time, number of films taken and patients radiation dose in terms of Kerma area product (KAP) were recorded and analysed in relation with the technical difficulty of ERCP according to the above grading scale.
RESULTS: Mean values for each Group are presented in the following table:

Grade of procedure	N pat's	Age	Time	Films	KAP
1	407	70.2	3.9	2.4	15.8
2	157	69.8	7	2.9	23.8
3	20	70.3	5.8	2.6	17.5

There was statistically significant difference between Groups 1 and 2 for all parameters (Mann-Whitney U, Wilcoxon W): Fluoroscopy time Z=-7,839 $p<0.001$, Films taken Z=-2,780 $P<0.005$ and KAP Z=-4,131 $p<0.001$, while there were no significant differences between all other groups. The relatively low KAP in Group 3 is presumably due to the small number of cases, compared with Groups 1 and 2, and that most of them were patients with Billroth II operations where most of the time was spent in cannulation rather than fluoroscopy.
CONCLUSION: Complexity and technical difficulty of interventional ERCP procedures increases both fluoroscopy time and KAP and thus patients radiation dose.
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Disclosure of Interest: None Declared
Keywords: Complexity and technical difficulty, Interventional ERCP, Patients radiation

P753 THERAPEUTIC ERCP IN CHOLELITHIASIS – A TEN YEAR - EXPERIENCE OF A SINGLE CENTER

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INTRODUCTION: Endoscopic Retrograde Cholangio-Pancreatography (ERCP) is the standard method of treatment of choledocholithiasis.
AIMS&METHODS: To evaluate the diagnostic success rate and the outcomes of therapeutic ERCP for bile duct stones, depending on the anatomical variants.

A total of 3097 consecutive ERCPs were performed in 2986 patients during a 9-year period (2002-2011) in our endoscopy department. The analysis of the results of therapy was performed depending on anatomic variants, age and opacification of the Wirsung duct.
RESULTS: The rate of successful cannulation was 98%. The patient's age and the diameter of the common bile duct were the factors influencing the probability of finding a gallstone (age over 74 years, AUC=0.547; $p<0.001$) and a CBD diameter larger than 12 mm (AUC=0.735, $p<0.001$). The number of cases with opacification of the Wirsung duct, the use of precut papillotomy and the inability of finding a stone significantly decresed with the increasing experience of operator ($p<0.001$). Stone removal was unsuccessful in 2.3%. Factors associated independently with unsuccessful extraction were previous surgical sphincteroplasty, stone size and Billroth I anastomosis. The precut sphincterotomy, required overall in 4.21% of cases, was significantly associated with the additional presence of an impacted stone ($p<0.001$), but did not correlate significantly with the other anatomical alterations. The use of the precut papillotomy technique decreased significantly with the increased expertise of the operators ($p<0.001$). The prevalence of pancreasum divisum in 866 patients with pancreatography was of 3.0%.
CONCLUSION: The endoscopic treatment of choledocholithiasis is highly effective, influenced partly by the experience of the operator; in experienced hands, however, the success rate is high even in case of anatomic variants and difficult calculi.
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Keywords: choledocholithiasis, endoscopic retrograde cholangio-pancreatography, extraction, success rate

P754 ENDOSCOPIC OSTIUM INCISION AT NON-MALIGNANT POST-SURGICAL BILIOENTERIC ANASTOMOTIC STRICTURE AFTER COMPLEX ABDOMINAL SURGERY

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INTRODUCTION: Bilioenteric anastomotic stricture is a well-known complication after bile duct surgery or liver transplantation. This study reports our experience with endoscopic ostium incision of high-grade or subtotal stricture at the non-malignant biliary
AIMS&METHODS: Over a 7-yr period among more than 7500 ERCPs, 38 patients (0.50%) after complex abdominal surgery were identified with high-grade/subtotal bilioenteric anastomotic stricture with failed cannulation or inaccessible ostium.
RESULTS: DBE enteroscopy (n= 19), push enteroscopy (n=7) or transstomal endoscopy via jejunostomy (n=12) were used to reach the bilioenteric anastomotic stricture and to intervene at the postsurgical stricture by ostium incision, guidewire canulation or dilation.
Results: From 38 patients with endoscopically identified high-grade or subtotal bilioenteric anastomotic stricture ostium incision was necessary in 23 patients (60.5%) to access the biliary tree, while in the remaining 15 patients (39.4%) guidewire probing or blunt bouginage/dilation was successful.
The ostium incision in 23 patients was made by either snare, needle knife and/or papillotome in 4 (17.3%), 3 (13.0%) and 18 patients (78.2%), respectively. Sucessful ostium incision was achieved in 20 of 23 patients (86.9%), allowing all further ERCP interventions successfully. Major complications included 1 perforation (5.2%) and 2 cholangitis (10.5% after transstomal approach).
CONCLUSION: Ostium incision at the strictured bilioenteric anastomosis may be required in a minority of postop patients. It represents a somewhat risky procedure, which should be performed only in experienced centers to avoid percutaneous transhepatic biliary approaches or re-operation.
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Disclosure of Interest: None Declared
Keywords: anastomosis stenosis, Liver transplantation, ostium incision

P755 THE UTILITY OF THE SECOND-GENERATION MULTIBENDING BACKWARDOBLIQUE VIEWING DUODENOSCOPE IN ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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INTRODUCTION: In the associated procedure for ERCP, the factors of patient's anatomy, or compressed tumor and all, make en face view of the papilla of Vater difficult. Those, also makes deep biliary cannulation and therapeutic techniques difficult. Therefore, we have developed multibending backwardoblique viewing duodenoscope (M-D scope) in conjunction with Olympus Medical Systems, Tokyo, Japan. Our pilot study of first-generation M-D scope showed (1); it allowed the endoscopic view "to look" up to the papilla while keeping a constant distance between the papilla and the endoscope tip, using swan-neck position. Especially, the M-D scope was useful for biliary cannulation in cases with Billroth I gastrectomy. However, biliary stenting was failed in a case of strong biliary stricture with Klatskin's tumor, and the M-D scope could not be inserted into duodenum in a case of duodenal stenosis due to pancreatic cancer. The reason of this technical failure was because the M-D scope with proximal bending portion did not get an adequate stiffness. To overcome this limitation, we newly developed the second-generation M-D scope (TJF-Y0022, Olympus Medical Systems, Tokyo, Japan).
AIMS&METHODS: The aim of the present retrospective study was to evaluate the utility of the second-generation M-D scope (S-M-D scope) in ERCP. To get an adequate scope stiffness, traction wire was strengthened, and proximal bending angle was changed from 70 degree of up/down to 45 degree. From July on 2012 to March on 2013, S-M-D scope was used in cases of biliary ERCP which were selected at random, or cases in which initial biliary cannulation with a conventional duodenoscope (JF-260V) was failed. Six endoscopists with various experience used S-M-D scope and were given questionnaire about when the proximal bending was used. Clinical and ERCP-related data such as serum amylase before and after the procedure, success of biliary cannulation were analyzed.
RESULTS: S-M-D scope was used in 53 cases of biliary ERCP related procedure including biliary stenting, sphincterotomy, stone removal and so on. The overall success rate of biliary cannulation with the M-D scope was 100%(53 /53), and all of the endoscopic procedures were successfully completed. Questionnaire showed proximal bending was used to obtain the ideal en face position for biliary cannulation in 9 cases (17%), and S-M-D scope was useful in 2 cases of 5 with Billroth I gastrectomy, In addition, stiffness of S-M-D scope never limited all procedures. Any complications were not found.
CONCLUSION: The S-M-D scope was very useful for therapeutic and diagnostic ERCP.
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Disclosure of Interest: None Declared
Keywords: Biliary, ERCP

P756 ENDOSCOPIC SNARE AMPULLECTOMY(ESP) FOR AMPULLARY TUMOURS - SINGLE CENTRE STUDY

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INTRODUCTION: Tumors of duodenal papillae may be malignant or premalignant. Endoscopic snare papillectomy (ESP) may be a minimally invasive solution to treat these lesions and can obviate the need for major surgical intervention. This retrospective single centre study evaluates the safety and outcome of ESP for ampullary tumors.
AIMS&METHODS: Patients with ampullary tumors treated with ESP during 6-years (Feb 2007 to Jan 2013) identified from our ERCP database. All underwent pre-ESP side-viewing duodenoscopy, EUS and relevant additional imaging to confirm localized disease and suitability for the procedure.
ESP was performed using a diathermy snare by fulcrum technique followed by biliary and pancreatic stenting –which were removed at 4 – 6 weeks with biopsies from the base for residual tumor. Patients with histology confirmed as adenocarcinoma were counseled for either close follow-up or surgical resection & with benign histology were closely followed up. Follow up done at 1, 3, 6, 12, 18, and 24 months& yearly thereafter.
RESULTS: 36 patients underwent ESP, mean age 63 years (33 – 83), males – 23. Initial presentation was abdominal pain 16(44%), obstructive jaundice 13(36%), anorexia 4 (11%) and cholangitis in 3(8%) patients. Mean tumor diameter was 18mm (7 – 37). Complications - 2 bleeds (managed with APC), one delayed biliary stenosis, stones & cholangitis (underwent ERCP & stenting) and one fatal pancreatitis after follow- up biopsy.
Histopathology: adenocarcinoma – 20(56%), adenoma – 15(41%), NET – 1.Margin positive 7 (19.4%) – adenocarcinoma– 4 (20%), adenoma – 3 (20%). Mean follow up 13.6 months (1 – 58).
4 (11%) lost to follow up – 2 each in carcinoma and adenoma group.
On follow up in adenoma group – patients without recurrence at mean 12-month (3 – 36) were – 10(67%),recurrence – 3 (treated by APC), NET 3-month no recurrence. Adenocarcinoma group –8(40%) underwent surgery. Of the remaining 12, 7(58%) – no recurrence at mean 26-month (14 – 58) ,recurrence -2 , fatal pancreatitis-1, lost to follow up- 2.
CONCLUSION: ESP for ampullary tumors is effective and safe. It can be curative for most ampullary adenomas.ESP for localized adenocarcinoma may be potentially curative in > 50% patients and may obviate need for major surgery. Negative resection margin status may be a predictor of improved ESP outcomes.
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Keywords: Adenoma, Ampullary Carcinoma, Endoscopic Ampullectomy, ERCP

P757 SAFETY AND EFFICACY OF DEXMEDETOMIDINE SEDATION FOR ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

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INTRODUCTION: Endoscopic retrograde cholangiopancreatography (ERCP) often requires deep sedation because it is an invasive procedure. Although

propofol and midazolam sedation have been widely used and accepted for ERCP, occasionally these agents cause respiratory depression. Dexmedetomidine, a highly selective α2-adrenoreceptor agonist with sedative activity and minimal effects on respiration, has recently been widely used for patients in the intensive care unit. However, its utility for endoscopic procedures remains unclear. In this study, we retrospectively investigated the safety and efficacy of dexmedetomidine sedation during ERCP.
AIMS&METHODS: Of the patients who underwent ERCP between January 2013 and May 2013, 20 cases were selected, excluding the elderly or the patients with reduced cardiac function. The patients were sedated with dexmedetomidine, intravenously infused at 3.0 μg/kg/h for 10 min and then continuously at 0.4 μg/kg/h. In addition, pentazocine and midazolam were administrated when further sedation was required as a result of restlessness or body movement. To evaluate patient consciousness, Bispectral Index monitoring and the Richmond Agitation-Sedation Scale (RASS) were used. During ERCP, the level of sedation between RASS-2 and RASS-3 was maintained. The examination completion rate and complication rate associated with sedation were evaluated.
RESULTS: In our patient cohort, the mean age was 63.7 years and the male-to-female ratio was 5:3. The mean examination time was 47 min. The mean dose of additional midazolam and pentazocine was 9 mg and 5 mg, respectively. The examination completion rate for each examination was 100%. In one case, a transient reduction in blood pressure was observed. There was no case that SpO_2 was 90% or less throughout the whole observation period.
CONCLUSION: In this study, we safely performed ERCP using dexmedetomidine combined with a small amount of other sedative agents. In conclusion, dexmedetomidine can be used as an alternative to conventional methods for deep sedation during ERCP.
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Disclosure of Interest: None Declared
Keywords: Dexmedetomidine, ERCP, sedation

P758 DIRECT PERORAL CHOLANGIOSCOPY IN A LARGE PROSPECTIVE COHORT ANLAYSIS

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INTRODUCTION: Direct cholangioscopy (DC) with ultraslim endoscopes and freehand cannulation of the common bile duct (CBD) is a promising technique for evaluating and treating cholangiopathy. However, its safety and success rates are as yet unclear.
AIMS&METHODS: Evaluation of the overall success rates and adverse events with the procedure in a single center academic tertiary referral center. Prospective cohort study with 100 DC procedures in 84 patients with biliary disease were evaluated prospectively.
RESULTS: In 34 cases with small or medium-sized sphincterotomies, sphincteroplasty was performed with a 10-mm dilating balloon before DC. The intraductal area of interest was successfully accessed in 87% of the procedures. The intended interventions were successfully carried out in 81 cases (93.1%), but failed in six (6.9%). In patients without significant strictures, intrahepatic exploration of the bile ducts beyond the level of the bifurcation was feasible in only 10.8% of cases. The mean total procedure time was 38.6 $\pm$ 12.2 minutes. Adverse events occurred in 12 procedures (12%) and were managed conservatively.
CONCLUSION: DC is safe and allows direct high-resolution examination and a wide range of therapeutic options in the bile ducts in the majority of patients with biliary disease. However, the range of access is limited to the main bile duct, and suspected pathology restricted to the proximal intrahepatic ducts beyond the bifurcation is therefore not a good indication for DC.
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Disclosure of Interest: V. Meves: None Declared, C. Ell Other: Speakers honoraria from Fujifilm, J. Pohl Consultancy for: Speakers honoraria from Fujifilm, Other: Speakers honoraria from Fujifilm
Keywords: Direct Cholangioscopy, Efficiacy , peroral cholangioscopy, Safety

P759 A MULTI-CENTER RETROSPECTIVE STUDY OF PHOTODYNAMIC THERAPY WITH POLYHEMATOPORPHYRIN FOR MALIGNANT BILIARY OBSTRUCTION: RESULTS OF 76 CONSECUTIVE APPLICATIONS

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INTRODUCTION: Photodynamic therapy (PDT) is a treatment modality for malignant biliary obstruction.
AIMS&METHODS: The aim of the present study was to retrospectively analyze the experience with PDT using polyhematoporphyrin as a photosensitizer at different Austrian referral centers for biliary endoscopy. At the participating institutions charts of PDT patients were screened for their underlying diseases, anti-tumor co-therapies, interventional complications, adverse events within 30 days post PDT and follow-up.
RESULTS: 47 patients (34 male, 13 female, median age 70 years, range 46 to 86 years) underwent a total of 76 PDT applications at 4 referral centers in Austria. Polyhematoporphyrin was used as a photosensitizer in all cases (2mg/kg body weight). The underlying conditions included 41 Klatskin tumors, 4 cases of metastatic colorectal cancer (mCRC) and 2 cases of distal cholangiocarcinoma (CCa). Prior tumor treatment included chemotherapy in 12 cases, liver surgery in 5 cases, radiofrequency ablation in 2 cases and 1 case each of external radiotherapy, ethanol instillation and selective internal radiotherapy. PDT could be performed without any complication in all patients. Within 30 days after PDT the following adverse events were recorded: 13 cases of cholangitis, 2 cases of E. coli sepsis and 1 case each of non-ST-elevated myocardial infarction, transfusion dependent anemia, Clostridium difficile colitis and acute renal failure. 30-day and 90-day mortality (referring to the first PDT procedure) were 2% and 12%, respectively. The median survival after PDT was 15.1 months (95% CI 11.6 - 18.5 months).
CONCLUSION: PDT using polyhematoporphyrin as a photosensitizer proved to be feasible and safe in this retrospective study. The number of adverse events within 30 days after PDT (including the rate of cholangitis), mortality rates and survival time were comparable to previous publications on PDT with different photosensitizers. PDT seems to be a valuable therapeutic option for patients suffering from malignant biliary obstruction.
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Disclosure of Interest: None Declared
Keywords: malignant hilar biliary obstruction, photodynamic therapy (PDT)

P760 WHAT IS THE BEST DIRECTION FOR USES OF THE NEW HISTOLOGY NEEDLE WITH REVERSE SIDE-BEVEL (ECHOTIP® PROCORE™) FOR EUS-GUIDED FINE NEEDLE BIOPSY? : AN EXPERIMENTAL STUDY.

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INTRODUCTION: Recently, ProCore as the EUS-guided histology needle was developed and widely used. The theoretical advantages of ProCore are 1) "core trap" within the needle which holds the core specimen, 2) "reverse side-bevel" which serves to cut the specimen, allow scraping away the tissue into the bevel and to gain a core tissue on withdrawal. In this regard, it is considered movement of the needle with whipping back may be able to obtain more tissue than movement at natural speed. In addition, the slow-pull technique which is performed with simultaneous minimal negative pressure provided by pulling the stylet slowly and continuously is recommended. Nevertheless, tissue yield with the ProCore is not consistent and no standard technique has been established.
AIMS&METHODS: The aim of this study is to determine what is the best direction for uses of the ProCore in experimental study. We performed fine-needle biopsy (FNB) with 22G ProCore for fresh chicken tenderloin and liver. Six techniques with moving back and forth 10 times of the needle per pass were evaluated: 1) needling with natural speed; without suction, with slow-pull technique, with 10ml suction, 2) needling with whipping back; without suction, with slow-pull, with 10ml suction. To perform whipping back, we made a handmade device attached stopper. The obtained tissue were entirely expressed onto a charta by reinsertion of the stylet, and measured total weight by electronic balance. In addition, the materials were evaluated whether a visible core for histology was obtained or not.
RESULTS: At FNB for tenderloin, the weight of obtaining tissue using natural speed technique was 0.36±0.07 (mean±SD, mg) in no suction group, 0.78±0.19 in slow-pull group, 2.59±0.68 in 10ml suction group, respectively. In using whipping back technique, the weight was 0.24±0.20 in no suction group, 0.44±0.22 in slow-pull group, 1.97±0.70 in 10ml suction group, respectively. At FNB for liver, in order of the above, 1.12±0.98, 5.2±2.13, 18.52±4.28, 2.2±0.82, 7.22±1.36, 16.98±3.74, respectively. In either target, many specimens were obtained with higher negative pressure, at any techniques ($P<0.001$). Moreover, visible core samples were constantly obtained in the groups with negative pressure.
CONCLUSION: Our experimental study indicates that EUS-FNB using ProCore should be performed with negative pressure (at least 10ml) in any needling techniques. Although ProCore has the reverse side-bevel, it is difficult to mention this mechanism was workable.
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Disclosure of Interest: None Declared
Keywords: EUS-FNA, EUS-FNB, ProCore

P761 ENDOSCOPIC ULTRASONOGRAPHY GUIDED-GALLBLADDER STENTING FOR PATIENTS SUFFERING FROM ACUTE CHOLECYSTITIS OR THOSE WITH LONG-TERM CHOLECYSTOSOTMY

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INTRODUCTION: Acute cholecystitis is traditionally managed by cholecystectomy. The uses of endoscopic methods to treat the condition have been described but did not gain popularity. Recently, a lumen apposing stent (AXIOS, Xlumena, CA, USA) designed for EUS guided-transmural gallbladder stenting (EUS-GBS) has become available. In this study, we present our experience of performing EUS-GBS for patients suffering from acute cholecystitis or on long-term percutaneous cholecystostomies.
AIMS&METHODS: All patients admitted to the Prince of Wales Hospital with a diagnosis of acute cholecystitis who were unfit for surgery and those who were

on long-term cholecystomies were recruited. EUS-GBS was performed with a linear array echoendoscope (GF-UCT180 Olympus, Japan). The gallbladder was punctured from the dudoenum or antrum. After initial puncture, the track was then dilated with a 8.5 Fr cystotome or 6Fr needle knife and a biliary balloon. The AXIOS stent was then inserted and deployed under EUS and endoscopic guidance. Follow-up cholecystoscopy was performed 3 months after the procedure. The stent was then removed if cholecystoscopy showed no residue stones. Outcomes measurements included technical and clinical success rates, morbidities, mortalities and recurrent biliary events.
RESULTS: Between June 2012 to April 2013, 10 patients were recruited to the study. The mean (S.D.) age of the patients was 82.5 (7.23) years old. 7 patients suffered from acute cholecystitis and 3 were on long-term percutaneous cholecystostomies. 7 patients were of American society of Anaesthesiology grading 3 and 3 patients were grade 4. The mean (S.D.) temperature and white cell counts of patients who suffered from acute cholecystitis on admission were 38.44 (1.11) degrees Celsius and 22.5 (10.3) x 10^9/L. Technical success and clinical success was achieved on all patients. An additional covered metallic stent was required in 2 patients. The mean (S.D.) procedural time was 35.5 (11.4) minutes. Procedural complications occurred in 3 patients, 2 with mal-positioning of the stent and 1 with pneumoperitoneum. Follow-up cholecystoscopy was performed in 5 patients and 1 patient had residue stones that required laser lithotripsy. 2 patients suffered from common bile duct stones after removal of the stent.
CONCLUSION: EUS guided-gallbladdder stenting and intervetions were feasible with the lumen apposing stent. It is a technically demanding procedure requiring dedicated instruments. However, it is a promising technique for treatment of acute cholecystitis and gallstones with acceptable morbidities.
Disclosure of Interest: None Declared
Keywords: Endoscopic ultrasonography drainage, Gallbladder drainage, Interventional endoscopic ultrasonography

P762 COMPARATIVE STUDY IN 100 CASES BY AN EXPERT USING 22G STANDARD AND FENESTRATED ASPIRATION NEEDLES, IN ENDOSCOPIC ULTRASOUND-GUIDED BIOPSY OF SOILD PANCREATIC LESIONS.

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INTRODUCTION: Endoscopic ultrasound-guided fine-needle aspiration(EUS-FNA) using standard needles (SN) has proven to be of high diagnostic value in the evaluation of solid pancreatic masses (SPM), Fenestrated needles (FN) have been promoted to improve the histopathological quality of the EUS-FNA.
AIMS&METHODS: To compare the histological quality and diagnostic yield in FN versus SN.Over a 2y period,we included patients with SPM > 2cm in size,EUS-FNA performed by the same senior endoscopist by a 22 Gauge needles either SN or Procore® FN by aspiration method while using an EUS GF-UCT140 scope(Olympus, Japan).Each needle pass was treated by a independent histopathologist (blinded to the type of needle used).We developed a quality scale to evaluate the histopathological contents of each slide following a 4 category grading levels,(A)absent 0%,(B)Minimal surface area/slide(SA/S)< 25%,(C)Moderate SA/S< 25%>50%,(D)Significant SA/S>50%,these grades were applied to evaluate the contents of(blood, digestive contamination,normal pancreatic tissue,necrotic tissue and tumoral tissue),the cellularity load was evaluated by number of cells/SA(fair<100,good 100to1000,excellent >1000),presence of biopsy microframents(number and size),the diagnostic yield(definite group(begnin or malignant),suspect group (atypical, suspicous,normal tissue),group non-adequate for reporting(NAR)for lacking of histopathological content),patient clinical data and exam related complications were registered.
RESULTS: 100 patients,(SN 50%,FN 50%),males(63%),females(37%),median age(68,4 years +/- 12,5y SD).Median lesion size (32mm+/-4,6mm SD),location (head72%,body18%,tail10%), the median N° of needle passes (SN=3,FN=2), for SN content:blood (A=12%,B=56%,C=26%, D=6%), tumoral tissue (A=14%, B=64%, C=20%, D=2%), N° of cells/SA (fair 10%,good 36%, excellent 54%), 34microfragments present in 46% of slides with a median size of 0.6mm +/- 0.5 SD, diagnostic yield is 90%(definite in 84%,suspect in 6%)and 10%was NAR.For theFN 1stpass, blood content (A=2%, B=44%, C=36%, D=18%),tumoral tissue (A=18%, B=48%, C=22%, D=12%), N° of cells/SA (fair 4%, good 28%, excellent 68%), 76 microfragments present in 60% of slides with a median size of 0.96mm+/-0.7SD,diagnostic yield is 94%(definite 68%,suspect 26%) and 6% was NAR.Global diagnostic yield for FN needle(-median N° of passes of 2)is 98%(definite 88%, suspect 10%) and 2% was NAR.
CONCLUSION: As compared to SN, FN shows improved histopathological quality grades of obtained material in EUS-FNA but with a relatively similar diagnostic yield in the first pass, nevertheless the global outcome of FN passes seems superior to that of SN.
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Disclosure of Interest: None Declared
Keywords: diagnostic accuracy, diagnostic yield, endosonography, Interventional endoscopic ultrasonography, pancreas

P763 ROLE OF ENDOSCOPIC ULTRASOUND (EUS) IN CHILDREN: A LARGE SINGLE CENTRE EXPERIENCE

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INTRODUCTION: Experience in the use of endoscopic ultrasonography (EUS) in children is limited. The aim of this study was to determine its feasibility and efficacy in children at a tertiary care gastroenterology referral centre in India.
AIMS&METHODS: Consecutive patients aged ≤ 18 years who underwent EUS from January 2009 to December 2012 were retrospectively identified through a computer database search. EUS was done using radial GF-UCT160 or curvilinear GF-UCT140 echoendoscopes.Indications, findings, interventions and complications of the procedures in these patients were recorded.
RESULTS: A total of 350 EUS procedures were performed in 347 children (246 males, mean age 14.9 ± 2.6 years); of which 44(12.6%) cases underwent EUS guided interventions .The main indications for EUS were recurrent acute pancreatitis in 123 (35.4 %), chronic pancreatitis(CP) in 100 (28.8%), select cases of acute pancreatitis in 36(10.4%), pancreatic pseudocyst in 26 (7.5%), abdominal pain of suspected pancreatobiliary origin in 22(6.4%), suspected biliary obstruction in 19(5.5%), mediastinal mass/lymph nodes in 13 (3.7%), pancreatic mass in 6 (1.7%), upper gastrointestinal submucosal lesion in 1 (0.3%), periampullary mass in 1(0.3%). Findings included CP in 90 (26%), indeterminate CP in 88(25%), pseudocyst in 37(10.6%), acute resolving pancreatitis in 40 (11.5%), lymph nodes (mediastinal -13, abdominal- 4)in 17(4.9 %) , normal in 21(6%), gall stones with normal common bile duct in 16 (4.6%), acute on chronic pancreatitis in 14(4%), acute peripancreatic fluid collection in 8(2.3%), necrotizing pancreatitis in 6 (1.7%).Uncommon EUS findings were choledochal cyst in 3(0.8%), biliary microlithiasis in 2 (0.5%), biliary hydatid cyst in 1(0.3%), insulinoma in 1(0.3%), pseudopapillary tumor of pancreas in 1 (0.3%), duodenal duplication cyst in 1(0.3%), and internal hernia in 1(0.3%).
EUS-guided pseudocyst drainage was performed in 20 (5.8%), fine needle aspiration in 16 (4.6%), celiac plexus block in 6 (1.7%), pancreatic duct (PD) puncture and stenting in 2 (0.6%) cases. In all patients anesthesiologist administered ketamine with midazolam (50:1) for induction, followed by propofol for maintenance .The procedure was successful in all patients. Post procedure mild abdominal pain was encountered in 2 patients who had undergone intervention.
CONCLUSION: EUS and EUS guided interventions in children are feasible and safe. Procedure is well tolerated under propofol sedation when given by anaesthetist.
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Disclosure of Interest: None Declared
Keywords: children, endoscopic ultrasound, Interventions

P764 DIAGNOSTIC ACCURACY OF CT, DW-MRI AND EUS IN RESECTABLE GASTRIC TUMORS: A RETROSPECTIVE STUDY

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INTRODUCTION: Assessment of the preoperative T-N staging is of pivotal importance for the therapeutic strategy in gastric cancer(GC). Until recently, computerized tomography (CT) has been the mainstay of preoperative staging for GC, but accuracy in T and N staging were often inadequate. Among multiple imaging tests for GC staging, endoscopic ultrasound (EUS) has emerged as the most accurate tool for pre therapeutic loco regional tumor staging, while there are few data regarding the new concept of diffusion-weighted magnetic resonance imaging (DW- MRI).
AIMS&METHODS: The aim was to assess the accuracy of EUS, CT and DW-MRI in the preoperative staging of GC, and the ability to correctly select patients for neoadjuvant therapy. Gold standard was histologic specimens. All patients who underwent preoperative clinical assessment of T/N stage with EUS, CT and DW-MRI and subsequent resection for GC between 2009 and 2011 were collected. Staging results from preoperative tools were compared with postoperative pathologic results. Main outcome parameter was the diagnostic value of different imaging techniques in distinguishing between early stage (T1/2N0) and locally advanced (T3/4 or any N+) in order to establish the accuracy of the preoperative work-up in selecting patients who may benefit from neoadjuvant therapy.
RESULTS: Sixty-six patients with GC underwent EUS, CT and DW-MRI followed by resection, including patients treated with preoperative chemotherapy (n=20). The overall T staging accuracy was 38.3% for EUS, 57.4% for CT and 40.6% for DW-MRI, whereas for N stage accuracy were respectively of 60%, 48% and 64.1%. Sensitivity of EUS in selection of advanced T stage patients (T3-4 vs T1-2) was better compared to CT and DW-MRI (86.2% vs 78.9% and 75% respectively). Patients with advanced tumors (T3-4/N+) were globally best selected by EUS (sensitivity: 89% EUS, 75% CT, 76% MRI). EUS under staged patients in 11% of cases, CT in 25%, DW-MRI in 24% of cases.
CONCLUSION: The concordance between EUS and pathologic results was lower than expected for individual T and N stages. Similar data are achieved by using the new DW-MRI. Conversely EUS achieved the best results in correctly select patients who may benefit from neoadiuvant therapy. EUS should be still adopted as routine procedure in preoperative work-up.
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Disclosure of Interest: None Declared
Keywords: Computed tomography, Endoscopic Ultrasound, Gastric cancer, magnetic resonance imaging

P765 THE ROLE OF ENDOSCOPIC ULTRASONOGRAPHY IN THE ETIOLOGICAL EVALUATION OF IDIOPATHIC ACUTE PANCREATITIS

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INTRODUCTION: Historically, no cause was identified in 10-30% of cases of acute pancreatitis and these patients were often labelled as suffering from idiopathic acute pancreatitis (IAP). Endoscopic ultrasonography (EUS) may play a significant role in the diagnostic evaluation of these patients.

AIMS&METHODS: The aim of this study was to evaluate the use of EUS in determining a probable etiology where conventional radiologic methods had failed to identify the cause of acute pancreatitis. Between June 2009 and June 2012 268 patients (158 male, 110 female; age range 47-78, mean age 67.5 years) were admitted to the emergency room of our hospital for biochemically proven acute pancreatitis. All patients were evaluated by conventional radiologic methods (transabdominal ultrasound, computer tomography and/or magnetic resonance cholangiography). The patients with no etiology established were considered affected by IAP and underwent EUS (Olympus linear echoendoscope Gf Type Uc140p-Al5; Olympus Co., Ltd., Tokyo, Japan) at Gastroenterology and Endoscopy Unit of "Ospedali Riuniti Marche Nord", Pesaro – Italy.
RESULTS: In 42/268 (15.7%) patients without prior colecistectomy (18 male, 24 female; age range 57-79, mean age 67 years) no etiology was found by conventional radiologic methods and diagnosis of IAP was done. A definitive diagnosis by EUS was done in 34/42 patients (80.9%). Cholelithiasis or microlithiasis (small gallbladder stones 1 to 5 mm) was identified in 24/42 patients (57.1%), choledocholithiasis (sludge and stones 2 to 4 mm) in 6/42 (14.3 %). All stones were confirmed by subsequent ERCP or cholecystectomy. 4/42 (9.5.%) patients were found to have chronic pancreatitis and in the remaining 8/42 (19%) patients no etiology was identified.
CONCLUSION: EUS provided additional diagnostic information in a large number of patients classified as having IAP by conventional radiologic examinations. In this study patients with IAP were reduced from 42/268 (15.7%) to 8/268 (3%) after EUS was done. Early identification of a biliary cause of acute pancreatitis, and early treatment, reduce the risk of recurrent pancreatitis, morbidity and mortality. EUS should be performed as first-line investigation in patients with acute pancreatitis especially when a biliary etiology is suspected.
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Disclosure of Interest: None Declared
Keywords: Endoscopic ultrasonography, idiopathic pancreatitis

P766 EUS IN PANCREATIC CANCER STAGING - A SINGLE CENTER PROSPECTIVE STUDY

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INTRODUCTION: Accurate preoperative staging of pancreatic cancer is important for proper treatment selection. EUS is considered an accurate tool in preoperative staging.
AIMS&METHODS: The aim of this prospective study was to evaluate the accuracy of preoperative EUS T- and N-staging of pancreatic cancer. Patients with histologically confirmed pancreatic carcinoma, that underwent preoperative EUS staging followed by surgery, were included in the study. The accuracy of EUS T-staging was evaluated by the comparison of EUS with final (histopathological or peroperative) T-staging and was calculated as a ratio of patients with agreement between EUS and final T-staging and total number of patients. Accuracy of all as well as each T-stage of pancreatic cancer were calculated. EUS-nodal staging was based on EUS image only. Two of four EUS signs of malignant lymph node involvement were necessary for an EUS diagnosis of malignant LN, with one beeing short axis diameter of≥10 mm. EUS and histopathological staging of LN were compared and accuracy of EUS N-staging was calculated.
RESULTS: A total of 87 patients (male: 62,1%, mean age±SD: 61,6±8,7 years) with pancreatic carcinoma, that underwent either surgical resection with histopathological staging (n=50) or exploration/paliative surgery with peroperative staging (n=37) were analysed. In the majority (76/87; 87,4%) of patients pancreatic carcinoma was localised within the head. In the wole study group, the agreement between EUS and final T-staging was 52,9% (46/87) with understaging occuring in 39,1% (34/87) and overstaging in 8% (7/87) of patients. The lowest agreement was in the T4- (6/22; 27%) and T3- (18/34; 52,9%) stage carcinoma groups, where understaging occured in 73% (16/22) and 47,1% (16/34), respectively. EUS-N-staging was analysed in 64 patients with the accuracy of 73,4% (47/64). EUS N-staging was false-negative in 11% (7/64) and false-positive in 15,6% (10/64) patients.
CONCLUSION: The overall accuracy of EUS T-staging of pancreatic cancer is inacceptably low, caused mostly by understaging of T4- and T3 pancreatic cancer. Therefore, a combination of EUS and CT/MRI is recommended in preoperative T-staging. EUS without FNA evaluates correctly 3/4 of lymph nodes in patients with pancreatic cancer.
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Disclosure of Interest: None Declared
Keywords: endosonography, pancreatic carcinoma, staging

P767 THE PROTOTYPE LONGER MINIATURE ULTRASOUND MINIPROBE "UM-3Y" DURING SINGLE-BALLOON ENTEROSCOPY (SBE) IN NEOPLASTIC LESIONS OF SMALL BOWEL

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INTRODUCTION: Single-balloon enteroscopy (SBE) is an endoscopic procedure useful for investigating patients suspected for having tumours, inflammatory bowel diseases or bleeding of small bowel with an anterograde or retrograde approach. The evaluation of neoplastic lesions of small bowel by an ultrasound miniprobe can be useful in spite of the difficulty to have a histological definition of these lesions.
AIMS&METHODS: The aim of the study was to evaluate the prototype longer ultrasound miniprobe UM-3Y (Olympus, Tokyo, Japan) in submucosal lesions of small bowel during SBE.
Between 2010 and 2012 we investigated a total of 15 patients (mean age 60), 6 males and 9 females for anaemia, radiological suspect of small bowel tumour, diarrhea and follow-up small bowel cancer. All patients after a negative esophagogastroduodenoscopy and colonoscopy underwent to capsule enteroscopy that showed a lesion of the small bowel. All patients underwent to SBE. For every patient histological samples were collected. During SBE a prototype longer miniature ultrasound miniprobe UM-3Y which incorporated a radial scanning system with a frequency of 20MHz was used, this was connected to an endoscopic ultrasonic observation unit (EU-M30; Olympus, Tokyo, Japan). The prototype has a length of 2700 mm and diameter 2.5 mm. After endoscopic examination of the small bowel and lesion detection with SBE, we inflated the overtube balloon to fix the endoscope in place and performed EUS-SBE.
RESULTS: In all cases we were able to insert EUS probe through the enteroscope channel and finally obtain a clear ultrasound image. In 2 of 3 patients the initial endoscopic diagnosis was a suspicion of submucosal mass and it has been characterized as neuroendocrine tumours by EUS-SBE and histology, in 2 of 2 patients adenocarcinoma was confirmed and in 2 patients we found respectively a GIST and a lymphoma. In the other cases ultrasonography allowed us to characterize duodenal cysts, an aggressive fibromatosis, an adenoma of the papilla of Vater and a jejunoileitis in this case excluding a lymphoma, in the other 4 cases EUS-SBE showed normal wall.
CONCLUSION: Endoscopic ultrasound with miniprobe UM-3Y is an important diagnostic tool for investigating with high accuracy small bowel lesions.
Disclosure of Interest: None Declared
Keywords: Ecoendoscopic Miniprobe, enteroscopy

P768 LONG-TERM OUTCOMES FOLLOWING ENDOSCOPIC ULTRASOUND-GUIDED CELIAC PLEXUS NEUROLYSIS

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INTRODUCTION: Endoscopic ultrasound-guided celiac plexus neurolysis (EUS-CPN) is reportedly a safe and effective method for alleviating pancreatic cancer-related pain. However, previous studies have primarily reported only the short-term outcomes of this treatment.
AIMS&METHODS: To evaluate the long-term outcomes following EUS-CPN, we retrospectively reviewed patients who underwent EUS-CPN for alleviating pancreatic cancer-related pain between July 2003 and July 2012. The EUS-CPN described in the present study included both conventional EUS-CPN as well as EUS-celiac ganglia neurolysis (EUS-CGN). Only patients who were followed-up until death were included in the analysis. Pain was evaluated using the visual analog scale (VAS), and the initial evaluation was performed 7 days after the EUS-CPN. Patients who exhibited a reduction in the VAS score to ≤3 were considered to show an effective response, whereas those who exhibited a reduction in the VAS score to ≤1 were considered to show a complete response. The duration of the EUS-CPN effect was defined as the duration between which EUS-CPN was performed and the time at which a narcotic agent was first administered or its dosage was increased since EUS-CPN. Univariate and multivariate analyses of the prognostic factors associated with the long-term effects of EUS-CPN until death were performed.
RESULTS: We evaluated 133 patients who underwent EUS-CPN (only conventional EUS-CPN, 73 patients; only EUS-CGN, 44 patients; both conventional EUS-CPN and EUS-CGN, 16 patients) for pancreatic cancer-related pain. The effective response and complete response rate at the initial evaluation was 69% and 36%, respectively. The median (95% CI) duration of the effect was 61.0 (36.6–85.3) days. We found that the statistically significant prognostic factors of the long-term effect of EUS-CPN until death included a reduction in the VAS score by ≥4 at the initial evaluation, complete pain relief (VAS score of ≤1 at the initial evaluation), bilateral distribution of ethanol, and relatively short duration of pain prior to EUS-CPN (≤120 days); the hazard ratio (95% CI) of these factors were 2.0 (1.2–3.2), 1.9 (1.2–3.1), 2.8 (1.8–4.4), and 2.8 (1.7–4.5), respectively. The difference of CGN or CPN did not affect the long-term outcomes.
CONCLUSION: Our findings indicate that the treatment effect of EUS-CPN may last longer in patients who exhibited a better response at the initial evaluation. Moreover, we believe that EUS-CPN should be performed at an earlier stage for the appropriate management of pancreatic cancer-related pain.
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Disclosure of Interest: None Declared
Keywords: EUS-CPN, pain relief

P769 ENDOSCOPIC ULTRASOUND-GUIDED CHOLECYSTOSTOMY FOR ACUTE CHOLECYSTITIS IN PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION

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INTRODUCTION: Although early laparoscopic cholecystectomy is the treatment of choice for patients with acute cholecystitis, percutaneous cholecystostomy has been performed in patients unsuitable for cholecystectomy. EUS-guided transgastric/transduodenal gallbladder drainage by using a plastic stent or covered self-expandable metal stent (SEMS) may be an alternative effective treatment for these patients
AIMS&METHODS: To evaluate the technical feasibility and safety of EUS-guided transgastric/transduodenal gallbladder drainage with single-step placement of a pigtailed plastic stent or a fully covered SEMS in patients with acute cholecystitis who are unsuitable for cholecystectomy. This study involved 15 patients with acute cholecystitis who did not respond to initial medical treatment and were unsuitable for cholecystectomy. EUS-guided transgastric/

transduodenal gallbladder drainage with single-step placement of a pigtailed plastic stent or a fully covered SEMS.
RESULTS: EUS-guided gallbladder drainage (pigtailed plastic stents =7, SEMS = 8) were successfully placed in all patients through the stomach (n= 3) or duodenum (n= 12). Fourteen patients among 15 patients achieved functional success within 3 days of stent placement. Bile leakage occurred in 2 patients and pneumoperitoneum occurred in 3 patients during or after the procedure, but all patients improved with conservative management. During follow-up (median 124 days, range 30-250 days), one patient experienced recurrent cholecystitis.
CONCLUSION: Placement of pigtailed plastic stent and fully covered SEMS after EUS-guided transgastric/transduodenal gallbladder drainage may be a feasible and safe alternative to treatments such as percutaneous cholecystostomy in patients with acute cholecystitis.
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Disclosure of Interest: None Declared
Keywords: cholecystostomy, Endoscopic Ultrasound

P770 A RETROSPECTIVE COMPARATIVE STUDY OF SLOW PULL VS. SUCTION TECHNIQUE IN ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION OF PANCREATIC SOLID LESIONS

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INTRODUCTION: Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) of pancreatic masses is an established procedure to obtain a pahthological diagnosis. However, the application of suction during EUS-FNA is still controversial due to increased blood contamination and the efficacy of slow pull technique, 10 to 20 to-and-fro movements with simultaneous minimal negative pressure provided by pulling the needle stylet slowly and continuously, was recently reported in new core biopsy needles. However, the efficacy of slow pull technique in EUS-FNA using a regular needle has not been fully elucidated.
AIMS&METHODS: Patients who underwent EUS-FNA for pancreatic solid lesions were retrospectively studied to compare suction and slow pull techniques using regular EUS-FNA needles. Primary endpoint was the diagnostic yield of malignancy. Secondary endpoints were cellularity and blood contamination on cytologic specimen. Subgroup analyses were performed based on the needle size (22- and 25- gauge). In addition, a multivariate logistic regression analysis for sensitivity of malignancy was performed, using tumor size (<25 mm vs. ≥ 25 mm), needle size (22- vs. 25- gauge), tumor location (head vs. body/tail) and FNA technique (suction vs. slow pull) as potential predictive factors.
RESULTS: A total of 389 passes (190 by suction and 199 slow pull technique) were performed during 103 EUS-FNA procedures in 98 patients with pancreatic solid lesions. Slow pull technique showed lower scores in cellularity (≥ 2 in 39.0% vs. 76.7%) but blood contamination scores were lower (≥ 2 in 27.1% vs. 66.7%) and sensitivity to diagnose malignancy was higher (90.6% vs. 67.9%) when a 25-gauge FNA needle was used. No significant differences were seen between two techniques when a 22-gauge needle was used. In a multivariate analysis of 86 cases with malignancy, slow pull technique (odds ratio [OR] 1.80, $p = 0.037$) as well as tumor size ≥ 25 mm (OR 3.70, $p < 0.001$) and tumor location in the body or tail (OR 2.82, $p < 0.001$) were associated with higher sensitivity.
CONCLUSION: Slow pull technique was associated with less blood contamination and can potentially increase the diagnostic yield compared with suction technique in EUS-FNA of pancreatic solid masses, especially with a 25-gauge FNA needle.
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Disclosure of Interest: None Declared
Keywords: EUS-FNA, Pancreatic Cancer

P771 THE BENEFITS OF THE COMBINED USE OF THE VIDEOCAPSULE AND BALLOON-ASSISTED ENTEROSCOPY IN PATIENTS WITH SUSPECTED SMALL BOWEL DISEASES

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INTRODUCTION: Both videocapsule endoscopy (VCE) and balloon-assisted enteroscopy (BAE) have their own specific limitations.
AIMS&METHODS: The aim: to estimate the benefits of combined use of CE and BAE. From 14.02.2007 to 30.04.2013 VCE followed by BAE were performed in 73 pts. (m-33, f-40, mean age 54,3±13,7 yrs., range 17-89) with suspected small bowel diseases. Obscure GI bleeding was an indication for VCE in 40 (54,8%) cases. The insertion route for BAE was determined according to the site of the suspected lesions detected by VCE.
RESULTS: In 8 (10,9%) pts. without a definite lesion on VCE there were no any abnormalities found by the BAE as well. In 1 (1,4%) case VCE revealed a cavernous haemangioma in the caecum missed by 2 prior colonoscopies. Small bowel lesions were suspected on VCE in 64 (87,7%) pts.: tumors in 32 (43,8%) pts.; enteritis in 20 (27,4%); vascular lesions in 12(16,4%).

Defined small bowel lesions	CE findings (pts.)	Insertion route for BAE (pts.)	BAE findings (pts.)	Biopsy taken (pts.)	Final diagnosis (pts.)	Treatment modality (pts.)
Tumors	32	Per os 22 Per rect. 4 Both 6	18	8	20	Endo 7 Surgery 11
Enteritis (incl. erosions and ulcers)	20	Per os 6 Per rect. 6 Both 8	20	16	20	Endo 2 Surgery 4
Vascular lesions	12	Per os 8 Per rect. 2 Both 2	11	1	7	Endo 9 Surgery 1
Total	**64**	**Per os 36 Per rect. 12 Both 16**	**49**	**25**	**48**	**Endo 18 Surgery 16**

The diagnosis was confirmed by BAE in 49 (75,4%) from 64 pts. Tumors were confirmed in 56,3% (18/32) pts. plus in 2 pts. with negative BAE we've performed laparoscopy and revealed tumors with extraorganic growth; inflammation and ulcerations - in 100,0% (20/20), however 1 case detected as an ulcer turned to be Meckel's diverticulum; vascular lesions - in 91,7% (12/11). Conservative treatment has been applied in 31 (48,5%) cases. Endoscopic treatment was performed in 18 (28,1%) pts.: APC and clipping in 9 cases, polyps removal in 7; bougienage strictures in Crohn's disease in 2. There were 16 (25,0%) pts. who underwent surgery: for tumors (11), Crohn's disease with a stricture (1), angioectasia and ulcers with recurrent GI bleeding (3), Meckel's diverticulum (1). The sensitivity, specificity, positive predictive value and negative predictive value, diagnostic accuracy of combined VCE and BAE for small bowel lesions were 100%, 93,7%, 98,4%, 100% and 80, 3%, respectively.
CONCLUSION: VCE can provide useful information on the indications and selection of the route for BAE. BAE can provide conservative management in 76,6% pts. (incl. 28,1% endoscopic treatment). Combined use of VCE and BAE has a high effectiveness (80,6%) in the diagnosis and management of patients with small bowel diseases.
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Disclosure of Interest: None Declared
Keywords: balloon-assisted enteroscopy, Capsule Endoscopy, Small Bowel

P772 DOUBLE-BALLOON ENTEROSOCOPY HAS HIGHER DIAGNOSTIC YIELD AND BETTER CLINICAL OUTCOMES IN PATIENTS WITH ACUTE OVERT-OGIB WITH SHORT-TERM FOLLOW-UP: COMPARED WITH CAPSULE ENDOSCOPY

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INTRODUCTION: Capsule endoscopy (CE) and double-balloon enteroscopy (DBE) have been reported to provide comparable diagnostic yields in patients with obscure gastrointestinal bleeding (OGIB). In addition, CE has been recommended as a first-line tool for investigation of patients with OGIB. However, few studies have directly compared the two modalities in patients with acute overt-OGIB. The current study was to compare the diagnostic yield of direct CE and DBE in patients with acute overt-OGIB and evaluate the outcomes of short-term follow-up.
AIMS&METHODS: Prospective study was conducted between June 2012 and December 2012. EGD and colonoscopy were tandem performed in patients with melena or hematochezia within 24hrs after registration. Tandem CE and DBE were performed within 2 weeks after non-diagnostic EGD and colonoscopy given CE retention. Initially, retrograde DBE route was selected based on consideration of difficulty in griping the intestine if antegrade DBE was firstly performed. The primary outcomes assessed were the diagnostic yields of the both tests. All patients received short-term follow-up, including assessment of rebleeding, readmission, further transfusion or interventions, and mortality.
RESULTS: A total of 39 patients were included (26 males; mean age: 38.87 years, range13-84years). DBE detected more lesions of bleeding than (35, 89.7%) than that of CE (28, 71.8%) (P=0.039), both CE and DBE detected bleeding in 27 patients. CE retention occurred in 4 patients and intestinal perforation occurred in 1 patient with MD diagnosed by DBE. Patients with positive findings received drug therapy or were submitted to surgical procedure (24 cases). Definite diagnosis was confirmed in 36 patients, including MD (11cases), Crohn's diseases(8 cases), Gastrointestinal mesenchymal tumors (4 cases), erosions (3 cases), multiple xanthoma (2 cases), multiple diverticulum (2 cases), ganglioneuroma (1case), single ulcer(1case), adenocarcinoma (1case), vascular abnormality(1case), intestinal duplication(1case), metastatic renal clear cell carcinoma(1 case). All the patients received a mean of 5.8 months follow-up (range 2.4-9.0 months) except one lost. 3 patients complained of slight rebleeding, respectively, and received medicine for hemostasis. Further transfusion or interventions and mortality were not reported.
CONCLUSION: For patients with acute overt-OGIB, DBE provides higher diagnostic yield than that of CE and better outcomes due to timely intervention. (**Chinese Clinical Trial Register** ChiCTR-DDT-12002465)
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Disclosure of Interest: None Declared
Keywords: balloon-assisted enteroscopy, capsule endoscopy, double-balloon enteroscopy, obscure gastrointestinal bleeding

P773 DIAGNOSTIC CONCORDANCE BETWEEN BALLOON-ASSISTED ENTEROSCOPY, VIDEOCAPSULE ENDOSCOPY AND CROSS-SECTIONAL IMAGING MODALITIES IN THE EVALUATION OF SMALL BOWEL DISEASE

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INTRODUCTION: Capsule endoscopy (CE), ballon-assisted enteroscopy (BE) and cross-sectional imaging modalities (computed tomography (CT) and magnetic resonance (MR)) are used for the detection of small bowel disease. Many studies evaluate the diagnostic yield of these procedures, however there are few reports establishing the concordance between the different methods.
AIMS&METHODS: We performed a retrospective single-center study describing the diagnostic agreement between CE, BE and CT or RM imaging in the evaluation of small bowel disease. The level of diagnostic concordance was quantified with the Cohen's kappa coefficient.
RESULTS: Ninety-nine patients (49 female, mean age 52±18 years) were submitted to 111 BE (59% antegrade procedures), performed between January 2011 and January 2013. Biopsy specimens were obtained in 44% of the procedures and endoscopic therapy was held in 20 exams. Complication rate was 0.9%, without serious adverse events. Sixty patients had been recently (<3 months) evaluated with capsule endoscopy and 29 had had cross-sectional imaging modalities (24 CT; 5 MR). The entire small bowel was examined in CE and BE, in 82 and 5 percent of the cases, respectively. Globally, in patients submitted to CE and BE, there was diagnostic agreement in 61% of cases (Kappa=0.44 – moderate). Diagnostic concordance between BE and imaging modalities was fair (Kappa=0.39).
CONCLUSION: BE is a safe diagnostic and treatment modality in small-bowel disease. BE and CE had a moderate concordance in our series. The agreement with CT and MR, in a smaller sample, was fair.
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Disclosure of Interest: None Declared
Keywords: agreement, capsule endoscopy, CT, double-balloon enteroscopy, MRI

P774 CO2-INSUFFLATION DURING SINGLE BALLOON-ENTEROSCOPY IMPROVES ORAL INTUBATION DEPTH IN PATIENTS WITH HISTORY OF ABDOMINAL SURGERY

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INTRODUCTION: The use of CO_2 as insufflation gas during endoscopic procedure has already shown advantages regarding procedure-related pain and discomfort compared to standard air-insufflation. Additionally, CO_2-insufflation leads to greater oral insertion depth during double-balloon enteroscopy. The aim of the present study was to examine whether CO_2-insufflation also leads to a reduction of abdominal pain in patients having undergone single-balloon enteroscopy (SBE) and facilitates a deeper insertion of the small bowel.
AIMS&METHODS: This study is a randomized, international multicenter trial comparing CO_2- vs. air-insufflation during SBE (ClinicalTrials.gov Identifier: NCT01524055). Patients were blinded with regard to the type of insufflation gas used. Patients' discomfort during and after the procedure were scored using a visual analogue scale.
RESULTS: 107 patients were enrolled in this study (52 in the CO_2 group and 55 in the air group). Sixty-two patients were examined via both routes, 36 only orally and 9 patients by anal approach only. In both groups, patients' characteristics were comparable (age, diagnosis, previous intestinal surgery, indication for endoscopy). The oral intubation depth was not significantly higher in the CO_2 vs. air group (254 ± 80 vs. 238 ± 55 cm, $P = 0.726$, mean ± SD). In patients with previous abdominal surgery, oral intubation depth was significantly higher in the CO_2-group compared with air (258 ± 84 vs. 192 ± 42 cm, $P < 0.05$). Via anal route, CO_2 showed no significant difference regarding intubation depth compared to standard air insufflation (86 ± 67 vs. 110 ± 68 cm, $P = 0.155$, mean ± SD). The diagnostic yield of balloon-assisted enteroscopy procedures was comparable and high for both groups (CO_2: 67 %, Air: 73 %). The procedure times and dosage of sedation did not differ between CO_2 versus air in both approaches.
Patients' pain and discomfort were significantly better in the CO_2 group at almost every questioned time point but reached only statistic significance at 1 hour after the anal examination ($P = 0.020$). No severe adverse events were observed in both groups.
CONCLUSION: This study underlines the advantage of CO_2 in balloon-assisted enteroscopy techniques, especially in patients with a history of previous abdominal surgery. The reduction of patient discomfort, especially in the anal approach, implies a general indication for the usage of CO_2 in balloon-assisted enteroscopy.
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Keywords: carbon dioxide insufflation, single-balloon enteroscopy

P775 SMALL BOWEL STRICTURE TREATMENT BY DOUBLE BALLOON ENTEROSCOPY AND REVIEW OF PUBLISHED STUDIES FOR STRICTURE DILATION WITH MODERN ENTEROSCOPY

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INTRODUCTION: Small bowel strictures may be well reached by modern enteroscopy using DBE, single balloon- or spiral enteroscopy (SBE, SpE). This study reports our experience with enteroscopic stricture treatment in comparison to 9 published studies using modern enteroscopy techniques.
AIMS&METHODS: Stricture treatment was achieved after DBE identification of one or more strictures by balloon dilation, either through the scope or through the overtube, and by steroid injection into the stricture. These results from our center were compared to published results available from nine studies (n=169 pts).
RESULTS: From 30 pts with endoscopically identified small bowel strictures, DBE balloon dilation could achieve short term remission in 22/30 pts (73%), long term remission (>12 mo) in 17/30 pts (56%), while 7pts (23%) got re-dilatations and/or steroid injection, and 6pts (20%) were referred to surgery. 2/30 pts (6%) with malignant strictures experienced perforations.
In the 9 published studies similar results (median, 25-75%) were found with a short or long term remission rate of 80% (72-95) or 71.5% (64-74) and necessity for surgery in 27% (20-38%). However, major complication rate varied up to 9% for perforation, 5% for bleeding, 4% pancreatitis and 3% for sedation related adverse events.
CONCLUSION: Small bowel stricture dilation with modern enteroscopy was currently performed in approximately 200 pts, primarily with the DBE technique. With some caution because 5-yr follow up data are scarce, it appears to be an effective treatment modality for 70% of pts, while 20-38% have still to undergo surgery because of recurrence, complex strictures or inaccessibility of the stricture for the enteroscope.
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Disclosure of Interest: None Declared
Keywords: double balloon enteroscopy , Small bowel strictures

P776 EFFICACY OF NARROW BAND IMAGING IN SINGLE BALLOON ENTEROSCOPY

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INTRODUCTION: The current technique and technology of image-enhanced endoscopy (IEE) is available to augment the detection, diagnosis and treatment of gastrointestinal lesions. The IEE techniques are applied to enhance microvascular contour and improve resolution of surface patterns and color differences. The advent of balloon-assisted enteroscopy has enabled assessment and treatment of small intestinal lesions. One of the most common diseases indicated for balloon-assisted enteroscopy is obscure gastrointestinal bleeding (OGIB). However, sometimes it is difficult to differentiate small lesions, angioectasia or clot or abrasion mark made by contact. Narrow band imaging (NBI) shows surface vessels in the mucosa as brown and deeper as green. We reported that angioectasia shows dark green colored area -which is called 'dark green sign'- contrary to abrasion mark or clot showing brown by NBI.
AIMS&METHODS: In this study, we evaluated the usefulness of NBI in single-balloon enterscopy (SBE) for angioectasia in the small intestine.Between March 2008 and October 2012, endoscopic treatment of angioectasias in small intestine was performed in 23 cases by SBE. We divided the suspected lesions into two groups, lesions with dark green sign (DG) and brown colored lesions (B) and assessed the result and efficacy of differentiation for two groups.
RESULTS: In 23 cases, 119 small lesions were detected each lesion was observed with NBI. Of 119 lesions, 61 lesions (51.3%) were DG group, while 58 lesions (48.7%) were B group. We recognized the DG group lesions as angioectasia and treated by argonplasma coagulation or clipping. We left the lesions in B group. One case had recurrent bleeding from the same lesion. Two cases had 2nd SBE for another angioectasia. We followed patients for an average of 18.3 months, and the rest of the cases didn't need further treatment.
CONCLUSION: NBI in SBE was effective for the diagnosis of angioectasia in the small intestine. IEE such as NBI could be useful for diagnosis of small intestinal diseases.
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Disclosure of Interest: None Declared
Keywords: angioectasia, image enhanced endoscopy, NBI, single-balloon enteroscopy

P777 USEFULNESS OF SINGLE-BALLOON ENTEROSCOPY FOR TREATMENT OF THE STENOSIS IN SMALL INTESTINE

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INTRODUCTION: Before the progress of balloon-assisted enteroscopy (BAE) and wireless capsule endoscopy, the stenoses of the small intestine were detected by CT or radiological enteroclysis. They were often difficult to diagnose, and surgery was selected for diagnostic therapy. BAE has enabled to make diagnosis and treat small intestinal lesions. We evaluated the efficacy of single-balloon enteroscopy (SBE) for treatment of small intestinal stenosis.
AIMS&METHODS: A total of 543 cases of SBE were performed between September 2005 and October 2012 at our center, and 60 stenotic cases of the small intestine detected by SBE were enrolled in the study. Stenosis was defined as difficulty in penetrating the enteroscope or sliding tube. Endoscopic balloon dilation (EBD) was performed to the suitable cases of benign stenosis. The indications of EBD were as follows: ①benign stenoses with the length being less than or equal to 5cm, ②strictures without deep ulcers, fistulas, or abscesses, and ③stenoses without sharp angle. Adopted cases were divided into two groups: 'CD' group with stenoses caused by Crohn's disesase, and 'non CD' group with benign stenoses caused by other factors. We assessed the first EBD success rate, restenotic rate, duration until restenosis, cumulative surgical free rate and occurrence of complications.
RESULTS: The causes of the stenosis cases included 21 Crohn's disease (CD, 47.7%), 4 postoperative stenosis (9.1%), 4 ischemic enteritis (9.1%), 6 adenocarcinoma (37.5%), 4 cases of invasion of small intestine from other carcinoma (25%), 6 malignant lymphoma (37.5%), 5 other cases (11.4%), and 10 cases of unknown etiology. Of the 60 cases, 19 were suitable for EBD therapy, and 10 cases were included in the 'CD' group while 9 cases (2 ischemic enteritis, 2 postsurgical stenoses, and 5 others) were in the 'non CD' group. The first EBD successful rate was 100% for each. Six of the 10 CD cases had restenosis, while restenosis occurred in one of nine non CD cases. The two groups had a significantly different restenotic rate ($P<0.05$). Duration until occurrence of restenosis was 11.5±4.5 months on average. The cumulative surgical free rate after EBD was 94.7% (18/19), and the observation period was almost 3 years. One case had a post-EBD bleeding, but perforation or other complications did not occur.
CONCLUSION: EBD was performed safely in most cases. The result suggests it is necessary to consider periodical SBE for stenotic lesions in the small intestine, especially in CD cases. There is a possibility that surgery can be avoided by doing EBD in cases of small intestinal stenoses.
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Disclosure of Interest: None Declared
Keywords: crohn disease, endoscopic balloon dilation, single-balloon enteroscopy, small intestinal stenosis

P778 SEDATION TECHNIQUES AND SAFETY IN DOUBLE BALLOON ENDOSCOPY – EXPERIENCE FROM A DISTRICT GENERAL HOSPITAL

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INTRODUCTION: Double balloon enteroscopy (DBE) is now used widely to examine the small bowel, using an antegrade or retrograde approach. To maximise the comfort and acceptability levels of this procedure, deep sedation using propofol is increasingly being used (as opposed to conscious sedation with benzodiazepines). Despite guidelines existing in favour of the safe use of propofol[1] in endoscopic procedures, there are still concerns about safety. As a result, propofol sedation is not in common use.
We review the data from our site with regards to safety and indicators of quality of DBE procedure.
AIMS&METHODS: Retrospective review of all DBEs performed at South Tyneside District Hospital between January 2010 and March 2013. Information reviewed; route of procedure, depth of insertion, duration of procedure, sedation used, complications. In our centre, propofol sedation is performed in the endoscopy unit, with administration of propofol and monitoring of the patient by an anaesthetist.
RESULTS: 56 DBEs have been performed on 46 patients (26 male, 20 female, median age 49.5 years (range 16-83). 29 procedures were antegrade, 24 retrograde. 13 were performed under propofol sedation, 43 under midazolam conscious sedation. No serious complications have been recorded. Depth of insertion, and duration of procedure are shown in table 1. Results shown are in the format: median (range).
Table 1.

Route	Measurement	Propofol*	Midazolam†
Antegrade	Time (mins)	50 (40-80)	48 (30-110)
	Depth (cm)	200 (75-250)	200 (75-350)
Retrograde	Time (mins)	65 (48-80)	59 (10-90)
	Depth (cm)	145 (140-150)	87.5 (10-200)

*n=13. 13 had depth recorded, 12 had time recorded. †n=43. 38 had depth recorded, 30 had time recorded
CONCLUSION: We conclude that in our centre, DBE performed under propofol sedation is safe, and non-inferior compared to midazolam sedation in terms of procedure duration and depth of insertion. It may in fact be superior with regards to depth of insertion during retrograde procedures, but numbers are too small to draw a confident conclusion.
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Keywords: double balloon enteroscopy, Safety, sedation

P779 A RETROSPECTIVE ANALYSIS OF PUSH ENTEROSCOPY IN A TEACHING HOSPITAL OVER 6 YEARS

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INTRODUCTION:
Push enteroscopy (PE) is used for the evaluation of the proximal small bowel. The diagnostic yield in gastrointestinal (GI) bleeding varies considerably from 38-75%[1]. A previous study showed that 64% of responsible lesions identified on PE were in reach of a standard gastroscope[2].
AIMS&METHODS:
The aim of our study was to analyse the PE data from Leeds and to establish the diagnostic yield, rates of endoscopic intervention and the proportion of cases where pathology was in reach of a standard gastroscope.
A retrospective analysis was conducted of all push enteroscopies performed between January 2006 and December 2011 at Leeds Teaching Hospitals Trust (LTHT). A list of all cases of PE was generated using the ADAM endoscopy software. For each case, we recorded patient demographics, indication, endoscopic findings, endoscopic management and distance from the pylorus.
RESULTS:
Over the 6 year period, a total of 135 Push enteroscopies were performed (58% female; mean age 59 years; range 19-91). The main indications were GI blood loss (61%), abnormal small bowel imaging (22%), suspected coeliac disease (5%) and assessment of crohn's disease (4%). Blood loss was either occult, in 52 patients with iron-deficiency anaemia (39%), or overt, in 30 patients with haematemesis and/or melaena (22%).
Overall an abnormality was identified in 101 cases out of 135 (75%). The diagnostic yield in the group referred with overt or occult GI blood loss was 55%. Angioectasia was by far the commonest abnormality which was seen in 69% of these cases. An ulcer (gastric, duodenal or jejunal) was found in 13%. Miscellaneous findings included small bowel tumour (4%), large hiatus hernia (4%), oesophageal varix (<1%) and haemobilia (<1%). The mean distance beyond the pylorus was 62cm (range 15 to 150cm). Lesions were within reach of standard gastroscope in 28 of the 45 (62%) with GI blood loss.
Endoscopic treatment was performed in 27% and biopsies in 41%. Argon plasma coagulation (APC) was performed in all 31 angioectasia, endoscopic clips placed in 6, adrenaline injected in 2 and polypectomy performed in 1 case of Peutz-Jeghers syndrome. There were no significant complications.
CONCLUSION:
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Gastrointestinal blood loss was the commonest indication to perform PE (61%). Significant pathology to account for the blood loss was found in 55%. Angioectasia was the commonest pathology accounting for 69% of abnormal findings. Lesions were in reach of a standard gastroscope in 62% of cases, emphasising the importance of a second look gastroscopy prior to performing PE.
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Disclosure of Interest: None Declared
Keywords: diagnostic yield, push enteroscopy

P780 ENDOSCOPIC MUCOSAL RESECTION FOR JEJUNAL POLYPS USING DOUBLE-BALLOON ENTEROSCOPY (DBE)

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INTRODUCTION: Endoscopic mucosal resection (EMR) is now a well-accepted and practiced method for treating esophageal, gastric and colon polyps and early carcinomas. Because the small bowel is less accesible and has a thinner wall as compared to other luminal parts of the GI tract, the experience using EMR here is very limited. Indeed, there is only one case report describing EMR of the jejunum in the literature.
AIMS&METHODS: To evaluate the feasibility and utility of double balloon enteroscopy assisted mucosal resection (EMR) in patients with familial and non-familial jejunal polyps.

Thirty-eight patients with jejunal polyp(s) (FAP, n= 14, PJS, n= 10, sporadic adenomas, n= 3, inflammatory pseudopolyps, n=3, lipomas, n= 4) undergoing DBE-assisted resection of their lesions at the University of Magdeburg Medical Center, Marienhospital Bottrop adn University of Alabama at Brimingham, USA between June 2007 and January 2013 were included and their data recorded in a prospectively collected database. For this case study we only selected patients undergoing EMR (n=9). Patients undergoing standard polypectomy were excluded.Mucosectomy technique: Before resecting the jejunal polyp the mucosal pit pattern analysis was performed using high definition white light and chromoendoscopy methods (standard and virtual chromoendoscopy). All lesions were resected using previous submcuosal injection.

RESULTS: : Nine (9) patients underwent DBE assisted jejunal EMR. Median age of patients was 42 years (range 24-62 years), male:female ratio 1.5:1. DBE was done through the antegrade (i.e. oral) route in all patients. Four patients had FAP; three had Peuth-Jeghers syndrome, one had a sporadic adenoma and one had a bleeding jejunal polyp, which on histological examination turned out to be lipoma. 4/9 underwent piece-meal EMR. Post EMR or DBE complications including perforation, bleeding or pancreatitis were not observed in any of these patients.

CONCLUSION: This is the first and largest study so far presenting the technique, feasibility and outocmes of EMR of the small bowel. EMR of the jejunum is feasible and safe during DBE.

Disclosure of Interest: None Declared

Keywords: double balloon enteroscopy, Small Bowel, small bowel polyps

P781 CLINICOPATHOLOGIC FEATURES OF SMALL BOWEL OBSTRUCTION: COMPARISON BETWEEN FINDINGS OF DOUBLE-BALLOON ENDOSCOPY AND ABDOMINAL CT SCAN

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INTRODUCTION: Small bowel obstruction (SBO) is a commonly encountered pathologic condition and is caused by a variety of etiologies. In case of strangulated bowel, emergent surgery is required for the lifesaving without preoperative diagnosis of etiology. However, differentiating the etiologies of SBO is critical to proper management of patients and to improve clinical outcomes. Abdominal CT scan with various protocols is a useful tool in the initial diagnosis and assessment of patients with SBO and widely performed especially in the emergent condition. The recently developed balloon-assisted enteroscopy system provides the capability of the exact diagnosis of small bowel diseases including malignancy. So, we evaluate the clinicopathologic features of SBO with the comparison between findings of double-balloon enteroscopy (DBE) and abdominal CT scan.

AIMS&METHODS: We retrospectively analyzed 22 consecutive cases between January 2009 and November 2012 for investigation of SBO without bowel strangulation. Both DBE and Abdominal CT scan were performed to all patients to confirm SBO. Pathologic, DBE and abdominal CT findings were collected and analyzed.

RESULTS: Total 23 DBE were performed in 22 patients (14 male, 8 female; mean age 49±25.3yrs). Antergrade approach was done in 12 patients while retrograde and both approaches were performed in 6 and 4 cases respectively. Abnormal findings were detected at DBE in 18 cases (81.8%). The most common pathologic findings were small bowel tumors (11 cases, 50 %) such as lymphoma (5), metastatic cancer (2), Peutz-jegher polyp(2), lipomatosis (1) and GIST (1). Strictures were found at seven cases; Crohn's disease (3), NSAID induced stricture (3) and idiopathic (1). We analyzed DBE findings according to abdominal CT findings. Small-bowel intussusceptions on CT were found at seven cases (31.8%). Four cases (57.2%) were small- bowel tumors; lymphoma (2), lipoma (1) and Peutz-jegher polyp (1) and no abnormal findings at DBE had shown in three cases (42.8%). Appearances of eccentric long-segment of small bowel on CT were found at three cases. All cases were small bowel tumors; two cases were lymphoma and metastatic cancer was found in one case. Normal findings on CT were found in two cases of stricture (Crohn's diseases, lymphoma).

CONCLUSION: DBE is a valuable diagnostic method for detecting the etiologies of SBO without bowel strangulation. Preoperative diagnosis of SBO with DBE might be essential for decision and change the treatment modalities of the patients with SBO.

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Disclosure of Interest: None Declared

Keywords: double balloon enteroscopy, small bowel enteroscopy, small bowel obstruction

P782 INDICATIONS, DIAGNOSTIC YIELD, THERAPEUTIC IMPACTS AND COMPLICATIONS OF BALLOON-ASSISTED ENTEROSCOPY OVER THE FIRST DECADE OF ITS USE IN KOREA: RETROSPECTIVE MULTICENTER STUDY

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INTRODUCTION: Since double-balloon enteroscopy was introduced in 2004 in Korea, balloon-assisted enteroscopy (BAE) can be used to explore a large part of the small bowel. Over the past decade, the BAE has been performed for the diagnosis and management of patients with suspected and established small-bowel diseases. However, technical difficulty and reimbursement policy by insurance system can affect the selectivity for BAE. We performed a retrospective study to assess indications, diagnostic yield, therapeutic impacts and complications of BAE during last 9 years and investigate the changes of them between different time periods in Korea.

AIMS&METHODS: The Small Intestine Research Group of the KASID constructed the multicenter retrospective BAE registry and 9 centers registered a consecutive of 1108 BAE cases from initial case to latest case performed their hospital. The registry includes the indications, the enteroscopic finding, and clinical outcomes of BAE. To evaluate the changes of the practice pattern of BAE over time, we compared in indication, diagnostic yield, and complications of BAE divided by the early stage (period of initial half: Jan. 2004–Jul. 2008, n=543 procedures) and late stage (period of later half: Aug. 2008–Dec. 2012, n=565 procedures).

RESULTS: The most common indication of BAE was obscure GI bleeding (50.9%, 556/1108). BAE to assess unexplained GI symptoms was more common in early stage (18.8% vs. 9.7%), whereas BAE to confirm the abnormal finding of imaging modality was more common in late stage (9.4% vs. 18.8%, $p<.001$). The diagnostic yields of BAE was 77.3% (838/1084), which did not showed a significant difference between early and late stage (72.0% vs. 76.6%, p=.085). Therapeutic intervention was performed during 213 BAE procedures (22.8%). The BAE-associated complications were occurred in 1.1% (12/1108), which was decreased significantly in late stage compared to early stage (1.8% vs. 0.4%, p=.020).

CONCLUSION: BAE is safe and useful tool for the diagnosis and treatment for small-bowel pathology. Over the first decade of its use in Korea, the usage of BAE for the exploration of symptoms appears to be replaced by other image modalities and the complications associated BAE are decreased.

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Disclosure of Interest: None Declared

Keywords: Complications, diagnostic yield, enteroscopy, indications

P783 EMERGENT SINGLE-BALLOON ENTEROSCOPY IN OVERT OBSCURE GASTROINTESTINAL BLEEDING - EFFICACY AND SAFETY

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INTRODUCTION: Endoscopic examination of the small bowel has dramatically improved with the advent of balloon-assisted enteroscopy (BAE) allowing both diagnostic and therapeutic procedures. There are few data concerning emergent BAE for Overt Obscure Gastrointestinal Bleeding (OGIB).

AIMS&METHODS: AIM: Evaluate the use of emergent BAE in active-overt OGIB and assess its impact on diagnosis and treatment. Furthermore, compare their effectiveness in active vs. inactive overt OGIB.

MATERIAL&METHOD: Retrospective analysis of all BAE performed for active-overt OGIB in our department. Demographics, clinical and endoscopic data were collected, as well as therapeutic procedures and complications. Single-balloon-enteroscopy (SBE) was used in all examinations. Emergent SBE was defined when performed for active-overt OGIB within a 24-hour period after confirmation of GI bleeding.

RESULTS: A total of 126 SBE were performed in 3 years, 99 for evaluation of the small intestine, of which 60.6% (60/99) for OGIB. Of these, 88.3% (53/60) of the examinations were conducted by overt OGIB (42 patients, 30 men, mean age 65.3 years) who were the object of our study; the remaining by occult OGIB. In the context of overt OGIB, there were 15 emergent SBE for active-overt OGIB (15/53). In these, the origin of small bowel bleeding was diagnosed in 15: angiodysplasia (n=5), erosion/ulceration (n=3), tumors (GIST 3, neuroendocrine 1), eroded polyps (n=2) and bleeding diverticulum (n=1). Hemostatic therapy performed: argon plasma coagulation - 5, adrenaline and hemostatic clips - 3 and polypectomy - 2. There were no complications regarding the examination or endoscopic treatment. Bleeding recurrence occurred in one (angiodysplasia, additional coagulation session needed). In SBE for inactive overt OGIB (38/53), the etiology detection rate was 65.7% (25/37). In comparative analysis between active vs inactive overt OGIB, bleeding etiology identification rate was significantly higher in active-overt OGIB ($\chi 2$ $p<0.05$).

CONCLUSION: The study revealed the important role of emergent enteroscopy in the diagnosis and treatment of active-overt OGIB, being a safe and effective tool.

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Disclosure of Interest: None Declared

Keywords: emergent enteroscopy, obscure gastrointestinal bleeding

P784 LEWIS SCORE IN SMALL-BOWEL CAPSULE ENDOSCOPY AND FAECAL CALPROTECTIN; AS GOOD AS IT GETS?

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INTRODUCTION: Lewis Score (LS) is one of the 2 inflammatory scores in small-bowel capsule endoscopy (SBCE). In a previous paper [1], we showed that LS shows only a moderate correlation with faecal calprotectin (FC) levels. The amount of calprotectin in faeces is directly proportional to the granulocyte migration to the gut mucosa and cell shedding in the intestinal lumen.

Hence, FC is considered a reliable, almost a 'gold standard', marker of gastrointestinal inflammation. Interestingly, both LS and FC are not disease-specific. One of the major factors that could potentially influence the correlation between FC and LS is the time lag from stool collection and FC measurement to SBCE [2].

AIMS&METHODS: We aim to assess the correlation between the FC and LS from a cohort of patients who underwent SBCE within 7 days from a FC measurement. A two-centre retrospective study; [Edinburgh (RIE) & Malmo (MUH)].

Methods: SBCE and biochemistry database cross check; SBCE videos of patients who underwent SBCE no later than 7 days from a FC measurement were reviewed for LS calculation. By convention, FC $<20\mu$g/g was transform to 0. Categorical data are described as mean±SD or median(IQR). FC/LS correlation was calculated using Kendall's tau-b rank coefficient. Furthermore, correlations of FC with each of the parameters/descriptors of LS were calculated; those with the higher tau-b values were selected and a second correlation was attempted between a "simplified LS" and FC.

RESULTS: 74 patients (55 RIE[§]/19 MUH; 20M/54F; mean age: 42±18.19) had a FC measurement within 7 days of their SBCE (median: 1.5; IQR: 5). 26 SBCE were performed with MiroCam® and 48 with PillCam®. 69 (93.24%) SBCE were complete to caecum; 2 capsules were delivered endoscopically in the duodenum. Median FC level was 127.5 (IQR:280); median LS was 135 (IQR:450). Kendall's correlation between FC and LS was –as previously shown[1]– only moderate (taub: 0.34). In detailed correlation sub-analysis, the strongest coefficients were between FC and summative villous score i.e. tertile 1+2+3 , summative ulcer score (tertile 1+2+3, but only ulcer number & size) and regular stenosis score at 0.21, 0.34 and 0.3, respectively. When the rank coefficient between the new summative "simplified LS" and FC was calculated, their correlation was at similar levels; tau-b: 0.33.

[§]**part of this cohort of patients presented previously (ref 1)**.

CONCLUSION: LS shows only moderate correlation to FC. This seems to be an inherit limitation of LS and consideration should be given to the creation of new, composite inflammation score/index for SBCE.

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Disclosure of Interest: None Declared

Keywords: calprotectin, capsule endoscopy, correlation, inflammatory index, Lewis score

P785 REVISITING THE "MASS OR BULGE" QUESTION IN CAPSULE ENDOSCOPY; PRELIMINARY RESULTS OF 3D SOFTWARE APPLICATION

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INTRODUCTION: Submucosal masses (SM) and innocent mucosal bulges (MB) often look similar on small-bowel capsule endoscopy (SBCE) [1]. Differentiating them is often a challenging task, even for experienced SBCE readers. Recently, software algorithms that enable three-dimensional (3D) reconstruction in SBCE have become available [2].

AIMS&METHODS: The aim of this study was to explore whether the application of such 3D reconstruction software helps readers of difference experience level in distinguishing SM from MB. 24 de-identified, short SBCE video clips containing either SM (5) or MB (19) were selected. In all cases, diagnosis (SM or MB) was confirmed by a reference standard (RS) (CT-enterography and/or device-assisted enteroscopy and/or surgery). Each video clip was reconstructed in 3D by means of a software developed in Mathworks©Matlab. For the evaluation process, a Matlab®program with user interface was devised (**fig. 1**). Two SBCE readers groups were involved in the evaluation: a group of SBCE experts (n=3; all > 1,000 SBCE reviews), and a group of novice readers (n=3; all < 5 SBCE reviews). All readers reviewed, blind to others and in a random order, first the standard 2D video clips and then (5-7 days later) the combined 2D+3D video clips. For each case, the diagnosis (SM or MB) reached after 2D and 2D+3D review -by each group- was compared with that of the RS. Diagnostic accuracy and precision were calculated. Inter-observer agreement (using the Randolph's free-marginal multirater *kappa*; *K*) for each group and each reviewing session was also calculated [3].

RESULTS: In 2D review, the diagnostic accuracy/precision of experts and novices were 0.87/0.65 and 0.79/0.5, respectively. In combined 2D+3D review, the diagnostic accuracy/precision for experts and novices were 0.81/0.52 and 0.87/0.79, respectively. In 2D review, the inter-observer agreement (*K*) of experts and novices was 0.78 and 0.44, respectively. In 2D+3D review, the *K* value for experts and novices was 0.5 and 0.56, respectively.

When false negative/true positive rate (FN/TP) was examined in 2D review, results for experts and novices were 2/13 and 4/11, respectively. In 2D+3D review, relevant results for experts and novices were 0/15 and 6/11, respectively.

Limitations: low number of video clips; high number of MB, as compared with SM included.

CONCLUSION: The application of 3D reconstruction software improves, although not significantly, the capability of novice SBCE readers in distinguishes MsM from ImB. Its integration in training SBCE videos should be considered.

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3. Online Kappa Calculator, available from: *http://justusrandolph.net/kappa/*

Disclosure of Interest: None Declared

Keywords: capsule endoscopy, mucosal bulge, reconstruction software, submucosal mass, three-dimensional

P787 THE ROLE OF TRANSNASAL CAPSULE ESOPHAGOSCOPE (E.G SCAN) FOR THE PREDICTION OF HIGH RISK ENDOSCOPIC LESIONS IN PATIENTS WITH UPPER GI BLEEDING: A PILOT TRIAL OF FEASIBILITY, SAFETY, AND UTILITY.

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INTRODUCTION: The optimal timing of urgent endoscopy (within 24 hours) for patients with upper GI bleeding (UGIB) remains controversial. Emergency endoscopy (EE) (within 4 hours) is indicated in patients with high risk laseions (Forrest I-IIA), but risk stratification (triage) based on only the clinical criteria can be insufficient to properly select these patients. A novel disposable transnasal capsule esophagoscope, the E.G.Scan (EGSC) allows direct visualization of the esophageal and gastric content.

AIMS&METHODS: The **aim** of the present study was to determine whether the application of EGSC in patients with acute UGIB could be useful to improve current pre-endoscopic risk stratification.

Patients and methods: We prospectively investigated 22 patients admitted with UGIB into our emergency department. UGIB was defined as a history of vomiting fresh or altered blood with or without melaena in the preceding 7 days. After hemodynamic stabilization, both nasogastric tube aspiration (NGA) and EGSC obtained before EE. The first generation EGSC system (Intromedic) was applied successfully without complications in all patients with a disposable ultrathin transnasal probe with camera capsule at the tip. Esophageal and gastric content was defined as clear, coffee ground material and bloody. Endoscopic findings were defined as high risk (HRL) (Forrest I, IIA-B) and low risk (LRL) (Forrest IIC, III) lesions. Finally results of NGA and EGSC were compared to the diagnosis EE.

RESULTS: In all but one patient there was an excellent correlation in the assessment of esophageal and gastric content between the EGSC and EE, in contrast in 8 out of 22 patients NGA and endoscopy demonstrated discordant results. Ongoing bleeding (bloody content) was demonstrated in 5 out of 6 patients with EGSC. More importantly, compared to EE Forrest HRL and LRL were differentiated with EGSC better than with NGA: PPV: 78% vs. 65%,; NPV: 87% vs. 100%, sensitivity: 78% vs. 100%, specificity: 85% vs. 46% and accuracy: 82% vs. 68%, respectively. 100% of patients with bleeding esophageal varices were also identified on EGSC.

CONCLUSION: EGSC is feasible, safe and valuable method to assess gastric and esophageal content in the emergency room setting. Our pilot study demonstrated that EGSC can be useful to predict high-risk endoscopic lesions in patients with UGIB. Further, randomized prospective study is needed to determine the diagnostic value of EGSC as to able to identify patients who would benefit from EE. The study was supported by Intromedic Co.

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Keywords: capsule endoscopy, Esophagus, upper gastrointestinal bleeding

P788 REPEAT VIDEO CAPSULE ENDOSCOPY (VCE)- IS IT WORTH IT?

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INTRODUCTION: Few studies have reported on the yield of repeat capsule endoscopy (CE) in the same patient and data regarding this diagnostic strategy are limited.[1,2] The aims of this work were to assess the indications for repeat capsule and to determine the diagnostic yield of repeat capsule in our trust.

AIMS&METHODS: A retrospective review of all patients who underwent CE at South Tyneside District Hospital between August 2004 and October 2012 was conducted. Patients who underwent a repeat CE were identified and divided into one of four subgroups. Findings were classified as positive or negative; positive findings were taken as presence on report of ulcers, tumours, strictures, polyps, blood or angioectasia.

RESULTS: A total of 1083 studies were performed, 83 were repeat studies. 7 patients were noted to have greater than 2 repeats.

Indications:

- Group 1 Gastric retention or technical failure (N=16)
- Group 2 Surveillance (N=7)
- Group 3 Poor views (as commented on by reporting physician on report) or incomplete (not seen to enter the colon) on initial study (N=31)

- Group 4 Ongoing symptoms/ assessment of disease extent/ unclear findings on initial VCE (N=36) (7 cases are reported in both group 3 and 4)
Yield: Overall yield, excluding gastric retention was 38% for the first study and 46% for 2nd study, of those with an initial negative study (42 patients), 21% of these had a positive repeat. (those with poor views had been given bowel preparation, those with an incomplete capsule study had a capsule recording time of 8-9 hours on both studies).
Positive findings:

Group	Positive findings 1st study	Positive findings 2nd study
1	N/A	5/16 (31%)
2	4/7 (57%)	4/7 (57%)
3	3/31 (10%)	10/31 (32%)
4	16/36 (44%)	17/36 (47%)

Subgroup analysis group 4:
- Ongoing symptoms with consistent with ?Crohn's or known Crohn's the yield remains the same on 1st and 2nd capsule 4/9 (44%).
- Ongoing IDA/ GI bleeding show an increased yield with 8/17 (47%) having a positive 1st study and 10/17 (59%) a positive 2nd study.
21 had a repeat despite a positive 1st study (excluding surveillance), 71% had positive repeat with resulting change in management in 73%. 9/15 done for ongoing symptoms, 6/15 for incomplete/ poor views.
CONCLUSION: Limited data exist regarding the yield of repeat CE, it is suggested by the literature that yield of a repeat study is better in those with GI bleeding/ anaemia. Our results suggest that the group with the highest yield (3 fold increase) on repeat are those with poor views or an incomplete initial study. There is an improvement in yield with 2nd study for those with ongoing symptoms of IDA or GI bleeding in keeping with previous literature.
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Keywords: capsule endoscopy, repeat procedure

P789 SAFETY OF OMOM CAPSULE ENDOSCOPY IN PATIENTS WITH PACEMAKERS AND IMPLANTABLE CARDIAC DEFIBRILLATORS: AN "IN VIVO" ELECTROPHYSIOLOGICAL STUDY.

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INTRODUCTION: The role of capsule endoscopy (CE) in small bowel investigation is well established. Once swallowed by the patient, capsule transmits images from the gut to an external recorder over a digital radiofrequency communication channel. Potential electromagnetic interferences with electronic cardiac devices (CD) have been postulated, so the manufacturers consider their presence as a contraindication for CE. Whereas safety data on the use of Given SB capsule in patients with pacemakers (PM) and automatic implantable cardiac defibrillators (AICD) are available, there are no studies on the OMOM capsule in this field.
AIMS&METHODS: We report the results of the first electrophysiological "in vivo" study about the use of OMOM capsule system (Wuhan Zhongxin Medical Instrument Co.) in 8 consecutive patients with CD prospectively evaluated over a 9-months period. Capsule ingestion was performed in the morning after a overnight fast and bowel preparation (2L of polyethylene glycol solution the day before). A full technical check of CD was performed before and after CE. During CE patients were continuously monitored with cardiac telemetry, performed in a hospital setting.
Table: P789

Patient CD		1 AICD Medtronic Protecta	2 PM Medtronic Advisa	3 PM Boston Sc. Altrua	4 PM Medtronic Advisa	5 AICD St. Jude Med. Atlas HF	6 PM St. Jude Med. Accent	7 AICD Boston Sc. Cognis	8 PM Medtronic Advisa
Results during CE exam	Changes in device parameters	NO	NO	NO	NO	NO	NO	NO	NO
	Inappropriate Shocks	NO	NO	NO	NO	NO	NO	NO	NO
	Inappropriate anti-tachycardia therapy	NO	NO	NO	NO	NO	NO	NO	NO
	Inappropriate Sensing	NO	NO	NO	NO	NO	NO	NO	NO
	Inappropriate Pacing	NO	NO	NO	NO	NO	NO	NO	NO
	Noise Detected	NO	NO	NO	NO	NO	NO	NO	NO
	Device Reset	NO	NO	NO	NO	NO	NO	NO	NO
	Programmation Changes	NO	NO	NO	NO	NO	NO	NO	NO
	Permanent Electrical Damages	NO	NO	NO	NO	NO	NO	NO	NO

RESULTS: In 7 cases the indication for CE was obscure gastrointestinal bleeding (OGIB) and intestinal polyposis (IP) in one. Mean age was 73 years (range 56-83); all the patients were males. CD parameters and results of recordings are reported in the table.
Capsule reached ileo-cecal valve in 6 cases. No complications related to capsule transit were observed. No technical problems related to imagine transmission were recorded. Causes of OGIB were found in 57,1% of cases. CE in IP patient was normal. No CD malfunction nor interference in sensing or pacing were recorded; no malfunction of CE caused by CD was registered.
CONCLUSION: Our results suggest that OMOM capsule can be safely performed in patients with different types of CD.
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Disclosure of Interest: None Declared
Keywords: capsule endoscopy, Electromagnetic interference, Implantable cardiac devices, OMOM capsule

P790 KINETICS OF COLON CAPSULE ENDOSCOPY: PILOT STUDY WITH PRUCALOPRIDE.

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INTRODUCTION: Up until now, the use of colon capsule endoscopy (CCE) has been limited by the inabilities to achieve a complete examination. A pilot study was conducted to determine the efficacy of a new preparation based on associating Prucalopride (Resolor) and polyethylene glycol plus ascorbic acid (Moviprep). Prucalopride is a highly selective serotonin 5HT4 receptor agonist which stimulate the release of acetylcholine necessary for smooth bowel muscle contraction and therefore peristalsis. After observing its benefits on the treatment for constipation, we believe that Prucalopride could be useful in the preparation of colon capsule endoscopy, speeding up intestinal transit and therefore making the examination shorter, increasing the excretion rate. This article presents the results obtained in terms of transit times, total examination time and expulsion rates.
AIMS&METHODS: Pilot study with 40 patients (cases) with the new preparation compared with 40 control patients with the standard preparation (PEG/ Fosfosoda/). Each video is read by two researchers.
Preparation protocol: - Two days of residue-free diet - Day before the test, liquid diet - Resolor 2 mg, 1 on each day of the diet and 2 on the examination day - Moviprep, 1 liter in the evening prior to the examination and 1 liter in the morning of the examination – Then 2 boosters of half a liter each in alarms 1 and 2.
RESULTS: A cohort with 32 men and 48 women, mean age of 53.3 years old (10-90). Expulsion rate over time of 87.5% in the cases with respect to 67.5% in the controls (p=0.188). The mean gastric transit time (75 vs. 49.5 minutes; p=0.12), intestinal transit time (81.4 vs. 42.4 minutes; p=0.001) and colon transit time (262 vs. 271.3 minutes; p=0.89) were shorten.
CONCLUSION: The higher excretion rate as well as the shortened gastric and intestinal transits, without modifying the colon transit, with the new preparation (Prucalopride+Polyethylene glycol plus ascorbic acid), allow conducting a higher quality study of the colon over time and with less adverse effects and better tolerance as a result of excluding sodium phosphate.
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This procedure may be considered as an alternative, particularly for patients in whom sodium phosphate-based preparations are contraindicated.

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Disclosure of Interest: None Declared
Keywords: kinetic, prucalopride, video capsule

P791 PATIENTS PERCEPTION OF COLONOSCOPY: ASTONISHING REASONS FOR COLON CAPSULE ENDOSCOPY PREFERENCE

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INTRODUCTION: Colonoscopy is considered to be the gold standard for colon evaluation and screening for colorectal cancer (CRCA). Classical colonoscopy (CC) is an invasive method with an unfavourable reputation amongst patients which may be a reason for noncompliance with CRCA screening programs. Colon capsule endoscopy (CCE) is an innovative non-invasive technique which has gained patients interest in CRCA screening despite the fact of being very costly.

AIMS&METHODS: The aim of this prospective, multicentric study was to assess reasons for preference for CCE over CC. The data from all consecutive patients scheduled to undergo CCE were obtained using a questionnaire.

RESULTS: From December 2010 to October 2012 one hundred patients (68 men, 32 women, average age 52 years) were included in the study. Seventy eight (78%) patients had university education and 20 patients (20%) were high school graduates. Seventy nine (79%) were senior managers with at least 10 or more employees. Sixty five (65%) had their salary at least four times the nation's avarage income. The main reasons of CCE preference were concerns about a patient's privacy and embarrassment (38 patients, 30 males, 8 females), concerns of pain (35 patients, 18 males, 17 females) , fear of a loss of discernment (20 patients, 15 males, 5 females). Forty six (46%) patients had undergone CC in the past. In this subgroup, privacy issue was main reason for 33 (71%) patients and pain for 13 (28%) patients. Forty two patients (42%) would never undergo a screening CC even though 19 (45%) of them had a positive family history.

CONCLUSION: The main reason for CCE preference over CC was mental discomfort and fear of embarrassment during CC, rather than concerns of pain. The results imply a need of improvement of our CC management.

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Disclosure of Interest: None Declared
Keywords: Capsule colonoscopy, preference

P792 URGENT CAPSULE ENDOSCOPY FOR BLEEDING SITE LOCALIZATION & LESION DIAGNOSIS OF PATIENTS WITH SEVERE HEMATOCHEZIA

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INTRODUCTION: There is no agreement about the best strategy for diagnosis of patients presenting with severe hematochezia.

AIMS&METHODS: For patients with severe hematochezia, our aims were: 1) to determine diagnostic yield of urgent capsule endoscopy (UCE) for bleeding site localization in the gut & for etiologic or lesion diagnosis & 2) to compare results with red blood cell (RBC) scan &/or angiogram (eg. standard angiography, CT, or MR angiogram) & with endoscopy (colonoscopy, upper endoscopy). We retrospectively reviewed charts of consecutive patients presenting with severe hematochezia, & without a recent history of hematemesis, melena,& a negative NG aspirate who underwent a UCE within 12 hours of GI consultation at our center. Demographics, clinical & laboratory data, results of RBC scanning, angiogram, UCE, endoscopies, & GI surgery were recorded. With the combination of endoscopic & surgical results as gold standard for lesion location & etiologic diagnosis, the diagnostic yield, sensitivity (Se) and specificity (Sp) of UCE were computed.

RESULTS: 15 patients (12M/3F, mean age [±SD] 57.9 years [±24.0]) had UCE for severe hematochezia. 13 (87%) patients had a final etiologic diagnosis: 2 colon angiodysplasia, 3 definitive diverticulosis, 3 presumptive diverticulosis, 3 Meckel's diverticulum, 1 jejunal Dieulafoy's lesion and 1 ileal tumor. CE was delayed in the stomach in 2 patients & failed to pass the pylorus in 1. All other patients had visualization of the entire small bowel & 47% had some colon visualization. All patients had endoscopies. 6 patients underwent RBC scan &/or angiogram. UCE had a higher diagnostic yield than RBC scan or angiography for bleeding site localization: 67% vs. 33%. But these techniques often failed to determine an etiologic or lesion diagnosis. Overall diagnostic yield of UCE for bleeding site localization in the gut was 67%. But for etiologic diagnosis, the yield of UCE was only 20% vs. 53% for endoscopy. The Se and Sp of CE were 80% and 60% respectively for bleeding site localization. The Se and Sp of CE were 15% and 50% respectively for lesion diagnosis.

CONCLUSION: In patients hospitalized for severe hematochezia and no sign of upper GI bleeding, the diagnostic yield of CE for localization of the bleeding site (67%) was higher than for RBC and/or angiogram, but the ability to make an etiologic diagnosis was low with all these procedures. The overall rate of bleeding site localization with UCE was 67%. These results suggest a potential important role for UCE as the initial approach for lesion localization in patients with severe hematochezia.

Disclosure of Interest: None Declared
Keywords: Bleeding, capsule endoscopy, colon

P793 UTILITY OF COLON CAPSULE ENDOSCOPY AFTER AN INCOMPLETE COLONOSCOPY. MULTICENTRIC SPANISH STUDY

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INTRODUCTION: Between 5-10% of colonoscopies are incomplete for a variety of reasons. With this in mind, it was proposed to complete the visualization of unexplored segments of the colon with Pillcam® Colon2® n capsule endoscopy (CCE) and to assess the number and type of lesions identified, improvement of diagnostic yield and modification of therapeutic interventions.

AIMS&METHODS: After ethics committee approval of all 10 participant hospitals, patients were accrued to the study from November 2010 to April 2013. Patients with incomplete colonoscopy due to technical reasons which were not contraindicated to the capsule procedure were included in the study.

RESULTS: 96 patients were enrolled, 68 women and 28 men, median age of 50 (22-86). The most common cause for incomplete colonoscopy was a repeated loop that could not be overcome with standard manoeuvres. Complete CCE visualization was obtained in 69 patients (72%). Of the 27 patients in which the capsule did not reach the hemorrhoidal plexus, CCE visualised the colonic segments not explored with previous colonoscopy in 20, so the combined approach (CCE plus colonoscopy) permited a completed visualization of colonic mucosa in 93% of the patients.

CCE was incomplete because of capsule delay in the stomach and small bowel in 4 cases, unsatisfactory bowel preparation in 3 and technical failure in 2 cases.

CEC revealed new lesions in 58 patients (60%). Polyps were the most frequent finding (41 patients), followed by diverticulae (8 patients); neoplasia (2 patients), and solitary colonic ulcers (2 patients) In 43 of these patients (45%) the new findings modified the therapeutic approach, which included a new trial of colonoscopy for polyp resection or surgery in case of colon neoplasia. Minor changes in therapeutics were made when colonic diverticulae were found.

CONCLUSION: CCE is potentially a useful diagnostic tool in the setting of incomplete colonoscopy, revealing a significant number of lesions in unexplored colonic mucosa. Results may produce favorable changes in the therapeutic approach for these patients.
The authors declare no confict of interest.
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Disclosure of Interest: None Declared
Keywords: colon capsule endoscopy, utility

P794 CAPSULE ENTEROSCOPY IN OBSCURE GASTROINTESTINAL BLEEDING: THE PARAMOUNT IMPORTANCE OF ANTITHROMBOTICS

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INTRODUCTION: Capsule enteroscopy (CE) plays a decisive role in the obscure gastrointestinal bleeding (OGIB) diagnosis. Antiplatelet and anticoagulant drugs may result in an increased digestive bleeding risk, both in patients with pre-existent lesions as well as through mucosal aggression.
AIMS&METHODS: Our aim was to analyze and correlate these drugs with potential bleeding lesions found in CE.
Unicentric retrospective study including 219 consecutive and complete CE performed in 5 years for OGIB diagnosis. The lesions observed during the CE were classified as P0 (no potential for bleeding), P1 (uncertain potential for bleeding) and P2 (high potential for bleeding). We also assessed antiplatelet and anticoagulant drug usage during the 30 days previous to the CE. Statistical analysis was performed with SPSS 17.0.
RESULTS: OGIB had a visible presentation in 17,4% of the patients. Approximately one quarter of the patients was taking antithrombotics (21,5% were on antiplatelet and 6,4% on anticoagulant drugs). Angiectasias (18%), erosions (15%) and ulcers (5%) were the most frequently observed lesions in the CE. Patients presenting with occult OGIB used antithrombotics significantly more often than the ones with visible OGIB (p=0,049).
We found no significant correlation between antithrombotics and P1 or P2 lesion findings in CE. However, when a sub-analysis was performed, there was a significant correlation between anticoagulant drugs and a higher incidence for P1-P2 lesions in the small bowel (p=0,045).
CONCLUSION: Antithrombotic drugs, whose usage was very frequent in patients presenting with OGIB, were significantly associated with an occult bleeding presentation.
Both uncertain bleeding potential (P1) and high bleeding potential (P2) small bowel lesions were more frequently found in the capsule enteroscopy when the patient was on anticoagulant drugs.
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Disclosure of Interest: None Declared
Keywords: antiplatelets, antithrombotics, capsule endoscopy, obscure gastrointestinal bleeding

P795 COMPARISON OF DIFFERENT COLONIC PREPARATION PROTOCOLS DURING COLONIC CAPSULE ENDOSCOPY BASED ON QUANTITATIVE COMPUTER ANALYSIS OF MUCOSAL VISIBILTY – A RANDOMIZED PROSPECTIVE STUDY

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INTRODUCTION: Development of new colonic preparation protocol (CPP) is needed to improve the overall accuracy of colon capsule endoscopy (CCE) and to diminish side effects. Recently we developed and validated a quantitative score of colonic cleanliness that was derived from the spectral color analysis of the CCE images.
AIMS&METHODS: The aim of the present prospective, randomized study was to quantitatively compare different CPPs during CCE. A quantitative assessment of colonic cleanliness and mucosal visibility was developed based on computer spectral analysis of red color intensities in the color bar (CB) of Rapid Reader with the software Colors ®™. The feasibility of this score was retrospectively tested in 28 CCE studies with the original CPP as we published earlier and these results were served now as controls. A prospective, randomized study was now conducted in 30 consecutive patients undergone CCE. The first-generation PillCam GIVEN CCE was applied. 16 patients were prepared with Fleet phospho-soda (FPS group) and a split dose of 3L of PEG, and the remaining 14 patients were prepared with Picoprep (sodium picosulfate) (SPS group) and a split dose of 3L of PEG. The red color intensity (RCI=R*R/G*B) of the total spectral color from the CB representing the whole colonic section was measured and then compared.
RESULTS: Anal capsule expulsion and complete CCE study was successfully accomplished 13 out of 14 (93%) in the SPS group and 13 out of 16 (81%) in the FPS group versus 19 out of 28 (68%) in the controls ($p < 0.05$). More importantly RCI was significantly higher in the SPS group than in the controls (5.1+1.1 vs. 4.4+0.6; p=0.015), whereas FPS group did not differ significantly from the controls (4.5+0.8 vs. 4.4+0.6; p=0.14). SPS group had significantly faster colonic capsule transit than the FPS group and the controls (157 min vs. 245 min vs. 259 min; p=0.047).
CONCLUSION: Quantitative assessment of colonic mucosal visibility with RCI is a useful method to compare different CPPs during CCE. Preparation and booster during CCE with SPS combined with split dose of PEG is superior to FPS based colonic preparation in respect of mucosal visibility, colonic transit time and anal capsule expulsion. Routine application of SPS (Picoprep) in the bowel preparation before CCE may further improve the diagnostic yield and patient acceptance with no or only minimal side effects.
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Disclosure of Interest: None Declared
Keywords: Capsule colonoscopy, capsule endoscopy, colonic, colonic cleanliness, COLONIC PREPARATION, sodium picosulfate

TUESDAY, OCTOBER 15, 2013 9:00-17:00
SURGERY II – Poster Area

P796 OPEN VERSUS LAPAROSCOPIC RIGHT HEMICOLECTOMY IN THE ELDERLY POPULATION

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INTRODUCTION: Laparoscopic colorectal surgery is associated with superior perioperative outcomes when compared to open surgery. However, in the elderly population these benefits are often overshadowed by co-morbidities and difficulties in achieving rapid discharge. Right hemicolectomies (RH) represent a distinct group of colorectal resections where the benefits of the laparoscopic approach may be reduced.
AIMS&METHODS: The aim of this study was to compare short term outcomes of elective laparoscopic and open RH in an elderly population.
All patients over the age of 70 undergoing elective RH at Ninewells Hospital, Dundee and Perth Royal Infirmary were included in our analysis. Intra-operative details and hospital length of stay was obtained from a prospective database. The primary endpoints for analysis were morbidity and mortality. Our secondary endpoints were operative duration, length of hospital stay and discharge destination.
RESULTS: 206 patients were included in our analysis. 125 patients underwent an open resection and 81 patients had a laparoscopic resection. The mean operating time was 139+/-36 minutes in the open group versus 197+/-53 minutes in laparoscopic (p=0.001). The mean length of hospital stay was 11.2 days in open and 9.6 days in laparoscopic. The incidence of post-operative morbidities was 27% in the open group and 38% in the laparoscopic group. Overall mortality was 0.8% in open procedures versus 1% in laparoscopic.
CONCLUSION: Laparoscopic RH was associated with a significantly longer operative time compared to open RH. In our study, laparoscopic RH was not associated with reduced post-operative morbidity or significantly shorter length of hospital stay.
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Disclosure of Interest: None Declared
Keywords: Elderly, Laparoscopic, Right hemicolectomy

P797 INCOMPLETE HISTOLOGICAL EVALUATION AS A RISK FACTOR FOR SURGERY OF MALIGNANT COLORECTAL POLYPS

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INTRODUCTION: Malignant colorectal polyp is the earliest form of clinically relevant colorectal cancer. It corresponds to 0,5-8% of the resected adenomas. After endoscopic resection additional surgery may be necessary, although decision criteria remain debatable.
AIMS&METHODS: Assess oncologic outcomes in terms of locoregional disease and study risk predictors and areas of work improvement that may facilitate patients' management.
Retrospective study of forty patients with T1 colorectal cancer endoscopically resected during the last 5 years. Clinicopathological features were assessed and correlated with locoregional disease.
From the associated risk factors (margins, depth submucosal and lymphovascular invasion, differentiation, budding) we could not evaluate depth invasion and budding.
RESULTS: Thirty-one patients underwent subsequent surgery while 9 were followed-up. After segmentectomy, residual disease was confirmed in 15 (48.4%) patients. No recurrence was detected in the follow-up group. Polyp configuration (p=0.03), differentiation (p=0.02) and margins status (p=0.02) were factors for residual wall disease. The presence of only one risk factor is determinant of poor outcome (p=0.08) while the presence of no risk factor is strongly associated with lower incidence of residual disease (p=0.13). We verified that 22 patients were operated because of inadequate evaluation, mainly consequence of piecemeal

resection, and half of them were disease free. Postoperative anastomotic leakage was highly associated with rectum anterior resection (p=0.03). Study main limitations were the sample size and retrospective design.
CONCLUSION: The need for surgery in case of any risk factor versus cautious follow-up if no risk factors was corroborate. Was also demonstrated a clear need for technical improvement in endoscopic resection and pathologic evaluation in order to prevent unnecessary surgeries, especially for rectal lesions.
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Disclosure of Interest: None Declared
Keywords: malignant polyp, postoperative complications, residual disease, risk factors, submucosal invasion

P798 KINETICS OF SERUM PROCALCITONIN IN THE SMALL BOWEL OBSTRUCTION'S MANAGEMENT

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INTRODUCTION: Small bowel obstruction (SBO) is a frequent intestinal disease that requires either conservative management (with a nasogastric tube) or surgical management in case of failure of the nasogastric tube. For the digestive surgeon, the timing before the necessity of the surgery is difficult because of the absence of preoperative markers. Procalcitonin (PCT) has been recently proposed as a marker for helping in this discrimination. The aim of this study is to determine the kinetics of PCT in patients with SBO and the best predictive timepoints to propose conservative management and surgical management.
AIMS&METHODS: Between January and April 2013, 23 patients were hospitalized in the Amiens Digestive Surgery Department for SBO. In all of these patients, serum PCT were taken every four hours for three days or until the transit was restored and measured with Kryptor TRACE analyzer. Patients were divided into subgroups considering the success (CM) or the failure (FM) of conservative management.
RESULTS: At admission, serum PCT is significantly lower in CM group (n= 18; 0.13 vs 0.35; $p < 0.01$) compared with the FM group (n=5). At 12 hours after the admission, a PCT > 0.21 ng/mL has a positive predictive value (VPP) of 89.6% and a negative predictive value (NPV) of 73.2% and at 24 hours, a PCT > 0.16ng/mL has a VPP of 83.2% and a NPV of 78.3% to predict conservative management failure. The Area under the Curve was 0.85 for conservative management failure.
CONCLUSION: serum Procalcitonin could help to discriminate patients with SBO in whose the surgical management has to be proposed. A larger effective is required to confirm this trend.
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Disclosure of Interest: None Declared
Keywords: procalcitonin, small bowel obstruction, surgical treatment

P799 PRESENTATION OF FEMORAL HERNIA AND ITS CONSEQUENCES: A POPULATION BASED STUDY USING LINKED PRIMARY AND SECONDARY CARE DATA

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INTRODUCTION: Emergency admission with femoral hernia is high compared to other hernias and the reasons for this are unclear.
AIMS&METHODS: Our aim was to determine the outcomes of patients admitted as an emergency with a femoral hernia and describe the mode of presentation to primary care. Computerized health care records of patients from the Clinical Practice Research Datalink (CPRD) linked to Hospital Episode Statistics (HES) data from the UK from 1997 to 2007 with a first hospital admission for a femoral hernia repair. The demographics of the emergency and elective patients were described with respect to age, gender, comorbidity and first presenting complaint to primary care either hernia or other presentation (groin pain, obstructive symptoms). Length of stay, bowel resection rates and 30 day mortality were calculated.
RESULTS: We identified 885 patients (78% female) who underwent a femoral hernia repair with 406 (45.9%) as an emergency. The median age of those presenting as an emergency was 77.5 years (IQR 68-84 years) which was significantly greater than those presenting electively 61.0 years (IQR 46-75 years) (Kruskal-Wallis $p < 0.0001$). The majority of emergency admissions (81.5%, 331/406) presented to their GP for the first time with symptoms of a hernia in the 7 days prior to admission compared with just 2% of elective admissions (Chi squared 585, $p < 0.0001$). Patients presenting for elective repair were 7 times more likely to present with a history of a hernia compared to those presenting as an emergency (Odds Ratio 6.7, 95% CI 4.95-9.12). In those presenting as an emergency 72.2 % (293/406) presented with evidence of small bowel obstruction or strangulation with 22.9% (93/406) having a bowel resection. The median length of stay in those undergoing elective surgery was 1 day (IQR 0-2) and for those undergoing emergency repair it was 5 days (IQR 3-9) (Kruskal-Wallis $p < 0.0001$). There were no deaths within 30 days in the elective group with a 1.7% 30 day mortality in the emergency group.
CONCLUSION: A substantial number of patients present as an emergency with a femoral hernia. These patients are older and present to primary care in a different manner in terms of timing and presenting complaint compared to those having an elective repair. Morbidity associated with these admissions is high and therefore preventing emergency admission is likely to improve outcomes.
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Disclosure of Interest: None Declared
Keywords: emergency intervention, femoral, hernia

P800 TREATMENT OF LOW RECTAL CANCER BY ELRR OR TETMR BY TEM

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INTRODUCTION: Surgical sphincter saving procedure in patients with low rectal cancer are hugely successful,but today there is still no universally adopted standardized technique.From the beginning of the 90's, the authors have introduced an original technique of loco-regional resection by Transanal Endocopic Microsurgery (TEM) named ''Endoluminal Loco-Regional Resection'' (ELRR).This technique is a valid alternative to traditional surgery for early rectal cancer (Tis-T1) and for T2N0 after neoadjuvant radio-chemotherapy (n-RCT). From 2008 authors have developed a new combined technique: Transanal Endoluminal Total Mesorectal Resection (TETMR) by TEM in patients not eligible for ELRR (T2-T3N0/N+).Transanal TME is achieved with a modified TEM rectoscope.Abdominal laparoscopic time is performed as usual, followed by colo-anal anastomosis and ileostomy**.**
AIMS&METHODS: From 2001 to 2013,115 patients (67 male,48 female,median age 65 years) affected by rectal cancer were selected. All patients were studied preoperatively with tumor markers assay (CEA,Ca19.9,Ca125),digital rectal examination,colonoscopy with macrobiopsies,vital staining and marking of the lesion,total body CT scan,pelvic MRI and endorectal ultrasound.One hundred and six patients with T1-T2N0 rectal cancer underwent to ELRR and nine patients with T2-T3N0/N+ underwent TETMR.All T2-T3 patients underwent to n-RCT.
RESULTS: Mean operative time for ELRR and TETMR was 138 min (range 40-300) and 450 (range 360-600) respectively.No intraoperative complication occurred for both procedure.Final staging was pT0N0(2), pTis(49), pT1(41), pT2(20), pT3N0(2), pT3N1(1).Ileostomy was performed in 5 patients underwent TETMR.Mean hospital stay was 4 days for ELRR and 16 days for TETMR.No late complications were observed in ELRR group.In TETMR group were observed 2 anastomotic leakage,2 anastomotic stenosis,1 rectovaginal fistula. Mortality was nil.
CONCLUSION: In patients with low rectal cancer quality of life should be considered as primary objective as well as oncological results.Nowadays TME is considered the gold standard surgical procedure,but high postoperative functional sequelae are observed.Many surgical alternative procedures are described in literature,but no universally standardized technique is still adopted.Modified TEM procedure (ELRR) is a valid alternative to traditional surgery in selected patients T1 or T2 after n-RCT.Authors described a new technique named TETMR to treat patients with T2-T3 rectal cancer.Main advantage is the preliminary identification of tumor distal margin,dissection of distal part of perineal muscle and fascia in order to detect perirectal tumoral invasion and verify the possibility to perform a sphincter saving procedure.
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Disclosure of Interest: None Declared
Keywords: ELRR, Rectal cancer, TEM, TETMR

P801 SECONDARY PROCTECTOMY AFTER COLECTOMY AND ILEORECTAL ANASTOMOSIS IN FAMILIAL ADENOMATOUS POLYPOSIS

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INTRODUCTION: Familial adenomatous polyposis (FAP) is a hereditary disease characterized by hundreds or thousands of polyps in the colon and rectum. The aim of surgery is to prevent otherwise almost inevitable colorectal cancer. Surgical treatment options include proctocolectomy and conventional ileostomy (IS), colectomy and ileorectal anastomosis (IRA), and proctocolectomy with ileal pouch-anal anastomosis (IPAA) [1]. The choice of surgery for each patient is made case by case, taking into account the patient's age, location and number of polyps, comorbidities, and patient's wish [2]. Also genotype has been suggested to guide the decision between IPAA and IRA [3]. Colectomy with IRA is considered to be safer than proctocolectomy with IPAA, but it is associated with an elevated risk of rectal cancer.
AIMS&METHODS: The aim of our retrospective study was to review the outcome of patients undergoing colectomy with ileorectal anastomosis (IRA) due to familial adenomatous polyposis (FAP) in Finland during the last 50 years.
The cumulative risk of rectal cancer and the rate of anus preservation were analyzed. Total of 140 FAP patients with previous colectomy combined with ileorectal anastomosis were included. Kaplan-Meier analysis was performed to evaluate cumulative risks.
RESULTS: Secondary proctectomy was performed for 39 (28%) of 140 patients. The median follow-up time after colectomy and IRA was 15 years (range 0-44 years, mean 16 years). The cumulative risk of secondary proctectomy was 53% at 30 years after colectomy with IRA. A total of 17 (44%) secondary proctectomies were performed due to cancer or suspicion of cancer, and another 17 (44%) secondary proctectomies were performed due to uncontrollable rectal polyposis. During our study, the anus preservation rate in secondary proctectomies was 49%. Estimated cumulative risk of

rectal cancer was 24% at 30 years after colectomy with IRA. The cumulative rectal cancer mortality 30 years after colectomy with IRA was 9%. Patients with attenuated FAP had no rectal cancer in our study.
CONCLUSION: Proctocolectomy and ileal pouch-anal anastomosis (IPAA) should be favored as a primary operation for patients not having technical or medical contraindications for it, because almost one-third of patients with colectomy and IRA will experience rectal failure and secondary proctectomy during 20 years after the operation and over half after 30 years. Approximately 10% will develop rectal cancer in 20 years and 20% in 30 year's follow-up, resulting in a cumulative mortality of 8% in 20 years. Patients with attenuated FAP form a group where IRA should still be the first choice as an exception.
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Disclosure of Interest: None Declared
Keywords: Attenuated familial adenomatous polyposis (AFAP), Familial adenomatous polyposis (FAP), Ileorectal anastomosis, Rectal cancer , Secondary proctectomy

P802 MODULATION OF VISCERAL SENSITIVITY BY ACUTE SACRAL NERVE STIMULATION IN RAT.

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INTRODUCTION: Fecal incontinence remains a therapeutic problem in patients when conservative measures fail and sphincter repair is unsuccessful or inappropriate. Sacral nerve stimulation (SNS) is an alternative surgical approach proposed initially to treat urinary incontinence, and has been used for the past decade as a successful treatment of fecal incontinence. Despite its overall efficacy that is reported to be between 70 and 80%, the mechanisms involved in this symptomatic effect remain unclear, and may involve modification of visceral sensitivity.
AIMS&METHODS: We assessed whether SNS could modify colorectal sensitivity to colorectal distension (CRD). These experiments were carried out in healthy rats and in a cross-organ hypersensitive rat model using acetic acid bladder instillation. We monitored the variation of arterial blood pressure (BP) as a marker of visceral sensitivity in anesthetized rats in response to graded CRD from 20 to 80 mmHg during either SNS or sham stimulation. In addition, c-fos protein (neuronal activation marker) expression was quantified by immunohistochemistry within the S1 sacral dorsal horn of the spinal cord, the solitary tract nucleus (NTS) and parabrachial nucleus (PBN) in response to 80 mmHg CRD during either NS or sham NS.
RESULTS: Graded CRD led to an increase of BP that was decreased by SNS in both models, with an effect that was more prominent in the hypersensitive model. The effect of SNS on visceral pain was prevented in both models by administration of intravenous (iv) or intrathecal naloxone, while L-Name administered iv had no effect. In addition, SNS prevented the increase of the number of c-fos immunoreactive cells in response to CRD in the lamina I of dorsal horn of the sacral spinal cord, in the NTS and in the PBN in both models.
CONCLUSION: Our study shows that SNS modifies visceral sensitivity in healthy and hypersensitive rat by acting on the central nervous system through an opioid (but not nitrergic) -dependent pathway. Further investigations are necessary to determine mediators involved both at the peripheral and central levels.
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Disclosure of Interest: None Declared
Keywords: colorectal distensions, opioids, Sacral nerve stimulation, visceral hypersensitivity

P803 TRIPLE TEST FOR EXCLUDING ACUTE APPENDICITIS IN ADULTS

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INTRODUCTION: Appendectomy is by far the commonest major emergency general surgical operation.
AIMS&METHODS: The present prospective clinical study was conducted to investigate whether a negative triple test (NTT) (total leukocyte count [TLC], neutrophil percentage [NP], and C-reactive protein [CRP] level) can rule out acute appendicitis in adults. It included 452 consecutive patients with suspected acute appendicitis. Children (<16 years) (n=91) and pregnant women (n=7) were excluded. The remaining 354 patients were enrolled but only those with a NTT (n=130) were analyzed. The NTT meant TLC <11,000/μL, NP <75%, and CRP <5 mg/L. Data collected included demographics, clinical presentation, laboratory tests, histopathology, and outcome. Negative predictive value (NPP) was calculated.
RESULTS: Eighty-seven patients (66.9%) were female and 43 (33.1%) were male. Their ages ranged between 16 and 52 years (mean 27.8 years). Most patients (87.7%) had their symptoms for 12-36 hours before hospital admission. The mean values for TLC, NP, and CRP were 7,693/μL, 55.61%, and 0.65 mg/L, respectively. Of the 130 patients with NTT, only one proved to have appendiceal inflammation (NPV=99.2%). Only 49 patients were operated upon, of whom 48 (98%) had a normal appendix, and the remaining patients were either discharged (n=56) or referred to other specialties (n=25). There were significantly more women (77.1%, 37/48) with negative appendectomy than men (22.9%, 9/38) (X^2= 21.1, p=0.0001).
CONCLUSION: Triple test (TLC, NP and CRP levels) should be measured upon hospital admission of adult patients with clinically suspected acute appendicitis. If used judiciously, they may spare the group of patients with a NTT an unnecessary surgical operation with its cost and potential risks.
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Disclosure of Interest: None Declared
Keywords: appendicitis, triple test

P804 MOLECULAR CHARACTERIZATION OF SERRATED POLYPS CAN DIFFERENTIATE MORE ADVANCED LESIONS

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INTRODUCTION: Serrated polyps could be premalignant acting through the serrated pathway of carcinogenesis.
AIMS&METHODS: The objective of our study was to compare a group of polyps with mutations in KRAS, BRAF and not mutated in order to determine molecular and histological differences between them.
We performed a retrospective study including 163 patients and determining the clinical and molecular feature of a total of 613 polyps belonging to these patients. We analyze KRAS and BRAF mutations in the DNA of polyps. Mutation analysis for KRAS (codons 12 and 13) was performed by DNA sequencing while BRAF mutation (V600E) was studied using allelic discrimination.
RESULTS: A total of 378 polyps were classified as adenomas. BRAF mutation was present in 0.6% of adenomas and KRAS mutation in a 6.8%. A total of 204 polyps were classified as serrated polyps, 188 (92,1%) were hyperplastic polyps (HPs), 10 (4,9%) as sessile serrated polyps (SSP) and 6 (2,9%) as traditional serrated adenomas (TSA). We observed that polyps harbouring BRAF mutation are more frequently larger than 10 mm than non-mutated polyps (70,4% vs 29,6%; p=0,03). When we compare mutations in BRAF and KRAS we can observe that BRAF mutated polyps appeared more frequently in the right colon (75% vs 25%; p=0,015). KRAS mutated polyps are located mainly in the left colon with an upward progression of the number of polyps to rectum (p<0,001). There were no differences in the morphology of serrated polyps depending on the BRAF or KRAS mutational status. On the other hand when we only considered the HPs polyps we observed that KRAS mutated polyps are smaller than 10mm (75%vs25%) and are located with statistical significance in rectosigmoid colon (p=0.002).
CONCLUSION: BRAF mutation is almost exclusive of serrated polyps. Serrated polyps showing BRAF mutation have more frequently features of advanced polyps, being higher in size and right-sided.
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Disclosure of Interest: None Declared
Keywords: molecular characterization, serrated pathway, serrated polyps

P805 EARLY CLOSURE OF TEMPORARY ILEOSTOMY, A LARGE PROSPECTIVE STUDY

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INTRODUCTION: A temporary ileostomy is a frequently used method to protect a distal colorectal anastomosis and to reduce the morbidity and mortality in case of an anastomotic leakage (AL). Usually, closure is performed 8 – 12 weeks after the primary operation although currently there is no evidence that this period is required for complete healing of the colonic anastomosis. During this prolonged period, stoma-related complications can occur and medical expenditures may rise.
AIMS&METHODS: The aim of this large prospective, single-center cohort study was to analyze the complications and stoma-related morbidity after early (7 – 14 days) and postponed closure of loop ileostomy in patients who received a colonic anastomosis between 2002 and 2011. All included patients underwent a bowel enema study, ten days postoperatively, to judge the presence of AL. When no clinical and/or radiological signs of anastomic leakage were present, early closure of ileostomy was attempted. Reasons to postpone ileostomy closure were analyzed. Patients were monitored from the primary construction of the loop ileostomy until one year after closure of the ileostomy.
RESULTS: Seventy-five patients were included in this study. Early closure of the loop ileostomy was performed in 42 patients. Late closure was necessary in 30 patients. In three patients the stoma was not closed. Reasons for postponing closure were clinical and/or radiological signs of AL (6), delayed recovery (20), gastroparesis (3), and logistic reasons (1). In the postponed closure group were more major surgery related complications (p<0.01): haemorrhages (n=3) and abcesses (n=2) for which a relaparatomy was performed. Intra-abdominal abcesses occurred in n=2 in the early group. Minor surgery related complications were not different in the early group vs the postponed group, p=0.06, although wound infection was more frequent in the early group. Total average in-hospital stay, from the initial operation until the day of discharge , was 18 days (11 – 107) in the early closure group and 27 days (16 – 63) in the late closure group.

CONCLUSION: This large prospective study shows that early closure of the temporary ileostomy is safe in patients without clinical and radiological signs of AL. The most important criterion for early closure of the ileostomy is the presence of a radiologically proven sufficient healed anastomosis in a clinically stable patient.
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Disclosure of Interest: None Declared
Keywords: anastomosis, surgical, Colon/surgery, Ileostomy/adverse effects, Postoperative Complications/etiology, Prospective Studies, Rectum/surgery

P806 EXTERNAL VALIDATION OF A PROGNOSTIC MODEL OF PREOPERATIVE RISK FACTORS FOR POUCH FAILURE

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INTRODUCTION: A prognostic model of preoperative risk factors for ileoanal pouch failure has been proposed by the Cleveland Clinic. The model incorporates four predictive variables: completion proctectomy, diabetes mellitus, handsewn anastomosis and Crohn's disease.[1]
AIMS&METHODS: Aim of the present study is to perform an external validation of this model in a new cohort of patients having had an ileal pouch-anal anastomosis (IPAA).
Validation was performed in a cohort of 371 consecutive patients who had an IPAA between 1999 and 2012 in a single tertiary referral center in the Netherlands. The proposed prognostic model was validated in this cohort using a Kaplan-Meier survival analysis and Cox regression analysis and the performance of the model was expressed using the Harrell's concordance error rate.
RESULTS: Kaplan Meier analysis showed a worse pouch survival for completion proctectomy (P=0.021) and no significant difference for diabetes (P=0.368). A trend was seen for handsewn anastomosis (P=0.072) and Crohn's disease (P=0.065). Although the observed hazard ratios for pouch failure were similar to those reported for the Cleveland Clinic sample, multivariable analysis showed no significant independent predictors in this cohort. Harrell's concordance error rate was 0.42, indicating poor performance.
CONCLUSION: Although no independent significant predictive differences were observed, the variables completion proctectomy, handsewn anastomosis and Crohn's disease were also associated with pouch failure in our cohort with relatively few events. However, the poor performance of this proposed prognostic model does not make it suitable for application in daily practice.
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Disclosure of Interest: None Declared
Keywords: External validation, Pouchfailure, Prognostic model, risk factors

P807 MUCINOUS AND SIGNET-RING CELL CARCINOMAS DIFFER FROM CLASSICAL ADENOCARCINOMAS IN TUMOR BIOLOGY AND PROGNOSIS

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INTRODUCTION: Most colorectal cancers are classical adenocarcinomas (AC). Less frequent subtypes include mucinous adenocarcinomas (MAC) and signet-ring cell carcinomas (SC). The histological subtype has no therapeutical consequences so far, although it may reflect different biological behavior.
AIMS&METHODS: To define the prognostic value of different histological subtypes of colorectal cancer. Between 1982 and 2012, a total of 3479 consecutive patients underwent surgery for primary colorectal cancer (AC, MAC, or SC). Clinical, histopathological, and survival data were analyzed.
RESULTS: ***MAC and SC were rare histological subtypes.*** Of all 3479 patients, 3074 cases were AC (88%), 375 cases were MAC (11%), and 30 cases were SC (0.9%). Although potentially induced by radiation, the prevalence of MAC and SC was not significantly altered after neoadjuvant treatment (p=0.200).
MAC and SC had distinct clinicopathological characteristics. MAC (51%, $p<0.001$) and SC (50%, $p=0.029$) occurred more frequently in right-sided tumors than AC (28%), and had poorer histological grading ($p<0.001$ for both). Subgroup analysis revealed higher rates of microsatellite instability for MAC and SC compared to AC (p=0.006). Rates of angioinvasion were lower in MAC than in AC (5% vs. 9%, $p=0.011$). Rates of lymphatic invasion were higher in SC than in AC (67% vs. 25%, $p<0.001$).
Only SC were an independent prognostic factor. Five-year cause-specific survival was 67±1% for AC, 61±3% for MAC, and 21±8% for SC ($p<0.001$ for difference between the groups). Compared to AC, tumor stages were higher in MAC and SC ($p<0.001$). After stage correction, survival of AC and MAC did not differ significantly (p=0.991), whereas SC remained an independent prognostic factor associated with worse survival compared to AC (HR=2.5, 95% CI 1.6–3.8, $p<0.001$).
CONCLUSION: MAC and SC are uncommon histological subtypes of colorectal cancer with different characteristics than classical AC. Both are diagnosed in more advanced tumor stages, but the dismal prognosis of SC appears to be caused by its intrinsic tumor biology. The consideration of the histological stubtyp in future classification systems could increase prognostic accuracy.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, histological subtype, tumor biology

P808 THE SACCHAROMYCES BOULARDI'S ROLE IN THE COMPLEX OF MEDICAMENTAL CORRECTION OF INTRAINTESTINE HOMEOSTASIS (IIH) IN EARLY POSTOPERATIONAL PERIOD (EPP) IN PATIENTS WITH ACUTE APPENDICITIS (AA) A CONTROLLED, RANDOMISED STUDY

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INTRODUCTION: Optimization of the diagnostic-medicative program which includes integrated surgical treatment of patients with AA is still an urgent problem.
AIMS&METHODS: The aim of the research is to optimize the medicamental therapy in epp of patients with AA considering results of the bacteriological examination of the peritoneal exudation. The patient's with AA medicamental and operational treatment in the Lviv Emergency Hospital in 2010-2011 was analyzed. The observation group consisted of 77 patients, by who simultaneously with antibacterial treatment (amenably to the schemes and standards to renew the adequate peristalsis) the probiotic Saccharomyces boulardi was also applied (in dosage 1 dose three times a day) to effect the correction of IIH starting from the 2-nd day of the treatment.
RESULTS: By extension of the illness period the patients per cent in which the signs of the peritoneal exudation infection are confirmed is increasing in geometrical progression, which has a huge negative influence on the movement of intestinal contents though the digestive tract and has an effect on the development of intestine wall microcirculatory malfunctions and can also provide to IIH malfunction.
The bacteriological examination data gave us information, that in peritoneal exudation prevailed pathogenic E.coli (75; 97,4%), in monoculture (27; 35%), and in association with other cultures (48; 62,4%): Enterococcus faecalis (14; 18,2%), Pseudomonas aerogenosa (13;16,9%), Enterobacter aerogenes (5; 6,5%), Hl. Pneumoniae (1; 1,3%), Pr. vulgaris (5; 6,5%), Streptococcus aureus (4; 5,2%), Streptococcus haemolyticus (6; 7,8%), there was no growth only in 2 cases (2,6%). The bacteriological research of defecation, made on the 3-rd and 7-th day of treatment confirmed the renewal of the large intestine microbiocenosis, we recorded reliable ($p<0,005$) quantitative growth of lactobacteria (з 6,88±0,19 до 7,91±0,15 lg CFU/ml) and bifidobacteria (з 7,71±0,23 до 8,62±0,21 lg CFU/ml) in 89,6% of patients.
CONCLUSION: The bacteriological examination of abdominal cavity exudation in patients with acute appendicitis confirmed, that the main microflora gained as a result of the examination is E.coli in monoculture - 35%, and in association with other cultures (62,4%), mainly with Enterococcus faecalis, Pseudomonas aerogenosa та Streptococcus haemolyticus. The antibacterial therapy in association with probiotic Saccharomyces boulardi promotes the elimination of the pathogenic microflora and helps to renew the IIH in 69 patients (89,6%).
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Disclosure of Interest: None Declared
Keywords: ACUTE APPENDICITIS , POSTOPERATIONAL PERIOD

P809 HOW WELL DO WE UNDERSTAND SEPSIS? A CROSS SECTIONAL SURVEY

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INTRODUCTION: Sepsis is a major cause of morbidity and mortality, with an incidence of 1 per 1000 population per year and mortality ranging from 20-50%. Sepsis, Severe sepsis, septic shock and SIRS are very clearly defined by the Surviving Sepsis Campaign, according to which, one of the most important influences on outcome is prompt recognition and subsequent equally prompt treatment to reduce morbidity and mortality.
AIMS&METHODS: The purpose of this study is to assess knowledge of medical students and junior doctors within the local hospital and within the Deanery. Medical students and junior doctors – house officers (F1) and Senior house officers (F2 and core surgical trainees) were questioned to see if there is any improvement of knowledge over time
Over a one month period in January 2013, 40 participants were provided questionnaires, 36 people completed this; 7 final year medical students, 11 F1, 8 F2 and 11 Core Surgical Trainees.
RESULTS: Medical students – 14% defined SIRS correctly,14% defined sepsis. 71% believed empirical antibiotics should be given in less than an hour for a patient identified with sepsis. None of the medical students had heard of local trust sepsis protocols, antibiotic policies and critical care outreach. F1 – 18% defined SIRS correctly, 72% defined sepsis. 9% could identify severe sepsis, and septic shock. 91% would give antibiotics in less than an hour after diagnosis. 54% didn't know their trust had a sepsis management protocol. F2 – 0% defined SIRS correctly, 75% defined sepsis as SIRS with evidence of infection, and 12.5% defined severe sepsis. 37.5% weren't aware their hospital had a sepsis protocol. 75% had used their trust antibiotic policy. Core surgical trainees – 9% defined SIRS correctly, 90% defined sepsis as SIRS plus evidence of infection, 9% defined severe sepsis. 90% would give antibiotics within an hour. 81% were aware of their trust's sepsis guidelines, and all used their hospital antibiotic policy and critical care outreach.
CONCLUSION: The awareness of what SIRS was found to be inadequate in all groups tested, but what was more worrying was that the more senior surgical trainees were less aware than juniors. However senior trainees seemed more aware of the management of sepsis.

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Correct identification of SIRS and sepsis is the first and most important step, as without identification, appropriate treatment cannot be implemented. This highlights the need for improved education to be introduced at all levels of junior medical training, from medical school, foundation level and core training in regards prompt recognition of this common but live threatening problem. The next step would be a repeat survey after steps are put in place to improve sepsis knowledge.

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Disclosure of Interest: None Declared
Keywords: questionnaire, sepsis

P810 COMPARISON OF PREOPERATIVE CT-BASED AND INTRAOPERATIVE PANCREATIC RISK ASSESSMENT IN PREDICTING PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY

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INTRODUCTION: Postoperative pancreatic fistula (POPF) remains the predominant cause of morbidity after pancreatoduodenectomy (PD). As previously shown, intraoperative evaluation of pancreatic texture and main pancreatic duct (MPD) size provides a reliable measure of risk for clinically relevant POPF (ISPFG grade-B/C (Ansorge Br. J.Surg 2012). Likewise, the preoperative CT-based determination of the remaining gland volume and MPD diameter can reliably predict the risk of POPF (Frozanpor WJS 2012).
AIMS&METHODS: To evaluate the predictive value of preoperative radiological features compared to intraoperative risk estimation for the development of clinically relevant POPF. In all 296 consecutive PDs at Karolinska University Hospital that had undergone preoperative CT determination of residual gland volume and MPD diameter were included. In 216 of these patients, a standardized intraoperative assessment of gland texture and MPD size were done. Both the preoperative and intraoperative risk assessments were conducted in three POPF-risk groups: low, intermediate and high risk. The risk estimates were calculated as OR and 95% confidence interval (CI).
RESULTS: Results of the radiological arm exhibits: low risk 4.3 % (OR 7.5; CI 3.1-18, $p<0.001$), intermediate risk 22 % (OR 2.4; CI 1.2- 4.5, $p<0.01$), high risk 41% (OR 5.0; CI 2.2-11, $p<0.001$). Results of the intraoperative risk assessment arm exhibits: low risk: 4.8 % (OR 8.6; CI 3.4-22, $p<0.001$), intermediate risk 26 % (OR 2.7; CI 1.3-5.7, $p<0.01$). high risk 39% (OR 4.7; CI 2.0-11, $p<0.001$).
CONCLUSION: The preoperative CT-based risk assessment and the intraoperative assessment done by experienced pancreatic surgeons had comparable POPF-predictive impacts.
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Disclosure of Interest: None Declared
Keywords: Computed tomography, Fistula, Pancreatic Cancer , Pancreatico-duodenectomy, postoperative complications, Whipple

P811 COMPLICATIONS AFTER ADJUSTABLE GASTRIC BANDING FOR OBESITY; THE ENDOSCOPIST'S POINT OF VIEW

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INTRODUCTION: Bariatric surgery is currently the most effective measure for treating morbidly obese patients. Laparoscopic adjustable gastric banding (AGB) is a restrictive, widely applied technique, with good results. The gastroenterologist who is called to evaluate the postoperative bariatric patient is obliged to face a completely new anatomy and must be able to recognize and, if possible, to manage the potential complications.
AIMS&METHODS: The files of 298 patients (36 men) submitted to laparoscopic AGB during an 8-year period by a single surgeon, were retrospectively reviewed. Postoperatively, all patients (mean age 41.5±11.4, range 16-70) were submitted at least once to upper endoscopy due to inadequate weight loss or symptoms that implicated complications or as part of a routine control, usually at 24 months after the operation. Mean follow-up time was 37.4±21.8 months (range 2-96). The postoperative complications, as diagnosed by endoscopy, were analyzed.
RESULTS: 91 patients had at least one kind of abnormal findings. A total of 106 abnormal endoscopic findings were recorded. Mean time of diagnosis was 35.2±17.9 months after operation. Sixty-nine of the patients had to be reoperated due to complications or inadequate weight loss.The endoscopic complications recognized were: esophagitis 12%, Barrett's esophagus 1.5%, pouch dilatation/gastric prolapse 5.5%, transgastric migration of ring 4%, inflammation of the mucosa covering the ring 1.2%, gastric bezoar 0.3%, proximal slippage of the ring 7.3%, stomal stenosis 1.8%, hemorrhage 0.6%, adenocarcinoma 0.3%. Patients with gastric bezoar and stomal stenosis were able to be treated endoscopically.
CONCLUSION: Endoscopic complications after laparoscopic AGB are frequent. The endoscopist must be aware of the surgically altered anatomy and the appearance of the potential complications.
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Disclosure of Interest: None Declared
Keywords: Bariatric surgery, Complications

P812 POST-CHOLECYSTECTOMY ACUTE BILE DUCT INJURIES: PRESENTATIONS AND OUTCOME

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INTRODUCTION: Management of post-cholecystectomy acute bile duct injuries (BDI) has been addressed in the literature less frequently than the management of established benign biliary strictures (BBS). We have reviewed our experience with management of acute BDI and reported the short term and long term outcome of the patients with acute BDI.
AIMS&METHODS: Retrospective analysis of prospectively kept data of 239 patients with post-cholecystectomy acute BDI that were managed in a single institution from January 1989 to Dec 2010 and in whom follow up information was available.
RESULTS: Of the 239 patients**, t**here were 77 males & 162 females patients with a median age of 40.0 (12-74) years. The index surgery was open cholecystectomy in 147, open cholecystectomy with common bile duct (CBD) exploration in 12 and laparoscopic cholecystectomy in 80 patients. Patients were referred to us at a median duration of 22 days (1-270) days after cholecystectomy.106/239(44%) had jaundice on presentation. 100/239(42%) patients had single or multiple pre-referral interventions.
Based on their clinical presentation, the patients with BDI were classified into external biliary fistula EBF(n=107), Bilioma(n-100), Bile ascites(n=10), Bile peritonitis(n=20) and 2 pts presented with only jaundice of which 1 underwent early repair, 1 refused surgery.
70 patients were managed conservatively, 112 had percutaneous intervention, 40 had endoscopic intervention, 37 were operated and 36 had combination of these procedures including surgery. 9/309(3%) patients died due to the complications of BDI and were excluded from the study. Post- intervention, on the basis of scintigraphy (HIDA), cholangiography (MRCP, ERCP, Tubogram), 138/239 (58%) had complete injury and 101/239 (42%) had partial injury
Early outcome (at 4 weeks of intervention): In pts. with complete injury, 79/158(57%) had controlled external biliary fistula whereas 85/101(84%) with partial injury had closure of fistula.
Late outcome (6 weeks to 3 months): 129/138(93%) of pts. with complete injury went on to have biliary stricture requiring surgical intervention compared to only 29/101(29%) in the group with partial injury.
CONCLUSION: Post-cholecystectomy BDI presents as EBF, Biloma, bile peritonitis, bile ascites, only jaundice and management differs in each of these presentations.
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Majority of patients with post-cholecystectomy BDI referred to surgical units have 'complete' injury.
The short term and long term outcome of the acute BDI could be predicted based on the clinical and radiological presentation of the patients.
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Disclosure of Interest: J. Abraham : none, V. Kapoor: None Declared, A. Prakash: None Declared, A. Behari: None Declared, A. Gupta: None Declared, R. Singh: None Declared, R. Saxena: None Declared
Keywords: Acute bile duct injury, Bile peritonitis, Biloma, External biliary fistula, Laparoscopic cholecystectomy, Open cholecystectomy

P813 REGENERATIVE OF THE BLADDER WALL FOR THE TREATMENT OF A BIOABSORBABLE POLYMER SHEET

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INTRODUCTION: If the segmental resection of the bladder wall where the rectal cancer invased is required, absorption thread is often used for the direct sutures. With a decrease in bladder capacity, it might be micturition and the long-term urethra catheter custody. The surgery to extend of the bladder with intestinal canal of caulescent may be stressful for the patients. Nowadays, there is no reinforcing materials which can substitute a defective part. Our group successes the renovation of various organs, such as an extrahepatic bile duct, and a gastric parietal using the bio absorbable polymer sheet ;BAPS In this study, we investigated the renovation of the bladder wall using BAPS.

AIMS&METHODS: The body weights with 20kg Mongrel (hybrid) pigs were laparotomized under general anesthesia. A 5×2-cm or 9×7-cm oval-shaped portion of the bladder wall was excised, and a BAPS was implanted with consecutive sutures at the excision site. BAPS is a porous fiber material composed of a 50:50 copolymer of polylactic acid and polycaprolactone and reinforced with polyglycolic acid fibers. The hydrolysis in the living body is absorbed in about 8 weeks. The pigs were relaparotomized at 4 weeks (5×4-cm, 9×7-cm, each n=3), and 20 weeks(5×4-cm, n=1) after implantation. The histological findings of the repaired diagrams were evaluated. We compared the bladder capacity with the BAPS non-transplant group (9×7-cm consecutive sutures at the excision site, n=2), BAPS transplant group

RESULTS: Four weeks later, neither group accepted the failure or the urinary leakage of the transplant part. Significant shrinkage was recognized at 30% in both 5×4-cm and 9×7-cm patches, and the regeneration of bladder wall was not found. The bladder capacity with the BAPS transplant group (9×7cm) was 400 cc , compared with 300cc of non-transplant group. It showed a slight increase at the bladder capacity. BAPS could not keep the dome-shape after the 9×7-cm excision and suturing, and this might be the reason of the shrinkage. Therefore, the plastic spherical prop/stent was inserted into the bladder to maintain the shape of the sheet site. In the results, there was no shrinkage at the implantation site after 4 weeks later.

CONCLUSION: BSAP repaired the defective bladder wall after partially bladder wall excision site. However, there was a problem for the remarkable shrinkage of BAPS in thebladder capacity by a more extensive loss. To avoid this shrinkage, we placed a stent to maintain the shape of the bladder after implantation, and this method was successfully to repair the bladder. It is suggested that this model which use BAPB for the defective tissue should approach the goal of clinical surgical use in future.

Disclosure of Interest: None Declared

Keywords: Bladder, Rectum/surgery, Regenerative medicine

P814 SIGNIFICANT ERRORS IN CODING OF GENERAL SURGICAL READMISSIONS IN A UK DISTRICT GENERAL HOSPITAL

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INTRODUCTION: The UK Department of Health have proposed ceasing payment for emergency hospital readmissions. This would affect 430,000 patient spells with an estimated loss in revenue of £790 million.

AIMS&METHODS: Aims were to establish the accuracy of recorded readmissions in a district general hospital in the UK over a six month period. The computerised hospital records of all general surgical readmissions between March and September 2012 were reviewed.

RESULTS: Of 1,320 admissions, 197 (14.2%) were readmissions in 169 patients. 194 readmissions in 166 patients were suitable for analysis. 72 (43.4%) were male, 94 (56.6%) female with a median age of 52.4 years (range 6.3 – 99.4). No difference was found in age group (p=0.1), or mean age (p=0.2), between gender. 174 primary admissions had one readmission, 17 had two readmissions, and one had five readmissions. 85/174 (48.9%) 1st readmissions were invalid, of which 58 (68.2%) were due to differing specialities at each admission, 14 (16.5%) readmissions were planned admissions, 9 (10.6%) were due to a flare of a chronic condition, 3 (3.5%) were readmitted with an unrelated pathology, and 1 (1.2%) patient self discharged at initial admission. Total hospital length of stay (LOS) for invalid readmissions was 542 days. For valid readmissions, no correlation was found between initial LOS and time to readmission (R^2 linear = 0.012) or LOS for readmission (R^2 linear = 0.006).

CONCLUSION: Robust systems need to be instituted to ensure that readmissions are coded correctly, to ensure hospital trusts are appropriately reimbursed.

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Disclosure of Interest: None Declared

Keywords: Complications, surgery

P815 CHOLECYSTECTOMY DOES NOT INFLUENCE GASTROINTESTINAL TRANSIT: RESULTS OF A PROSPECTIVE STUDY USING RADIO-OPAQUE MARKERS

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INTRODUCTION: Cholecystectomy has been shown to lead to changes in gastrointestinal (GI) transit by reducing transit time through the colon, though this remains disputed. However, studies in this area are sparse, and have often used lactulose, which in itself influences transit times.

AIMS&METHODS: We aimed to assess prospectively whether cholecystectomy affects GI transit using a radiological procedure developed at our unit.

Twenty-four patients (21 female, 3 male), prior to elective cholecystectomy, ingested 10 radio-opaque rings daily for 6 days, dividing the dose in two on the final day to improve measurement of fast colonic transit. On day 7, 20 radio-opaque spherical markers were added, and the positions of markers were observed every 30 minutes using fluoroscopy for a maximum of 8 hours. Gastric emptying time, small intestinal transit time (SITT), oro-anal transit time (OATT) and segmental colonic transit times were determined. The procedure was repeated 3 months post-operatively and pre- and post-operative transit times were compared.

RESULTS: No difference was shown between pre-operative median gastric emptying time (2.65 hours, range 0.4-8.6) and post-operative times (2.80 hours, range 0.3-5.3; Z=-1.759, p=0.079, Wilcoxon signed rank test), nor between pre-op SITT median (5.30 h, range 1.2-73.3), and post-op SITT (6.00, 2.0-21.7; Z=-0.556, p=0.578). Colonic segmental transit times were also unchanged: pre-operative median right colon segmental transit time was 0.5 days (range 0-1.0), compared to 0.5 days post-operatively (0-1.9; Z=-0.825, p=0.410); pre-op transverse colonic transit 0.15 days (0-0.9), post-op 0.3 days (0-0.9; Z=-0.141, p=0.888) and pre-op left colonic transit 0.6 days (0-3.1), post-op 0.55 (0-1.3; Z=-0.786, p=0.432). Median total oro-anal transit time pre-operatively was 1.6 days (0.4-4.9) and post-operatively 1.7 days (0.4-3.1; Z=-0.540, p=0.589), again showing no measurable effect after cholecystectomy.

CONCLUSION: Cholecystectomy does not appear to affect a change in gastric emptying, small bowel transit time, segmental colonic transit times, or oro-anal transit times in a 3-month prospective follow up. Longer follow-up periods may be of value to establish whether changes are induced in the longer term.

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Disclosure of Interest: None Declared

Keywords: cholecystectomy, transit

P816 DERANGEMENT OF THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM AND GLYCAEMIC CONTROL AFTER COLECTOMY

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INTRODUCTION: There is increasing evidence that colon is an active metabolic organ, removal of which leads to sodium and water depletion, chronic activation of renin-angiotensin-aldosterone system (RAAS), hyperaldosteronism and abnormal glucose tolerance[1]. Previous work has studied patients who have undergone colectomy for inflammatory bowel disease[2]. This is the first such study in patients with familial adenomatous polyposis (FAP). Patients with FAP undergo prophylactic colectomy to prevent development of colorectal cancer and so long term metabolic abnormalities resulting from the surgery would be of immense clinical interest.

AIMS&METHODS: We aimed to determine the prevalence of metabolic disturbance in patients with FAP following colectomy.

30 FAP patients who had undergone either colectomy and ileo-rectal anastomosis or restorative proctocolectomy at our institution were recruited. After fasting, urine and blood samples were collected to measure sodium loss, hydration status and RAAS activation. An oral glucose tolerance test was performed as per the World Health Organisation recommendation. Health related quality of life was assessed using Short Form 36 (SF-36) Health Survey (Version 2) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) (Version4) questionnaires.

RESULTS: Median time since prophylactic colectomy was 11.5 years. Fourteen patients (47 per cent) demonstrated fasting hyperaldosteronism (>250pmol/L) leading to higher urinary losses of potassium (p=0.01) and creatinine (p=0.002). Thirteen patients (43 per cent) also demonstrated abnormal glucose tolerance in the form of hypoglycaemia. Patients with hypoglycaemia had a significantly higher early insulin secretion (p=0.04, insulinogenic index) without the expected reduction in tissue insulin sensitivity, resulting in inappropriately low blood glucose levels. Patients exhibiting hypoglycaemia had significantly lower body mass index (p=0.005), lower energy levels with increased fatigue. However, there were no significant differences between the two groups with regard to age (p=0.29) or time elapsed since colectomy (p=0.09).

CONCLUSION: Our work suggests that prophylactic colectomy in FAP patients results in metabolic disturbances leading to a negative impact on the quality of life.

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Disclosure of Interest: S. Mallappa Other: Ms S Mallappa has been awarded the Royal College of Surgeons of England Surgical Research Fellowship, M. Samarasinghe: None Declared, S. Gabe: None Declared, R. Phillips: None Declared, M. Robertson: None Declared, S. Clark: None Declared

Keywords: Aldosterone, Colectomy, Glucose tolerance

P817 COMPLIANCE WITH THE ERAS (ENAHANCED RECOVERY AFTER SURGERY) PROTOCOL IN AN OPEN INTESTINAL SURGERY.

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INTRODUCTION: Modern perioperative care (ERAS, Fast Track) after elective intestinal surgery decreases postoperative complications and shortens hospital stay (1) and is more comfortable for patients than traditional care. These programs arising from EBM are difficult to implement and to follow (2). Randomized study was carried in between 2005-2007 at the authors' work place (3). The intervention group was managed strictly according to the ERAS protocol. The ERAS protocol became standard perioperative care in the department after that.

AIMS&METHODS: The aim of this study was to audit compliance with the ERAS protocol after a prospective study finishing.

Data of the 91 patients (54% women, mean age 36,9 years) who underwent planned open abdominal surgery during the period 9/2010-3/2011 was processed retrospectively. All patients underwent resection of the small or large intestine, proctectomy was performed in 17 patients.

RESULTS: Preoperative oral intake (D-1) was an average of 2418 ml (SD ± 1014), all patients drank PreOp (Nutricia) evening and morning before surgery (average 5,7 units, SD ± 1,4). Nasogastric tube (NGT) was not introduced during surgery in any patient, in 4 patients (4%) it was necessary to introduce it in the postoperative period. Urinary catheter was not inserted in 63 (69%) patients primarily, of which 51 patients (81%) urinated spontaneously and in 12 (19%) was necessary to introduce the catheter for urinary retention. Mean postoperative oral intake was at the day of surgery 738 ml (SD ± 522), postoperative days (POD) 1-4: 1176 ml (SD ± 606 ml), 1477 ml (SD ± 687 ml), 1761 (SD ± 750 ml), 1998 ml (SD ± 611 ml). An epidural catheter for postoperative analgesia was introduced in 82 patients (90%), in 13 (16%) patients was dysfunctional. Analgesia as measured by VAS (visual analgesic scale) was superior in patients with epidural catheter, within the 2nd POD significantly (mean VAS 0,96; SD ± 0,92 vs. 1,7, SD ± 0,99, p = 0,0039). The average length of hospital stay was 8,3 days (SD ± 5,0). Surgical site infection rate was 14,3% (13 patients). SSI I was noted in 7 (7,7%) patients, SSI II and III in 3 (3,3%).

CONCLUSION: All patients (100%) preoperatively drank maltodextrin cocktail, 96% underwent postoperative period without NGT and 56% without urinary catheter. Epidural catheter was established in 90% of the patients and reduced postoperative pain significantly. Length of hospital stay was comparable to that as in a prospective randomized study conducted in the workplace. Compliance with the ERAS protocol for its extensive introduction into practice remained high.

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Disclosure of Interest: None Declared

Keywords: Complicance, ERAS, Open Intestinal Surgery

TUESDAY, OCTOBER 15, 2013 9:00–17:00

IBD II – Poster Area

P818 IMMUNOSUPPRESSANT EFFECT OF MESENCHYMAL STROMAL CELLS ON MUCOSAL T CELLS FROM CROHN'S DISEASE PATIENTS

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INTRODUCTION: Mesenchymal stromal cells (MSC) are multipotent non-hematopoietic stem cells able to promote tissue repair and to exert potent effects on all cells involved in immune response. Crohn's disease (CD) is caused by a dysregulated T cell response towards components of the intestinal microbiota, of which the muramyl dipeptide (MDP), a peptidoglycan constituent of the bacterial wall, plays a crucial role in triggering the inflammatory cascade leading to intestinal injury.

AIMS&METHODS: We investigated the *in vitro* effects of MSC on mucosal T cells in terms of mortality, proliferative response, immunophenotype and cytokine production upon specific antigen stimulation.

A pure population of bone marrow-derived MSC at passage 3 was obtained from 3 adult CD patients. T cells were isolated from inflamed and not-inflamed colonic mucosa of 6 CD patients (F/M 4/2, mean age: 32 years, range 18-56) and 4 healthy controls (F/M 1/3, mean age: 43 years, range 27-52), and expanded *in vitro* through weekly cycles of stimulation with interleukin (IL)-2 (40 U/ml). Parallel cultures were settled in the presence or absence of allogeneic MSC (MSC:T ratio 1:20, 1:200) and MDP (10 mg/ml). The T cell mortality rate and immunophenotype were assessed by flow cytometry, the proliferation rate by incorporation of [^{3}H]-thymidine (0,5μCi/well) upon MDP stimulation. The following cytokines were detected by ELISA assay (SearchLight): transforming growth factor (TGF)-β1, interferon (IFN)-g, IL-6, IL-8, IL-10, IL-21. Student *t* test was applied for statistical analysis.

RESULTS: T cells from inflamed CD mucosa showed a lower mortality rate upon MDP stimulation in comparison with those unstimulated (18% vs 43%, $p<0.05$). MSC at both ratios were able to revert this finding ($p<0.01$), whilst they did not affect the mortality of T cells from not-inflamed CD and healthy control mucosa. A reduction of the activation marker CD25 and an increase of the CD69 in T cells cultured with MSC at both ratios ($p<0.01$), together with a reduction of the inflammatory cytokines IL-21 and IFN-g and an increase of TGF-β1 ($p<0.01$), were found. Finally, MSC inhibited T cell proliferative response upon MDP ($p<0.005$ and <0.05 for inflamed and not-inflamed mucosa, respectively) at both MSC:T cell ratios.

CONCLUSION: MSC display a robust immunosuppressant effect *in vitro* on antigen-reactive pathogenic T cells, thus paving the way to a possible therapeutic use in CD.

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Disclosure of Interest: None Declared

Keywords: Crohn's disease, cytokine, Stem Cells, t cells

P819 VITAMIN D POTENTIATES THE IMMUNOSUPPRESSIVE EFFECT OF ANTI-TNF INDUCED REGULATORY MACROPHAGES

A. Levin[1,*], M. Wildenberg[1], C. Vos[1], F. Bloemendaal[1], G. D'Haens[1], G. Van den Brink[1]. [1]*Department of gastroenterology and Hepatology and Tytgat institute for Liver and Intestinal Research, AMC, Amsterdam, Netherlands*

INTRODUCTION: We have previously shown that anti-TNF-α antibodies induce a distinct population of macrophages with immune regulatory and wound healing properties. An environmental factor that has been shown to induce tolerogenicity in dendritic cells is Vitamin D. Interestingly, epidemiological studies have shown that Crohn's disease patients have a high prevalence of vitamin D deficiency. These results incited us to investigate the role of Vitamin D in anti-TNF induced macrophages.

AIMS&METHODS: The aim of this study was to see if the Vitamin D receptor pathway is involved in the induction of anti-TNF induced macrophages and if Vitamin D can potentiate immunosuppressive effect of these macrophages.

PBMC's were isolated from peripheral blood of healthy donors. Mixed lymphocyte reactions were established by co-culturing PBMC's of two healthy individual donors in a 1:1 ratio. Cultures were treated with anti-TNF to induce anti-TNF induced macrophages. Inflammatory M1 type macrophages were generated by culturing of monocytes in the presence of IFN-gamma. Gene expression of anti-TNF compared to M1 macrophages was determined by microarray followed by pathway analysis.To determine the effect of Vitamin D on the immunosuppressive effect of anti-TNF induced regulatory macrophages, cell culture experiments were performed in the presence or absence of 1,25-dihydroxyvitamin D. Macrophages were isolated with CD14 microbeads and co-cultured with activated T-cells from a third donor. Proliferation was measured by 3H thymidine incorporation.

RESULTS: Anti-TNF induced macrophages displayed an increased expression of a number of components of the vitamin D receptor pathway, including the vitamin D receptor (VDR) and osteopontin (OPN). Addition of 1,25-dihydroxyvitamin D to the cultures did not result in enhanced numbers of regulatory macrophages. However, macrophages generated in the presence of 1,25-dihydroxyvitamin D did show an increased inhibition of T-cell proliferation, indicating increased immunosuppressive function.

CONCLUSION: Anti-TNF induced macrophages show an increased activation of the vitamin D receptor pathway. Furthermore the immunosuppressive properties of wound healing macrophages induced by anti-TNF-α can be potentiated by 1,25-dihydroxyvitamin D.

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Disclosure of Interest: None Declared

Keywords: anti-TNF, macrophage, Vitamin D, Inflammatory Bowel Disease

P820 QUORUM SENSING DRIVEN BY N-ACYL-HOMOSERINE LACTONE IN INFLAMMATORY BOWEL DISEASES ASSOCIATED DYSBIOSIS

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INTRODUCTION: Dysbiosis is a key factor in inflammatory bowel diseases (IBD) physiopathology. Quorum sensing (QS) driven by N-acyl-homoserine lactone (acyl-HSL), a bacterial communication network, has not been studied in the human gut microbiota yet and could be involved in dysbiosis.

AIMS&METHODS: The aims of this study were to look for acyl-HSLs in human gut microbiota and to investigate their features in IBD associated dysbiosis.

Fecal samples from 19 IBD patients in remission (n=10) and during flare (n= 9) and from 11 healthy subjects (HS) were analyzed. After extraction, an acyl-HSL profile was determined for each sample using HPLC coupled with tandem mass spectrometry. Concentrations were estimated by AUC of each peak (arbitrary units +/- SEM). Acyl-HSL biologic activity was validated on a bacterial biosensor system (*Agrobacterium tumefasciens* NTL4). In parallel, fecal microbiota composition was assessed by real-time quantitative PCR. For statistical analysis, a non parametric test was used.

RESULTS: Nine acyl-HSLs were identified in fecal samples while 2 were prominent: acyl-HSL at *m/z* 216.1 (3-OH-C6-HSL) and acyl-HSL at *m/z* 294.2 (3-oxo-C12:2-HSL or C13:2-HSL) recognized by NTL4 biosensor. Their concentrations

differed between IBD patients and HS: acyl-HSL at *m/z* 216.1 was significantly increased in inactive IBD compared to HS (AUC=2897+/-572 vs 1242 +/-353, P=0.04) and acyl-HSL at *m/z* 294.2 was significantly decreased in active IBD (AUC=2726+/-2726) compared to HS (AUC=30532+/-12230, P=0.007) and to inactive IBD (AUC=26409+/-12291, P=0.02). In parallel, dysbiosis was observed in active IBD: low counts in Firmicutes (*C. coccoïdes* P=0.01 and *C. leptum* P=0.003 including *F. prausnitzii* P=0.04), significant increase in Lactobacilli (P=0.002) and non significant increase in *E. coli* (P=0.6). In samples with high acyl-HSL at *m/z* 294.2 (concentration above median), *C. leptum* was significantly more represented (10.22+/-0.07 vs 9.72+/-0.19 log/g of feces, P=0.046). In these samples, there was also a trend towards higher counts in *C. coccoïdes* (P=0.06) and lower counts in *E. coli* (P=0.09).

CONCLUSION: Our study showed for the first time that QS driven by acyl-HSLs occurs in human gut microbiota. Moreover, in IBD, acyl-HSLs profile characterized by prominent acyl-HSL at *m/z* 216.1 and a decrease in acyl-HSL at *m/z* 294.2 during flare differs from HS. The lack of this acyl-HSL was associated with low counts in Firmicutes. These results invite us to investigate acyl-HSL functional role in dysbiosis onset and in host physiology.

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Keywords: Gut microbiota, Inflammatory bowel disease (IBD)

P821 MAGNETIC RESONANCE COLONOGRAPHY IN RATS WITH TNBS-INDUCED CHRONIC COLITIS. A FEASIBILITY AND VALIDATION STUDY

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INTRODUCTION: Magnetic resonance colonography (MRC) has been recently developed to assess bowel inflammation in IBD patients.

AIMS&METHODS: We aimed to assess the feasibility of MRC in rats with TNBS-induced chronic colitis and to confront results to model features.

Chronic colitis was induced in rats by weekly intrarectal injection of increasing doses of TNBS (n=9) for 6 wks while controls received vehicle (n=7). Fibrosis was assessed histologically. Fibrosis mediators were measured at wk7. Bowel wall thickness, wall signal intensity on T1 and T2w images, thickening diameter, presence of stenosis and mucosal detachment were recorded.

RESULTS: Chronic colitis was associated with significant body weight loss, higher colon weight/length as compared to control (p=0.0002). Inflammatory parameters were significantly higher in TNBS than in control: IL1β (4531 vs 1067pg/ml, p=0.011) and COX2 (0.8 vs 0.2, p=0.001). Fibrosis mediators were increased: IL13 (68.1 vs 3.6pg/ml, P=0.015), αSMA production (0.9 vs 0.6pg/ml, p=0.03). Fibrosis score was higher in TNBS than in control (p=0.03).

Colon wall thickness was higher in the TNBS than in control: maximal thickness (2.4 vs 0.7mm, p=0.0002) and minimal thickness (1.3 vs 0.5mm, p=0.0002). The wall signal intensity on T2w images was significantly higher in TNBS than in control (9040 vs 6192, p=0.002). Thickening diameter was significantly more important in TNBS than in control (50 vs 10%, p=0.0002). Stenosis was observed in 7/9 TNBS and in 0/7 control (p=0.002). Mucosal detachment was found in 4/9 TNBS and 0/7 control (p=0.04).

MRI data were associated with inflammation and fibrosis parameters:

	Colon weight/ length	Fibrosis score	TNFα	IL1β	COX2	IL13	αSMA
Maximal thickness	**<0.0001**	**0.0013**	0.2556	**0.0184**	**0.0005**	0.0634	**0.0425**
Minimal thickness	**<0.0001**	**0.0141**	0.0555	0.1798	**0.0007**	0.0538	**0.0113**
T2w signal	**0.0010**	**0.0047**	0.2454	0.0677	**0.0005**	0.0594	0.2545
Thickening diameter	**0.0076**	0.0769	**0.0131**	0.3121	**0.0014**	0.0579	**0.0187**

CONCLUSION: MRC is feasible and easily distinguished control from colitic rats. MRC signs are strongly associated with fibrosis parameters. MRC evaluation may be part of new anti-fibrotic drug assessment in experimental models of chronic colitis.

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Disclosure of Interest: None Declared

Keywords: chronic colitis, IBD, magnetic resonance colonography, Rat, TNBS

P822 DIFFERENT INFLAMMASOME TYPES COLLABORATE IN HUMAN INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: Recently, intracellular danger – and pathogen receptor activation has been described in the gut. Inflammasome activation in the cytosol of myeloid and epithelial cells leads to potent caspase-1 mediated pyrogene and alarmin secretion (such as IL-1β and HMGB1) that might be involved in the pathogenesis of IBD[1]. Moreover, inflammasome activation has been shown to be pivotal in a murine model of IBD colitis[2]. However, the functional importance of the combined inflammasome subtype activation during IBD pathogenesis remains unknown.

AIMS&METHODS: This study investigated whether there are different inflammasomes activated in colonic mucosa of active IBD patients before and after anti-TNF-α therapy. Therefore, gene expression of genes involved in inflammasome activation was investigated in colonic mucosa from 43 active IBD patients [24 ulcerative colitis (UC) and 19 Crohn's disease (CD)] before and 4-6 weeks after their first infliximab (IFX) infusion and from 6 normal controls. Total RNA was used to analyze gene expression via Affymetrix Human Genome U133 Plus 2.0 Arrays and qRT-PCR. Data was analyzed using Bioconductor software. Protein localisation of AIM2, IFI16, cleaved IL-1-β, CASP1 and HMGB1 was determined by immunohistochemistry (IHC) on formalin-fixed, paraffin-embedded mucosal biopsies of IBD patients and controls. dsDNA-induced intracellular IL-1β cleavage was determined by western blot in protein lysates from intestinal FHC cells.

RESULTS: Gene expression analysis showed a significant (false discovery rate $<5\%$) increase in colonic expression of *AIM2, IFI16* and a borderline significant increase of *NLRP3* in active IBD vs. controls. Moreover, after IFX therapy, a significant decrease in expression of *AIM2* and *IFI16* was observed in IBD responders showing complete mucosal healing when compared to their baseline samples. Interestingly, IHC demonstrated an epithelial expression pattern for AIM2 with minor expression in inflammatory cells. In contrast, we observed positive staining for IFI16 in lymphocytes and epithelial cells. Finally, we confirmed the presence of active IL1-β, CASP1 and HMGB1 in tissue sections of inflamed mucosa and we endorsed the epithelial presence/activation of an AIM2/IFI16-mediated inflammasome since dsDNA (AIM2/IFI16 specific stimulus) could induce IL-1β cleavage in intestinal FHC cells.

CONCLUSION: For the first time we have shown combined transcriptional and functional activation of the different inflammasome subtypes NLRP3, AIM2 and IFI16 in the inflamed colon of active IBD patients, accompanied with expression levels of activated CASP1, IL-1β and HMGB1.

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Keywords: AIM2, IFI16, Inflammasome, Inflammatory bowel disease (IBD), NLRP3

P823 DETERMINATION OF IMMUNE SURVEILLANCE IN CEREBROSPINAL FLUID (CSF) IN PATIENTS WITH CROHN'S DISEASE: INITIAL RESULTS OF THE TOSCA STUDY

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INTRODUCTION: Natalizumab (N), a therapeutic monoclonal antibody (MAb) for Multiple Sclerosis and Crohn's Disease (CD), increases progressive multifocal leukoencephalopathy (PML) risk. It blocks $\alpha_4\beta_1$ and $\alpha_4\beta_7$ integrins, and inhibits both CNS and gut lymphocyte trafficking. This results in marked reduction in CSF total and CD4+ lymphocytes, and inverted CD4:CD8 ratio, signs of deficient immune surveillance, and the putative mechanism contributing to PML due to JC virus infection/reactivation.[1]PF-00547659 (PF) is an investigational, fully human, anti-MAdCAM MAb designed to reduce gut lymphocyte homing, to treat inflammatory bowel disease. Because of the low incidence of N associated PML, comparing risk between these drugs in clinical trials is not feasible. However, 6 weeks after 1 injection of N, a dramatic drop in CSF lymphocytes and CD4 cells occurs.[2] An alternative approach to assess drug-induced PML risk may be to assess the effect of a new agent on CNS T lymphocytes. The purpose of this study is to see if PF alters trafficking of the lymphocyte population to the CNS reflecting immune surveillance in CD patients (pts).

AIMS&METHODS: TOSCA is a 2 cohort open-label study of PF. Cohort 1 explored baseline CSF values at 2 different lumbar puncture (LP) visits before PF administration, while cohort 2 will investigate CSF composition before and after induction with PF. We present here the data from Cohort 1, along with concurrent data from 5 healthy subjects. CSF from adults with moderately-to-severely active CD, who failed prior immunosuppressants (IS) and anti-TNF treatment was analyzed by FACS

RESULTS: Of 10 CD pts, 8 were men, age (mean±sd) was 40.8±16.0y, CD duration was 13.5±6.1y and HBI was 8.6±2.8 for 7 pts (3 had stomas). Data from 2 pts were discarded because of inaccurate cell counting. 3 pts did not have a 2nd LP because of headache. FACS data, in cells/mL, are shown below

Population	Total Lymphs	CD3+	CD4+	CD8+	CD4:CD8
LP1 (n=8)	678 (64.4)	571 (72.2)	408 (74.3)	178 (142.0)	2.3 (140.2)
LP2 (n=5)	832 (65.9)	796 (63.2)	551 (73.8)	206 (55.9)	2.7 (67.7)
Healthy Subjects (HS) (n=5)	672 (66.4)	654 (66.4)	498 (65.6)	199 (60.1)	2.5 (23.3)
Geometric mean values (CV%)					

CONCLUSION: CSF lymphocyte counts are similar in HS and pts with moderate-to-severe CD. Repeat testing showed stable CSF lymphocyte populations, showing lack of inflammatory changes after LP. This is a promising approach to assess risk of anti-integrin therapy

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Keywords: CSF, Immune Surveillance

P824 ROLE OF TOPICAL CALCIUM BUTYRATE IN INFLAMMATORY AND PROLIFERATIVE COLON DISEASES

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INTRODUCTION: Butyric acid (BA) is a physiological component of colonic environment endowed with anti-inflammatory properties. Moreover BA is a pivotal regulator of cell-cycle since it inhibits histone deacetylase, and activates acid sphingomyelinase leading to production of antiproliferative molecules such as ceramide and sphingosine.

AIMS&METHODS: To investigate the topical anti-inflammatory activity of BA calcium salt (calcium butyrate, CB) in chemically-induced colitis in rat, and to evaluate "in vivo" and "in vitro" its anti-proliferative properties.

i) The anti-inflammatory activity of CB (10-30 mg) was evaluated in rat in the dinitrobenzene (DNB)-induced colitis test, after intracolonic instillation for 6 consecutive days starting 3 days before colitis induction. ii) The "in vivo" anti-proliferative activity of CB (3.5 mg) was evaluated in F344 rat in the azoxymethane (AOM)-induced aberrant crypt foci (ACF) test, after intracolonic instillation six days a week for four weeks. iii) The "in vitro" anti-proliferative activity of CB (2.5-5-10 mM) was assessed by incubation for 48h with HT29, SW620 and HCT116 tumour cell lines evaluating the rate of [^{3}H]thymidine incorporation.

RESULTS: i) In DNB-induced colitis, the intracolonic instillation of CB 30 mg completely prevented the decrease of body weight of the animals, and counteracted the local noxious effects of the irritant by reducing both the colon swelling (-23%) and the mucosal damaged area (-48%) respectively. ii) In AOM-induced aberrant crypt foci test, the intracolonic instillation of CB significantly reduced the number of ACF in the whole colon (-22.7%). iii) CB, incubated with HT29, SW620 and HCT116 tumour cell lines, induced in all strains a significant anti-proliferative dose-dependent effect measured by reduction of [^{3}H]thymidine incorporation.

CONCLUSION: CB, when directly applied to the mucosa of the colon of the rat, is able to ameliorate the colonic inflammation, suggesting a possible beneficial role in the treatment of inflammatory colon diseases. Moreover, CB showed "in vivo" and "in vitro" interesting anti-proliferative activities, whose clinical relevance needs to be confirmed in additional clinical investigations.

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Disclosure of Interest: None Declared

Keywords: Calcium Butyrate, Inflammatory bowel disease (IBD), Proliferative Colon Diseases

P825 CROHN'S DISEASE-ASSOCIATED ADHERENT-INVASIVE ESCHERICHIA COLI MANIPULATE HOST AUTOPHAGY BY IMPAIRING SUMOYLATION

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INTRODUCTION: Crohn's disease (CD) is an inflammatory intestinal disorder involving genetic and environmental factors, as well as microbiota. It has been established that intestinal mucosa of CD patients is abnormally colonized by pathogenic adherent-invasive *Escherichia coli* (AIEC) able to adhere to and to invade intestinal epithelial cells (IECs). SUMOylation is a reversible modification in which SUMO, a ubiquitin-like polypeptide of about 10 kDa, is covalently linked to target proteins. SUMOylation has been emerged to regulate numerous cellular processes, such as transcription and protein stability.

AIMS&METHODS: Here, we investigated the role of SUMOylation in host defense against AIEC infection. SUMO-conjugated protein levels in human intestinal epithelial cells T84 and in mouse intestinal epithelia were analyzed by Western blot. The number of intracellular AIEC in cells over-expressing SUMOs was determined by bacterial invasion assay and confocal microscopy. SUMOylation status of ATG5 and ATG16L1 was assessed by immunoprecipitation analysis. Autophagic activity was characterized by Western blot and immunofluorescent analyses of LC3 and p62 levels.

RESULTS: AIEC infection markedly decreased the levels of SUMO1-, 2- and 3-conjugated proteins in IECs. This was also observed in IECs from AIEC-infected mice. Over-expression of SUMO1, 2 or 3 significantly decreased the number of intracellular AIEC in IECs. As we previously showed that the intracellular replication of AIEC is tightly controlled by autophagy, the involvement of SUMOylation in such process was investigated. We observed that autophagic activity was increased in T84 cells transfected with SUMOs as shown by increased LC3-II and p62 protein levels. Bioinformatics prediction revealed ATG5 and ATG16L1, two key elements of autophagy induction, as potential targets of SUMOs. Immunoprecipitation and Western blot analyses confirmed the SUMOylation of these proteins in IECs, which was decreased upon AIEC infection. Plasmids encoding ATG5 or ATG16L1 wild-type or mutated for the SUMO-binding site were respectively transfected in ATG5 or ATG16L1-deficient MEFs. Absence of SUMOylation of ATG5 and ATG16L1 in MEFs resulted in a less efficient autophagy response to AIEC infection.

CONCLUSION: Our results suggest that AIEC infection inhibits host autophagy response to replicate intracellularly via a SUMOylation-mediated mechanism.

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Disclosure of Interest: None Declared

Keywords: adherent-invasive E. coli, autophagy, Crohn's disease, sumo

P826 AUTONOMIC NERVOUS SYSTEM FUNCTION PREDICTS THE INFLAMMATORY RESPONSE OVER A THREE-YEAR FOLLOW-UP

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INTRODUCTION: The autonomic nervous system (ANS) modulate disease activity in several animal models of intestinal inflammation. The parasympathetic nervous system (PNS) acts anti-inflammatory via the vagus nerve, while the sympathetic branch (SNS) is considered pro-inflammatory. However, clinical evidence confirming such an influence of the ANS on gut or systemic inflammation in patients with inflammatory bowel disease (IBD) is sparse.

AIMS&METHODS: We aimed to investigate whether ANS function is associated with severity of inflammation at onset of ulcerative colitis (UC), and whether ANS function at onset predicts the evolution of inflammatory parameters longitudinally.We followed 49 patients from onset of UC for 3 years. Three months after inclusion, ANS activity was assessed by HRV analysis of 24-hour Holterrecordings. RMSSD was used as an indicator for PNS activity and LF/HF for SNS activity. Blood and stool samples were obtained at the visits to assess inflammatory parameters. Rectal biopsies were obtained for analysis of mucosal cytokine mRNA levels. Linear regression analysis was used to test associations between ANS activity and inflammation at onset; linear mixed models were used to test if ANS function at onset predicts the evolution of inflammation over the next 3 years.

RESULTS: SNS was significantly associated with higher levels of several systemic inflammatory parameters at onset (Table 1A). Moreover, SNS activity was also positively associated with mucosal IL-8 mRNA (β=0.52±0.24, p=0.035). PNS activity predicted the evolution of systemic inflammation, assessed by sedimentation and WBC count, over the 3 year period (Table 1B). Moreover, trends were found for both SNS (β=13.4±8.0, p=0.099) and PNS (β=-2.3±1.3, p=0.075) activity to predict the course of mucosal inflammation (fecal calprotectin) during follow-up. Over all analyses, signs are consistently positive for SNS activity and negative for PNS activity, confirming their pro- and anti-inflammatory properties, respectively, as found in animal studies.

Table1. Beta coefficients from linear regression analysis[1], Beta coefficients from linear mixed models[2]

A.Onset[1]	Symp,LH/HF	p	Parasymp,RMSSD	p
Sedimentation Rate	**1.44±0.51**	**0.007**	-0.10±0.061	0.12
CRP	**5.67±1.79**	**0.0029**	-0.27±0.22	0.22
IL17	*0.44±0.24*	*0.080*	-0.04±0.025	0.11
TNF	**0.63±0.28**	**0.028**	-0.06±0.034	0.11
B.Followup[2]				
Sedimentation Rate	0.20±0.46	0.66	**-0.13±0.06**	**0.027**
WBC count	0.006±0.10	0.95	**-0.03±0.01**	**0.007**

CONCLUSION: In patients with UC there is a close interplay between ANS activity and the inflammatory response, which might be an important contribution to understand the pathogenesis of UC, to predict the inflammatory activity and improve treatment.
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Disclosure of Interest: None Declared
Keywords: ANS, inflammation, prediction, ulcerative colitis

P827 RELATIONSHIP OF VASCULAR DAMAGE TO DISRUPTION OF MUCOSAL EPITHELIUM IN DEXTRAN SULPHATE SODIUM-INDUCED COLITIS IN MICE

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INTRODUCTION: Ulcerative colitis (UC) is a multifactorial disorder of unknown cause. Dextran sulphate sodium (DSS)-induced colitis in mice is often used as a model of UC, but the pathogenesis of the colitis is also poorly understood. We focused on the mucosal blood vessels in this model in order to define their relationship to epithelial damage.
AIMS&METHODS: Eight-week-old C57BL/6J mice (n = 48) were administered 3% DSS in their drinking water, which was freely accessible, for 7 days. Six mice were euthanized each day from the start of the administration. The large intestine of three of the mice was extirpated after the vessels had been perfused with rhodamine B isothiocyanate (RITC)-labeled gelatin. Thick sections of the excised tissue were stained with anti-CD31 and anti-α-SMA antibodies. The distribution and morphology of the vessels were observed with a confocal laser scanning microscope, and three-dimensional reconstruct images were obtained. From the other three mice, we prepared paraffin sections of the colon, stained them with hematoxylin-eosin and immunohistochemically with anti-Ki67 antibodies, and assessed the mucosal damage microscopically.
RESULTS: The animals had begun to lose weight from the fourth day and passed bloody stools from the fifth day. On day 3, we observed leakage of RITC-labeled gelatin from blood vessels in the lamina propria just above the muscularis mucosa, and detachment of vascular endothelial cells from pericytes. Immunostaining with anti-Ki67 antibodies during the same period revealed signal reduction in the crypt proliferative zone, indicating a decrease in epithelial-cell proliferation. Damage to the mucosal epithelium became evident histopathologically on day 5. The vascular damage progressed through day 7.
CONCLUSION: In the early stage of DSS-induced colitis, the cell cycle of crypt cells in the proliferative zone is arrested. Concurrently, and before inflammation develops in the mucosa, bleeding from blood vessels running in the lamina propria occurs. Our results suggest that in DSS induced-colitis, mucosal epithelial-cell damage is preceded by damage to mucosal blood vessels, resulting in decreased blood flow in the lamina propria. After mucosal epithelial damage has occurred, the mucosal barrier may be disrupted, leading to exacerbation of the colitis. Study of the colonic vasculature in UC may help in clarifying the pathogenesis of the disease.
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Disclosure of Interest: None Declared
Keywords: Dextran Sulphate Sodium, rhodamine B isothiocyanate, ulcerative colitis

P828 VITAMIN D SUPPLEMENTATION DOES NOT IMPROVE ACUTE DSS COLITIS

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INTRODUCTION: Vitamin D (vD) plays an important role in the regulation of the immune system and its deficiency is associated with an increased risk of developing IBD. Studies have shown that patients with IBD often have low serum 25(OH)D3 levels compared to healthy controls and suggest that vD supplementation may serve as a novel treatment strategy for this prevalent health problem. The purpose of this study is to investigate the possible benefical role of vD on the severity of dextran sulfate sodium (DSS)-induced acute colitis model.
AIMS&METHODS: The purpose of this study is to investigate the possible benefical role of vD on the severity of dextran sulfate sodium (DSS)-induced acute colitis model. We utilized the murine DSS colitis model. BALB/c mice were divided into 4 specific treatment groups: Group 1 was provided a normal diet; Group 2 was given a vD deficient diet; Groups 3 and 4 were given a diet supplemented with *1 IU/g and 5 IU/g vD, respectively. Groups 2-4 were supplemented four weeks prior to and then during* 2% DSS administration in drinking water. Clinical assessment was monitored daily using a validated DSS Colitis Disease Activity Index (DAI). The mice were sacrificed 5 d after DSS administration. Colon length to weight ratio and histological damage were also scored.
RESULTS: In preliminary experiments, mice receiving 3% DSS had 50% mortality by day 5. We thus proceeded with 2% DSS, found to induce significant acute colitis, without mortality. vD failed to abrogate the weight loss associated with DSS induced colitis. Overall DAI scores and colonic weight/length ratios were lower in vD supplemented mice that received 2% DSS, although the differences did not achieve statistical significance. DAI and other measures as above were not statistically different in the mice on a vD deficient diet. Histopathology analyses also revealed non-significant differences between dietary groups. vD serum levels are pending.
CONCLUSION: Taken together, our data do not provide evidence that dietary supplementation with vD improves acute colitis in the DSS model. Limitations include the very short duration of the study, limited number of animals per group and the acute nature of the inflammatory colitis.
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Keywords: DSS colitis, treatment, Vitamin D, Inflammatory Bowel Disease

P829 MUCOSAL MICRORNA EXPRESSION IN PATIENTS WITH ULCERATIVE COLITIS BEFORE AND AFTER INFLIXIMAB TREATMENT

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INTRODUCTION: MicroRNAs (miRNAs) are increasingly recognized as major regulators of gene expression in many processes, including inflammation and tissue remodeling. Recently, altered expression of miRNAs has demonstrated association with ulcerative colitis (UC).
AIMS&METHODS: In this study, we investigated the effect of infliximab therapy on the miRNA expression in UC colonic mucosa. Therefore, colonic mucosal biopsies were obtained during endoscopy from 7 UC patients before and after infliximab induction therapy (infusions at weeks 0, 2 and 6) and from 10 normal controls. Endoscopic response was assessed at 14 weeks after start of infliximab and was defined as a Mayo endoscopic subscore of 0 or 1 (inactive UC). Endoscopic non-response was defined as a Mayo endoscopic subscore of 2 or 3 (active UC). Total RNA, including small RNA, was extracted from the biopsies and used to analyze the miRNA expression via Affymetrix GeneChip® miRNA 2.0 arrays. Data were analyzed with Bioconductor software. A false discovery rate $<5\%$ and >2-fold change was considered as significant.
RESULTS: Compared to normal controls, we identified 58 significantly differentially expressed miRNAs in active UC at baseline before therapy (18 up- and 40 downregulated). Between inactive UC after therapy and controls, still 33 significantly dysregulated miRNAs were seen (15 up- and 18 downregulated), with 17 out of 33 miRNAs common to the significant miRNAs between active UC and controls.
Four out of 7 patients showed endoscopic response. In these 4 endoscopic responders, 4 mature miRNAs were significantly upregulated (hsa-miR-10b-5p, hsa-miR-375, hsa-miR-378a-3p and hsa-miR-422a) and 6 were downregulated (hsa-miR-21-5p, hsa-miR-31-5p, hsa-miR-146b-5p, hsa-miR-155-5p, hsa-miR-330-3p and hsa-miR-3187-3p) after infliximab therapy when compared to their baseline samples. These miRNAs were predominantly immune-cell derived and have been implicated in inflammation and autoimmunity. By contrast, infliximab did not significantly affect miRNA expression in the 3 non-responders.
For prediction of response to infliximab therapy, we compared endoscopic responders and non-responders before treatment. No significant differences in miRNA expression were observed.
CONCLUSION: Infliximab therapy has a profound effect on the mucosal expression of miRNAs. This suggests the involvement of miRNAs in pathways affected by infliximab therapy and implies a role for mucosal miRNAs as potential biomarkers for response to infliximab therapy.
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Keywords: infliximab, microarray, mucosal microRNA expression profiling

P830 INFLAMMATION DRIVEN FIBROSIS IN ULCERATIVE COLITIS – INVESTIGATION OF A NEGLECTED PROBLEM

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INTRODUCTION: Intestinal fibrosis in Crohn's disease is a chronic inflammation driven process leading to an increase of myofibroblasts in all layers of the intestinal wall. However strictures and stenosis in Ulcerative Colitis (UC), which classically affects the mucosa and submucosa but occasionally leads to transmural disease, are very rare. It is suggested that a thickening of the muscularis propria predominates this process. There is however no systemic evaluation of fibrostenosing UC available.
AIMS&METHODS: We aimed at investigating whether there is a different fibrotic load in acute vs longstanding UC and whether the degree of fibrosis in UC correlates with the severity and extent of inflammation.
Colectomy specimens from all UC patients operated at the AMC between 2009-2012 were reviewed. Specimens from patients with recent onset ($<$ 2 years) and longstanding UC ($>$ 10 years) were selected. On H&E stainings the cumulative

Geboes histological inflammatory activity score (0-22 points) was determined. Sirius Red stainings were done for collagen, and α-smooth muscle (α-SMA) was stained immunohistochemically for detection of myofibroblasts and smooth muscle cells. From every patient the surgical resection margin and the microscopically most inflamed region were selected, so that every patient served as its own control. Staining signals were investigated by image analysis software (Image J, NIH).

RESULTS: We compared 8 resection specimens from patients with recent onset refractory UC, and 10 from patients with longstanding UC operated for dysplasia.

Patients with short disease duration had a higher cumulative Geboes score gradient (maximal inflamed area–resection margin) compared to patients with longer disease duration (6 vs 14 points, p=0.02).

There was no difference in increase of collagen deposition in early vs longstanding UC (4.2% vs 2.0%) or α-SMA positivity (=number of α-SMA positive vs total number of cells; 3.6% vs 1.6%).

In both early and long UC duration, we did not find a correlation between collagen deposition and α-SMA expression.

In early vs long UC the muscularis mucosa (MM) was not significantly thicker (0.9 vs 1.8 mm). There was no correlation between MM thickness and collagen or α-SMA expression.

CONCLUSION: In our series of colectomy specimens, no association between disease duration and increased collagen deposition or myofibroblast activation could be found. In addition, no correlation between the severity of inflammation and deposition of collagen or expression of α-SMA could be detected. Fibrosis in UC does not appear to increase significantly over time.

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Keywords: Fibrosis, inflammation, Pathology, ulcerative colitis

P832 A WATER-SOLUBLE EXTRACT FROM GANODERMA LUCIDUM FUNGUS MYCELIA (DESIGNATED AS MAK) PREVENTS INDOMETHACIN-INDUCED SMALL INTESTINAL INFLAMMATION.

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INTRODUCTION: "*Ganoderma lucidum*" Karst also known as "Reishi", is a traditional food in China and Japan, and we have previously reported that MAK has anti-inflammatory effects in murine colitis induced by trinitrobenzene sulphonic acid. However, its effects on small intestinal inflammation is unknown. The present study was designed to investigate the preventing effects of MAK on indomethacin-induced ileitis in mice.

AIMS&METHODS: To assess the preventive role of dietary MAK, the C57BL/6 mice were sacrificed after 24 hours of indomethacin treatment and the intestinal inflammation was evaluated. Mucosal lymphocytes taken from the small intestine of treated mice were stimulated in vitro for 48 hours, and mucosal lymphocytes taken from small intestine of non-treated mice were stimulated in vitro with MAK for 48 hours, then the concentration of interferon-gamma (IFN-gamma) was determined by ELISA. In addition peritoneal macrophages (PMs) were stimulated in vitro with MAK and adoptively transferred intra-peritoneally to C57BL/6 mice, which were then given indomethacin. After 24 hours, the intestinal inflammation was evaluated. PMs stimulated with MAK and labeled with fluorescent dye were adaptively transferred intra-peritoneally to treated mice, we determined the localization by confocal microscopy.

RESULTS: The shortness of the small intestine was prevented in MAK administered mice. Indomethacin-induced small intestinal injury was inhibited by feeding with MAK in a dose-dependent manner. The IFN-gamma production from intraepithelial lymphocytes of indomethacin treated mice was increased compared to control group. In vitro stimulation of intraepithelial lymphocytes, but not lamina propria lymphocytes, the IFN-gamma production from intraepithelial lymphocytes was inhibited by MAK. The development of macroscopic lesions, the number of ulcers, and vascular permeability by indomethacin were significantly prevented in the transfer of PMs that had been stimulated in vitro with MAK compared to PMs from the control group. The transferred PMs were detected in mesenteric lymph node, the submucosa and lamina propria of a small intestine.

CONCLUSION: MAK is effective in the prevention of acute intestinal inflammation by indomethacin. PMs stimulated by MAK were detected in small intestine, and appear to contribute to the anti-inflammatory response.

Disclosure of Interest: None Declared

Keywords: Indomethacin, MAK, small intestine

P833 CD80 SIGNALING MANIPULATION AFFECTS TUMOR IMMUNOSURVEILLANCE IN EXPERIMENTAL COLITIS-ASSOCIATED CANCER

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INTRODUCTION: In patients with ulcerative colitis (UC), the inconsistency between cumulative risk of colon cancer and cumulative rate of dysplasia suggests the presence of an immunosurveillance mechanism. In a previous study, we observed a significant overexpression of the costimulatory molecule CD80 in the colonic mucosa of UC patients with dysplasia and its down-regulation at more advanced stages of carcinogenesis.

AIMS&METHODS: The aim of this study was to explore the role of CD80 in an experimental model of colitis-associated cancer. To this end, the AOM/DSS murine model of inflammation-related colon carcinogenesis was used. Neutralizing antibodies against CD80 or its inhibitory receptor CTLA4 were administered after the last DSS cycle in order to inhibit or enhance CD80 signalling, respectively. Animals were randomized to receive specific abs or isotype control and sacrificed after 0, 7, 28 or 56 days. Colons were processed for microscopic examination of histopathologic and inflammatory changes.

RESULTS: Invasive carcinoma frequency was increased in mice treated with antiCD80 compared to isotype control mice. Notably, no evidence of invasive carcinoma was observed in mice treated with antiCTLA4, instead (p=0.02). High grade dysplasia (HGD) foci number and extension were significantly augmented in mice treated with antiCD80 and minimal in those treated with antiCTLA4 (p=0.005). The extension of LGD was not different among the three groups. Inflammatory score was significantly lower in mice who received antiCD80 but it was similar in isotype control and antiCTLA4 treated mice.

CONCLUSION: After the oncological damage is arrested at a relatively early stage half of the mice spontaneously clear off HGD demonstrating the presence of an active immunosurveillance mechanism at the level of the colonic mucosa. This mechanism is significantly impaired if CD80 signaling is altered. Indeed, CD80 signaling blockade leaded to carcinogenesis progression, while its enhancement triggered a reduction of HGD frequency and extension. The inhibition did not affected LGD, suggesting that CD80 signaling is the checkpoint of LGD to HGD progression.

Disclosure of Interest: None Declared

Keywords: AOM-DSS colitis, CD80, colonic carcinogenesis, colonic dysplasia, CTLA-4, ulcerative colitis,

P834 HYPOXIS HEMEROCALLIDEA CORM AMELIORATES ACUTE EXPERIMENTAL COLITIS

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INTRODUCTION: The preventive effect of *Hypoxis hemerocallidea* corm (African potato, AP), a plant widely used in South Africa as a natural remedy for its anti-inflammatory and hypoglycaemic properties, was evaluated. Anti-inflammatory activity has been ascribed to hypoxoside, one of the major constituents of the plant, which is transformed to rooperol in the gut. Rooperol is a biologically active compound that balances the immune system.

AIMS&METHODS: The aims of the present study was to evaluate an AP dietary extract (APE) supplementation on acute ulcerative colitis (UC) and deep insight into possible mechanisms of action involved.Seven week old female C57BL/6J mice were randomized into three groups (n=14): two of them received a standard diet during 35 days, while the third group was fed with the standard diet supplemented with APE powder 0.67 % for the same interval. The supplied APE powder for the experiment contained 58.0 % of hypoxoside. UC was induced by the addition of 3 % dextran sulfate sodium (DSS) in the drinking water on day 26 and for 5 days, followed by a regime of 5 days of tap water. Control healthy mice were allowed to drink only water. Disease activity index (DAI) was evaluated and colonic inflammation was determined by both histological and biochemical assays.

RESULTS: DSS administration caused severe colon damage, as indicated by body weight loss and colon shortening, increased DAI and myeloperoxidase (MPO) levels. Furthermore, an acute inflammation with neutrophil infiltration as well as haemorrhagic foci developed on colons from DSS-control animals. On the contrary, treatment with APE-supplemented diet significantly attenuated macroscopic colonic damage as well as MPO activity, compared to non-treated colitic animals. DSS exposure also caused significant expression of cyclooxygenase (COX)-2 and inducible nitric oxide synthase (iNOS), which were reverted to the control levels in the APE-supplemented diet group. P38 and c-Jun N-terminal kinase (JNK) mitogen-activated protein kinases (MAPKs) phosphorylation and the nuclear factor kappa B (NFkB) expression were also significantly increased by DSS. By contrast, these changes were prevented in animals fed with the APE-supplemented diet.

CONCLUSION: Dietary enrichment with APE reduces the damage in acute colitis model, alleviating the oxidative events and returning pro-inflammatory proteins expression to basal levels probably through JNK MAPK and NF-kB signalling pathways. *H. hemerocallidea* corm diet might provide a basis for developing a new strategy in dietary supplementation for the prevention of UC.

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Disclosure of Interest: None Declared

Keywords: DSS induced colitis, MAPK , NF-kappaB

P835 DISTINCT CELL SIGNALLING MECHANISMS DRIVE THE TUMOUR NECROSIS FACTOR ALPHA AND INTERFERON GAMMA-INDUCED TRANSCRIPTIONAL DOWNREGULATION OF AQUAPORIN 3 RNA EXPRESSION

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INTRODUCTION: Altered absorption and secretion of water, resulting in diarrhea, is a key characteristic of inflammatory bowel diseases (IBD). Although aquaporins (AQP) are known to be involved in water movement, the role of AQP3 in the barrier dysfunction that characterizes IBD remains unknown. *We hypothesized that AQP3 transcription was inhibited in intestinal inflammation by the cytokines tumour necrosis factor (TNF) α and interferon (IFN) γ.*

AIMS&METHODS: 1. C57Bl/6 mice were administered 2.5% dextran sodium sulfate (DSS) in drinking water for up to 7 days to induce colonic inflammation. AQP3 protein expression was assessed using western blot of mucosal scrapings and immunofluorescence of fixed tissue. **2.** The human adenocarcinoma cell line HT29 was used for treatments with either human recombinant TNFα (25 ng/mL) or human recombinant IFNγ (500 U/mL). AQP3 pre-mRNA and mRNA expression were assessed by real-time RT-PCR. Inhibitor studies to reverse the cytokine-induced downregulation of AQP3 were performed using a 1 hr inhibitor pre-treatment prior to the addition of cytokine.

RESULTS: 1. AQP3 protein expression was downregulated early in colonic inflammation at 3 days post-commencement of DSS with diminished basolateral membrane staining in epithelial cells lining colonic crypts. These changes were no longer evident at 7 days, where surviving epithelial cells expressed similar levels of AQP3 compared to controls. However, there was an increase in AQP3 positive, E-cadherin negative cells in regions lacking normal crypt architecture. **2.** Similarly, HT29 cells treated with TNFα or IFNγ resulted in an early decrease in AQP3 pre-mRNA expression at 2 hr, which was followed by decreased mRNA expression at 6-12 hr, suggesting transcriptional repression of AQP3 expression. Commercially available AQP3 antibodies are unable to detect human AQP3 protein. The IFNγ-induced decrease in AQP3 mRNA expression at 12 hr was reversed using a broad-spectrum JAK inhibitor (JAK Inhibitor I, 10 μM), but not a JAK2 specific inhibitor (JAK2 Inhibitor II, 10 μM). In contrast, the TNFα-induced decrease in AQP3 mRNA expression at 12 hr was not reversed by inhibitors of the PI3K, AKT, NF-κB, ERK/MAPK and p38 MAPK pathways (LY294002, 10 μM; Triciribine, 1 μM; BAY11-7082, 30 μM; U0126, 10 μM and SB203580, 10 μM respectively), even though all of the above pathways were activated by TNFα and significantly inhibited by their respective inhibitors.

CONCLUSION: The data suggest that alterations in AQP3 expression represent early events that occur in colonic inflammation. *In vitro*, both TNFα and IFNγ are independently capable of decreasing AQP3 mRNA transcription through distinct mechanisms.

Disclosure of Interest: None Declared

Keywords: aquaporin, DSS induced colitis, HT-29 cell, interferon gamma, transcriptional downregulation, tumor necrosis factor-alpha

P836 TISSUE-SPECIFIC OVEREXPRESSION OF UPR-RELATED C/EBP HOMOLOGOUS PROTEIN IMPAIRS MUCOSAL TISSUE REPAIR

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INTRODUCTION: Loss of epithelial cell homeostasis and apoptosis highly contribute to intestinal inflammation. While endoplasmic reticulum and mitochondrial unfolded protein responses (UPR) have been implicated in chronic intestinal inflammation, functional correlation between UPR-related C/EBP homologous protein (CHOP) expression and CHOP-mediated programming towards inflammation-related disease susceptibility remains to be elucidated. In this study, we generated and characterized a novel transgenic mouse model expressing high levels of HA-tagged CHOP in intestinal epithelial cells ($Chop^{IEC\ Tg/Tg}$).

AIMS&METHODS: We characterized mice by gene expression profiling of colonic epithelial cells and analyzed the consequence of CHOP overexpression on intestinal homeostasis in response to infection-driven and Dextran Sodium Sulphate (DSS)-induced colitis, as well as mechanical injury.

RESULTS: Transcriptional profiling of disease-free transgenic mice identified a set of CHOP-dependent target genes related to inflammatory and microbial defense program in the intestinal epithelium. Under conditions of acute colonic inflammation, transgenic mice are not affected by *Citrobacter rodentium* infection, but reveal more severe inflammation and tissue injury in response to acute DSS-induced colitis, resulting from transcriptional activation of CHOP-HA protein. Delayed recovery from DSS-induced colitis and impaired closure of mechanically-induced mucosal wounds clearly indicate a role of CHOP in epithelial cell homeostasis in response to injury.

CONCLUSION: In conclusion, transgenic epithelial cell-specific overexpression of CHOP aggravates intestinal inflammation associated with the loss of epithelial cell restitution as well as impaired tissue healing and repair, supporting a disease-conditioning role of UPR-related CHOP expression in the epithelium.

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Disclosure of Interest: None Declared

Keywords: CHOP, mucosal heanling

P837 OLIGOSACCHARIDE ALTERATIONS OF IGA IN CROHN'S DISEASE INDUCE INFLAMMATORY-TYPE IMMUNE RESPONSES

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INTRODUCTION: Immunoglobulin (Ig) A serves as the first line of defense against pathogenic antigens in intestinal mucosa and plays a crucial role in the maintenance of intestinal homeostasis. Recent reports have revealed that monomeric IgA (mIgA) induces inflammatory immune response by neutrophils, whereas, secretary IgA (sIgA) reduces pathogen-mediated proinflammatory cytokines, such as TNF-α, IL-6 and IFN-γ. We have recently reported that *N*-acetylgalactosamine (GalNAc) in *O*-linked oligosaccharides of IgA was significantly decreased in IBD patients and the alteration was a novel biologic marker for Crohn's disease[1]. However, biological functions of altered IgA on mucosal immune system are unknown.

AIMS&METHODS: We aimed to investigate the influence of alteration in IgA glycan composition on inflammatory response and immune tolerance. GalNAc-deficient mIgA and control mIgA were purified from sera of Crohn's disease patients and healthy volunteers, respectively. Altered sIgA was obtained by the removal of oligosaccharides using *O*-glycanase and sialidase from purified human colostral IgA. Neutrophil migration toward mIgA was evaluated with common migration assay. Leukotriene B4 (LTB4) production was determined by ELISA. Differentiation of a human monocytic cell line THP-1 into macrophage-like cells (THP-1 macrophage) was induced by PMA and IL-4. Binding and uptake of sIgA by THP-1 macrophage were analyzed by flow cytometry. Cytokine production of sIgA-stimulated cells was evaluated by qRT-PCR.

RESULTS: To investigate whether oligosaccharide alteration of mIgA in Crohn's disease modifies neutrophil function, we first performed neutrophil migration assay. Neutrophil migration toward GalNAc-deficient mIgA was significantly enhanced compared to control mIgA. Moreover, LTB4 production from activated neutrophils was significantly elevated in GalNAc-deficient mIgA compared to control mIgA. We next studied the influence of oligosaccharide alteration on homeostatic-type of immune responses of sIgA. Ligand-lectin interaction and endocytosis of sIgA in THP-1 cells were not different between altered sIgA and control sIgA. However, both IL-6 and TNF-α levels were significantly elevated when the THP-1 macrophages were incubated with altered IgA compared to those with control IgA.

CONCLUSION: These results suggest characteristic functions of altered mIgA and sIgA on the induction of neutrophil migration and inflammatory cytokine production, respectively. Thus, oligosaccharide alteration of IgA may enhance the intestinal inflammation in pathological conditions of IBD.

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Disclosure of Interest: None Declared

Keywords: crohn's disease, IgA, interleukin-6, macrophage, neutrophil granulocytes, tumor necrosis factor-alpha

P838 PROTEIN CARBONYLATION PROFILE IN PATIENTS WITH ULCERATIVE COLITIS: A COMPARATIVE PROTEOMIC STUDY

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INTRODUCTION: The IBDs (Crohn's disease, ulcerative colitis) are chronic idiopathic inflammatory disorders of the intestine and/or colon, characterized by the presence of large numbers of leukocytes such as neutrophils, monocytes, and lymphocytes in the intestinal and/or colonic interstitium. Although the primary etiology of IBD is multifactorial, gut leakiness and diffusion of intraluminal pro-inflammatory molecules are considered to be reasonable initial steps for subsequent intestinal inflammation. The mechanisms of inflammatory intestinal injury, leading to mucosal barrier dysfunction, are not completely clear. However, it is known that chronic gut inflammation is associated with enhanced production of ROS/reactive nitrogen species (RNS) and protein oxidation, which may be responsible for mucosal barrier dysfunction [1]. The presence of ROS is generally measured indirectly by the levels of oxidatively damaged molecules (lipid, DNA and protein). The most frequently used biomarkers of protein damage are carbonyl groups [2]. Increased levels of ROS and protein carbonyls were found in the inflamed mucosal lesions of Crohn's disease and ulcerative colitis biopsies [3] but the proteomic analysis of the protein oxidation profile have not yet been performed.

AIMS&METHODS: The aim of this study was to identified the proteins of the intestinal mucosa that undergo carbonylation in ulcerative colitis (UC). We compared the oxidized proteome of inflamed to that of non-inflamed colonic biopsies from 6 UC patients in order to establish a baseline of markers, which are associated to the inflammatory state related to active UC. The oxidative proteome of whole colonic biopsies were characterized using two-dimensional gel electrophoresis followed by Western blot analysis with antibodies against carbonylated proteins [4].

RESULTS: A total of 50 protein spots displayed a statistically different degree of carbonylation level between inflamed and non-inflamed tissue in the patient group.

CONCLUSION: The proteomic results show a clear sign of oxidative stress in inflamed colonic biopsies. Since oxidation does not appear to affect all proteins at the same extent, we are currently analyzing these carbonylated proteins and identifying them by means of MALDI-TOF analysis.
REFERENCES:
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Disclosure of Interest: None Declared
Keywords: oxidative stress, protein carbonylation, proteomics, two-dimensional electrophoresis, ulcerative colitis

P839 INHIBITION OF EOTAXIN-1 (CCL-11) AMELIORATES DSS-INDUCED COLITIS – A NOVEL POTENTIAL THERAPEUTIC APPROACH FOR INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Eotaxin-1 (CCL-11) plays an important role in the regulation of eosinophil recruitment in colonic inflammation. Elevated eotaxin-1 is a feature in biopsy specimens from patients with IBD, which was shown to be positively correlated with disease severity. Targeting eotaxin-1 (CCL-11) may modulate the trafficking of eosinophils into inflammatory sites.
AIMS&METHODS: AIM - To evaluate the effect of anti-eotaxin-1 antibodies on the severity of dextran sodium sulfate (DSS)-induced colitis in mice.
METHODS - Experimental colitis was induced in BALB/c mice (N=10), by supplementation of DSS (3.5%, w/v) in drinking water for 7 days. Mice were divided into 2 groups. Group A was treated on days 0 and 4 with i.p injections of anti eotaxin-1 (100 mcg/animal) and group B was treated on the same days with isotype control antibody. Mice were monitored for body weight loss. On day 8 mice were sacrificed, 10 cm colon weight was measured. A Disease activity index (DAI) was calculated for each mouse using bleeding and diarrhea's severity.
RESULTS: I.p administration of anti eotaxin-1 resulted in significant smaller weight loss compared to the control group (15.7 and 23.2%, for group A vs. group B, respectively, $p<0.05$). DAI was decreased for anti-eotaxin-treated mice (4.8 and. 8, for group A vs. group B, respectively, $p<0.05$) and increased 10cm colon weight was recorded in the control mice (294.1 and 195 mg, for group B vs. group A, respectively, $p<0.001$).
CONCLUSION: Inhibition of eotaxin-1 (CCL-11) resulted in significant amelioration of DSS colitis in BALB/c mice. These results indicate the importance of eotaxin-1 in regulating intestinal mucosal inflammation, and its potential as a future therapeutic target in inflammatory bowel disease.
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Disclosure of Interest: T. Adar: None Declared, S. Shteingart: None Declared, D. Livovsky: None Declared, A. Bar Gil Shitrit: None Declared, M. Mahamid: None Declared, B. Koslowsky: None Declared, E. Goldin Financial support for research from: The study is funded in part by a grant from Immune pharmaceuticals
Keywords: DSS induced colitis, eotaxin-1

P840 IRSOGLADINE MALEATE, AN ANTI-ULCER DRUG, HAS PROPHYLACTIC EFFECT ON THE DEVELOPMENT OF SPONTANEOUS COLITIS IN INTERLEUKIN-10 GENE-DEFICIENT MICE THROUGH SUPPRESSING TH 1 AND TH 17 RESPONSES

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INTRODUCTION: Irsogladine maleate [2,4-diamino-6-(2,5-dichlorophenyl)-s-triazine maleate] (IM) has been approved for peptic ulcer and acute gastritis in Japan since 1989. Recently we demonstrated that IM prevented the development of spontaneous colitis in interleukin (IL) -10 gene-deficient (IL-10 KO) mice, prompting us to investigate whether IM can regulate Th1 and Th17 responses in the colonic tissue.
AIMS&METHODS: The aim of this study is to elucidate the mechanisms by which IM prevents the spontaneous colitis of IL-10 KO mice in terms of Th1 and Th17 responses. IL-10 KO mice aged over 20 weeks were chosen and fed with normal chow diet or the diet mixed with 100 ppm of IM for 10 consecutive weeks ("aged mice group"). Five-week-old IL-10 KO mice were also grown with normal diet or the diet mixed with IM as well ("young mice group"). After the mice were euthanized, colons were removed and evaluated morphologically. Expression levels of mRNAs, such as tumor necrosis factor α (TNFα), IL-1β, interferon γ (IFNγ), IL-12p35, IL-12p40, IL-17A, and IL-23p19 in the colon tissues were measured by quantitative PCR (qPCR) using comparative CT method.
RESULTS: The differences of the body weight, colon weight, and colon length in the aged mice were not significant between control and IM group (29.5 ± 2.72 vs 22.9 ± 0.87 g and 1.60 ± 0.22 vs 1.16 ± 0.22 g and 10.5 ± 0.41 vs 9.82 ± 0.28 cm, respectively). In contrast, the differences of the colon weight and length in the young mice were significantly different between control and IM group (0.64 ± 0.03 vs 1.02 ± 0.07 g and 8.6 ± 0.2 vs 8.1 ± 0.1 cm respectively), suggesting that efficacy of IM in preventing colitis was remarkable in younger mice. The results of qPCR of the aged mice showed that IM tended to decrease the mRNA expression of IFNγ, IL-12p40, and IL-17A compared to control mice (26.0 ± 8.8 vs 12.6 ± 1.3, 22.6 ± 2.2 vs 17.4 ± 1.8, and 30.1 ± 7.9 vs 15.2 ± 7.9, respectively) but they were not significant. However, the results of qPCR in the young mice showed that IM markedly and significantly reduced the mRNA expression of TNFα, IL-1β, IFNγ, IL-12p35, IL-12p40, IL-17A, and IL-23p19 compared to control mice (2.5-, 5.4-, 4.5-, 21.0-, 3.4-, 113.0-, and 4.2-folds, respectively).
CONCLUSION: IM has prophylactic effect on the development of spontaneous colitis in IL-10 KO mice by down-regulating Th1 and Th17 responses, especially when administrating IM in their younger age.
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Disclosure of Interest: None Declared
Keywords: IL-10 KO mice, Th 17, Th1

P841 ASTHMA PREVALENCE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The relation between Inflammatory bowel diseases (IBD) and asthma is not clear and whether it is an extraintestinal manifestation it is unknown. In non-IBD population asthma is present in around 5% of people.
AIMS&METHODS: The aim of the study was to assess the prevalence of asthma in IBD patients. **Methods:** A prospective study was designed. The case-studies consisted of consecutive patients with IBD (Crohńs disease (CD) and ulcerative colitis (UC)) over 18 years of age who attended the monographic IBD unit for 6 months and who agreed to participate in the study. All patients completed the European Community Respiratory Health Survey (ECRHS) questionnaire. A spirometry with bronchodilator, a fractional exhaled nitric oxide (FeNO) test and a skin allergy test using the skin prick test method (SPT) were also performed. Probable asthma was considered as affirmative answer to one of the questions of the ECRHS questionnaire: 1) Have you been woken by an attack of shortness of breath at any time in the last 12 months?; 2) Have you been woken by an attack of coughing at any time in the last 12 months?; 3) Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?; 4) Have you had an attack of asthma in the last 12 months?; 5) Are you currently taking any medicines including inhalers, aerosols or tablets for asthma?. Confirmed asthma was diagnosed in cases with Probable asthma if values in the FeNO test were over 30 ppb or a change in the FEV1 was over 12% and 200 ml. Results are shown in percentages.
RESULTS: 132 patients were consecutively included, 53 (40.1%) CD; 79 (59.9%) UC, having a mean age of 45 years, ranging from 18 to 77, 65 (49.2%) being female. Regarding asthma determination, 31 patients (23.5%) presented asthma symptoms according to the ECRHS questionnaire. The prick test was positive in 31.3% of patients, the FeNO test was over 30 ppm in 24.1% of patients and a positive bronchodilator test was observed in 30.5% of patients. Overall a probable asthma was observed in 23.5% of all IBD patients and confirmed asthma in 16.9% of our sample. These figures are clearly higher than that observed in a general population.
CONCLUSION: Asthma prevalence seems to be high among IBD patients, being superior to that of the average population
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Disclosure of Interest: None Declared
Keywords: asthma, inflamatory bowel disease

P842 INFLUENCE OF EXTRAINTESTINAL MANIFESTATIONS IN HEALTH-RELATED QUALITY OF LIFE IN INFLAMMATORY BOWEL DISEASE PATIENTS

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INTRODUCTION: Inflammatory bowel disease (IBD) patients are frequently associated with extraintestinal manifestations (EIM).
AIMS&METHODS: The aim of this study was to assess if the presence of EIM was associated with a worse health-related quality of life (HRQOL) in IBD patients regardless of the activity of the disease. **Methods:** A cross-sectional, prospective study with consecutive patient recruitment was designed. All patients with IBD who attended our IBD Unit were consecutively included. Patients were examined for the main reactive and non-reactive EIM of IBD. Reactive conditions were defined as those related to acute gut inflammation, i.e. dermatologic lesions, eye complications and peripheral osteoarthritis. Non-reactive conditions were those unrelated to gut inflammation, such as ankylosing spondylitis, sacroileitis and sclerosing cholangitis. Remission was defined as a Harvey-Bradshaw score $<=4$ for Crohńs disease (CD) and as a Mayo score $<=2$ in ulcerative colitis (UC). To assess quality of life we used the IBDQ, which included five dimensions. Total scores range from 36 to 252. We also used the SF-36 questionnaire, which included 8 scales. Total scores range from 0 to 100. In both cases, higher scores indicate better HRQOL. Results are shown as mean and standard deviation; the t-student test was used for comparing means.
RESULTS: 799 patients were consecutively included, 323(40.7%) CD; 470 (59.3%) UC, mean age of 44.63 years, range 18-81, 422 (52.8%) were female and 319 patients (39.8%) had a relapse. 159 patients (19,9%) presented any EIM. In Table 1 the means and p values of IBDQ and SF-36 dimensions are shown.
CONCLUSION: Patients with EIM have worse quality of life than those without EIM irrespective of the activity of the disease. The worse quality of life affects both physical and psychological aspects of the patients.
Disclosure of Interest: None Declared
Keywords: extraintestinal manifestations, quality of life

Table: P842

IBDQ Questionnaire

EIM	Bowel Symptoms	Systemic Symptoms	Functional Impairment	Social Impairment	Emotional Function
Yes	5.14 +- 1.16	4.74+-1.14	4.88+- 1.45	5.56 +- 1.12	4.94+- 1.46
No	5.53+- 1.16	5.26+- 1.12	5.48+- 1.39	5.88 +- 1.05	5.47+- 1.36
p	0.01	0.01	0.01	0.02	0.01

SF-36 Questionnaire

EIM	General Health	Physical Functioning	Role-Physical	Vitality	Role-Emotional	Social Functioning	Bodily Pain	Mental Health
Yes	39.77+-19.24	71.06+- 24.15	52.33+-45.46	44.16+-24.08	63.11+-44.72	67.50+-28.74	51.20+-25.75	58.80+-23.10
No	48.93+-21.59	80.17+-25.39	68.33+-42.52	56.95+-24.69	72.55+-39.56	76.82+-25.66	67.93+-27.04	67.56+-21.74
p	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01

P843 PREVALENCE AND ETIOLOGIES OF CHOLESTASIS IN INFLAMMATORY BOWEL DISEASES PATIENTS IN THE SWISS IBD COHORT.

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INTRODUCTION: Patients with inflammatory bowel diseases (IBD) may present with cholestasis during the course of their disease. Causes are multiple including drug-induced liver toxicity (e.g. Azathioprine), specific liver diseases complicating IBD (e.g. primary sclerosing cholangitis (PSC)) or para-inflammatory (TNF-α induced). Prevalence of cholestasis in IBD is unknown. Cholestasis, plays a significant role in the absorption of vitamins and drugs; bile acids are thought to play a role in dysplasia, intra-cellular signalling as well as interaction with the intestinal flora. The aim of this study is to establish the prevalence of clinical and biological cholestasis in IBD patients using the clinical data and biosamples of the Swiss IBD Cohort (SIBDC).
AIMS&METHODS: All patients of the SIBDC with serum samples available were included. Total bile acid (TBA) assay was performed (ELISA). Cholestasis was defined as a TBA > 8 μmol/l. In a second time bile acid profile, using HPLC, was performed in serum samples from patients with high TBA as well as in a cohort of patients with low TBA. Clinical data were collected from the SIBDC.
RESULTS: 1342 patients were included; 96 patients had TBA > 8 μmol/l with a mean level of 21.8 μmol/l (8-483). This represents a prevalence of 7.15% cholestasis in the SIBDC. In univariate analysis, cholestasis (TBA>8) was associated with male sex (63% vs 51%, p=0.034), less smoking (17% vs 27%, p=0.023), a higher alcalin phosphatase (108 vs 70, p=10E-12), a lower albumin (38 vs 40, p=0.016), more PSC (5% vs 1%, p=0.00007), supplementation with calcium or vitamin E (p=0.047) and treatment with tacrolimus (3% vs 1%, p=0.038) or ursodesoxycholic acid (10% vs 1%, p=10E-8). Age, IBD subtypes and mean activity index were comparable. In multivariate analysis, PSC (OR=4.64, p=0.012) and treatment with tacrolimus (OR=5.5, p=0.017) were significant factor associated with cholestasis.
CONCLUSION: Prevalence of cholestasis in the SIBDC was high (7%). PSC, IBD inflammatory flare or adverse effect of treatments could be an explanation. In some cases, the exact cause of the cholestasis remains unclear. Further analysis on the subtypes of biliary acids is underway and should help understanding the causes of cholestasis.
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Disclosure of Interest: None Declared
Keywords: cholestasis, Inflammatory bowel disease (IBD)

P844 QUALITY OF LIFE IN A EUROPEAN INCEPTION COHORT OF INFLAMMATORY BOWEL DISEASE PATIENTS IN 2010 - AN ECCO-EPICOM STUDY

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INTRODUCTION: Inflammatory Bowel Disease (IBD) is a chronic condition impairing patients' quality of life (QoL). The EpiCom population-based inception cohort of unselected IBD patients was initiated in 2010 in 31 centres from 14 Western and 8 Eastern European countries, covering 10 million in background population[1].
AIMS&METHODS: The Short Form 12 (SF-12) and the Short Inflammatory Bowel Disease Questionnaire (S-IBDQ) were used to investigate the differences in Health-Related Quality of Life (HRQoL) in IBD patients across Europe. Patients completed the questionnaires at time of diagnosis (0-3 months) and at 1 year follow up (±3months).
RESULTS: Out of 1515 IBD patients, 842 completed S-IBDQ at time of diagnosis, 199 (24%) from Eastern Europe (Crohn's Disease (CD): 78 (39%), Ulcerative Colitis (UC): 118 (59%), IBD Unclassified (IBDU): 3 (2%)) and 643 (76%) from Western Europe (CD: 220 (34%), UC: 344 (54%) IBDU: 79 (12%)). Higher mean S-IBDQ scores were observed in Western European UC patients (49 (Range: 11-70)) compared to Eastern European patients (45 (Range: 18-67)), p<0.05. 369 (44%) patients completed the S-IBDQ questionnaire at follow up, the mean scores increased over time in both regions and reached levels equal to or above a good quality of life (S-IBDQ score ≥50). 7 of 30 centres (23 %) had mean S-IBDQ scores >50 at time of diagnosis and 24 (80 %) centres at follow up. 841 patients completed the SF-12 questionnaire at time of diagnosis, 202 (24%) from Eastern Europe (CD: 80 (40%), UC: 119 (59%), IBDU: 3 (1%)) and 639 (76%) from Western Europe (CD: 217 (34%), UC: 342 (54%), IBDU: 80 (12%)). 362 (43%) patients completed the SF-12 survey at follow up. Summary scores of Mental and Physical health are shown in Table 1.

Table 1. SF-12 summary measures

		Eastern Europe			Western Europe		
		CD	UC	IBDU	CD	UC	IBDU
At diagnosis:							
	Physical Summary measure	44,5	44,2	56,3	42,3	47,0 *	46,3
	Mental Summary measure	42,5	43,3	43,3	43,1	43,8	43,9
At follow up:							
	Physical Summary measure	49,8**	50,9**	60,9	49,1**	49,3	49,6
	Mental Summary measure	49,9**	51,0**	52,7	47,4**	48,6**	50,8**

*= difference in mean score between regions p<0.05.
** = difference in mean score between time of diagnosis and follow up p<0.05.
CONCLUSION: Generic and disease specific QoL increased within a year from diagnosis in both regions of Europe. However, the differences in HRQoL between the two areas were not statistical significant. The association of QoL and disease course and outcome are currently being investigated.
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Disclosure of Interest: None Declared
Keywords: Cohort study, Inflammatory bowel disease (IBD), population-based, quality of life, sf-12, s-IBDQ

P845 EARLY DISEASE COURSE IN INFLAMMATORY BOWEL DISEASE: RESULTS FROM AN INCEPTION COHORT STUDY IN ASIA-PACIFIC

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INTRODUCTION: Early disease progression and complications of inflammatory bowel disease (IBD) have not been assessed in population-based settings across Asia-Pacific.

AIMS&METHODS: We evaluated early disease outcome in incident IBD cases in Asia-Pacific. IBD patients diagnosed between 2011 and 2012 were prospectively followed-up for up to 18 months from seven countries in Asia and Australia. Data on disease phenotype, mortality medical and surgical treatment over one year were entered into a web-based database. We determined risk of disease behavior change and probability of surgery.
RESULTS: 164 IBD cases (Australia 41; Asia 123) were included [79 ulcerative colitis (UC), 74 Crohn's disease (CD), and 11 indeterminate colitis (IC)]. Median age at diagnosis was 37 (IQR: 27-51) and 59% were male. After 18 months, probability of CD behavior change from B1 to B2/B3 was 7.7% and 12.5% in Australia and Asia, respectively. In UC, proximal disease extension was observed in 17% with proctitis or left sided colitis in Asia. Probability of surgical resection for CD was 11.5% in Australia and 4.2% in Asia ($p = 0.337$). Probability of surgical resection for UC was 11.1 % in Australia and 0% in Asia (p=0.114), after 18 months of disease duration. Five CD patients in Australia had surgery for perianal disease. There was no mortality in Australia and one CD patient in Asia died of sepsis. Total steroid exposure was higher in Australia than Asia (51.2% vs. 16.3%; $p<0.001$) but immunosuppressant (36.6% versus 35.8%; p=0.93) and anti-TNF antibody exposure (7.3% vs. 4.1%; p=0.414) was not significantly different between Australia and Asia.
CONCLUSION: Early disease course for IBD, immunosuppressant use and surgical rates in Asia are comparable to that of Australia.
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Disclosure of Interest: None Declared
Keywords: disease outcome, Inflammatory bowel disease (IBD), surgery

P846 ANORECTAL COMPLICATIONS AND FUNCTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: 14 YEARS FOLLOW-UP

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INTRODUCTION: Little is known about the long-term sequelae of perianal disease in IBD with regard to function. The long term follow–up with anorectal function tests may clarify the course of the perianal lesions.
AIMS&METHODS: The aim of the study was to prospectively evaluate the course of anorectal complains and anorectal function in inflammatory bowel disease (IBD) patients with perianal lesions.
Between 1993-2000, 56 patients with IBD (43 Crohn's disease, 13 ulcerative colitis) with perianal complaints underwent anorectal function tests. For follow-up, the patients were approached in 2010-2012 by sending questionnaires including Inflammatory Bowel Disease Questionnaire (IBDQ), Perianal Disease Activity Index (PDAI), fecal incontinences scale (Vaizey) and an invitation for anorectal function tests.
RESULTS: At follow-up, 46 (82%) were available, 9 patients (16%) were lost and 1 patient (2%) had died. Seventeen patients were interviewed by phone and 30 patients returned the questionnaires of whom 17 also underwent anorectal function tests. Median follow-up was 14 years (IQR 25-75: 13-15 years). In 25 of the 46 patients (54%) perianal complaints persisted: fecal incontinence (n=5); soiling (n=17); fecal incontinence and soiling (n=2); fistula pain (n=1). Eighteen (39%) and 5 (11%) patients had an active fistula at baseline and follow-up respectively. Two of the five fistulas at follow-up were new (rectovaginal fistula and complex fistula). Mean IBDQ, Vaizey and PDAI were 178 (SD 29), 7 (SD 5) and 4.2 (SD 3.0) respectively. Anal endosonography showed healing in 9 of the 10 fistulas. Anal rest and squeeze pressures as well as rectal compliance remained unaltered.
CONCLUSION: After 14 years, 54% of the IBD patients with perianal lesions, still have mild complaints. Quality of life of patients with IBD and perianal lesions remained moderate over a long period, which is concerning.
Disclosure of Interest: None Declared
Keywords: anal disease, anal endosonography, anorectal manometry, Inflammatory bowel disease (IBD)

P847 ANEMIA IN CROHN'S DISEASE

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INTRODUCTION: Anemia is a common complication of patients with Crohn's disease (CD). The aim of this study is to estimate the characteristics of anemia in CD.
AIMS&METHODS: We performed a retrospective study in patients with CD followed-up between 2011 and 2013 in the Sixth Affiliated Hospital of Sun Yat-sen University. 175 proved CD patients underwent the analysis according to age, signs, clinical course and activity of the disease. Complications and treatment options were recorded. The routine blood test, erythrocyte sedimentation rate (ESR), high sensitive C-reactive protein (hs-CRP) were tested for each patient at first visit and subsequent visits at 3 months interval.
RESULTS: 175 CD patients were included. 56.5% (n=99) were diagnosed as anemia at first visit. Microcytic anemia accounted for 54.8% of anemia in CD, 45.2% were normocytic anemia and no macrocytic anemia occurred.The mean age was 29.77±12.87. 56.6% (n=56) had bachelor degree at least, 34.3% were high school. The incidence rate of manifestations including diarrhea (n=56 57.1%), abdominal pain (n=75 76.5%), hematochezia (n=25 25.8%), abdominal distension (n=16 7.9%), fever (n=29 29.6%), oral ulcers (n=25 25.5%), arthralgia (n=11 11.2%),abdominal mass (n=1 1%) were diverse. At first visit, 72.5% (n=72) were mild anemia, 22.2% (n=22) were moderate and only 2% (n=2) were severe. 17.2% (n=17) of patients were less than 18 years old, 70% were aged from 18-45, 11% and 1% were aged as mid-age and old-age respectively. 45% (n=45) still had anemia at 3-month visit, a key point when glucocorticoid therapy sufficiently taking effect, and 87% was mild anemia and 13% was moderate anemia. The incidence rates of anemia at 6, 9 and 12 month were 44%, 21% and 50% respectively (Fig 1).At first visit, the average hs-CRP was 9 mg/L, 55.1% (n=86) of them had hs-CRP≥10 mg/L. It was 36.2% , 43.2%, 36.8% , 50% at 3,6,9 and 12 month respectively. For CD with anemia at first visit, 62.8% (n=54) had hs-CRP more than 10 mg/L, and 41.3%, 48.1%,44.1%,54.5% at 3,6, 9 and 12 month, respectively. But Logistic regression analysis showed that hs-CRP seemed not to be correlated with anemia (p=0.052, OR 1.898, 95%CI, 0.995-3.624), while weight ($p<0.05$, OR 0.886 95%CI 0.819-0.958) and ESR ($p<0.05$, OR 1.057 95%CI 1.020-1.095) seemed to be the independent risk factors for anemia in CD.
CONCLUSION: Patient with CD has high morbidity of anemia, and microcytic anemia is the most common type. Though there was no significant relationship between anemia and hs-CRP in our cohort, CD patients with anemia seem to have higher hs-CRP than those without. The incidence and severity of anemia seem to parallel to the change of hs-CRP. Weight and ESR seem to be the independent factors to anemia.
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Disclosure of Interest: None Declared
Keywords: anemia, CROHNS DISEASE

P848 IS THERE A DIFFERENCE IN HEALTH QUALITY OF CARE IN A EUROPEAN INFLAMMATORY BOWEL DISEASE INCEPTION COHORT? – AN ECCO-EPICOM STUDY

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INTRODUCTION: The ECCO-EpiCom study and inception cohort[1] was initiated in 2010 in 31 centres from 14 Western and 8 Eastern European countries, covering 10 millions in background population.
AIMS&METHODS: To investigate whether there is a difference between Eastern and Western Europe in Health Quality of Care (HQoC) of patients with inflammatory bowel disease (IBD), a HQoC questionnaire was developed in the EpiCom group consisting of 16 questions covering 5 items: time interval between the onset of symptoms and diagnosis-2 questions (q), information-6q, education-3q, empathy-4q and access to health care providers-1q.

Table: P848

Question	East	West	Question	East	West	Question	East	West
Q1. How long did you have IBD symptoms prior to IBD diagnosis?			**Q4. Did you get sufficient answers to your questions?**			**Q8. Are you satisfied with your current status of information?**		
0-12 months*	86%	74%	Yes	33%	38%	Yes	80%	83%
>1 year*	13%	24%	**Q5. Have you sought out information regarding your disease by yourself?**			**Q9. Do you have a specific nurse addressed to you regarding IBD questions?**		
Q2. If you received information, who gave it to you?			Yes*	76%	68%	Yes*	4%	21%
Specialist*	100%	94%	**Q6. If yes, what sources did you use?**			**Q10. Does your doctor indicate interest in how your IBD impacts your Quality of Life?**		
IBD nurse*	0%	8%	Internet*	72%	61%	Yes*	94%	72%
Patient organization	1%	3%	Booklets*	17%	24%	**Q11. Do you have easy access to the IBD staff?**		
Q3. Was the time the nurse spent with you relevant?			**Q7. Have you received IBD related education?**			Gastroenterologists*	80%	68%
Yes*	13%	37%	Yes*	76%	41%	Nurses*	47%	57%

RESULTS: Out of 1515 patients 947(n=217 East/730 West) answered the HQoC questionnaire: 84% of patients from Eastern and 57% of patients from Western Europe; m/f=519/428; median age at diagnosis: 38 years (Range: 15,2-89); 38% of patients had Crohn's disease, 51% had ulcerative colitis, 11% had indeterminate colitis. Excerpts from the HQoC questionnaire are shown in Table 1.

Table 1. Excerpts from the EpiCom HQoC questionnaire

* $p < 0,05$

CONCLUSION: HQoC differs significantly between Eastern and Western Europe in all items. As IBD is a more common disease in Western Europe, IBD nurses play a very important role in decreasing the burden of disease. Use of IBD nurses should be introduced in Eastern Europe, since in many countries the incidence of IBD is increasing.

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Disclosure of Interest: None Declared

Keywords: inflammatory bowel disease, quality of health care

P849 EPIGENETIC ALTERATIONS IN INFLAMMATORY BOWEL DISEASE: NEW INSIGHTS INTO DISEASE PATHOGENESIS

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INTRODUCTION: The rising incidence of inflammatory bowel disease (IBD) in Asia relates to changes in environmental factors. The exact mechanisms by which these factors predispose to IBD are not clear. Epigenetics may mediate effects of environment, genetic predisposition and intestinal microbiota on IBD pathogenesis[1,2]. Genome-wide association studies have shown that IBD-associated genetic variants differ between Caucasians and Asians,[3] but little is known of IBD epigenetic profiles.

AIMS&METHODS: In a screening cohort of 9 Crohn's disease (CD) and healthy control tissues, we evaluated the expression of 128 genes specifically related to epigenetic chromatin remodeling factors and chromatin modification enzymes using customized Real-time PCR (RT-PCR) based array. SAM and ANOVA were used to identify the most deviated candidate genes between healthy tissues and inflamed CD tissues as confirmed by histology. The expression levels of candidate genes were further validated by RT-PCR using independent set of primers in a larger cohort consisting of 56 tissue samples from CD, ulcerative colitis (UC) and healthy controls.

RESULTS: PCR array in the screening cohort showed that nine genes encoding bromodomain proteins, polycomb group proteins, inhibitor of growth family members, histone methyltransferase, acetyltransferase and demethylase were significantly down regulated in inflamed CD samples compared with control samples ($p < 0.01$). RT-PCR in the validation cohort confirmed that expression of ash1 (absent, small, or homeotic)-like (Drosophila) (ASH1L), bromodomain and WD repeat domain containing 3 (BRWD3), lysine(K)-specific demethylase 5C (KDM5C), and lysine(K) acetyltransferase 2B (KAT2B) were significantly downregulated in inflamed CD compared with control tissues ($p < 0.05$). In contrast, these genes did not show statistical significant changes in inflamed UC samples compared with controls.

CONCLUSION: This study identified novel chromatin-modifying genes associated with IBD. Concordant down-regulation of these genes may disrupt the transcriptome of the colon and small intestine leading to pathogenesis of IBD. The development of UC and CD appeared to be associated with different epigenetic alterations. Functional characterization of the downstream epigenetic changes will provide unique insights into the biological pathways of CD and UC that may translate into new therapeutic approaches.

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Keywords: Epigenetics, Inflammatory bowel disease (IBD)

P850 ULCERATIVE COLITIS PATIENTS UNDERGOING POUCH SURGERY HAVE ALTERATIONS IN GENE EXPRESSION BEYOND THE POUCH

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INTRODUCTION: Pouchitis is an inflammation developing in an a priori normal small bowel (SB) reservoir created in ulcerative colitis (UC) patients undergoing pouch surgery.

AIMS&METHODS: UC pouch patients were stratified to normal pouch (NP), chronic pouchitis (CP), and Crohn's-like disease of the pouch (CLDP). Biopsies were obtained from the pouch, the corresponding proximal SB, and SB of healthy volunteers (normal control (NC)). Gene expression was analyzed by microarrays. Significant alteration was defined a fold change ≥ 2, and corrected $p \leq 0.05$. We conducted an additional direct comparison between pouches and the corresponding proximal SB in each group.

RESULTS: Thirty-six subjects were included: NP (n=7), CP (n=10), CLDP (n=5), NC (n=14). All NP and CP patients had a normal appearing proximal SB, 3 CLDP patients had inflammation in the proximal SB. We detected 162 significant alterations in pouches of NP, 482 in CP, and 1132 in CLDP groups. The proximal SB of NP patients demonstrated only 9 alterations. In contrast, proximal SB of CP and CLDP patients demonstrated 80 and 230 alterations respectively. Overall, 76% and 97% of alterations detected in proximal SB of CP and CLDP overlapped with alterations detected in the pouches of each group. Two thirds of the changes in proximal SB of NP and CP overlapped with alteration detected in proximal SB of CLDP. Gene ontology analysis for the proximal SB alterations revealed many associated biological processes including inflammatory response, NOD-like receptor signaling pathway, response to nutrients and vitamins. Direct comparison of alterations in the proximal SB to those within the pouch revealed only few significant differences: none in the NP group, two in the CP group and 12 in the CLDP group.

CONCLUSION: Significant alterations were detected not only within pouches but in SB proximal to the pouch as well. Pouch and proximal SB mucosal alterations were comparable. The findings may suggest that the inflammatory process is not limited to the surgically manipulated region of the pouch but rather extends proximally, potentially exposing it to further inflammation.

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Keywords: gene expression, pouchitis

P851 ATG16L1 GENOTYPE IS ASSOCIATED WITH RESPONSE TO ANTI-TNF

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INTRODUCTION: We have previously shown that infliximab (IFX) treatment of mixed lymphocyte reactions results in the induction of macrophages with immunosuppressive and wound healing properties. In patients who respond to IFX treatment, the number of these macrophages increases significantly in the intestine. In contrast, no increase is seen in non-responders, indicating the clinical importance of this cell population. Genetic studies have shown an association between various autophagy related genes and the development of Crohn's disease. The aim of this study was to determine whether autophagy is involved in the induction of regulatory macrophages by IFX and whether autophagy related polymorphisms influence the response to IFX.

AIMS&METHODS: Peripheral blood was isolated from 28 healthy volunteers and rs_2241880 genotype was determined by pcr. After isolation of PBMC mixed lymphocyte reactions containing cells from 2 donors per reaction were established for 150 separate donor combinations. Cultures were treated with IFX or control IgG and incubated for 6-7 days. Cells were analyzed by gene array, immunofluorescence, flow cytometry and thymidine incorporation.

RESULTS: Anti-TNF induced regulatory macrophages displayed increased numbers of autophagosomes as well as an increased expression of autophagy related transcripts including *atg5*, *atg7*, *atg9* and *atg16l2*, suggesting induction of autophagy by IFX treatment.

Of all donors, 7 were homozygously carrying the CD associated risk allele, 14 were heterozygous and 7 were homozygous for the WT allele.

The number of CD14+ regulatory macrophages correlated significantly with the number of WT alleles present in each individual culture, with the largest number of macrophages found in cultures containing 3 or 4 WT alleles (2 WT donors or 1 WT and 1 heterozygous). Similarly, expression of CD206, which is associated with the immunosuppressive function of macrophages, positively correlated with the number of WT alleles present. To confirm the functional consequences of these findings, IFX mediated suppression of T cell proliferation was determined. Again, the level of suppression correlated significantly with the number of WT alleles present in the respective donor combinations.

CONCLUSION: Induction of regulatory macrophages by IFX is associated with induction of autophagy. In vitro, the number and function of IFX induced macrophages correlate with the number of WT alleles for ATG16L1. Given the association between induction of regulatory macrophages and clinical response, this suggests that an intact autophagy pathway is important for effectiveness of anti-TNF therapy.

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Keywords: anti-TNF, autophagy, macrophage

P852 IDENTIFICATION OF DISEASE-ASSOCIATED DNA METHYLATION IN BLOOD FROM PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: It is well known that inflammatory bowel disease (IBD) is caused by a complex interplay between genetic predispositions of multiple genes, combined with an abnormal interaction with environmental factors. Germline variation in the IBD implicated by genome-wide association studies (GWAS)

only accounts for approximately 25% of estimated heritability. The contribution of epigenetic alterations to disease pathogenesis is emerging as a research priority. In this study, we extended this approach to identify IBD-associated changes in DNA methylation in blood from 12 IBD patients [6 Crohn's disease, CD and 6 Ulcerative colitis, UC].

AIMS&METHODS: The promoter methylation status of 22 genes (ATF2, CCL25, CXCL14, CXCL3, CXCL5, CXCL6, FADD, GATA3, IL10RA, IL12A, IL12B, IL13, IL13RA1, IL15, IL17C, IL17RA, IL4R, IL6R, IL6ST, IL7, INHA, TYK2) whose involvement in inflammation and autoimmunity were profiled using the Human Inflammatory Response and Autoimmunity EpiTect Methyl II Signature PCR Array profiles.

RESULTS: Using this approach with strict statistical analysis, we identified concerning the CD that the CCL25, CXCL14, CXCL3, CXCL6, GATA3, IL15, IL17RA, IL4R, IL6R, IL6ST, IL7, INHA, TYK2 were hypomethylated compared to healthy individuals. Regarding the UC cases the CCL25, CXCL3, IL10R, IL12A, IL13, IL15, IL17RA, IL7, INHA and TYK2 were found to be hypomethylated, whereas the CXCL14, CXCL5, GATA3, IL12B, IL17C, IL4R and IL6R were found to be hypermethylated compared to the controls.

CONCLUSION: IBD- and subtype-specific changes in DNA methylation were identified in blood from IBD patients. Many of these genes have important inflammatory and autoimmunity response functions. These data provide an important insight into the impact of epigenetic mechanisms in the pathogenesis of IBD.

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Keywords: IBD, METHYLATION

P853 CONTRIBUTION OF MDR1 GENE POLYMORPHISMS ON IBD PREDISPOSITION AND RESPONSE TO GLUCOCORTICOIDS IN IBD IN CHINESE POPULATION

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INTRODUCTION: Glucocorticoids (GCs) play a pivotal role in inducing remission of inflammatory bowel disease (IBD), however, the sensitivity to GCs vary from person to person. Genes such as Multidrug resistance 1 (MDR1), NACHT leucine-rich-repeat protein 1 (NALP1), Glucocorticoid receptor (GR/NR3C1) and its co-chaperone FK506-binding protein FKBP5 participate in modulating the metabolism of GCs. Variations of these genes were reported influencing on GCs response and MDR1 polymorphisms also associated with the susceptibility to IBD. This article aims to evaluate whether the polymorphisms of these genes influence the response to GCs in Chinese IBD patients as well as investigate the relationships between MDR1 and IBD susceptibility.

AIMS&METHODS: 8 single nucleotide polymorphisms (SNPs) were selected from genes mentioned above. These SNPs were genotyped in 156 IBD patients (including 117 Crohn's disease and 39 Ulcerative colitis cases) and 223 healthy controls by MALDI-TOF MS assay. Patients included were all treated with GCs and defined as GCs responders, dependants and resisters after one year follow up. The influences of these variations on GCs response or MDR1 effect on IBD susceptibility and clinical phenotypes were analyzed.

RESULTS: Among the 8 SNPs, the CC genotypes of rs1128503 (C1236T) (P=0.019, OR: 6.583 1.760-24.628, 95%CI 1.760-24.628) and rs1045642 (C3435T) (P=0.009, OR: 3.873, 95%CI 1.578-9.506) in MDR1 gene were more frequent in GC dependants compared with the respond patients of CD, while the other SNPs have no association with GCs response. In addition, the G allele of MDR1 rs2032582 (G2677A/T) was less frequent among CD cases in comparison to controls (P=0.014, OR: 0.668, 95%CI 0.484-0.921); Patients who carried G allele of MDR1 rs2032582 decreased risk for developing non-stricturing and non-penetrating CD (P=0.023, OR: 0.661, 95%CI 0.462-0. 946) and ileocolonic CD (P= 0.024, OR: 0.669, 95% CI 0.472-0.948). There was no significance finding in UC.

CONCLUSION: Our results revealed polymorphisms of MDR1 have an effect on GCs response and the predisposition to IBD in Chinese population. More studies are needed to further confirm our results and elucidate the role of these SNPs as genetic markers for GCs response.

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Keywords: polymorphism, glucocorticords, IBD, MDR1

P854 HLA-DRB1 AND THE DEVELOPMENT OF ANTIBODIES TO INFLIXIMAB IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Infliximab (IFX) has proven to be a successful treatment in patients with inflammatory bowel disease. Unfortunately 15-20% of patients are primary non-responders and 40% of IFX treated patients will lose response over time. This can be partially explained by the formation of antibodies to IFX (ATI). This immunogenic response is seen in approximately 6-17% of patients treated with scheduled IFX. Little is known about host factors that determine immune responses to IFX but genetic factors may play a crucial role.

AIMS&METHODS: We hypothesized that the formation of ATIs is associated with specific HLA class II molecules. We retrospectively identified 78 ATI-positive patients and matched them with 58 controls. Controls required at least 2 years of therapy with 6 IFX trough level (TLI) measurements and no detectable ATI. ATI and TLI were measured with an in-house-developed ELISA. HLA class II alleles were imputed using immunochip data and HLA*IMP software. Imputation call thresholds were applied according to Dilthey's et al.[i] The number of allele carriers for the different class II HLA types were compared between cases and controls using the two tailed Fisher Exact test.

RESULTS: There was no difference between the number of allele carriers for HLA-DPB, HLA-DQA and HLA-DQB in the case and control group. For HLA-DRB1 however, we found that 23% of the cases carried the DRB1*0301 allele compared to 9% of controls (P=0.036; OR=3.18 [1.10-9.16]). When considering the total number of alleles, we found that 13% of the alleles in cases were DRB1*0301 positive compared to 6% in the control group (P=0.12; OR=2.28 [0.87-5.97]). As a drug holiday may influence ATI formation, we re-analyzed patients who had maintenance treatment only (61 cases and 40 controls) and found similar results (23% of the cases carried the DRB1*0301 allele compared to 8% of controls), although not significant (OR=3.67 [0.98-13.74], P=0.057) probably due to the small sample size.

CONCLUSION: The formation of ATI is influenced by specific HLA class II molecules as has also been shown for the formation of antibodies to interferon-β in multiple sclerosis. Although this retrospective study is impaired due to its small sample size and imputation of HLA alleles instead of direct typing, we did see a clear trend towards an association between HLA-DRB1*0301 and positive ATI. We therefore strongly feel that these findings warrant thorough examination in larger cohorts of patients.

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Keywords: Anti infliximab antibodies, HLA-DR4, immunogenicity, Inflammatory bowel disease (IBD), infliximab

P855 THE NOTCH SIGNALING PATHWAY COULD BE INVOLVED IN THE EARLY POST-SURGICAL RECURRENCE OF CROHN'S DISEASE

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INTRODUCTION: Our group previously reported singular molecular phenotypes in the inflamed areas of ileo-cecal resection specimens of patients with Crohn's disease (CD) [Zabana Y. JCC-sup 2012; 6 (1):S186]. However, their accuracy in predicting further post-surgical recurrence (PSR) was limited, possibly due to the predominance of inflammatory features in the studied samples.

AIMS&METHODS: To describe the functional genetic characteristics of non-inflamed intestinal areas of surgical resection specimens from CD patients and their relationship with the development of early PSR.**Methods:** Non-inflamed and inflamed samples were harvested from 15 CD patients undergoing ileo-cecal resection. Follow-up colonoscopies were performed at six, twelve, and eighteen months after surgery. Patients were grouped according to the development (n=5) or not (n=10) of endoscopic recurrence. Human whole genome microarray (Codelink) was performed. Transcriptomic profile of surgical samples was compared between recurrent versus non-recurrent patients. LIMA-R package was carried out for normalisation and comparisons. Changes in gene expression were considered significant when they occurred with a Fold Change (FC) of ± 1.5 and $p < 0.005$. Clustering of genes according to phenotype was done using *Qlucore* software, and biologic function prediction and genetic update were obtained using GeneCodis, gene set enrichment analysis (GSEA) and informatics database consultation (PubMed)

RESULTS: Macroscopically healthy intestinal tissue of patients with early PSR showed 16 up-regulated (DNAH3, GOLGA1, etc.) and 6 down-regulated genes (MAML2, CABYR, etc.) as compared to patients without PSR. These differently expressed genes are related to ciliar motility, extracellular matrix activity and, particularly, to the Notch pathway. This biological activity was also found in the profile obtained from inflamed ileal tissue (like SAMD4 and NFIC), but was not outstanding probably because the high inflammatory background.

CONCLUSION: Transcriptomic exploration of macroscopically healthy ileal tissue identified the ciliar motility/Notch pathway axis as a mechanism possibly related to early PSR in CD. Alterations of this biological activity have been

recently shown in the development of spontaneous colitis of murine models [Obata, et al, J Immunol, 2012].
Disclosure of Interest: None Declared
Keywords: crohn disease, notch pathway, post-surgical recurrence

P856 EARLY POST-OPERATIVE ENDOSCOPIC RECURRENCE IN CROHN'S DISEASE PATIENTS: DATA FROM AN ITALIAN GROUP FOR THE STUDY OF INFLAMMATORY BOWEL DISEASE (IG-IBD) STUDY ON A LARGE PROSPECTIVE MULTICENTER COHORT

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INTRODUCTION: The incidence of endoscopic recurrence (ER) in Crohn's disease (CD), following curative resection, is up to 80% at 1 year. Endoscopy has proved to be the most sensitive method to detect the earliest mucosal changes and the severe ER at 1 year (Rutgeerts' score≥i2) seems to be predictive of clinical relapse
AIMS&METHODS: The aim of this prospective study was to evaluate the incidence of early ER 6 months after curative resection for ileal/ileo-colonic CD. 170 patients [pts](99 males [58%]; mean age at diagnosis 32.7±12.7) were included, in 11 Italian referral centers for IBD (April '05-June '10), in a trial designed to assess the role of AZA vs 5-ASA as early treatment of severe ER. All the pts started oral 5-ASA 2.4 gr/die 15 days after surgery. We evaluated as predictors of severe ER: sex, age at diagnosis, smoking habit, site/duration of disease, type of anastomosis, previous surgery, previous immunosuppressive treatment. Multivariable analysis was performed if at least two variables were significant (p-value <0.05) at univariable analysis
RESULTS: ER was observed within 6 months in 62% of pts (105/170). Of these 82/105 (78%) had severe ER. At univariable analysis only ileo-colonic disease was associated to a lower risk of severe ER (p=0.04; OR 0.52, 95% CI 0,277-0.974). The overall ER rate (≥ i1) was 61.7% (105/170) despite the treatment with 5-ASA
CONCLUSION: In this series ER at 6 months, in pts operated-on for ileo-colonic CD, was high with a significant rate of severe ER (78% of all ER vs 83% [at 1 year] in Rutgeerts' study). This suggest that post-surgical endoscopic evaluation should be performed at 6 months instead of 1 year. Ileo-colonic disease was associated to a lower risk of severe ER at 6 months. The percentage of early ER was similar to that reported in the placebo arm of other studies, suggesting a weak role of 5-ASA in the prevention of early ER
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, Endoscopic recurrence, surgery

P857 DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN CROHN'S DISEASE: VALIDATION OF QUANTITATIVE INDEX OF ACTIVITY

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INTRODUCTION: Diffusion-weighted imaging (DWI)-MRI is useful for assessing inflammation in ileal Crohn's disease (CD)[1].
AIMS&METHODS: We aimed to compare the performances of the Apparent Diffusion Coefficient (ADC), the quantitative parameter of the DWI sequences, compared to the MaRIA (Magnetic Resonance Index of Activity) score calculated from injected sequences (reference standard)[2] in defining active CD; to define the best ADC threshold in discriminating active versus non-active CD; and to perform an external validation of the DWI-MaRIA score (Clermont Score)[1] in assessing ileal inflammation in CD. 130 patients from the Clermont-Ferrand IBD unit, France, underwent consecutively and prospectively MR Enterography (MRE) with gadolinium injection and DWI sequences between July 2011 and December 2012. 7 segments (jejunum, proximal and distal ileum, right, transverse and left/sigmoid colon, and rectum) were defined except for operated-patients, thus 848 digestive segments were evaluated. Each examination was interpreted independently by 2 radiologists.
RESULTS: 175 segments (20.6%) were active (small bowel=111, colon/rectum=64) defined as MaRIA score ≥ 7. Using a ROC curve, we determined an ADC threshold of $1.9x10^3 mm^2/s$ which yielded a sensitivity and a specificity in discriminating active from non active CD, of 96.9% and 98.1%, respectively, for the colon/rectum, and 85.9% and 81.6%, respectively, for the ileum. ADC was better correlated to MaRIA score ≥ 7 than related contrast enhancement obtained with injected sequences ($p<0.001$). Clermont score (=1.646 x bowel thickness – 1.321 x ADC + 5.613 x oedema + 8.306 x ulceration + 5.039) was highly correlated with the MaRIA score (rho=0.98) in CD involving distal ileum but not in colonic CD (rho < 0.80). Inter-observer agreement was high for ADC measurement (correlation and concordance > 0.9, p< 0001).
CONCLUSION: ADC is accurate to differentiate active from non active colonic CD. The Clermont score is a validated tool in assessing inflammation in ileal CD. In this context, DWI-MRE should be wider spread in CD and could avoid gadolinium injection in daily practice.
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Keywords: colon, CROHNS DISEASE, Diffusion Weighted Imaging, magnetic resonance imaging enterography, Small Bowel

P858 PERIPHERAL BLOOD BIOMARKERS FOR THERAPY RESPONSE IN CROHN'S DISEASE

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INTRODUCTION: Monitoring of remission induction therapy for active Crohn's disease is hampered by the lack of objective markers for therapy response. This also impedes development of new drugs since only subjective markers for therapeutic response can be used in clinical trials. CRP levels are rarely increased and thereby often inappropriate to monitor therapy response. As an alternative, consecutive colonoscopies to assess mucosal healing may be too burdensome. Therefore, measurements of objective biomarkers in peripheral blood are best applicable in daily clinical practice to assess therapy response and monitor individual patients during the remission induction phase.
AIMS&METHODS: This study aimed to identify biomarkers in peripheral blood to distinguish responders from non-responders at an early stage of remission induction therapy. Whole blood RNA was obtained by PAXgene blood RNA tubes before therapy and after 3, 7, 14 and 56 days of remission induction from 10 responders and 10 non-responders. To identify a biomarker for therapy response in general and not for a specific treatment, both anti-TNF and prednisone remission induction strategies were included. Response was defined by improvement in CDEIS at colonoscopy before and 8 weeks after start of therapy, improvement according to the global physician's assessment, as well as improvement in subjective questionnaires (CDAI, IBDQ), next to normalization of inflammation markers. Gene expression profiles were obtained by R2 software analysis of differential gene expression between responders and non-responders at consecutive timepoints, and confirmed by qPCR.
RESULTS: Our first analyses showed several genes to be differentially expressed between responders and non-responders. Within the first 2 weeks of remission induction therapy, responders could be differentiated from non-responders by more expression of ARAP3 ($p<0.01$), and triggering receptor expressed on myeloid cells-1 (TREM1) ($p<0.01$). ARAP3 was recently described as an inhibitor of neutrophil activation. Furthermore, EIF2S1 appeared to be more abundant in responders ($p<0.01$), and is known to regulate autophagy.
CONCLUSION: Here we describe several genes that are differentially expressed in peripheral blood making a distinction between responders and non-responders to Crohn's disease remission induction therapy. These genes might serve as candidate biomarkers for therapy response in peripheral blood.
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Disclosure of Interest: None Declared
Keywords: biomarkers, Crohn's disease, Efficiency of treatment, gene expression

P859 BODY COMPOSITION IN CROHN'S DISEASE PATIENTS BUT NOT IN ULCERATIVE COLITIS PATIENTS IS DIFFERENT COMPARED TO HEALTHY CONTROLS

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INTRODUCTION: Chronic illness, various intestinal and extraintestinal disease manifestations, and malnutrition affect the health status of inflammatory bowel disease patients. An impaired health status can be accompanied by changes of the body composition. The bioelectrical impedance analysis (BIA) is a widely used method to examine body composition in patients suffering from chronic diseases. In this study we compared the body composition/phase angle of Crohn's disease (CD) and ulcerative colitis (UC) patients with pair-matched controls.
AIMS&METHODS: We evaluated the body composition of 38 CD patients (19 male and 19 female) and 34 UC patients (16 male and 18 female). The four groups were compared to 72 pair-matched healthy individuals. Matching criteria were body mass index (± 2 kg/m^2), age (± 5 years), and gender. Body composition was assessed by BIA. Additionally, we measured biochemical markers of inflammation and nutrition as well as clinical activity indices.
RESULTS: The phase angle in female CD patients was 5.5° and significantly lower than in healthy controls (6.0°, p=0.037). Comparing male CD patients with healthy controls we also found a significant difference (6.3° versus 6.8°, p=0.015). Interestingly, no significant difference of body composition/phase angle was observed when comparing UC patients with matched healthy controls.

We observed no general correlation of any of the disease activity markers with the phase angle as a parameter of body composition.
CONCLUSION: Our observations demonstrate a significant difference of the phase angle as a global parameter of body composition between CD patients and healthy controls. No significant differences were found when comparing UC patients and healthy controls. These observations may reflect the different nature of both diseases (course of disease, affected parts of the gastrointestinal tract, medications, etc.). Generally, BIA seems to be an appropriate method to assess the health status in IBD patients.
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Disclosure of Interest: None Declared
Keywords: bioelectrical impedance analysis, body composition, Crohn's disease, ulcerative colitis

P860 LOWER PREVALENCE OF COLONIC DIVERTICULOSIS IN PATIENTS AFFECTED BY ULCERATIVE COLITIS THAN IN ADULT PATIENTS IN A SINGLE CENTRE

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INTRODUCTION: Diverticulosis of the colon is an acquired condition that results from herniation of the mucosa and submucosa through defects in the muscular layer. The true prevalence of colonic diverticulosis is difficult to measure because most individuals are asymptomatic. In particularly, in literature, there are few study about the prevalence of colonic diverticulosis in patients affected by ulcerative colitis (UC).
AIMS&METHODS: Aim of this study has been to investigate the prevalence of colonic diverticulosis in UC and in adult patients referred in a single centre. Computerized data of consecutive patients, referred to our Institution to undergo a colonoscopy for colorectal cancer screening and/or for UC control, between January 1, 2009 and December 31, 2009, were retrospectively studied. From this study were excluded patients who had previous history of colonic surgery, affected by proctitis and without a complete colonoscopy.
RESULTS: Six hundred and five consecutive patients were retrospectively studied. Of these patients, 438 (72.4%) underwent colonoscopy for colorectal cancer screening (Group A) and 167 (27.6%) for UC assessment (Group B). In group A 224 patients (51.1%) were male (average age of 62.7 ± 14.2 SD years, range 35-86 years), in group B 102 (61.1%) were male (average age of 57.6 ± 12.1 SD years, range 25-84 years). Prevalence of colonic diverticulosis was higher in group A (122 patients, 27.8%) than group B (18 patients, 10.8%) a difference statistically significant ($p < 0.0001$, Fisher's exact test). Female gender in patients with colonic diverticulosis was higher in group A than group B (68 patients, 55.7% and 4 patients, 22.2%, respectively) with a difference statistically significant ($p = 0.0106$, Fisher's exact test). In group A sigma and left colon was involved in 119 (97.6%) patients versus 12 (66.7%) of Group B, with a difference statistically significant, ($p=0.0001$, Fisher's exact test), in Group B the right colon was involved in 4 (22.2%) patients versus 1 (0.8%) of Group A, a difference statistically significant, ($p=0.0009$, Fisher's exact test). No difference was found between the presence of colonic diverticulosis and extension of UC.
CONCLUSION: Results of our study demonstrated that prevalence of colonic diverticulosis was significantly lower in patients with UC than in adult population, underlining, nevertheless, the relevance of the coexistence of UC and colonic diverticulosis that could make be difficult the clinical management of these patients.
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Disclosure of Interest: None Declared
Keywords: COLONIC DIVERTICULOSIS , ULCERATIVE COLITIS

P861 REAL TIME EVALUATION USING CONTRAST ENHANCED ULTRASOUND IN COMPLICATED CROHN'S DISEASE PATIENTS

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INTRODUCTION: Crohn's disease (CD) is associated with penetrating complications such as phlegmons and intra-abdominal abscesses. As the management of the patients is influenced by the presence and characterization of such complications, a readily available tool for the diagnosis of extramural complications in CD is needed. Ultrasonography has a good diagnostic accuracy and can be used as the first-line imaging technique in complicated CD patients. Preliminary findings suggest that the assessment of vascularity within intra-abdominal masses may distinguish between phlegmons and abscesses.
AIMS&METHODS: Aim of our study was to evaluate the use of contrast enhanced ultrasound (CEUS) to distinguish between phlegmons and intra-abdominal abscesses in CD patients. From November 2011, consecutive patients with complicated CD were enrolled. Indications of patient evaluations by CEUS were symptoms, signs and biochemical exams indicating penetrating behavior (abdominal pain, mass, fever, elevated CRP and leukocytosis). A total of 17 CD pts (10 M; median age 27 yrs, range 21-54; disease duration: median 48 mos, range 6-360; CD site: ileal in 9 pts, ileo-colonic in 8 pts; CD behavior: penetrating in 16 pts, stricturing in 1 pt; previous ileocolonic resection in 6 pts) were included. Clinical evaluations by an IBD expert and other cross sectional imaging techniques (MR and CT) were considered as gold standard.
RESULTS: CEUS detected abscesses in 7 pts and phlegmons in 10 pts. Five out of 7 abscesses were confirmed by CT-Enteroclysis and these pts underwent surgery during the follow up. The remaining 2 pts with abscesses were treated with antibiotic therapy and are still in follow up (10 mos). In the group of patients with phlegmons, 4 out of 10 patients were evaluated by CT or MRI that confirmed phlegmons in 3 cases but in one patient a deep abscess was identified and surgery was scheduled. Six out of 10 pts were clinically followed up (median: 6 mos). Two patients developed an abscess after one week from CEUS despite medical treatment. Overall CEUS correctly identified 14 out of 17 lesions on the basis of cross sectional imaging modalities and clinical follow up used as final diagnosis.
CONCLUSION: Our preliminary results indicate that CEUS is a non-invasive, radiation free and real time imaging modality able to differentiate phlegmons from abscesses driving a prompt clinical management in complicated CD patients.
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Disclosure of Interest: None Declared
Keywords: Complications, cross sectional imaging techniques, non invasive technique

P862 CORRELATION BETWEEN THE CROHN'S DISEASE ACTIVITY INDEX AND A WEB-BASED SELF-REPORTING SYMPTOMS DIARY OF CROHN'S DISEASE

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INTRODUCTION: Crohn's Disease Acitivity Index (CDAI) is known to be complex, time-consuming, and impractical.
AIMS&METHODS: The aim of this study was to investigate whether a newly-developed, simple web-based self-reporting symptoms diary of CD (CDSD) was equally effective in assessing disease severity. CDSD consisted of 5 clinical items (general well being, abdominal pain, number of liquid stools, abdominal mass, and complications) which could be easily recorded through online web site (www.CDSD.or.kr). Images were inserted to help patients better understand the complications. All patients were asked to visit and record their symptoms on weekly bases. CDAI and CDSD were recorded on patients visit to the hospitals. Data were analyzed to determine if scores from the CDAI correlated with those from the CDSD for defining disease remission.
RESULTS: Analysis of 288 data pairs showed a positive correlation between scores. The correlation between the systems was 0.673 (Spearman correlation coefficient). Through ROC curve, the score ≤ 5 points of CDSD was identified to correspond to a CDAI score ≤ 150 points (clinical remission). Using cutoff value 5 points of CDSD, the positive and negative predictive value for the clinical remission were 92.4% and 86.8%, respectively.
CONCLUSION: This study demonstrates that results from the CDAI correlated well with those from CDSD. Use of CDSD might permit simpler and patient-friendly CD activity assessment which can provide useful early-phase information of patients with CD in the long term clinical study.
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Disclosure of Interest: None Declared
Keywords: activity index, Crohn's disease

P863 SUSTAINED HIGH PERFUSION IN THE GASTROINTESTINAL WALL IN PATIENTS WITH CROHN'S DISEASE DURING MEDICAL TREATMENT INDICATES LACK OF RESPONSE

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INTRODUCTION: Crohn's disease is characterized by periods of remission and relapse. To improve patient management objective measurements of the degree of local inflammation in the gastrointestinal wall should be made. Increased microvessel density and perfusion are typical features of acute inflammation. Indirect measurements of these parameters could be measured using contrast-enhanced ultrasound (CEUS).
AIMS&METHODS: The study aim was to investigate whether CEUS can provide prognostic information about patients treated medically for an acute exacerbation of Crohn's disease. 13 patients with Crohn's disease were prospectively recruited in a pilot study at Haukeland University Hospital. All patients received medical treatment for an acute exacerbation with systemic steroids, adalimumab or infliximab. Patients who had to change treatment regime during the follow-up were categorized as having insufficient treatment effect. The patients were examined at time 0, 1, 3 and 12 months after initiation of the treatment with clinical scoring, blood tests and CEUS. Ultrasound was performed with a Logiq E9 ultrasound scanner (GE Healthcare, Milwaukee, USA) and contrast agents (Sonovue, Bracco, Milan Italy). The perfusion analysis was performed with commercially available software (Vuebox, Bracco Suisse SA, Geneva Switzerland). The program analyzes the contrast intensity in a selected area, fits the data to a standardized curve and derives variables such as peak contrast intensity, area under the curve and slope of the curve.
RESULTS: In six of the 13 patients, the treatment regime was changed during the study period. There were no significant differences in perfusion between the two groups at the start of the treatment or examinations after 3 and 12 months. There was, however, a significant difference between the two groups for peak contrast intensity ($p=0.022$), wash in area under the curve ($p=0.014$) and slope (wash in rate: $p=0.035$, wash out rate: $p=0.014$, respectively) at the examination one month after the initiation of the treatment.

CONCLUSION: Perfusion analysis of the intestinal wall with CEUS one month after starting treatment in patients with Crohn's disease can provide prognostic information regarding treatment efficacy.
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Keywords: Crohn's disease, inflammatory bowel disease, perfusion, treatment response

P864 ELEVATED MATRIX METALLOPROTEINASE-3 LEVELS IN SERUM CORRELATED WITH CROHN'S DISEASE SEVERITY: EFFICACY AS CLINICAL BIOMARKER

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INTRODUCTION: Matrix metalloproteinase-3 (MMP-3), a 59-kDa protein and 1 of 4 known stromelysins among MMPs, has been reported to be up-regulated in inflamed areas in Crohn's disease (CD) and is considered to play an important role in tissue destruction. However, MMP-3 levels in serum and its clinical effects in CD patients remain unknown.
AIMS&METHODS: We investigated whether serum MMP-3 levels are correlated with clinical and endoscopic evidence of CD. This study was prospectively conducted from November 2011 to September 2012 at 2 hospitals in Japan. Patients with an artificial anus and coexisting collagen disease were excluded. Serum samples were measured at the first visit and serum MMP-3 levels were assessed in regard to CD activity index (CDAI). MMP-3 in serum was also measured within 1 week before undergoing a complete ileocolonoscopy, with those patients scored according to a simple endoscopic score for CD (SES-CD), defined as follows: 0-3, inactive; 4-10, mildly active; and >11, moderately to severely active. We then assessed the correlation of serum MMP-3 levels with SES-CD results.
RESULTS: Sixty-two patients with CD (mean age 36.7±8.8 years; 44 males, 18 females) were enrolled in this study. The mean serum MMP-3 level was significantly higher in the active (n=20, 97.1±51.4 ng/ml) as compared to the inactive (n=42, 61.9±23.0) phase ($p<0.001$). In addition, that level was significantly correlated with CDAI (Spearman's rank correlation coefficient r=0.28, p=0.03). A complete ileocolonoscopy was performed 56 times in 44 patients during the study period. In those cases, the mean serum MMP-3 level was 62.5±28.3 ng/ml for inactive (n=16), 69.7±38.5 ng/ml for mildly active (n=20), and 101.8±48.0 ng/ml for moderately to severely active (n=20) SES-CD cases. Serum MMP-3 levels in cases with moderately to severely active SES-CD were significantly elevated as compared to both inactive (p=0.004) and mildly active cases (p=0.03), and showed a significant correlation with SES-CD (r=0.42, p=0.002).
CONCLUSION: Our results showed that serum MMP-3 levels were elevated during active phases of CD and had a significant correlation with ileocolonoscopy findings. Thus, MMP-3 may be useful as a clinical biomarker measurement in CD patients.
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Disclosure of Interest: None Declared
Keywords: clinical biomarker, Crohn's disease, matrix metalloproteinase-3

P865 INFLUENCE OF STRESS IN THE CLINICAL COURSE OF INFLAMMATORY BOWEL DISEASE PATIENTS

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INTRODUCTION: Psychological stress has been defined as a process in which environmental equal or exceeds the adaptative capacity of an organism. There is a long but inconsistent history of studies about the relationship between stress and Inflammatory Bowel Disease (IBD).
AIMS&METHODS: The aim of this study was to assess the influence of stress on the clinical course of IBD patients. **Methods:** A prospective observational, cohort study was designed. Crohńs Disease (CD) and Ulcerative Colitis (UC) patients older than 18 years of age were included. Stress was assessed with the Spanish version of the Perceived Stress scale (PSS). This scale is a self-reported instrument that assesses the level of perceived stress during the previous month, PSS consists of 14 items with a response format of a five-point scale (0 = never, 1 = hardly ever, 2 = once in a while, 3 = often, 4 = very often). The sum score obtained indicates that a higher score corresponds with a higher level of perceived stress (range 0-56). In order to assess the clinical course of IBD, during a follow-up period of 18 months all emergency visits and hospitalizations related with IBD were recorded. The influence of stress on clinical course was analyzed by Multiple Regression analysis.
RESULTS: 716 patients were included; 343 (47.9%) male, mean age 44.5 years, range from 18 to 86 years, 297 (41.8%) patients with CD and 413 (58.2%) with UC. The mean in the PSS was 23.67, with an SD of 9.59. The mean of emergency visits was 1.05 (SD: 1.68, range 0-14) and for hospitalizations it was 0.35 (SD: 0.94, range 0-9). At month 18 higher stress at baseline was related with more emergency visits in the follow up (B=0.11; CI95%: 0.01-0.03; p=0.005) but not with more hospitalizations (B=-0.02; CI95%: -0.01-0.01; p=0.685). Only the type of disease (CD) (B=-0.13; CI95%: -0.39-0.11; $p<0.0001$) and presence of relapse at baseline (B=0.22; CI95%: 0.29-0.57; $p<0.0001$) were related with more hospitalizations after 18 months.
CONCLUSION: A higher perception of stress in IBD patients is related with an increased number of emergency visits related with the disease in the following months. These patients could probably benefit from a psychological intervention that would improve their psychological status.
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Disclosure of Interest: None Declared
Keywords: inflamatory bowel disease, stress

P866 USE OF FAECAL CALPROTECTIN AS PREDICTOR OF RELAPSE IN INFLAMMATORY BOWEL DISEASE (IBD) PATIENTS UNDER MAINTENANCE TREATMENT WITH INFLIXIMAB

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INTRODUCTION: In inflammatory bowel disease (IBD) predicting relapse by measuring non-invasive biomarkers could allow early changes to treatment. Data is scarce regarding the usefulness of close monitoring with calprotectin to predict relapse.
AIMS&METHODS: The aim was to evaluate the predictive value of a faecal calprotectine test checking for flares in patients with IBD under maintenance treatment with Infliximab. **Methods**: A prospective and observational study was designed. Inclusion criteria were Crohn's disease [CD] and ulcerative colitis [UC] patients in clinical remission under maintenance 5 mg/kg Infliximab therapy. Fresh faecal calprotectin was measured using a rapid test in the stool sample collected just before the drug infusion. Clinical examination was performed the day of the infusion and after two months. Relapse was defined as a Harvey–Bradshaw score >4 in CD and as a Mayo score >2 in UC. The U-Mann–Whitney test and the ROC analysis were performed in SPSS.
RESULTS: 53 patients were included; mean age 46±12 years; 28 (52.8%) female, 62.3% with CD and 37.7% UC. After two months, 41 (77.4%) patients remained in remission and 12 (22.6%) presented a relapse. For patients in remission mean calprotectin levels were 110±170 µg/g (95% CI 225-439). Calprotectin levels in patients relapsing during the follow up had a mean of 332±168 µg/g (95% CI 57-164). Patients who flared had significantly higher calprotectin levels than those who maintained remission ($p < 0.005$). These differences were found in both CD and in UC. A further ROC analysis (flare vs remission) suggested that a calprotectin level > 110 µg/g was the best cut-off point showing high sensitivity (100%) to predict the flare. The area under the curve was (95% [CI]) = 0.888 (0.801 - 0.975) with good accuracy ($p < 0.005$).
CONCLUSION: In IBD patients under infliximab maintenance therapy calprotectin levels highly correlate with a predictor of relapse. Remission is associated with low calprotectine levels. More studies and an increased number of patients should confirm the usefulness of calprotectin to modulate therapy during medical checks.
Disclosure of Interest: None Declared
Keywords: calprotectin, inflamatory bowel disease, infliximab

P867 EFFECTS OF PHYSICAL EXERCISE ON BONE MINERAL DENSITY IN PATIENTS WITH ULCERATIVE COLITIS

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INTRODUCTION: A higher incidence of osteoporosis and fractures is a recognized complication of ulcerative colitis (UC). The cause of metabolic bone disease in this population is believed to be multifactorial and may include the disease itself and associated inflammation, high-dose corticosteroid use, weight loss and nutritional deficiencies, a lack of exercise and physical activity, and an underlying genetic predisposition to bone loss. Measures to prevent and treat osteoporosis in this high-risk group have not yet been well established and despite the benefits of specific exercises being well documented in healthy populations, the role of physical activity and exercise in the prevention and treatment of UC-related bone loss has received little attention.
AIMS&METHODS: The aim of this study was to evaluate the effects of a 1-year exercise training program on bone mineral density (BMD) in patients with UC. Sixty patients (M/F=32/28, median age 46 years) with quiescent UC and low BMD (T-score $\leq$ 1.1) were enrolled in the study. Patients were randomly assigned into control group (n=30) and exercise group (n=30). In exercise group, a mQuiz Ref IDoderate-intensity physical activity progressed to 60 minutes, 3 days per week was prescribed. Both groups received supplementation with 1 g calcium carbonate and 800 IU vitamin D per day. BMD (g/cm^2) was measured at baseline and at 12 months at femoral neck (FN) and lumbar spine (LS) by dual-energy X-ray absorptiometry.
RESULTS: Fifty-two patients completed the study. Significant increases compared with baseline in BMD were observed for both groups at 1 year, with significantly higher increases for exercise group compared with control group. Exercise group showed a BMD increase (± SD) at the LS of +5.7% (±2.1) compared with +3.6% (±2.0) observed in control group ($p<0.05$). Similarly, exercise group showed better performance compared with control group for BMD increase at the FN, with an observed increase +5.5% (±1.9), compared with a change of +3.2% (±1.8) observed in control group ($p<0.05$).
CONCLUSION: Our study has demonstrated that the association of physical exercise and supplementation with calcium and vitamin D is better than

supplementation alone to increase BMD in patient with UC. Physical exercise is a potentially effective method of increasing BMD and reducing the risk of osteoporotic fracture in UC patients.
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Disclosure of Interest: None Declared
Keywords: bone mineral density , physical exercise , ulcerative colitis

P868 DEVELOPMENT OF THE ULCERATIVE COLITIS PATIENT-REPORTED OUTCOMES (UC-PRO) QUESTIONNAIRE

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INTRODUCTION: Well-defined and reliable patient-reported outcome (PRO) measures are needed to provide direct evidence of treatment benefit in clinical trials evaluating new therapeutic agents for the treatment of ulcerative colitis (UC).
AIMS&METHODS: To develop a new instrument covering the signs, symptoms and impacts of UC important to patients with this condition. To determine instrument content and structure, concept elicitation from six focus groups (n=38) and ten 1:1 interviews were conducted in moderate to severe UC patients. Content analysis was performed by independent coders, with data organized using qualitative data analysis software (NVivo or ATLAS.ti). Based on the analytic findings and input from clinical experts, a draft instrument was developed. Two subsequent rounds of 1:1 cognitive interviews were conducted in UC subjects (n=16) to examine readability, interpretability, and comprehensiveness. Saturation was evaluated throughout the data collection process.
RESULTS: Of the 64 participants, 24 (38%) were male; mean age was 44 years (SD=14.3). The most important and relevant UC signs and symptoms were: frequency of bowel movement (BM), consistency of BM, blood in BM, pain in stomach area, joint pain/general body pain, tiredness, urge/need to have a BM right away, mucus in BM, gas, bloating, weakness, loss of appetite, and feeling dehydrated. Important impacts included the use of daily coping strategies and effects on emotional well-being and daily life. No new concepts were identified toward the end of data collection, indicating saturation had been achieved. Based on findings, the UC-PRO was developed to measure the UC signs, symptoms and impacts elicited from and important to the patients themselves. Given the day-to-day variability described by subjects, daily recall is used for recording signs and symptoms (14 items) and coping strategies (8 items), with a one-week recall used for assessing UC impact on activities of daily life (9 items) and emotions (8 items). During cognitive interviews, patients found items in the instrument clear, easy to understand, and relevant.
CONCLUSION: The UC-PRO was developed based on patient input and addresses signs and symptoms of UC, coping strategies, daily life impact, and emotional impact. Research examining the quantitative performance properties including reliability, validity, and ability to detect change, is currently underway.
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Keywords: inflammatory bowel diseases, symptom assessment

P869 SURVEILLANCE OF INTRAEPITHELIAL NEOPLASIA IN ULCERATIVE COLITIS: CHROMOENDOSCOPY-GUIDED ENDOMICROSCOPY VS. RANDOM BIOPSIES

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INTRODUCTION: Ulcerative colitis (UC) is associated with an increased risk of colorectal cancer. Chromoendoscopy with intravital staining techniques showed better results than random biopsies (RB) in surveillance studies aiming high-risk patients, particularly those with history of primary sclerosing cholangitis (PSC) and/or intraepithelial neoplasia (IEN).
AIMS&METHODS: Aims: Compare chromoendoscopy-guided endomicroscopy (CGE) with RB for IEN detection in patients with long-standing UC and no history of PSC and/or IEN. Determine confocal laser endomicroscopy (CLE) performance in IEN detection.
Patients and methods: 113 patients with distal/extensive UC with $\geq$ 8 years of disease and no history of PSC and/or IEN, were prospectively randomized at a 1:1 ratio to undergo RB or CGE. In the RB group (n = 55) 4 random biopsies every 10 cm and targeted biopsy/polypectomy of the detected lesions were performed. In the CGE group (n = 58) the circumscribed lesions identified by chromoendoscopy were evaluated by CLE and then targeted biopsy/polypectomy was performed.
RESULTS: 9 IEN, all low-grade, were detected. These included 4 IEN in the RB group and 5 IEN in the CGE group ($p > 0.05$), distributed by 2 patients in the RB group and 4 in the CGE group ($p > 0.05$). Regarding the number of biopsies performed, it was 36.0 ± 6.4 in the RB group and 5.0 ± 5.2 in the CGE group ($p < 0.001$). The proportion of biopsies with IEN was 1/496 in the RB group and 1/58 in the CGE group ($p < 0.01$). Colon screening takes on average 42.0 ± 8.5 min in the RB group and 61.5 ± 16.6 min in the CGE group ($p < 0.001$). Of the 88 circumscribed lesions identified in the CGE group, IEN was found in 5. IEN detection by CLE revealed: sensitivity = 80.0%, specificity = 97.6%, positive predictive value = 66.7% and negative predictive value = 98.8%.
CONCLUSION: In patients with long-standing UC and without history of PSC and/or IEN, CGE doesn't perform significantly better than RB in detecting IEN. CGE takes longer than the RB, but it decreases the number of biopsies performed and significantly increases the proportion of biopsies with IEN. CLE has a good performance in IEN detection, with a particularly high negative predictive value.
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Disclosure of Interest: None Declared
Keywords: Chromoendoscopy-guided endomicroscopy , Colon surveillance, Intraepithelial neoplasia , Random biopsies , Ulcerative colitis

P870 PATIENT'S DEFINITION OF A FLARE COMPARED TO HBI / SCCAI

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INTRODUCTION: Inflammatory bowel disease (IBD) is a chronic relapsing remitting disease, with flares of disease activity, often requiring escalation in treatment. Harvey-Bradshaw index (HBI) and simple clinical colitis activity index (SCCAI) are two validated clinical scores to assess activity of Crohn's disease (CD) and ulcerative colitis (UC) respectively. Although these two scores are widely used in clinical research and practice, there are no studies comparing patient's perception of a flare with them.
AIMS&METHODS: This was a prospective cross-sectional survey conducted among consecutive patients with CD or UC attending an IBD clinic in a single teaching hospital. All patients completed HBI and SCCAI questionnaires, and demographic data were collected. Participants were also asked if they were attending the clinic due to a flare of disease activity. We cross-tabulated the results using a 2x2 table, assuming HBI and SCCAI to be the gold-standard for defining a flare of disease activity (a score >4 for both), in order to calculate sensitivity, specificity, and positive and negative predictive values (PPV and NPV) for patient's perception of a flare of disease activity. We also calculated a kappa value (K) in order to measure the agreement between the two factors.
RESULTS: 281 patients with IBD were recruited (143 (51.1%) female, 156 (55.7%) CD, 47 (16.8%) smokers, 115 (41.1%) non-drinkers, mean age 46.3 years (range 17 to 89)). In CD 32 (20.5%) patients attending clinic self-reported a flare of disease activity, whereas 69 (44.2%) met criteria for a flare according to HBI. Sensitivity of a patient's self-report of a flare was 36.2%, specificity was 91.9%, PPV was 78.1%, and NPV was 64.2% (K value = 0.30). In UC 50 (39.7%) self-reported a flare, while 51 (40.5%) met criteria for a flare on SCCAI. Sensitivity was 62.7%, specificity 76.0%, PPV 64.0%, and NPV 75.0% (K value = 0.39)
CONCLUSION: Agreement between a patient's report of a flare of disease activity and available validated scores is modest, at best. This may have implications when therapies are altered based on patient's opinion of disease activity alone.
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Disclosure of Interest: None Declared
Keywords: Harvey Bradshaw Index (HBI), Inflammatory bowel disease (IBD), Simple Clinical Colitis Activity Index (SCCAI)

P871 DIFFUSION WEIGHTED MRI OF INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The management of Crohn's disease (CD) is largely dictated by the degree of inflammatory activity within the bowel. Current methods of assessing this include endoscopy and clinicopathological markers of disease activity but these have limitations. Diffusion weighted - MR enterography (DW-MRE) is a recently introduced noninvasive, non-ionising imaging technique that provides comprehensive evaluation of small and large bowel disease. Preliminary studies have suggested that restricted diffusion is seen in segments of inflamed bowel in CD, thought to be due to the presence of an inflammatory cell infiltrate reducing the extravascular extracellular space, and thus restricting the movement of water molecules (1, 2).
AIMS&METHODS: The aim of this study was to compare apparent diffusion coefficient (ADC) measurements on DW-MRE in the inflamed terminal ileum in patients with histologically proven CD compared to the control population. A retrospective study was performed on 59 consecutive patients (median age 35 years, range 16-72 years, 30 female, 29 male) with terminal ileal CD who underwent DW-MRE between January and December 2011. During this same time period, 54 patients (median age 34 years, range 14-73 years, 23 female and 31 male). underwent DW-MRE for investigation of small bowel symptoms with no

endoscopic or histopathological evidence of CD who then served as the controls. One radiologist reviewed the DW images and ADC maps for both patients and controls, with ADC measurements obtained by drawing a standardised region of interest over the wall of the terminal ileum. Analysis was performed using diffusion analysis software on an open source Mac-based Dicom Viewer (Osirix 3.9).
RESULTS: There was a significant difference in ADC measurements between patients with terminal ileal disease and controls, with the median (range) ADC value of inflamed and normal terminal ileum measured as 1.249 (0.900-1.629) $x10^{-3}$ mm^2/s and 2.276 (1.279-3.325) $x10^{-3}$ mm^2/s respectively ($p < 0.0001$, Mann Whitney).
CONCLUSION: Restricted diffusion is present in Crohn's patients with terminal ileal disease, with mural ADC measurements significantly lower than in control subjects. This study supports the hypothesis that diffusion may well have a role as an imaging biomarker in assessing disease activity.
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Disclosure of Interest: None Declared
Keywords: Apparent Diffusion Coefficient, Crohn's disease, Diffusion Weighted Imaging, IBD, MRI

P872 OBSERVATION OF PEYER'S PATCH USING NARROW BAND IMAGING WITH MAGNIFYING ENDOSCOPY IS USEFUL IN PREDICTING THE RECURRENCE IN ULCERATIVE COLITIS PATIENTS

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INTRODUCTION: Peyer's patches (PPs) are aggregates of lymphoid follicles mainly located in distal ileum, which play a major role in mucosal immunity. Using narrow-band imaging with magnifying endoscopy (NBI-ME), we recently reported that patients with ulcerative colitis (UC) have alternate PPs, but its clinical significance is unapparent.
AIMS&METHODS: The aim of this study was to evaluate the relationship between images of PPs using NBI-ME and clinical findings in UC patients. Sixty-three UC patients under 65 years who underwent total colonoscopy from April 2009 to March 2013 were prospectively enrolled, and images of PPs from NBI-ME were collected. Alteration in the villi of PPs were evaluated by ''villi index'' as previously reported (Hiyama S. et al, *Digestion* in press); the sum of three categories; irregular formation, hyperemia, and altered vascular network pattern. Patients were divided into two groups based on ''villi index'', low (L) type = 0 or 1, and high (H) type = 2 or 3. Clinical background data, including age, gender, clinical activity, endoscopic score, extent of involvement, and clinical course were obtained, and factors which contribute to the alteration in PPs were analyzed. Twenty-three patients with mucosal healing (Mayo endoscopic subscore = 0) were followed and were evaluated for the clinical recurrence rate within six months after colonoscopy.
RESULTS: UC patients included 36 men and 27 women, and mean age was 39.9 (17-64) years. Fifty-one percent (32/63) of the patients had L type PPs, while 49% (31/63) had H type. Gender, age, clinical activity, endoscopic score and extent of involvement did not affect the alteration in PPs. All the patients with chronically active course (8/8) had H type PPs, which was significantly higher proportion than in patients with relapsing-remitting or first attack type [42% (23/55); $p < 0.01$]. Additionally, among 23 patients who showed mucosal healing (L type, 12; H type, 11) at the time of endoscopic examination, patients with H type PPs had significantly higher recurrence rate within six months compared to those with L type PPs [64% (7/11) vs 17% (2/12), $p < 0.05$].
CONCLUSION: Alteration in PPs was associated with chronically active disease course and clinical recurrence in UC patients. Observation of PPs using NBI-ME may be a useful method to differentiate treatment-resistant patients in UC.
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Disclosure of Interest: None Declared
Keywords: Inflammatory bowel disease (IBD), narrow band imaging, peyer's patch, ulcerative colitis

P873 DEVELOPMENT OF A NOVEL INDEX OF CT ENTEROGRAPHY FOR EVALUATING SEVERITY OF CROHN'S DISEASE

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INTRODUCTION: The use of computed tomography enterography (CTE) for assessment of patients with Crohn's disease (CD) is expanding. For evaluating severity of the small and large bowel lesions in patients with CD, we developed a novel ''CTE index'' as a parameter of disease activity.
AIMS&METHODS: Patients underwent CTE and double balloon endoscopy (DBE) after oral administration of polyethylene glycol solution on the same day. CTE parameters evaluated in this study included bowel wall thickening (WT), mucosal hyperenhancement (MH), submucosal fat deposition (SF), mural stratification (target sign), stenosis/sacculation (S/S), mesenteric hypervascularity (comb sign), increased fat density (FD), fibrofatty proliferation (FP) and enlarged lymph nodes (LN). Each CTE parameter was graded in a scale of 0 (no), 1 (mild) or 2 (severe). Endoscopic findings were evaluated by the parameters in the Simple Endoscopic Score for Crohn's Disease (SES-CD). The small and large intestine was divided into 3 and 4 distinct anatomic segments, respectively. The segments observed by both CTE and DBE were subjected to evaluation in this study. We sought to determine CTE parameters that were best correlated with endoscopic findings using Spearman's rank correlation and multiple regression analysis to develop "CTE index".
RESULTS: Seventy four segments from 14 patients with CD were observed by both CTE and DBE and subjected to analysis. Spearman's rank correlation showed that most CTE parameters highly correlated with a subtotal score of SES-CD in each segment. Next, regression formulae for each endoscopic parameter were obtained by the multiple regression analysis; Presence and size of ulcers=0.3+0.8*FD+0.4*LN. Extent of ulcerated surface=0.4+1.2*FD. Extent of affected surface=0.7+0.9*FD+0.6*S/S. Presence and type of narrowings=0.7*WT-0.5*MH+S/S. Finally, subtotal score for each segment was found to correlate with the following regression formula; [CTE index (segment)=1.4+2.5*FD +1.2*LN+S/S] ($r=0.66$, $p < 0.0001$). Interestingly, endoscopic findings were more strongly correlated with extraenteric CTE parameters such as increased fat density and enlarged lymph nodes rather than enteric CTE parameters such as wall thickening, mucosal hyperenhancement.
CONCLUSION: This study demonstrated that CTE parameters highly correlated with endoscopic parameters in the small and large bowel lesions of CD. A novel "CTE index" validated by the endoscopic parameters should be useful in non-invasive assessment of disease activity in CD.
Disclosure of Interest: None Declared
Keywords: Crohn's disease, CT enterography

P874 PREDICTING MUCOSAL HEALING IN CROHN'S DISEASE USING PRACTICAL CLINICAL INDICES WITH REGARD TO THE LOCATION OF ACTIVE DISEASE

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INTRODUCTION: Only a few reports have examined the relationship between balloon-assisted enteroscopy (BAE)-based mucosal lesion severity in Crohn's disease (CD) with clinical variables such as serum levels of disease activity markers and Crohn's Disease Activity Index. We analyzed whether clinical variables are useful to predict mucosal healing (MH) in various CD types.
AIMS&METHODS: A total of 173 CD patients who underwent BAE were enrolled. Endoscopic findings were assessed by Modified Rutgeerts Score (MRS). MRS was scored by the following five point scale: 0, no lesions or scar; 1, ≤ 5 aphtous lesions; 2, ≥ 5 aphtous lesions with normal mucosa between the lesions; 3, diffuse aphtous mucosal lesions including smaller ulcers (0.5-2cm); 4, diffuse inflammation with already larger ulcers (>2cm). MH was defined as MRS 0-1. MRS was scored in the most affected area. In this study, all observed intestine, small bowel and large bowel were individually scored. The ''predominantly ileum group'' included patients with MRS ileum score greater than or equal to the MRS colon score (n = 139), whereas the ''predominantly colon group'' included patients who had the ileum score greater than or equal to the MRS colon score (n = 56).
RESULTS: Spearman's rank correlation between MRS and practical clinical parameters were stronger in the predominantly colon group than in the predominantly ileum group. C-reactive protein (CRP) was the most accurate marker for predicting MH in all groups. ROC analysis revealed that the predominantly colon group had better correlativity for the prediction of MH than the predominantly ileum group. The MH index using CRP and serum albumin obtained from logistic regression analysis improved the accuracy in the prediction of MH. A decision-tree model using CRP and serum albumin levels was built; 83.6% (133/159) of all patients and 76.1% (54/71) of patients who underwent second BAE attempts were correctly classified.
CONCLUSION: In the dominant ileal CD, clinical practical parameters such as CRP and serum albumin were less affected by active mucosal lesions. Therefore we need to pay attention to the slight changes of CRP and serum albumin not to overlook active mucosal disease especially for dominant ileal CD. In this context, combination of these parameters or decision-tree model can be used as a guide to predict MH probability in the clinical settings.
Disclosure of Interest: None Declared
Keywords: balloon-assisted enteroscopy, Crohn's disease, mucosal healing

P875 SERUM CHEMERIN LEVELS ARE INCREASED IN IBD PATIENTS AND ASSOCIATED WITH THE DEVELOPMENT OF OSTEOPOROSIS

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INTRODUCTION: Chemerin has been found to play an important role in inflammation by signaling autocrine/paracrine actions. Inflammatory bowel disease (IBD) is characterized by a chronic inflammatory process and a high prevalence of bone loss. Our aim was to examine the serum levels of chemerin in a Greek IBD population in comparison with healthy controls (HC) and to investigate for possible correlation between chemerin and the bone mineral density.

AIMS&METHODS: One hundred and twenty five consecutive IBD patients were included in the study [64 Crohn's disease (CD) and 61 ulcerative colitis (UC)]. All patients underwent bone densitometry by dual energy x-ray absorptiometry at the femoral neck and lumbar spine, and body mass composition with GE-Lunar Prodigy along with host software Encore. Chemerin serum levels were measured in IBD patients and in 98 matched healthy controls (HC) using commercially available enzyme-linked immunosorbent assays. The results of body mass composition include measurements of soft tissue, fat tissue, lean body mass, free fat mass, % total body mass, BMI and total body weight.
RESULTS: Mean (±standard deviation) serum chemerin levels were 14.1±6.6 ng/ml in CD patients, 13.5±3.3 ng/ml in UC patients and 7.8±2.7 ng/ml in healthy controls ($P<0.0001$). No difference between CD and UC was found. No association with disease activity and no difference between males and females were demonstrated.Subgroup analysis of correlation of chemerin levels with clinical characteristics showed significant association only with indices of osteoporosis. Chemerin serum levels were found significantly correlated with T score both at the femoral neck and lumbar spine (r= 0.25 P=0.007 and r =0.19, P=0.03 respectively). No association between chemerin levels and all examined parameters of body mass composition was found.
CONCLUSION: Serum chemerin levels are significantly elevated in IBD patients compared with HC and positive correlated with the development of osteoporosis.
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Disclosure of Interest: None Declared
Keywords: chemerin, IBD, osteoporosis

P876 DISTRIBUTION OF DIAGNOSTIC CRITERIA FOR COLLAGENOUS COLITIS – POOLED ANALYSIS OF 2 EUROPEAN CLINICAL TRIALS

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INTRODUCTION: INTRODUCTION: The diagnosis of collagenous colitis (CC) relies on the histological evaluation of colonic biopsies. There is uncertainty about where and how many colonic biopsies should be obtained to make a reliable diagnosis.
AIMS&METHODS: AIMS: To determine the topographical distribution of diagnostic histopathological criteria of CC.
METHODS*:* We analyzed patients with active CC from 2 prospective multicenter trials (BUC60/COC, BUC63/COC) in whom biopsies from multiple colonic segments have been obtained during baseline colonoscopy. Collagen band thickness and chronic lamina propria inflammation were assessed for each colonic segment based on H&E and van Gieson staining.
RESULTS: RESULTS*:* 187 patients were available for analysis including 79 patients with biopsies from all 5 segments. While chronic lymphoplasmocytic (LP) inflammation was evenly distributed throughout the colon, the mean collagenous band thickness in the rectum (15,8 mm) and sigmoid (18,9 mm) was significantly lower compared to descending (21 mm), $p<0.0001$, $p=0.018$) and ascending colon (20,9 mm, $p<0.0001$, $p=0.043$). Thus, the diagnostic criteria of a collagenous band >10 mm was significantly more common in the ascending (89,9%) compared to the sigmoid (75.9%, $p=0.043$) and the rectum (55.7%, $p<0.0001$). Biopsies taken from the ascending, transverse and descending colon resulted in a diagnostic yield for a collagenous band >10 mm of 96.2%.
CONCLUSION: CONCLUSION: To establish the diagnosis CC it is advisable to perform a complete colonoscopy as the thickened collagenous layer is mainly found in the right colon. In this disease a chronic inflammation in the lamina propria seems to be present in the whole colon which should prompt the pathologist to look for the characteristic findings of CC
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Disclosure of Interest: None Declared
Keywords: collagenous colitis, microscopic colitis

P877 IS FECAL CALPROTECTIN USEFUL IN THE FOLLOW-UP OF CROHN'S DISEASE PATIENTS WITH ANTI-TNF THERAPY ?

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INTRODUCTION: The assessment of Crohn's disease (CD) activity is amenable to endoscopic examination and subsequent histological analysis, but these methods are time-consuming, expensive and invasive. So, if quantifying low calprotectin levels after treatment indicates response of disease activity, this non-invasive marker can become routinely used in optimizing treatment and compliance.
AIMS&METHODS: Aim: to evaluate the role of fecal calprotectin in monitoring the anti TNF-alpha treatment in patients with CD. **Methods:** We prospectively included 25 patients (44±3 years) with moderate to severe ileocolonic CD (CDAI 250-450), who were about to receive either Infliximab i.v. (13 patients) or Adalimumab s.c. (12 patients). Stool samples were collected and calprotectin was measured before starting the treatment and after the induction period (lateral flux immunchromatography technique). In addition, clinical activity was measured using CDAI index before and after induction treatment. For mucosal healing assessment, colonoscopy was performed before and after 6 months of anti-TNF treatment and CDEIS (Crohn's Disease Severity Index) index was assessed. Statistics was done using the U-Mann-Witney test from SPSS.
RESULTS: Clinical response (expressed by CDAI drop) at 6 months was obtained in 19 out of 25 patients (76%) - 8 with Infliximab and 11 with Adalimumab. Calprotectin value was $>300\mu g/g$ before starting the treatment in all patients and after the induction period between 50-200μg/g in 19 patients. Of the 25 patients, 18 (72%) showed an endoscopic response to treatment and 9 of these achieved endoscopic remission (CDEIS<3) and calprotectin concentration below 50μg/g. Patients with clinical and endoscopic response had significantly lower calprotectin levels than the others ($p< 0.05$).
CONCLUSION: Fecal calprotectin has great potential to become widely use as a simple, non-invasive, cheap marker of response to treatment in patients with clearly established diagnosis of Crohn's disease. Further studies with increased number of patients should confirm its role in monitoring the response and the mucosal healing during anti-TNF therapy.
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Disclosure of Interest: None Declared
Keywords: anti TNF therapy, calprotectin, Crohn' disease

P878 SUPERFICIAL SMALL BOWEL CROHN'S DISEASE - AN EMERGING NEW NOSOLOGIC ENTITY?

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INTRODUCTION: The diagnosis of small bowel Crohn's disease has been facilitated by imaging modalities, particularly CT and MRI enterocolysis. However, capsule endoscopy (CE) may be more sensitive for detecting superficial erosions not obvious on CT or MRI enterocolysis. We use faecal calprotectin as a gatekeeper for invasive investigations for patients referred to the outpatient department, with elevated values suggesting intestinal inflammation and leading to further investigations. We describe patients with a long established diagnosis of IBS that have consequentially been diagnosed with a superficial small bowel Crohn's disease by CE.
AIMS&METHODS: We retrospectively analysed all patients who had undergone CE over between 2007 and 2011 (1903 studies). Patients with abnormal studies were then looked up on the integrated hospital electronic database for clinical details, faecal calprotectin, radiology, endoscopy and pathology results.
RESULTS: Most patients reviewed had a clear precipitant or pre-existing diagnosis (e.g. normal, IBD, NSAID-use, radiation enteropathy, etc.). However, there were 15 patients, 8 (53%) male and 7 (47%) female, median ages 47 years and 40 years, respectively) with a firm clinical diagnosis of (mostly) diarrhoea -predominant IBS for an average of 4 years, range 6 months to 10 years, who (apart from one) had raised faecal calprotectin (median 247 g/L, range 10-1384 (normal range < 50). In all cases, superficial aphthous ulceration was detected at CE, predominantly in the terminal ileum. All had normal colonoscopic and large-bowel histological findings. CT or MRI enterocolysis showed no evidence of mural wall thickness, fistulae or stricturing disease. None had an alternative explanation for the aphthous ulceration. All were treated by conventional means as Crohn's disease (variably steroids, 5-aminosalicylic acid, Azathioprine) with improvement in inflammatory activity (reduction or normalization of calprotectin). Four patients required biologics (anti-TNF agents). No patients have developed small bowel strictures to date.
CONCLUSION: The combined use of faecal calprotectin and capsule endoscopy has identified a superficial form of small bowel disease characterized by aphthae and inflammation that responds to conventional Crohn's disease treatment. The disease severity is not trivial, as 4 (25%) required biologics for symptomatic control. These findings represent either 'early' small bowel Crohn's disease or a hitherto unrecognized form of the disease that does not progress to stricturing disease.
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Disclosure of Interest: None Declared
Keywords: Capsule Endoscopy, Crohn's disease, Faecal Calprotectin (FC), Inflammatory bowel disease (IBD)

P879 INFLIXIMAB (IFX) DOES NOT INCREASE THE RISK OF CYTOMEGALOVIRUS (CMV) INFECTION AND CMV IS NOT ASSOCIATED TO RESISTANCE TO IFX THERAPY

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INTRODUCTION: Cytomegalovirus (CMV) infection has also been implicated in resistance to successive lines of immunosuppressive therapies in ulcerative colitis (UC) (1). In contrast to corticoid and anti-calcineurin therapies, the use of anti-TNF antibodies (infliximab, IFX) seems to have a limited impact on CMV infection but limited data are currently available (2).

AIMS&METHODS: The aims of our work were to evaluate (i) if the use of IFX was associated to an increased risk of CMV infection, (ii) if CMV infection is associated to failure of IFX, and (iii) if the intestinal CMV DNA load is increased when using IFX for treatment of UC acute flare. A first prospective cohort included 53 patients exhibiting UC with a Mayo endoscopic score of at least 2. When an acute flare was diagnosed, 2 biopsies of the inflamed mucosa were analysed for CMV DNA load by real-time PCR. A second retrospective cohort included 20 patients exhibiting a positive DNA load in inflamed mucosa and receiving IFX; after 8 to 12 weeks of IFX, the CMV DNA load was measured.
RESULTS: The 53 patients (mean of age: 49.4 years; sex ratio M/F: 0.7; 28 cases of E3) included prospectively exhibited a total of 82 acute flares. A total of 26 CMV infection of the inflamed mucosa was observed: it was observed in 12 cases (26.7%) when flare occurred under IFX therapy whereas in 14 cases (37.8%) of flare without IFX (not statistically significant). The median of CMV DNA load was higher in flares without IFX compared to those under IFX (P=0.06). Among the 12 flares that occurred under IFX, all patients xere optimised with the same dose (10mg/kg). After optimisation at 8W, 6(30%) recovered with IFX and 6 (23.1%) failed to IFX treatment (not statistically significant). Of note, the median of CMV DNA load tends to be higher in case of failure to IFX (P=0.13). For the 20 patients (10 patients naïve for IFX therapy), the follow-up of the intestinal CMV infection after 8 to 12 weeks of IFX showed that the CMV DNA load was undetectable in 4 cases, still positive but decreased in 2, stable for 12 patients, and increased only in 3 patients. No relation was observed between the CMV DNA load and the dose of IFX.
CONCLUSION: The use of IFX was not associated to an increased risk of CMV infection and CMV infection did not increase the risk of IFX failure after optimisation. The mean of CMV DNA load did not increase when using IFX for treatment of the UC acute flare; moreover, the viral DNA load is lower when using IFX. IFX therapy should be recommended for the treatment of UC acute flare when associated to a CMV infection.
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Keywords: Cytomegalovirus, ulcerative colitis

P880 THE PLATELET-CRIT IS A VALUABLE BIOMARKERS FOR ACTIVE CROHN'S DISEASE

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INTRODUCTION: Platelet indices is a set of parameters of the standard full blood count tests, measuring the size variability of thrombocytes. We investigated whether platelet indices are biomarkers of active disease in patients with CD.
AIMS&METHODS: We performed a retrospective study, in order to examine if platelet indices variation could be biomarkers of active CD. In total, 89 patients with Crohn's disease (CD) were enrolled in the study group, and 20 age- and-sex-matched healthy volunteers were included as the control group. A CD activity index >150 in patients with CD indicated active disease. In addition to platelet indices including platelet counts(PLT), mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR) and platelet-crit (PCT), high sensitive serum C-reactive protein levels(hsCRP), erythrocyte sedimentation rates(ESR) and red cell distribution width (RDW) were measured.
RESULTS: The PLT, PCT and PDW level were significantly higher in patients with active CD than in normal controls and in remission patients. ($p<0.001$). PLT(r: 0.261 $p<0.001$),PDW (r: -0.232 p: 0.002) and PCT (r: 0.268 $p<0.001$) had a significant correlation with CD disease activity. A ROC curve analysis indicated that for a PCT cut-off of 0.285, the sensitivity for detecting active CD was 67%, and the specicity was 63% (area under curve [AUC], 0.672; $p<0.001$). PCT was the third sensitive and specific marker for active CD only weaker than hsCRP and ESR. In those patients which hsCRP were lower than 10mg/l, PCT turned to be the most sensitive and specific marker for active CD. In those patients, a ROC curve analysis indicated that for a PCT cut-off of 0.285, the sensitivity for detecting active CD was 71%, and the specicity was 85% (area under curve [AUC], 0.763; $p<0.001$).
CONCLUSION: PLT, PDW and PCT were elevated in active CD in comparison with healthy controls and remission patients. Our pilot study demonstrated that PCT may be a sensitive and specific biomarker for determining active CD, especially in those patients which hsCRP are lower than 10mg/l.
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Disclosure of Interest: None Declared
Keywords: biomarker, Crohn's disease, thrombocyte

P881 TNF- ALPHA EXPRESSION PREDICTS RESPONE TO INFLIXIMAB

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INTRODUCTION: Crohn's disease (CD) is characterized by aberrant mucosal immune response and over expression of T-helper 1 cytokines such as tumor necrosis factor-alpha (TNF-alpha). Antibodies targeting TNF-alpha are the most efficient therapy. However, primary non response, and loss of response are common.
AIMS&METHODS: We hypothesized that pretreatment TNF- alpha expression may predict response to anti- TNF-alpha therapy in CD patients.
CD patients treated with infliximab were prospectively recruited. Response was defined either by post-treatment Crohn's Disease Activity Index (CDAI) lower than150 or 70 points reduction, or a senior gastroenterologist evaluation in the face of pretreatment CDAI < 150. Serum TNF-alpha was assessed using ELISA. TNF-alpha expression was analyzed using immunohistochemistry and the area of lamina propria positive for TNF-alpha was semi-quantified by computerized software.
RESULTS: Out of 69 recruited CD patients with serum or tissue samples, 41patients were responders (59.5%). No difference in age, gender, infliximab level or pretreatment CRP level was documented between groups .Twenty seven patients had pretreatment biopsies and 51-serum samples. Nineteen out of twenty seven (70.5%) infliximab loading patients were primary responders. Lamina propria TNF-alpha expression among responders was significantly higher compared to non responders: 15.4% vs.5.7%, P=0.012. TNF-alpha positive area>12% had a PPV of 100% and NPV of 58%. A correlation (R sq linear=0.74) between lamina propria TNF-alpha expression and treatment efficacy as evaluated by CDAI score reduction was found. Non significant higher serum TNF-alpha levels were detected among nonresponders: 65.2vs. 41.5 pg/ml, p=0.47.
CONCLUSION: High TNF-alpha expression in the lamina propria of CD patients predicts response to treatment with Infliximab. This may be used to improved stratification of CD patients into infliximab responders.
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Disclosure of Interest: None Declared
Keywords: infliximab, lamina propria, TNF-Alpha

P882 USE OF ANTI-TNF TROUGH LEVELS IN CLINICAL PRACTICE

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INTRODUCTION: Anti-TNF trough levels are frequently assessed in clinical trials. Although the value of drug levels are limited in clinical practice because a lot of questions are still unresolved (e.g. optimal trough level, consequences), in general gastroenterologist determine these values to evaluate clinical situations (e.g. control of adherence, side effects, loss of response).
AIMS&METHODS: To limit costs and work load, we wanted to construct a local protocol in order to decrease the current variability in indications for ordering drug levels and to clarify the clinical consequences of the test results to local IBD doctors and nurses. All IBD patients at our hospital (tertiary referral center) who received either adalimumab or infliximab in the year 2011 and / or 2012 (n=353) were retrospectively evaluated with respect to trough levels during the period 2010 – March 2013. We identified 4 reasons for ordering trough levels: (1) complaints / loss of response; (2) to titrate the dosis actively; (3) for clinical interest; and (4) to control trough level after a medication change. Medication change is defined as change in dosis of immunomodulator and / or anti-TNF. Our trough levels are performed by sanguine (Amsterdam) in mg/L.
RESULTS: A total of 342 trough levels were ordered in 228 patients. In Table 1 the indication of the trough level and the results are shown. In the control group, in 27 cases the first trough level was < 3 and after medication change the trough level was > 3 in 12 cases. In just 2 cases with undetectable trough levels (n=7) at the first measurement, these were still undetectable after medication switch. Changes to medication were made in 72 cases (41.4%) of the complaints group, in 20 cases (51.3%) of the titration group, and in 34 (37.8%) cases of the clinical interest group. Overall, in 49 cases the dose of anti-TNF was increased, in 46 cases the dosis was decreased and in 25 cases the current anti-TNFdrug was stopped.
Table 1

	Reason of ordering trough level				
Trough level (mg/L)	Complaints	Titration	Clinical interest	Control	Total
< 0.002	10	4	4	2	20
0.002 – 3	34	3	12	13	62
3-7	45	13	27	13	98
>7	85	19	47	11	162
Total	174	39	90	39	342

CONCLUSION: Each individual doctor and nurse practitioner at our center has gained clinical experience with anti-TNF trough levels. When the exact clinical implications of trough levels are known, the values can help to give optimal individual treatment and will reduce costs. Till then we suggest to assess trough levels at least (1) when stopping an anti-TNFdrug, for any reason, to evaluate the possibility of future re-introduction, (2) before stopping an anti-TNF drug in case of loss of response to exclude low drug levels as the reason for failure.
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Disclosure of Interest: None Declared
Keywords: ANTI-TNF-ALPHA THERAPY, trough levels

P883 MUCOSAL TNF-ALPHA PROTEIN LEVELS AND OTHER PRO-INFLAMMATORY CYTOKINES ARE SUPPRESSED AFTER CLINICALLY EFFECTIVE ADALIMUMAB TREATMENT IN CHRONIC, ACTIVE COLLAGENOUS COLITIS

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INTRODUCTION: Collagenous colitis is a common diarrhoeal disorder of inflammatory origin that in rare cases can present with a chronic, active course despite prior treatment with high dose budesonide and methotrexate. We describe 3 consecutive patients who were given adalimumab (ADA) as a third line therapy and where colonic biopsies were investigated for mucosal cytokine protein levels before and after ADA treatment.
AIMS&METHODS: Three patients (2 women, mean age 45 years and 1 man, 74 years old) were included. ADA was given in doses 160 mg s.c. (baseline), 80 mg (week 2) and 40mg (week 4). The patients were followed clinically and histopathologically and biopsies were taken at baseline and after 6 weeks. Protein levels of IFN-γ, IL-1b, -2, -4, -5, -6, -10, -12p70, -13, -17A, -21, -23 and TNF-α in colonic biopsies were analysed with Luminex. Results are given in pg/mg tissue.
RESULTS: The two women tolerated the treatment well and achieved clinical remission at week 6 with a decrease of mean stool frequency/day from 11 to 2. The mean stool weight/24 hours changed from 600g to185g and the QoL improved drastically. There were no changes in histology. The man developed, despite clinical response, side effects (vomiting, abdominal pain) after 80 mg adalimumab and the treatment was stopped as side effects reoccurred after rechallange. In the two female patients the mucosal TNF-α protein levels were suppressed from mean 1.3 pg/mg to undetectable levels after treatment. Furthermore, the pro-inflammatory cytokines IFN-γ, IL-1b, IL-6, IL-12p70 and IL-17A were suppressed from 1.4, 0.9, 1.4, 1.5, 0.6 pg/mg to undetectable levels whereas IL-23 decreased from 16.4 to 8.8 pg/mg. The levels of the anti-inflammatory cytokines were more or less unchanged in IL-13 (3.6 vs 3.4); and decreased in IL-4 (2.7 vs 2.3); IL-10 (0.6 vs undetectable).
IL-2 declined from 7.3 pg/mg to undetectable levels after treatment in one patient, whereas IL-21 levels were slightly increased, from 4.1 to 4.9 pg/mg.
IL-5 was not found in any of the biopsies.
CONCLUSION: Adalimumab seems to be effective and improves Quality of Life in patients with chronic, active collagenous colitis. ADA treatment leads to suppression of TNF-α and other pro-inflammatory cytokines to undetectable protein levels in colonic biopsies.
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Disclosure of Interest: None Declared
Keywords: adalimumab, collagenous colitis, cytokines, Microscopic colitis

P884 EFFICACY AND SAFETY OF ADALIMUMAB IN MODERATE TO SEVERE PAEDIATRIC CROHN'S DISEASE: SINGLE TERTIARY CENTRE OUTCOME

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INTRODUCTION: The role of Adalimumab in the treatment of paediatric Crohn's disease (CD) is increasingly recognised. The aim of our study was to evaluate the efficacy and safety of Adalimumab in children with Crohn's disease who failed conventional treatment.
AIMS&METHODS: All patients with CD receiving Adalimumab between September 2006 and January 2013 were identified retrospectively. All patients had either failed to respond to Infliximab, lost response or had allergic reaction before commencing Adalimumab. Clinical response and long term outcomes were assessed.
RESULTS: Twenty-one patients (10 females) with median age 12.7 years (8.8y-16.6y) at the time of first Adalimumab injection were included. Seventeen patients (17/21, 81%) showed sustained clinical response to Adalimumab with symptomatic improvement and increased time between relapse (if at all) over a mean period of 2 years 6 months. Ten patients (10/12, 83%) responded to combined therapy of Adalimumab and Methotrexate, compared to four patients (4/4, 100%) responding to Adalimumab and Azathioprine. For the remaining four patients where treatment failed to work over a mean of 11 months, medical treatment was escalated with other immunosuppressive agents, but disease progression remained. Links were also found indicating that those with a higher atopic activity (IgE) and lower inflammatory status (ESR) tended to respond better to the drug. Lastly, there was no major difference in age between groups, with 12.4 years for the responders compared to a mean of 11.7 years for the non-responders. Methotrexate and Azathioprine were the most successful adjuvants, when combined with Adalimumab. No adverse reactions were recorded with the use of Adalimumab during the study period.
CONCLUSION: Adalimumab was efficacious in 81% of children and adolescents with moderate to severe CD unresponsive to Infliximab and should therefore be considered as a treatment option. Adalimumab was additionally found to be safe as no adverse reactions recorded. Results linked to IgE and ESR warrant further studies.
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Disclosure of Interest: None Declared
Keywords: adalimumab injection therapy, CROHŃS DISEASE, Humira, Inflammatory bowel disease (IBD), paediatric

P885 PREDICTOR OF EFFECT OF ORAL TACROLIMUS ON REFRACTORY ULCERATIVE COLITIS

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INTRODUCTION: Patients who received tacrolimus (TAC) administration for refractory ulcerative colitis (UC) at our hospital were divided into those who did and did not achieve clinical remission (clinical remission and non-remission groups, respectively), and a predictor of the effect of TAC was investigated.
AIMS&METHODS: Twenty-nine patients treated with TAC between February 2010 and March 2013 were divided into the clinical remission group consisting of 24 patients (12 males and females) and non-remission group consisting of 5 patients (5 males). TAC was administered in a fasting state or before meals at a single dose of 0.025-0.075 mg/kg, twice daily, as a rule. The target blood level was set at a trough level of 10-15 ng/ml after 2 weeks of administration, and the trough level after 2 weeks was adjusted to 5-10 ng/ml. The clinical activity was evaluated using the Lichtiger score (CAI) before the initiation of TAC administration and at the time when the blood TAC level reached the target level. The CAI score before TAC administration was 10 or higher in all patients. Clinical remission was defined as a condition with a CAI score of 4 or lower after 4 weeks of TAC administration.
RESULTS: The endoscopic findings before the introduction of TAC were evaluated using the UCAI and EAI, and the clinical background was investigated with regard to the gender, age, affected area, duration of illness, total dose of PSL administered 4 and 2 weeks before introduction of TAC, CRP and Hb on admission, CAI before TAC administration, and time required for the blood TAC level to reach the target level, but no significant difference was noted in any item. However, a significant difference was noted in the CAI score at the time when the blood TAC level reached the target level between the clinical remission (7.0 ± 2.5) and non-remission (12.6 ± 2.3) groups ($p<0.005$). When the interval estimation of the mean CAI score was compared between those on admission and at the time of reaching the target TAC level, the reduction rate was 40.1-54.5% in the clinical remission group and 72.1-103.5% in the non-remission group.
CONCLUSION: The rate of reduction of the CAI score from that before TAC administration to that at the time of reaching the target blood TAC level may be an important predictor of the effect.
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Keywords: IBD, Japan, Tacrolimus (FK506), ulcerative colitis

P886 SMALL BOWEL ILEITIS AS DETECTED BY CAPSULE ENDOSCOPY AS A PREDICTOR OF RESPONSE TO IMMUNOMODULATOR THERAPY - A 3 MONTH MUCOSAL HEALING ASSESSMENT

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INTRODUCTION: Mucosal healing and deep remission confer improved long-term outcomes in Crohn's disease(CD) as opposed to clinical indices alone. While immunomodulator therapies have demonstrated improved symptomatic response in CD and their early use and mucosal healing may allow for modification of the natural history of CD, little is currently known of this with regard to Ileitis, which is increasingly diagnosed using Wireless Capsule Endoscopy(WCE).
AIMS&METHODS: To assess clinical, biochemical and ileal mucosal response to therapy in a cohort with established CD at baseline and 12 weeks using WCE. Following informed consent and successful patency exam, symptomatic patients commencing on immunomodulator therapy for CD were invited to participate. Baseline demographics, Harvey Brashaw Index (HBI), Work Productivity and Activity Index(WPAI) and EuroQol(EQ-5D) questionnaires, along with C-reactive protein(CRP) and calprotectin samples were collected at WCE (Given SB2). Calprotectin levels were assessed with a commercially available ELISA kit (MedLab Pathology). A Lewis score (LS) was used to assess severity of ileitis. At week 12 of treatment all parameters were reassessed. Mucosal healing was defined as absence of visible small bowel ulceration. Results at baseline & week 12 were compared using two-tailed Wilcoxon analysis, a p value of <0.05 was considered significant.
RESULTS: To date, 30 patients have been enrolled, 17(56%) female, mean age 38 (range 19-63). Overall, 16(53%) have undergone 12 week assessment, 12 were commenced on adalimumab, 3 on azathioprine and 1 remains on steroids only. Baseline and 12 week values are expressed as a mean in Table 1. Overall there was a statistically significant reduction in all clinical and biochemical parameters at week 12. In all, 13 (81%) had a decrease in LS with 2 $<$135. No patient achieved mucosal healing or deep remission by week 12.
Table 1 Baseline values and 12 week response to treatment values (n=30)

Parameter (normal values) p value	Baseline Values [mean (range)]	12 Week Values [mean (range)]
HBI (<5) $p<0.05$	7 (0-15)	4 (0-14)
WPAI (0-10) $p<0.05$	3 (0-8)	2 (0-7)
EQ-5D (0-100) $p<0.05$	60 (40-100)	70 (40-100)
Calprotectin($<50\mu g/g$) $p<0.03$	195 (30-1600)	65 (0-700)
Lewis score (<135)	552 (225-5050)	318 (0-3000)
CRP (<5mg/dl) $p<0.03$	5 (1-160)	2 (1-17)

CONCLUSION: Symptomatic and biochemical response in our CD ileitis cohort has not been mirrored by mucosal healing at this early stage. This may be due to a lag in mucosal healing that will eventually "catch up" with symptomatic response. Repeat mucosal healing assessment at one year from treatment baseline is warranted to further assess for deep remission rates.

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Keywords: Capsule Endoscopy, Crohn's disease, mucosal healing, Small bowel disease

P887 REDUCTIONS IN CORTICOSTEROID USE IN PATIENTS WITH ULCERATIVE COLITIS OR CROHN'S DISEASE TREATED WITH VEDOLIZUMAB

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INTRODUCTION: Long-term corticosteroid use in ulcerative colitis (UC) and Crohn's disease (CD) leads to adverse effects/dependence. Vedolizumab (VDZ), an anti–$\alpha_4\beta_7$ integrin antibody, has been studied in UC and CD patients (pts) on corticosteroids.

AIMS&METHODS: Two phase 3 UC/CD studies involved induction (wks 0-6) and maintenance (wks 6-52), during which pts received placebo (PB) or VDZ 300 mg intravenously every 8 or 4 wks (Q8W/Q4W). Pts on corticosteroids at wk 0 with a clinical response began corticosteroid tapering at wk 6. Wk 52 corticosteroid-free remission rates (prespecified) and wk 6 associations with wk 52 corticosteroid-free remission (post hoc) were assessed.

RESULTS: In UC, VDZ led to greater wk 52 corticosteroid-free remission rates and decreased corticosteroid use for up to 180 d than did PB. Of pts in wk 6 remission, more in the VDZ Q4W group than the PB group had corticosteroid-free wk 52 remission. In pts with wk 6 mucosal healing, wk 52 corticosteroid-free remission rates were higher with VDZ than PB. In CD, VDZ also led to greater wk 52 corticosteroid-free remission rates (Q8W, Q4W) and decreased corticosteroid use for up to 180 d (Q8W) than did PB. In pts in wk 6 clinical remission, no significant differences from PB in VDZ wk 52 corticosteroid-free remission rates were seen.

	UC			CD		
	VDZ			VDZ		
	Q8W n=70	Q4W n=73	PB n=72	Q8W n=82	Q4W n=80	PB n=82
Wk 52 CS-free remission, %	31.4	45.2	13.9	31.7	28.8	15.9
p value	0.0120	<0.0001	-	0.0154	0.0450	-
Wk 52 remission and CS free for 90 d, %	30.0	45.2	13.9	30.5	25.0	15.9
p value	0.0192	<0.0001	-	0.0240	0.1433	-
Wk 52 remission and CS free for 180 d, %	28.6	42.5	11.1	30.5	23.8	14.6
p value	0.0082	<0.0001	-	0.0139	0.1353	-
Wk 6 mucosal healing and wk 52 CS-free remission, %	**n=48** 41.7	**n=56** 50.0	**n=51** 15.7	- -	- -	- -
Wk 6 remission and wk 52 CS-free remission, %	**n=23** 39.1	**n=29** 58.6	**n=23** 17.4	**n=29** 48.3	**n=29** 37.9	**n=35** 28.6
p value	0.1230	0.0030	-	0.1449	0.3418	-

p values versus PB; CS=corticosteroid.

CONCLUSION: VDZ led to corticosteroid-free remission in UC and CD. Future studies are needed to confirm whether 6-week clinical remissions and/or mucosal healing are predictive of 52-week steroid-free remissions.

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Keywords: corticosteroid, corticosteroid-free remission, Crohn's disease, ulcerative colitis, vedolizumab

P888 ENTERO-URINARY FISTULAS TREATED WITH ANTI-TNF: OUTCOMES AND PREDICTORS OF RESPONSE

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INTRODUCTION: The success of medical treatment for entero-urinary fistulas (EUFs) in CD has so far been modest and surgery is the standard treatment. The advent of anti-TNF therapy has provided a powerful new potential treatment option. The aim of this study was to evaluate the effectiveness and predictors of response of anti-TNF therapy for inducing remission of EUF in CD patients and avoiding the need for surgery.

AIMS&METHODS: In this multicentre observational study a retrospective search was performed for CD patients with EUF treated with any anti-TNF. We defined remission as the absence of clinical symptoms with a radiological confirmation of EUF closure. Multivariate Cox regression analysis was performed to determine factors predictive of achieving remission without need for surgery.

RESULTS: Thirty-three patients received anti-TNF therapy (21 infliximab, 9 adalimumab and 3 both) and were included in the study. Twenty-five (75%) patients were male. Mean (SD) age at diagnosis of EUF was 33 (13) years and median disease duration was 31 months (IQR 12-97). Seventeen patients (51%) were treated concomitantly with an immunomodulator (IMM). Fifteen patients (45%) achieved sustained remission (median follow-up from remission 34 months, IQR 18-44) without needing surgery (10 with infliximab and 4 with adalimumab) and 14 of these continued on anti-TNF therapy. A further 15 (45%) patients achieved sustained remission after surgery (median follow-up 59 months; IQR 26-74). Three patients were in partial response at the last follow-up visit and continued on anti-TNF therapy. In the Cox analysis (adjusted for age, gender, fecaluria and/or pneumaturia, concomitant IMM or antibiotics and type of anti-TNF), only patients with concomitant IMM showed a tendency towards an increased rate of remission without need for surgery (HR 0.42, 95% CI 0.16-1.12; $p<0.08$).

CONCLUSION: Anti-TNF therapy was effective for EUFs in CD, with 45% of patients achieving sustained remission without need for surgery. There was a trend in favour of the concomitant use of IMM.

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Keywords: adalimumab, CROHNS DISEASE, enterourinary fistula, infliximab, internal fistula

P889 NEED FOR INFLIXIMAB DOSE INTENSIFICATION IN PATIENTS WITH CROHN'S DISEASE AND ULCERATIVE COLITIS AND ASSOCIATED COSTS

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INTRODUCTION: In Crohn's disease (CD) patients the annual risk for loss of infliximab (IFX) response and needing for IFX dose intensification is around 15% per patient/year. The requirement for IFX dose intensification in ulcerative colitis (UC) is not well known. The need for dose intensification is one of the main drivers of the increased direct drug costs.
AIMS&METHODS: The aim of the study was to compare the costs of IFX in two cohorts of patients (CD or UC). We also estimated the impact of the requirements for dose intensification on costs. All consecutive CD and UC patients who received IFX were enrolled in the study. We compared the differences in the rates of patients requiring dose intensification per month with IFX treatment in both cohorts. We also compared the interval between first IFX induction dose and the first escalated IFX dose. The primary endpoint was the pharmacological costs derived from the IFX administration (patient per kg/year) (IFX, pre-medication, and day hospital costs) in patients of each cohort who were in treatment for at least 1 year.
RESULTS: Seventy-nine patients were in treatment for at least 1 year (51 CD and 28 UC). The rate per month of patients who needed intensification was 1.5% vs 3.6% (p=0.008) respectively. In patients who underwent IFX optimization, median time between the first IFX induction dose and the first escalated IFX dose was 10 months vs 6 months (p=0.021) for CD patients and UC patients, respectively. In the survival analysis, the cumulative probability of avoiding IFX dose intensification was significantly higher in CD patients (p=0.006). In the multivariate analysis, disease (UC vs CD) was the only factor significantly associated with dose intensification. The costs per patient per kg were significantly higher in UC patients than in EC ($p < 0.001$). In the multivariate analysis, only the need for IFX dose intensification was associated with increased cost (p=0.008).
CONCLUSION: Direct (one-year) cost of IFX is significantly higher in patients with UC compared with CD patients. The increased costs of IFX in the UC cohort was driven by the higher rate per month of UC patients who needed IFX dose intensification. Our data provide a rational basis for economic planning in patients with UC selected for IFX therapy.
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Keywords: costs, CROHNS DISEASE, infliximab, intensification, ulcerative colitis

P890 OPTIMISING OF ANTI TUMOR NECROSIS FACTOR ALPHA STRATEGY IN IBD PATIENTS: WHO NEED AND WHO BENEFIT?

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INTRODUCTION: From 25 to 40% of IBD patients who initially benefit from anti-TNFα will develop intolerance, adverse events or lose of response while on maintenance treatment. Optimisation of anti-TNFα based therapies may help to overcome theses loses of response. Strategies available to optimise an anti-TNFα before switch to another agent include shortening the dosing interval, increasing dose, re-induction or introduction of an immunosuppressive drug. The aim of our study was to identify patients who need optimisation and those who will benefit from it.
AIMS&METHODS: This retrospective study was performed in a single tertiary care centre. All IBD patients who received anti-TNFα treatment from September 2009 to September 2011 were analysed. Demographics, IBD type and characteristics according to Montreal classification as well as treatments received, modalities of treatment optimisation and theirs results were collected. Optimisation failure was defined as a need for surgery, switch to other anti-TNFα, ciclosporin or experimental drugs. Characteristics of patients requiring and benefiting from optimisation were compared to patients succeeding on standard anti-TNFα dosage using univariate analysis.
RESULTS: 300 patients of mean age 37± 11 years with 56% of female were included. IBD type was Crohn's disease (CD) in 70.7%, ulcerative colitis (UC) in 26%. CD was of ileo-colic location in 62%, of non-inflammatory phenotype in 13% and with perianal disease in 44%. In UC patients 54% had pancolitis. Extra digestive manifestations were present in one third. In 74% of the cases the first anti-TNFα treatment was infliximab and combination therapy was used in 70% mainly with azathioprin.
Optimisation was required in 104 patients (40%). Strategies used were shortening dosing interval (n=59, 57 %), increasing dose (n= 13, 12 %), combination of both (n= 19, 18%), introduction of an immunosuppressive drug (n=3, 3 %). Optimisation's requirement was more frequent in female (p=0.02) and in CD (p=0.04). Among patients who were optimised, 76 (73.1%) of them had benefit. Optimisation's success was associated with female ($p < 0.0001$), absence of perianal disease (p=0.047) and tended to be more frequently achieved with infliximab (p=0.055).
CONCLUSION: Optimisation of anti-TNF treatment is required in 40% of IBD patients while on maintenance therapy. These strategies avoided unfavourable outcome and anti-TNF failure in 74% of cases. Female and CD patients were more likely to require optimisation while female and absence of perianal disease were associated with optimisation success.
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Keywords: anti TNF therapy, IBD, optimisation

P891 EFFICACY OF INFLIXIMAB IN PAEDIATRIC ULCERATIVE COLITIS: SINGLE TERTIARY CENTRE EXPERIENCE

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INTRODUCTION: The role of Infliximab in the treatment of paediatric ulcerative colitis (UC) is increasingly recognised. The aim of our study was to evaluate the efficacy of Infliximab in children with ulcerative colitis who failed conventional treatment.
AIMS&METHODS: All children with UC who received Infliximab between April 2006 and October 2012 in our centre were identified. Clinical response and long term outcomes were assessed.
RESULTS: Twenty eight (28) patients with moderate/ severe UC were included in the study (17 males). Median age at histological diagnosis was 11.6 years (range 2.6y-15.2y), with median duration of disease prior to first Infliximab infusion 1.6y (5 weeks-5.5y) and median follow up post Infliximab regardless of outcome 1.6y (0.5y- 5.4y). Fifteen patients (15/28, 53.5%) responded initially to the treatment. Nine patients (9/15, 60%) had sustained clinical response at 5mg/kg 8 weekly with histological evidence of mucosal healing, with median duration of treatment 1.6y (0.7y-5.4y). In six patients (6/15) Infliximab had to be discontinued due to either loss of initial response or allergic reaction. Out of 13 patients with partial or no response to Infliximab (13/28, 46.4%), 6 failed escalation of medical treatment with other immunosuppressive agents , including Adalimumab and Sirolimus, and underwent colectomy 1 month-11 months later (median 0.6y), at median age 13.7y (8.9y-15y).
CONCLUSION: Infliximab was efficacious in 53.5% of children with ulcerative colitis who failed conventional treatment, with response maintained in 60% of those patients. Therefore, Infliximab should be considered not only as rescue treatment, but also as maintenance treatment in children with refractory disease.
Disclosure of Interest: None Declared
Keywords: inflammatory bowel disease, infliximab, paediatric, ulcerative colitis

P892 EFFICACY OF ADALIMUMAB IN CHILDREN AND ADOLESCENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS

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INTRODUCTION: Adalimumab is licensed for treating moderately to severely active ulcerative colitis (UC) in adults whose condition has responded inadequately to conventional therapy, but data on its role in paediatric UC are lacking. The aim of our study was to evaluate the efficacy of Adalimumab used as indicated above in children and adolescents treated in a single tertiary UK centre.
AIMS&METHODS: All patients with UC who received Adalimumab between April 2008 and October 2012 in our hospital were identified. Clinical response and long term outcomes were assessed.
RESULTS: Ten patients (7 females) with median age 14 years (6.8y-16.6y) at the time of first Adalimumab injection were included in our study, with median follow up 1.9 years (1y-3y). All patients had failed Infliximab after 6.5 months median duration of treatment (2–24 months). Three patients (3/10, 30%) showed sustained clinical response to Adalimumab with histological evidence of mucosal healing (follow up 16, 22 and 24months respectively). All three received concurrent treatment with Azathioprine or Methotrexate and one of them was successfully weaned off Adalimumab after 21 months, without relapse to date. For the remaining 7 patients, medical treatment was escalated with other immunosuppressive agents, with 4 of them ending up with colectomy (4/10, 40%).
CONCLUSION: Adalimumab was efficacious in 30% of children and adolescents with moderate/ severe ulcerative colitis who failed Infliximab and should therefore be considered as treatment option in refractory disease in this age group.
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Disclosure of Interest: None Declared
Keywords: adalimumab injection therapy, Humira, Inflammatory bowel disease (IBD), paediatric, ulcerative colitis

P893 ORAL BECLOMETHASONE DIPROPIONATE VERSUS 5-AMINOSALYCILIC ACID ENEMA IN ACTIVE ULCERATIVE COLITIS PATIENTS: LOWER EFFICACY BUT BETTER COMPLIANCE

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INTRODUCTION: Treatment of patients with mild-moderate active ulcerative colitis (UC) is based on combination of oral and topical sulfasalazine or 5-aminosalycilic acid (5-ASA), or use of oral and topical glucocorticosteroids, but prolonged use of steroids is limitated by the risk of side effects. A new

glucocorticosteroids, beclomethasone dipropionate (BDP), with the same efficacy as traditional ones, but with more favourable safety profile was developed.
AIMS&METHODS: Aim of this study has been to define the efficacy and safety of oral BDP compared to 5-ASA enema in left-sided active UC. In eight-week, investigator blind comparative study, patients with left-sided mild-moderately active UC were randomized to receive oral 5-ASA (2.4 g/day) plus oral BDP (10 mg/day) or 5-ASA enema (4 g/day). Efficacy was evaluated by the Disease Activity Index (DAI). Safety was evaluated by monitoring adverse events, haematochemical parameters and adrenal function.
RESULTS: Sixty-two outpatients were enrolled and randomly treated with BDP (n= 30) or 5-ASA enema (n= 32). Twelve patients did not complete the study: 2 (6.7%) in the BDP group and 10 (31.3 %) in the 5-ASA group, with a difference statistically significant (p=0.0226). According to *intention-to-treat* (ITT) analysis complete remission was achieved in twelve out of thirty patients in BDP group (40%) and in fourteen out of thirty-two patients in 5-ASA group (43.8%) with a difference not statistically significant. According to *per protocol* (PP) analysis, complete remission was achieved in 42.9% of BDP patients vs 63.6% of 5-ASA, a difference not statistically significant. Mild signs of hypothalamic-pituitary-adrenal axis suppression were observed in 4 (14.3%) patients of BDP group.
CONCLUSION: Oral BDP gave an overall treatment result in patients with left-sided active UC with few signs of systemic side-effects, so it can be considered, a useful therapeutic regimen in patients not compliant to 5-ASA enema.
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Keywords: 5-AMINOSALYCILIC ACID ENEMA, ORAL BECLOMETHASONE DIPROPIONATE , ULCERATIVE COLITIS

P894 EFFICACY AND SAFETY OF INFLIXIMAB SALVAGE THERAPY FOR PATIENTS WITH ULCERATIVE COLITIS WHO FAILED TO TACROLIMUS

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INTRODUCTION: Tacrolimus and anti-TNFα therapy are effective for the treatment of patients with moderate or severe corticosteroid-dependent/refractory ulcerative colitis. However, regarding treatment for these patients, whether tacrolimus therapy should precede anti-TNFα therapy as a secondline therapy remains controversial. To address this issue, we retrospectively investigated the efficacy of infliximab salvage therapy for patients with severe or moderate ulcerative colitis who failed to respond to tacrolimus.
AIMS&METHODS: We assessed retrospectively clinical backgrounds and therapeutic outcomes at baseline, 8, and 30 weeks for 16 patients receiving infliximab between beginning of 2009 and the end of 2012 for severe or moderate ulcerative colitis who showed refractoriness or loss of response to tacrolimus, or no tolerance.
RESULTS: Mean partial Mayo score was significantly decreased ($P<0.05$) to 5.75, 3.38, and 2.38 at baseline, 8, and 30 weeks, respectively. Five of 16 patients (31.2%) showed clinical remission at 8 weeks and seven (43.8%) showed clinical remission at 30 weeks. Two patients who did not respond to infliximab finally underwent colectomy. Rates of clinical remission at 8 and 30 weeks were 28.6 and 42.9% in tacrolimus responders, and good remission rates of 33.3 and 44.4%, respectively, were also obtained in tacrolimus nonresponders. There was no factor which was useful in predicting response to infliximab. No serious adverse events were encountered.
CONCLUSION: Infliximab salvage therapy following tacrolimus appeared to be efficacious in both tacrolimus responders (loss of response or no tolerance) and in nonresponders (refractoriness), and 14 (87.5%) of 16 patients avoided colectomy. Sequential therapy may thus prove useful and well tolerated. Infliximab was thus considered to be a therapeutic option. In addition, we should avoid missing the proper timing of colectomy, and care is warranted regarding adverse events.
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Disclosure of Interest: None Declared
Keywords: infliximab, tacrolimus, ulcerative colitis

P895 DAIKENCHUTO (TU-100) RAISES PLASMA LEVELS OF ADRENOMEDULLIN IN PATIENTS WITH CROHN'S DISEASE: POSSIBLE MECHANISM OF CLINICAL ACTION

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INTRODUCTION: Daikenchuto (TU-100), a traditional Japanese medicine, reportedly up-regulates the adrenomedullin (ADM)/calcitonin gene-related peptide (CGRP) system, which is involved in potent tissue repair and anti-inflammatory actions in the intestine. TU-100 exerted beneficial effects in a Crohn's disease (CD) mouse model through the induction of ADM release, and a clinical study involving the use of TU-100 in humans with CD is in the planning stage. However, nothing is known about the effect of TU-100 on ADM/CGRP release in the treatment of human CD. The primary objective of this study was to evaluate the efficacy of TU-100 treatment on circulating ADM/CGRP levels in patients with active CD. Additional objectives included the assessment of disease activity and a safety evaluation.
AIMS&METHODS: The plasma levels of total ADM (tADM) and mature form-ADM (mADM) and the serum levels of CGRP were measured in 17 patients with active CD and 24 healthy subjects using enzyme-linked immunosorbent assays (ELISAs), for the measurement of tADM [detection limit, 2 fmol/mL] and mADM [1 fmol/mL], for CGRP [7.8 pg/mL]). Then, 10 patients with active CD received 15 g of TU-100 (Tsumura & Co., Japan) daily for 8 consecutive weeks in an open-label treatment protocol while the baseline anti-inflammatory therapy was continued. The pre- and post-treatment plasma levels of tADM and mADM were measured. The response to treatment was evaluated clinically using the international organization for the study of inflammatory bowel diseases (IOIBD) score.
RESULTS: The plasma tADM and mADM levels were higher in the patients with active CD than in the healthy subjects (mean $\pm$ SEM**:** 16.4 ± 1.1 vs**.** 11.8 ± 0.4 fmol/mL, $P < 0.001$; 1.7 ± 0.1 vs**.** 1.4 ± 0.1 fmol/mL, $P = 0.008$, respectively). Simultaneous determinations of the serum CGRP level were not detectable in most of the subjects. After 8 weeks of treatment with TU-100, the patients showed elevated levels of plasma tADM (16.4 ± 1.1 vs. 20.2 ± 1.7 fmol/mL, $P = 0.0218$) and plasma mADM (1.7 ± 0.1 vs. 2.2 ± 0.1 fmol/mL, $P = 0.0284$). The patients' IOIBD scores also improved, with a significant decrease in the score from 3.9 ± 0.5 to 2.4 ± 0.4 ($P = 0.0284$). Of the 10 components of the IOIBD score, the scores for 2 components (''abdominal pain'' and ''abdominal tenderness'') decreased significantly ($P = 0.014$ and $P = 0.046$, respectively). No side effects were observed.
CONCLUSION: This pilot study showed that the pharmacologic action of TU-100 is related to changes in the ADM levels. Treatment with TU-100 may have a place in the management of CD.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, daikenchuto, TU-100

P896 EFFICACY OF PROBIOTIC TREATMENT WITH BIFIDOBACTERIUM LONGUM 536 FOR INDUCTION OF REMISSION IN ACTIVE ULCERATIVE COLITIS: A RANDOMIZED, DOUBLE-BLINDED, PLACEBO-CONTROLLED MULTICENTER TRIAL

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INTRODUCTION: Probiotic treatment in patients with ulcerative colitis (UC) has been focused on improving the intestinal microbial balance and cytokine profile. We have previously reported that upregulation of T-bet and tight junction molecules by *Bifidobacterium longum 536* (BB536) improves colonic inflammation in patients with UC. Therefore, to investigate the efficacy of BB536 supplementation for induction of remission in patients with active UC, we conducted a randomized, double-blinded, placebo-controlled multicenter trial.
AIMS&METHODS: A total of 56 consecutive patients with mild-to-moderate UC (27 male, 29 female; mean age 44±14) were enrolled in the study. Eight patients of these (14%) were affected with pancolitis and 31 (56%) had left-sided colitis; 17 (30%) had proctitis. Patients were randomly treated with 2–3 $\times 10^{11}$ freeze-dried viable BB536 (28 patients) or placebo (28 patients) for 8 weeks.
RESULTS: Twenty-four patients in the BB536 group and 23 patients in the placebo group completed the study (86% and 82%, respectively). In 7 of the remaining 9 patients, other treatments were needed because of exacerbation. One patient from the BB536 group withdrew from the study because of a mild side effect, and 1 patient from the placebo group withdrew from the study on entry. In total, 63% of patients receiving BB536 showed clinical remission (UC disease activity index [UCDAI], ≤ 2) at week 8 compared to 52% of those receiving placebo ($p = 0.395$). There was a significant decrease in UCDAI scores from 3.5 ± 1.9 at baseline to 2.5 ± 1.7 at week 8 in the BB536 group ($p = 0.034$), whereas there was no significant decrease in these scores in the placebo group. The Rachmilewitz endoscopic index (EI) score also decreased significantly for the items of granulation scattering reflected light (from 1.8 ± 0.7 to 0.8 ± 1.0, $p < 0.001$) and vulnerability of mucosa (from 1.4 ± 1.2 to 0.6 ± 0.9, $p < 0.001$) in the BB536 group. One patient (1.8%) in the BB536 group reported a mild side effect (dry cough), but no other serious adverse reactions were observed.
CONCLUSION: Supplementation with BB536 was safe and efficacious in reducing UCDAI scores in patients affected by mild-to-moderate UC. Moreover, BB536 improved EI scores in patients with active UC after 8 weeks of treatment.
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Keywords: probiotics, randomised controlled trial, ulcerative colitis

P897 EFFECT OF A PROBIOTIC PREPARATION(VSL#3) IN THE PATIENTS WITH ULCERATIVE COLITIS: ITS EFFECT ON CYTOKINES

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INTRODUCTION: Ulcerative colitis is chronic inflammatory disease. Probiotics could possibly induce remission in the treatment of active UC. Assess the efficacy of VSL#3 on induction and maintenance of remission and evaluate cytokine concentration change in patients withactive UC.
AIMS&METHODS: We evaluated the clinical efficacy of probiotic preparation VSL#3 and assessed cytokine concentration changes in the treatment of mild to moderate UC patients.Thirteen eligible patients with mild to moderate UC between the ages of 20 to 70 received VSL#3 4 sachets daily in 2 divided doses

for 8 weeks. The disease activity pre- and post-VSL#3 therapy was assessed by Mayo ulcerative colitis endoscopic score; colonic tissue cytokine profiling done at baseline and at week 8.
RESULTS: Thirteen patients (8 males and 5 females) were enrolled in the open-label VSL#3 study and completed 8 weeks of VSL#3 treatment. VSL#3 treatment outcome demonstrated remission (defined as UCDAI $\leq$2) in 61.5% of subjects (n=8); response (decrease in UCDAI $\geq$2) in 15.4 % (n=2); no response 15.4 % (n=2); worsened in 7.7 % (n=1).
CONCLUSION: Our study demonstrated that using VSL#3 in the treatment of mild to moderate UC is effective in induction of remission / response. Those who responded to VSL#3 treatment had a significant decrease in their UCDAI scores and colonic tissue pro-inflammatory cytokine levels.
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Keywords: probiotics, ulcerative colitis

P898 THE EFFICACY OF TACROLIMUS IN PATIENTS WITH ULCERATIVE COLITIS REFRACTORY TO CORTICOSTEROIDS AFTER FAILURE OF INFLIXIMAB REMISSION INDUCTION THERAPY

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INTRODUCTION: The calcineurin inhibitor, tacrolimus (Tac) and the anti-tumour necrosis factor (TNF)-alpha antibodies like infliximab (IFX) are alternative medications for patients with severe corticosteroids-refractory ulcerative colitis (UC). However, currently, there is no guideline pertained to the order or the timing of these medications.
AIMS&METHODS: This study was to investigate the efficacy of Tac in patients with active UC refractory to corticosteroid who failed to respond to IFX remission induction therapy. In a single centre, open-label setting, 94 patients with corticosteroid-refractory UC, average age 38.3yr, range 15-79yr were given IFX (5mg/kg bodyweight) at weeks 0, 2 and 6 as remission induction therapy. At week 8, 26 patients had not achieved remission. Seventeen of these IFX refractory patients were given Tac, orally, aiming for an initial blood trough level of 10-15ng/ml as remission-induction therapy and then at 5-10ng/ml blood as maintenance therapy for longer than 3 months. The other 9 patients were given alternative medications (without Tac). Efficacy was assessed by applying the Mayo disease activity index (DAI). DAI equal or smaller than 2 meant remission, while at least a 30% decrease in the DAI score was defined as response to therapy.
RESULTS: In the Tac arm (n=17), before Tac remission induction therapy, the DAI score was 8.95+/-1.17 and C-reactive protein level was 2.37+/-2.45mg/dL, indicating active UC in spite of IFX administration. Eight weeks after Tac administration, the rates of remission induction, clinical response and no-response were 29.4% (5 of 17 patients), 58.8% (10 of 17 patients), and an 11.7% (2 of 17 patients), respectively. The maintenance rate and the surgery rate one year after Tac treatment were 20% (1of 5 patients) and 17.6% (3 of 17), respectively. The maintenance rate in the without Tac arm was 0% while the surgery rate was 44.4% (4 of 9 patients). Side effects were tremor, kidney disfunction and thrombosis 1 patient each.
CONCLUSION: The efficacy of Tac in patients with UC refractory to corticosteroids who failed to achieve remission within 8 weeks of initiating IFX remission induction therapy is potentially interesting. A randomized study in a large cohort of patients including a control arm is warranted to fully evaluate the efficacy and safety of Tac in patients with UC refractory to corticosteroids and anti-TNF biologics.
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Disclosure of Interest: None Declared
Keywords: after failure of infliximab, taclolimus, ulcerative colitis

P899 TIMING OF SWITCHING FROM INFLIXIMAB TO ADALIMUMAB IN THE TREATMENT OF CROHN'S DISEASE

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INTRODUCTION: Patients who receive infliximab (IFX) for Crohn's disease (CD), at some time point may require dose escalation or shortening of infusion interval for maintaining an adequate efficacy level. This is often called loss of response to IFX. Switching from IFX to adalimumab (ADA) has been considered as an alternative strategy for minimizing adverse side effects and overcoming the loss of response.
AIMS&METHODS: In this investigation, we were interested to better understand the timing of switching from IFX to ADA in patients who had developed active CD in spite of IFX dose escalation or shortened infusion interval. In this endeavour, we retrospectively evaluated CD patients who were treated with anti-tumour necrosis factor (TNF)-α agents from November 2010 to September 2012 and assessed the efficacy of ADA among patients with anti-TNF-α naïve (naïve group), switching from 5mg/kg of IFX (5mg/kg group), and from10mg/kg of IFX or reducing the interval of IFX infusion (dose-escalation group).
RESULTS: A total of 60 patients with CD were included, 15 were anti-TNF-α naïve, and 45 had switched from IFX to ADA. Seven patients had switched to ADA because of IFX infusion reaction. 12 of 15 patients (80%) who were anti-TNF naïve together with 24 of 45 patients (53%) who had switched from IFX to ADA could continue the treatment with ADA up to week 52. 11 of 15 patients in the 5mg/kg group could continue the treatment with ADA up to week 52 compared with 11 of 28 patients in the dose-escalation group (73% vs 39%, P = 0.033). The CD activity index (CDAI) in the naïve group was significantly lower than in either the 5mg/kg group or the dose-escalation group at 52 weeks after the start of ADA administration (P = 0.02). Further, both CDAI and C-reactive protein levels in the 5mg/kg group were significantly lower than the dose-escalation group at 52 weeks (P = 0.02, and P = 0.006, respectively).
CONCLUSION: In CD patients with the loss of response to IFX, switching to ADA before IFX dose escalation appears to be a clinically relevant therapeutic decision.
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Disclosure of Interest: None Declared
Keywords: anti TNF therapy, Crohn's disease

P900 LONG-TERM OUTCOME AFTER DISCONTINUATION OF INFLIXIMAB IN PATIENTS WITH CROHN'S DISEASE ACHIEVING CLINICAL REMISSION

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INTRODUCTION: The STORI trial showed that in CD patients who stop infliximab (IFX) for remission but continued immunomodulators (IMM), half will relapse within 1 year after discontinuation, while biologic or endoscopic features of persistent inflammation were predictors of relapse. We investigated the long-term outcome of CD patients who discontinued IFX, while in clinical remission (CR) and searched for predictors of sustained clinical remission (SCR) after IFX cessation including serum levels of IFX.
AIMS&METHODS: Observational, retrospective, single-centre study of 90 CD patients [36 males, median age at last follow up 43 (IQR 35-56)] years who discontinued IFX therapy due to CR after a median of 7.6 (IQR 1.4-17.6) months and a median of 4 (IQR 2-6) infusions. The majority had been treated with episodic IFX, n=70 (78%), 12 with maintenance from the start (13%) and 8 (9%) had switch from episodic to maintenance therapy. After stopping IFX, 76 (84%) patients continued on IMM (AZA, n=60), while 14 (16%) received 5-ASA or no therapy. Primary outcome was SCR after discontinuation of IFX and secondary objectives included the identification of predictors for SCR. SCR was defined as maintained disease remission without any biological or surgical treatment until the end of follow up. Serial IFX trough (TR) and intermediate (IM) levels in prospectively collected serum samples were analyzed by an in house ELISA.
RESULTS: With a median follow up of 9.4 (IQR 7.6-11.2) years, 49/90 (54.5%) had SCR [22/49 (45%) treated mainly for fistulising, 27/49 (55%) for luminal disease]. The median time between stop of IFX and relapse was 4.7 (IQR=3.5-7.0) years. In univariate analysis, potential factors associated with SCR included long-term partial or complete mucosal healing (MH) 2-48 months after stop of IFX [OR=4.427 (95% CI, 1.74-11.267), n=49, $p<0.001$], while there was a trend for albumin >35g/l at the time of last IFX [OR=1.156 (95% CI, 1.018-1.313), n=71, p=0.055]. Logistic regression analysis did not reveal any independent factor predicting SCR. Median TR and IM levels at different available time points of treatment (w2, w6 for those with an induction phase, n=27 and at the time of discontinuation of IFX, n=18) were not able to predict SCR.
CONCLUSION: In this single centre cohort, 54% of CD patients who discontinued IFX therapy while in CR remained in SCR and mainly with continued IMM treatment. This implies that within the variable responses to IFX some patients may achieve indefinite remission after IFX discontinuation. Unfortunately we were not able to identify any independent factor predicting SCR.
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Keywords: CROHNS DISEASE, infliximab, trough levels

P901 AZATHIOPRINE ACHIEVES MUCOSAL HEALING IN PATIENTS WITH EARLY-ONSET CROHN'S DISEASE

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INTRODUCTION: Although azathioprine (AZA) may prevent relapses of steroid-dependent Crohn's disease (CD) its healing effects range between 16.5 (SONIC trial) and 85%. This may be due to patient selection, disease activity, definition of mucosal healing (MH) and timing of colonoscopy after starting AZA. We aimed to assess MH in patients with early onset CD receiving AZA monotherapy.

AIMS&METHODS: Retrospective analysis of prospectively acquired data in patients followed in a single center from 2006 to 2013. Eligible patients had a recent onset of luminal CD (≤6 months of symptom onset and diagnosis), ileocolonoscopy and full laboratory assessment at disease diagnosis and were received AZA at or within 6 months of diagnosis. Patients received budesonide or classical steroids with AZA (2.5 mg/kg); steroids were tapered off within 8-12 weeks. Patients were followed by a strict protocol including regular clinical examination and laboratory tests. Patients maintained in clinical (CDAI < 150) and serological (CRP < 0.6 mg/dL) remission underwent ileocolonoscopy between 22-26 months after starting AZA. Exclusion criteria were AZA intolerance, relapse despite adequate AZA dose, or lost to follow up. At baseline ileocolonoscopy, the SES-CD was used to describe and localize lesions. At follow up colonoscopy, MH was graded in 4 categories compared to baseline endoscopy: complete MH (no lesions); near-complete MH (occasional aphthae, residual superficial erosions, or thickened folds); partial MH (length of inflamed areas shortened but still considerable numbers of persisting ulceration and/or cobblestone), and unchanged/worse (lesions same or more severe than baseline).

RESULTS: Of 65 patients who received AZA 20 were excluded [8 adverse events, 10 persisting activity, 3 lost to follow up); 45 patients fulfilling the study criteria were identified [20 males, mean age 28 (range 16-67)y, smokers 23, ileitis (9), ileocolitis (21), colitis (13), median CDAI 265 (range 170-320), 20 steroid-dependent]. Patients had achieved steroid-free clinical and serological remission (SFR) between months 5-7 after starting AZA and maintained remission until follow up colonoscopy. MH at 2 years was complete in 53% (23/43); near-complete in 16% (7/43); partial in 19% (8/43) and unchanged in 12% (5/43) patients. Ileal lesions were more resistant than colonic lesions; healing rate in ileocolitis was higher for colonic than ileal lesions.

CONCLUSION: AZA can effectively heal luminal CD if started early after the onset of CD but is more effective for colonic lesions. Maintenance of SFR does not imply MH. MH should be assessed after 12 months in deep-remission.

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Keywords: azathioprine, CROHN'S DISEASE, mucosal healing

P902 EFFECTS OF ANTI-TNF THERAPY IN THE MONITORING OF HISTOLOGICAL ACTIVITY IN PATIENTS WITH CROHN'S DISEASE

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INTRODUCTION: Crohn's disease (CD) is a chronic inflammatory disorder characterized by periods of clinical remission alternating with periods of relapse. Historically, clinical response and remission have been the primary treatment goals. A working definition of sustained deep remission which includes long-term biological remission and symptom control with defined patient outcomes has been proposed. However, the optimal treatment goal should be the complete resolution of the inflammatory process, and this can only be confirmed by the corresponding histological assessment.

AIMS&METHODS: Our objective was to assess the clinical, biochemical, endoscopic and histological effects of anti-TNF therapy in patients with Crohn's disease. The inflammatory bowel disease clinic at the National Medical Center "20 de Noviembre" currently gives follow-up to 11 patients with moderate to severe Crohn disease. We conducted a retrospective review of 6 female patients and 5 male, whose ages were within a range of 17 to 62 years, of which 4 were smokers and 3 had history of appendectomy. The variables studied were: clinical features (Montreal's classification and the CDAI score), biochemical (erythrocyte sedimentation rate and C reactive protein), endoscopic (CES-CD scale) and histopathological findings (lymphoid aggregates, plasmocytosis, granulomas and cellular hyperplasia).

RESULTS: Below, the results are presented in frequencies and measures of central tendency. According to the Montreal's classification, the patients were classified as following: 6 in A3 and 5 A2, 6 in L3 and 5 L2, 7 in B1 and 4 B2. Prior to the anti-TNF therapy, the CDAI score was calculated, with a maximum value of 386 and a minimum of 240 with an average of 307.63. After therapy, the minimum value was 110 and maximum of 280 with an average of 183 points. Pretreatment average of ESR value was 43.54 and PCR 48.6; and post-treatment 25.36 and 8.55 respectively. A maximum value of 10 was obtained with the CES-CD scale and a minimum value of 4, with an average of 6.90 and at the end a maximum of 7 and a minimum of 3, with an average of 4.72.

Histopathological findings are expressed in table 1

Histopathological findings	Pre	Post
Lymphoid aggregates	11	8
Plasmocytosis	9 moderate 2 intense	7 mild 3 moderate
Granulomas	3	0
Celullar hyperplasia	7	5
Fibrosis	11	11

CONCLUSION: Histological healing would substantially improve the evaluation of the actual effectiveness of a given treatment. Histological assessment is widely available and has a low cost. In our population, anti-TNF therapy has shown that after 48 weeks of treatment, there are changes in most of the evaluated biopsies.

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Keywords: anti TNF therapy, crohn disease, histological follow-up

P903 PHARMACOLOGY OF ETROLIZUMAB IN A PHASE 2 STUDY IN MODERATE TO SEVERELY ACTIVE ULCERATIVE COLITIS

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INTRODUCTION: Etrolizumab, a humanized antibody to the integrin b7, blocks a4b7 binding to MAdCAM-1 as well as aEb7 interactions with its ligand, E-cadherin. We examined pharmacodynamic (PD) effects of etrolizumab at two dose regimens in peripheral blood and colonic tissue in a Phase2 study of patients with ulcerative colitis (UC).[1]

AIMS&METHODS: Patients (n=124) were randomized in a 1:1:1 ratio to either 2 dose levels of etrolizumab (100mg SC on wks 0,4, and 8 or 300mg SC on wks 2,4, and 8 + 420mg wk 0) or placebo. Two types of biomarkers were assessed by flow cytometry in peripheral blood and colonic biopsy tissue:an Occupancy Biomarker to confirm etrolizumab binding to b7-expressing cells and an Expression Biomarker to track b7-expressing cells in the presence of drug.

RESULTS: Demographics and baseline characteristics were similar across patient groups. Etrolizumab administration resulted in maximal occupancy of b7 on mucosal-homing CD4+ and CD4- T and CD19+ B cell subsets in peripheral blood in both dose cohorts (0% vs >85% available b7 in active vs placebo). Receptor occupancy correlated with elevated numbers of circulating b7-expressing mucosal-homing lymphocyte subsets (~20-80% median increase), consistent with the proposed MOA of blocked homing. Maximal occupancy of b7 receptors (a4b7 and aEb7) on T cells in colonic tissues was also observed in both etrolizumab cohorts (<10% available b7) with no apparent occupancy in placebo patients (>90% available b7). Additionally, occupancy of b7 in colonic tissue coincided with occupancy in peripheral blood in all assessed patients.

Occupancy: Median % Available Beta7 Expressing Cells

	Treatment (n)	Day 43	Day 71
Blood Mucosal Homing CD4+ T cells	100mg (29)	0	0
	300mg (34)	0	0
	Placebo (39)	87	111
Tissue aEb7+ CD4- T cells	100mg (5)	4	8
	300mg (7)	2	7
	Placebo (9)	107	94

CONCLUSION: These studies confirmed etrolizumab target binding and demonstrated biological effects of target engagement in blood and at the site of disease pathogenesis. Examination of etrolizumab pharmacologic effects was central to the elucidation of MOA and provided proof of concept to support Phase3 studies in UC. Analysis of exposure-response relationships and modeling of these data would aid regimen refinement moving forward.

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Keywords: biomarkers, drug occupancy, etrolizumab, mechanism of action, pharmacodynamics, pharmacology

P904 INFLIXIMAB IS EFFECTIVE AT PREVENTING RESTENOSIS AFTER THE ENDOSCOPIC BALLOON DILATATION THERAPY IN PATIENT'S WITH CROHN'S DISEASE.

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INTRODUCTION: Crohn's disease (CD) has a characteristic of fibrotic stenoses caused by healing process from chronic ulceration. Endoscopic balloon dilation (EBD) is very useful to dilate stenotic lesions and can prevent the patients from receiving surgical operation, however patients sometimes have restenosis several months after EBD. Recently, Regueiro et al. reported that administration of infliximab (IFX) after intestinal resective surgery is effective at preventing endoscopic and histologic recurrence of CD. We therefore evaluated whether IFX can also prevent CD patients from having restenosis after EBD.

AIMS&METHODS: The aim of this study is to evaluate the efficacy and the safety of IFX at preventing restenosis after EBD.

We enrolled 13 CD patients with severe stenoses at our hospital from March 2009 to April 2013. We first measured the distance of stenosis by endoscope and did not perform EBD if the stenosis was over 3 cm in distance. We dilated the stenosis to 10-18 mm in diameter by EBD, and then started or continued IFX. Seven patients started IFX after EBD, and six patients have already treated with IFX before EBD. Every two months the patients were evaluated with their symptoms and blood examination. The definition of restenosis is to be needed EBD again or to have abdominal symptoms caused by gastrointestinal stenosis. All patients were followed up for 22.8 months (11 to 45 months) on average.

RESULTS: We performed EBD for 22 stenotic lesions of 13 CD patients. The average number of stenoses in the patient was 1.6 ± 0.9 (one to four stenoses). Seven patients had stenoses of ileocecal valve, four had stenoses of ileum, two had stenoses of surgical anastomosis, and three had stenoses of anal or rectum. We succeeded to dilate the stenoses to 14.6 mm (10 to 18 mm) in diameter on average. There were no any complications related to EBD. Ten patients had no resteoses by administration of IFX. Five of them received endoscopy and had no restenoses endoscopically. Two patients were required EBD again, and one patient was required a surgical operation. One of the patients had treated with IFX before EBD, and the others started IFX after EBD. One of the patients had continuous positive for CRP although the patient was relieved symptoms of obstruction after EBD. The patients who had no restenoses had been negative for CRP. The predict marker for restenosis after EBD was not determined in this study, however continuous positive for CRP may be the risk for restenosis.

CONCLUSION: IFX is very useful treatment to prevent CD patients from having restenosis after the EBD.

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Disclosure of Interest: None Declared

Keywords: crohn's disease, endoscopic balloon dilation, Infliximab

P905 IMPACT OF CYTOMEGALOVIRUS AND ITS TREATMENT ON INFLAMMATORY BOWEL DISEASE FLARE-UPS

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INTRODUCTION: Impact of latent cytomegalovirus reactivation on inflammatory bowel disease (IBD) flare is debated. It is either considered as a worsening factor or as a simple bystander of severe flare.

AIMS&METHODS: The aim of our retrospective study was to evaluate the impact of antiviral treatment on IBD control in patients hospitalized for IBD flare with CMV reactivation.

One hundred and five patients (23 Crohn's disease [CD], 82 ulcerative colitis [UC]) hospitalized for IBD flare with systemic and/or colonic CMV reactivation (plasma PCR, n=80; PCR in colon biopsies, n=28) were indentified in the database of 3 tertiary centres. Viral load significance threshold was defined according to the techniques in use (500 to 2500 copies /mL for plasma PCR, semi-quantitative method for PCR in colon biopsies). Short-term (10 ± 4 days) and middle-term evolution from CMV reactivation diagnosis were compared between patients with antiviral treatment and those without. Results are shown as mean and standard deviation. On analysis, Mann Whitney test, paired Wilcoxon test, Chi2 test or logrank test were used when appropriate.

RESULTS: Among the 80 patients with systemic CMV reactivation, no difference was observed between treated (n=49) and untreated (n=31) patients at inclusion regarding age, gender, IBD type, immunosuppressant, CRP and haemoglobin level. No significant difference was observed between treated and untreated patients regarding decrease of CRP level at 10 days (11.0 ± 49.4 vs 17.7 ± 27.3 mg/L, p=0.6) and colectomy rate at 3 months (10.6% vs 13.3%, p=0.7). Antiviral treatment was associated with lower serum albumin level at inclusion (30.1 ± 5.9 vs 26.8 ± 4.6g/l, p= 0.03) and longer hospitalization (16.3 ± 10.6 vs 8.3 ± 5.8 days, $p < 0.0001$). In the severe colitis UC subpopulation (Lichtiger score ≥ 10), no significant difference was observed between treated and untreated patients regarding decrease of CRP level at 10 days (20.6 ± 46.1 vs 7.0 ± 15.2 mg/L, p=0.4), decrease of Lichtiger score (4.1 ± 4.7 vs 6.2 ± 3.4, p=0.35) or colectomy rate (logrank : p=0.8). In the treated group, hospitalization was longer than in the untreated group (15.3 ± 8.3 vs 8.8 ± 4.8 days, p= 0.04). Similar results were observed for colonic CMV reactivation.

CONCLUSION: Treatment of systemic or colonic CMV reactivation in IBD patients hospitalized for flare-up does not seem to impact on IBD evolution. These results should be confirmed prospectively.

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Keywords: Cytomegalovirus, Infection, Inflamatory bowel disease

P906 THE SAFETY OF BIOLOGICAL TREATMENT OF INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The present clinical practice of biological treatment (BT) of inflammatory bowel disease (IBD) in the Czech Republic includes using of two drugs (infliximab and adalimumab), where the active substance are antibodies against tumor necrosis factor alpha (TNF-α). The therapeutical effect is very good not only for induction of remission of the intestinal inflammation, but also for a long-term maintenance treatment. For some patients, however, BT is associated with the occurrence of sometimes serious side effects. Their pathogenesis is not known yet and in some cases these serious side effects are the cause of the termination of the treatment.

AIMS&METHODS: In the period 2007-2012, 126 patients with IBD TNF-α were treated at the Department of Internal Medicine II of the University Hospital in Olomouc. In this set of patients, the occurrence of serious side effects of TNF-α was observed within the dispensarization. The difference in the occurrence of side events was compared with the control set of 102 patients with IBD, who underwent only conventional therapy (aminosalicylates, corticosteroids, immunosuppressants). The observed side effects included skin, articulary, ocular, infectious, metabolic and hematopoietic disorders. The data were statistically processed using standard descriptive methods for continuous data.

RESULTS: The serious side effects were documented in 11 (8.7%) patients with TNF-α therapy; the most common complications were skin complications (54.3%). In the set of patients under the conventional therapy, the side effects of the treatment have been reported in 7 (6.9%) patients, mostly involving hematopoietic disorders (61.2%). The observed difference of occurrence of serious side effects was not statistically significant ($p = 0.11$).

CONCLUSION: In the last decade, the introduction of BT has caused a significant change in the routine clinical treatment of IBD. It turns out that this treatment is relatively safe, the incidence of serious side effects is not higher than when using conventional drug therapy. It is necessary to indicate the TNF-α treatment properly, the patient must be carefully examined before the initiation of the treatment and intensively monitored during the course of the treatment.

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Disclosure of Interest: None Declared

Keywords: biological treatment , complications, inflammatory bowel disease

P907 LONG-TERM EFFICACY OF A PH-DEPENDENT RELEASE MESALAMINE FORMULATION, ASACOL IN PATIENTS WITH ULCERATIVE COLITIS WHO SHOWED INADEQUATE RESPONSE TO A TIME- DEPENDENT RELEASE MESALAMINE FORMULATION, PENTASA: A PROSPECTIVE STUDY

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INTRODUCTION: Mesalamine has been a first-line medication for inducing and maintaining remission in patients with mildly to moderately active ulcerative colitis (UC). However, there is no evidence for efficacy difference between the pH-dependent release mesalamine formulation, Asacol and the time-dependent release formulation, Pentasa.
AIMS&METHODS: We were interested to evaluate the efficacy of Asacol instead of low dose (≤2.25g/day), moderate dose (3.0g/day) or high dose (4.0g/day) Pentasa for inducing and maintaining clinical remission in UC patients who had active disease while on Pentasa for ≥4 weeks. In a single-centre prospective setting, 180 consecutive patients with mildly to moderately active UC willingly switched from Pentasa (mean dose 2.9±0.8g/day; range 1.5-4.0/day) to Asacol (3.6g/day). At entry and week 4, patients were assessed for clinical and endoscopic response. Clinical response was defined as Rachmilewitz's clinical activity index (CAI) ≤4, essentially CAI ≤ 1 meant remission. Mucosal remission was defined as Rachmilewitz's endoscopic index (EI) ≤1. Patients who switched to Asacol and achieved remission received maintenance Asacol at 2.4 or 3.6g/day, and were followed for 52 weeks. Long-term outcomes were evaluated by using the Kaplan-Meier survival analysis.
RESULTS: The CAI fell from 5.8±1.7 at entry to 3.0±2.6 at week 4 (n=180, $P<0.001$). Similarly, the EI fell from 6.8±1.7 to 2.2±2.4 (n=37, $P<0.001$). Sixty patients (33.3%) achieved clinical remission, 76 (42.2%) achieved response level. Further, the CAI in patients on low dose (≤2.25g/day) Pentasa subgroup fell from 5.6±1.3 to 2.4±2.6 (n=51, $P<0.001$), from 5.7±1.8 to 3.1±2.3 (n=95, $P<0.001$) in moderate dose (3.0g/day), and from 6.7±1.7 to 3.4±3.4 (n=34, $P<0.001$) in high dose (4.0g/day) Pentasa, showing significant efficacy for Asacol at 3.6g/day. After 52 weeks, 33 of 59 (55.9%) patients with CAI ≤1 at week 4 had maintained clinical remission, compared with 15 of 42 (35.7%) patients with CAI ≥2 at week 4 ($P<0.05$). Likewise, 15 of 19 (78.9%) patients with EI ≤1 vs 6 of 13 (46.2%) with EI ≥2 ($P<0.05$) had maintained complete remission. The Kaplan-Meier survival analysis showed higher remission rate in CAI ≤1 or EI ≤1 subgroup ($P<0.05$).
CONCLUSION: This study showed that patients who do not respond well to Pentasa might benefit from switching to Asacol at 3.6g, regardless of Pentasa dose. Further, a low CAI together with mucosal healing after induction of remission should be a good predictor of long-term maintenance of remission.
Disclosure of Interest: None Declared
Keywords: Asacol, Clinical remission, Mucosal healing, Ulcerative colitis

P908 INFLUENCE OF MELATONIN ON THE COURSE OF ULCERATIVE COLITIS

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INTRODUCTION: Melatonin is one of the essential hormones, which regulates circadian rhythms, has anticancerogenic, antioxidant, immunomodulating effects, inhibits proliferation of the colon mucosa, influents on microbiota, modifies peristaltics and the gut transit. A significant amount of extrapineal melatonin is produced in the large intestine. Administration of melatonin can be one of the new therapeutic options in the treatment of ulcerative colitis (UC).
AIMS&METHODS: Aim: to investigate the efficacy of melatonin in comparison with standard treatment of UC.
Methods: double-blind, randomized clinical study in 62 patients with mild and moderate UC in acute phase of disease was performed. Clinical severity of UC was based on Mayo score assessment. Endoscopic (EI) and histological (HI) indexes were evaluated. Melatonin containing EC-cells were identified by Sevka's method. Immunohistochemistry was performed using monoclonal mouse antibodies raised against the mucins (Muc2, Muc3, Muc4), trefoil factor-3 (TFF3) and CD3, CD20, CD34, CD68. All patients received standard treatment of UC (5-ASA, topical steroids) during 30 days. 32 patients were treated with melatonin (2 mg per day orally) in addition to the base therapy (1-st group). 30 patients who didn't receive melatonin were considered as 2-nd group.
RESULTS: Before the therapy total Mayo index in all UC patients's group consisted 7.6+0.9 score points. The severity of UC correlated with the extensive of inflammation in the large intestine. The level of staining of Muc2 and Muc3 in all patients with UC was low, up to its complete absence (59.2% and 53.1% cases, p=0.05). Muc4 and TFF3 had high and medium staining intensity. Low quantity of EC-cells in the colon mucosa was found. After the treatment the most pronounced improvement was found in patients who received melatonin in addition to the standard treatment. Clinical remission was achieved earlier in the 1-st group (day 12.2+4.1) with Mayo index 1.9+0.5 score points in contrast to the 2-nd group: remission on 18.3+7.2 days, index Mayo 2.7+0.8 ($p\leq0.05$). The significant evidence of mucosal healing was mentioned in patients with melatonin: EI 1.1+0.5, HI 1.8+0.8, which were accompanied with increasing of Muc2 and Muc3 production (up to 75% cases), quantity of EC-cells, changes of CD3, CD20, CD34, CD68 in the colon mucosa.
CONCLUSION: melatonin application in addition to the standard treatment of UC was more effective than standard therapy alone. Melatonin showed significant improvement in the course of disease, earlier achievement of remission phase, evidence of deep histological remission in patients with UC.
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Disclosure of Interest: None Declared
Keywords: deep remission, melatonin, ulcerative colitis

P909 THE MAJORITY OF PATIENTS ARE NOT AWARE OF INFLAMMATORY BOWEL DISEASE MEDICATION SIDE EFFECTS

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INTRODUCTION: Inflammatory bowel disease (IBD) is a chronic condition requiring long-term treatment with potentially toxic medications. It is not known how much patients know about the potential medications that they are being prescribed to treat their inflammatory bowel disease.
AIMS&METHODS: To assess patients' knowledge of medication side effects.**Methods:** This is a questionnaire-based, cross-sectional study of 204 adult IBD patients attending the gastroenterology and biologic clinics in the University of Alberta Hospital. Multiple-choice questionnaires assessed patient knowledge of side effects of commonly used IBD treatments (amino salicylates, corticosteroids, immunomodulators (imuran and methotrexate) and biologics)
RESULTS: Questionnaire response rate was 98% (200/204). Sixty-eight percent had Crohn's disease (136), 29% =ulcerative colitis, and 3% indeterminate colitis). The average age was 41.1±SD, range 18-79years. Half the patients were male (100/200).
Medication Side Effect % (N) Knowledge Respective
Sulfasalazine Reversible male infertility 7.8% (4/51)
Leukopenia 9.8% (5/51)
Mesalamine Kidney problem 14.5% (23/159)
Hepatitis 12.6% (20/159)
Prednisone Osteoporosis 47.3% (88/186)
Risk of infection 24.1% (45/186)
Thiopurine Analogue (Imuran, 6-MP)
Leukopenia 41.9% (67/160)
Pancreatitis 22.5% (36/160)
Hepatitis 35.6% (57/160)
Lymphoma 9.3% (15/160)
Methotrexate
Folate deficiency 24.6% (15/61)
Reversible male infertility 8.2% (5/61)
Anti-TNF (Infliximab, Adalimumab) Risk of infection 57% (86/151)
Lymphoma 24.5% (37/151)
Tuberculosis 23.2% (35/151)
Sulfasalazine :Reversible male infertility 7.8% (4/51) Leukopenia 9.8% (5/51). Mesalamine: Kidney problem 14.5% (23/159) Hepatitis 12.6% (20/159). Prednisone :Osteoporosis 47.3% (88/186) Risk of infection 24.1% (45/186):Thiopurine Analogue (Imuran, 6-MP) Leukopenia 41.9% (67/160) Pancreatitis 22.5% (36/160) Hepatitis 35.6% (57/160) Lymphoma 9.3% (15/160). Methotrexate: Folate deficiency 24.6% (15/61) Reversible male infertility 8.2% (5/61). Anti-TNF (Infliximab, Adalimumab) :Risk of infection 57% (86/151) Lymphoma 24.5% (37/151) Tuberculosis 23.2% (35/151)
CONCLUSION: Fewer patients were aware of the potential side effects of mesalamine and sulfasalazine than of prednisone and immunosuppressive medications. . The majority of IBD patients are not aware of important side effects of medications they have been prescribed for treatment of their IBD.
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Disclosure of Interest: None Declared
Keywords: awareness, IBD, medications, Side effects

P910 PREDICTIVE FACTORS OF RESPONSE TO ORAL TACROLIMUS THERAPY IN REFRACTORY ULCERATIVE COLITIS: THE DEVELOPMENT OF A NOVEL PREDICTION FORMULA

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INTRODUCTION: Tacrolimus has been shown to be effective and safe as salvage therapy for steroid-refractory or steroid-dependent patients with ulcerative colitis (UC). However, some patients fail to respond and need to consider other treatments including colectomy. To predict effectiveness of tacrolimus therapy should contribute to early clinical decision-making.
AIMS&METHODS: The aim of this study is to identify predictive factors and to develop a reliable prediction formula of response to oral tacrolimus treatment. Included patients were those with moderate to severe steroid-refractory or steroid-dependent UC who had undergone oral tacrolimus treatment between July 2009 and April 2012 at a tertiary referral centre in Japan. Oral tacrolimus was started at a dose of 0.1 mg/kg body weight per day and trough levels were maintained at 10-15 ng/ml for 14 days. Then the trough levels were decreased and maintained at 5-10 ng/ml for 3 months. Primary endpoint of this study was clinical remission (Lichtiger score ≤ 4) at week 12 after starting oral tacrolimus. Demographic and clinical parameters obtained in 14 days after starting oral tacrolimus treatment were analysed by univariate (Chi-squared test or Mann-Whitney U test) and multivariate (multiple logistic regression analysis) statistics.
RESULTS: Thirty-six patients were included in this study (41.7% male with the average age of 41.0 ± 13.1 years). The average Lichtiger score when starting oral tacrolimus was 10.0 ± 3.2 (6-17). Nineteen patients (52.8%) had obtained remission at week 12 after starting oral tacrolimus and all of them avoided colectomy, 17 patients (47.2%) had failed to obtain remission and six of them underwent colectomy. Stepwise multiple logistic regression analysis identified three independent predictive factors of response to oral tacrolimus: stool frequency on the first day (="SF"), platelet count ($\times10^4/\mu$L) on day 14 (="PLT") and C-reactive protein value (mg/L) on day 14 minus that on the first day (="ΔCRP"). The calculation formula [$49.0 - 1.7 \times SF - 1.3 \times PLT - 0.27 \times \Delta CRP > 0$] was shown to predict remission with an accuracy of 88.9%, positive predictive value of 94.7% and negative predictive value of 82.4%.
CONCLUSION: This study indicates that disease remission status at week 12 can be predicted with a high accuracy by combination with three simple clinical items obtained in 14 days after starting oral tacrolimus therapy for UC. This

finding should be useful for acceralating early clinical decision-making when treating patients with UC.
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Disclosure of Interest: None Declared
Keywords: oral tacrolimus therapy, Predictive factors, refractory ulcerative colitis

P911 LOCALISED PHARMACOLOGICAL ACTIVATION OF MUCOSAL HYPOXIA INDUCIBLE FACTOR REVERSES COLITIS THROUGH ACCELERATED EPITHELIAL RESTITUTION

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INTRODUCTION: Crohn's disease (CD) is characterised by repeated wounding and inflammation of the intestinal mucosa. During mucosal inflammation, changes in metabolic activity and vascular damage, lead to a reduction in tissue-oxygen tension (hypoxia), in which healing processes such angiogenesis, cell migration and re-epithelialisation occur. Previous work has shown that pharmacological induction of hypoxia-inducible factor (HIF), a global transcriptional regulator of the hypoxic response, by prolyl hydroxylase inhibitors (PHDi) is protective in murine models of colitis. This appears to involve increased epithelial barrier function and restitution. Little is known about the role of HIF in mucosal wound healing. In a series of *in vitro* assays we identified induction of integrin $\beta1$ (ITGB1) during hypoxia. As integrins play critical roles in epithelial wound healing, we hypothesised that HIF activation accelerates epithelial restitution.
AIMS&METHODS: Employing chemically-induced Trinitrobenzene sulfonic acid (TNBS) murine models of colitis, our aims were to 1) investigate the relative induction of ITGB1 in epithelial cells with the mucosal protection afforded by PHDi, 2) examine the efficacy of PHDi with oral and systemic delivery. Colitis was induced in C57/Blk6 mice by rectal instillation of TNBS. Disease severity was monitored endoscopically over 7 days. At the peak of disease, as measured by endoscopy, mice received PHDi ([5mg/Kg] Akebia-4924, Aerpio Therapeutics) by i.p. injection or oral gavage. Mucosal healing was monitored and mice were euthanised at daily timepoints, where tissue was harvested for qPCR and western blot analysis.
RESULTS: TNBS colitis led to a significant increase in mucosal ITGB1 transcript and protein (7-fold increase). Integrin induction was most prominent in the epithelium (3-fold). A clear association (R2=0.78) between peak ITGB1 expression and mucosal recovery as measured by endoscopy score was observed across all groups. Mice treated with PHDi demonstrated increased epithelial HIF expression and an earlier, increased induction of ITGB1, which led to mucosal healing by day 7. Administration of PHDi by oral gavage led to a localisation of HIF and ITGB1 expression to the GI tract, with reduced HIF expression in the lungs, kidney and heart compared to i.p. injection.
CONCLUSION: These results suggest that epithelial HIF activation, through oral delivery of PHDi, promotes mucosal healing by accelerating the induction of ITGB1 expression in the epithelium and may represent a new therapeutic strategy for the management of IBD.
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Disclosure of Interest: None Declared
Keywords: Hypoxia-induced factor, Inflammatory bowel disease (IBD), mucosal inflammation

P912 THIOPURINE METABOLITES MEASUREMENT MORE EFFECTIVE IN GUIDING IBD MANAGEMENT WHEN DONE DURING DISEASE FLARE AS SUPPOSED TO DURING REMISSION.

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INTRODUCTION: In the setting of inflammatory bowel diseases (IBD), measurement of the thiopurine metabolites; 6-thioguanine nucleotide (TGN) and 6-methyl mercaptopurine (MMP) has been proposed to help explain the failure of therapeutic efficacy and toxicity. The levels associated with efficacy is within 235 to 450 pmol/8x10^8 for 6-TGN and hepatotoxicity for 6MMP is >5700 pmol/8x10^8. There is a scarcity of guidelines in terms of the timing of measurement
AIMS&METHODS: AIMS
The aims of this analysis are to determine the effect of measuring thiopurine metabolites on subsequent management strategy during disease flare and remission and to compare metabolite-based thiopurine dosing versus weight-based dosing.
METHODS
Metabolites were prospectively performed on consecutive IBD patients taking thiopurines and their medical records reviewed. Disease activity at the time of metabolite measurements (categorised to ''flare'' or ''remission'' based on blood tests, endoscopy and physician assessment) and any subsequent management decision (thiopurine dose increase/adjust, use of allopurinol, therapy escalation, no action) were assessed. Weight based dosing (calculated at 1mg/kg 6-Mercaptopurine, 2mg/kg Azathioprine) were compared to metabolites-determined thiopurine maintenance dose.
RESULTS: In total, 30.9% of patients (44/142) reviewed were on thiopurines and 126 metabolites levels were measured between the years 2008 to 2012. Of these, 47.6% (60/126) were done during disease flare and 52.3% (66/126) during remission. Measurement of thiopurine metabolites was subsequently followed by increasing/adjusting thiopurine dose in 38% (23/60) during flare and 13.6% of tests (9/66) during remission ($p<0.001$). 15% (9/60) and 4.5% (3/66) of patients were identified as metabolite 'shunters' and started on allopurinol during flare and remission, respectively ($p<0.001$). Therapy escalation (ie. biological agent, drug trial, surgery) followed metabolites measurement in 20% (12/60) during flare and 0% of tests (0/66) during remission. No action was taken after 26.6% (16/60) and 81.8% (54/66) ($p<0.001$) of tests when done during flare and remission, respectively. 68% (30/44) of patients were on a lesser thiopurine dose when determined by metabolites level as supposed to weight. On average, patients on 6-MP were taking 48% less (71.2% less on 6-MP/allopurinol) and patients on azathioprine 27.1% less dose (70% lower on azathioprine/allopurinol).
CONCLUSION: Measurement of metabolites level during IBD flare plays a useful role prior to management change. Metabolite-based thiopurine dosing may allow more patients to be on thiopurine due to potentially less toxicity risk.
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Disclosure of Interest: None Declared
Keywords: IBD, Thiopurine metabolites

P913 SERUM VITAMIN D LEVELS IN INFLAMMATORY BOWEL DISEASE, EFFECT OF ORAL SUPPLEMENTATION

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INTRODUCTION: Vitamin D (vitD) has multiple physiologic effects. Deficit may predispose to inflammatory bowel disease (IBD) or disease activity. Epidemiology of vitD levels was studied on relatively small sample sizes and little information is available on effect of oral supplementation and optimal dose in IBD.
AIMS&METHODS: Aim of this study was to assess levels of vitD in patients with inflammatory bowel disease in late winter with and without vitD supplementation.
Methods: Study included 126 IBD patients (91 Crohńs disease [CD], 35 ulcerative colitis [UC]). Serum 25 hydroxyvitamin D (25OHD) levels were determined by chemiluminescent assay (cut off > 75 nmol/l) during late winter (February to April). Demographic data and information dealing with vitD supplementation, steroid therapy and IBD were retrospectively obtained from patients electronic database.
RESULTS: Group of 52 women and 74 men, mean age 39.3 ± 15.2 years, duration of the disease 8.5 ± 7.4 years was studied. Active disease was present in 22.2 % CD and 19.2 % UC, steroid therapy in 15% patients (prednisone mean dose 11.7± 6.1mg/day). Mean 25OHD level was 51.8 ± 6.8 nmol/l in unsubstituted group without difference between men and women (p=0.57), CD and UC (p=0.53), on /off steroids (p=0.01), disease activity (p=0.27) and did not correlated with age (p =0.89) or disease duration (p=0.38). Only 13.8% subjects had normal levels of 25OHD and in 57.4 % of patients were levels < 50 nmol/l. 32 patients recieved oral cholecalciferol (mean 25OHD 56.6 ± 18.7 nmol/l) in dose 1337 ± 961 IU/day. In 41% was deficit relevant (< 50 nmol/l). There was no significant difference between levels in supplemented and unsupplemented group (p= 0.27). 25OHD levels do not correlated with supplementation dose of vitD (p= 0.31).
CONCLUSION: Vitamin D deficit is very common in IBD patients in late winter. Oral vitamin D supplementation even in doses about 1300IU/day has no significant influence on plasmatic levels. This result supports recommendation of higher supplementation dose in patients with IBD. Insufficient patients compliance must be however taken into account in such situation.
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Disclosure of Interest: None Declared
Keywords: CROHŃS DISEASE, inflamatory bowel disease, ulcerative colitis, vitamin D

P914 CLINICAL PHARMACOLOGY AND SAFETY OF AMG 181, A HUMAN ANTI-A4B7 ANTIBODY FOR TREATING INFLAMMATORY BOWEL DISEASES

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INTRODUCTION: AMG 181 is currently in Phase 2 clinical trials for treating subjects with Crohn's disease (CD) and ulcerative colitis (UC).
AIMS&METHODS: To evaluate the safety and pharmacokinetics/pharmacodynamics (PK/PD) of AMG 181 in healthy volunteers (HVs) and CD and UC, we have conducted a randomized, double-blinded, placebo-controlled, ascending multiple-dose study. 36 male HVs (age 18-44 yr, weight 57-113 kg) were randomized 6:2 to receive AMG 181 (7, 21, 70, or 210 mg) or placebo SC monthly for 3 months. 8 CD and 8 UC subjects were to be randomized 3:1 into 4 groups (N=4/group) to receive AMG 181 (21 or 210 mg) or placebo SC monthly for 3 months. Subjects were followed for 3-9 months after the last dose. AMG 181 PK and binding anti-AMG 181 antibodies (ADAs) were quantified. ADA positive samples were analyzed for neutralizing anti-AMG 181 antibodies (nADA) using a cell based assay. Blood was collected to assess $\alpha_4\beta_7$ receptor occupancy (RO) and CD4+ T cell counts using a validated whole blood 6-color flow cytometric assay with complete blood cell counts obtained from a hematology analyzer.
RESULTS: In HVs (completed), time to C_{max} was 1-14 days after dosing, with 1.22-2.03-fold accumulation from Dose 1 to 3. Both C_{max} and $AUC_{(0–4weeks)}$ increased dose-proportionally within the 21-210 mg dose range. The linear elimination half life was 30 (range: 20-46) days. The target-mediated disposition phase occurred at concentrations <1 μg/mL. The $\alpha_4\beta_7$ RO on CD4+ naïve T cells was maintained ~80-90% at 7 mg for 3 months, and >90% for 3.5, 5, and 7

months at 21, 70, and 210 mg, respectively. Absolute counts of CD4+ total, naïve, or memory T cells did not change significantly from baseline. Two HVs tested ADA positive for binding and neutralizing antibodies, and were followed until negative. To date, the AMG 181 PK profiles from the enrolled UC subjects (N=4; on-going) were contained within the range observed in HVs under the same doses. No ADAs were detected in UC. Blinded safety data showed no AMG 181-related serious adverse events, deaths, dose-limiting toxicities, or withdrawals due to adverse events. No clinically significant changes in electrocardiograms or neurological examinations were observed.
CONCLUSION: The safety and PK/PD profiles of AMG 181 under once-a-month multiple fixed SC doses of 7 to 210 mg have supported its further clinical development in Phase 2 clinical trials in UC and CD.
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Keywords: AMG 181, Anti-$\alpha 4\beta 7$ Antibody , Inflammatory bowel disease (IBD), T Cell Trafficking

P915 CLINICAL PHARMACOLOGY, SAFETY, AND EFFECTS OF ANTI-IL-23 ANTIBODY AMG 139

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INTRODUCTION: The human monoclonal anti-IL-23 antibody AMG 139 has been developed for treating inflammatory diseases. It is in Phase 2 clinical trial in Crohn's disease (CD) subjects (Clinicaltrials.gov: NCT01714726).
AIMS&METHODS: To evaluate safety, pharmacokinetic/pharmacodynamic (PK/PD), and effects of AMG 139, we conducted 2 randomized, double-blind, placebo controlled studies. In the single-ascending-dose (SAD) study (NCT01094093; completed), 56 healthy volunteers (HV) and 17 psoriasis (PsO) subjects received AMG 139 or placebo (PBO) (6:2 HV; 3:1 PsO) subcutaneously (SC; 7 [HV only], 21, 70, or 210 mg) or intravenously (IV; 210 [HV only], 420 [HV only], or 700 mg). In the multiple-ascending-dose (MAD) study (NCT01258205), AMG 139 or PBO (6:2) was administered once-a-month for a total of 3 doses to 40 HV at 70, 210, 420, or 700 mg IV or 210 mg SC, and will be administered to 8 CD subjects (3:1; on-going) at 210 or 700 mg IV. Safety, PK/PD, anti-AMG 139 antibodies (ADAs), psoriasis area severity index (PASI; single-dose), and Crohn's disease activity index (CDAI; multiple-dose) were measured.
RESULTS: In the SAD study, AMG 139 PK was linear within the 21-700 mg range (half-life=22-37 days; SC bioavailability 64-86%). AMG 139 effects in PsO was achieved as PASI 90 to 100 was reached by Day 85-113 and fewer differentially regulated genes were observed between lesional and nonlesional tissues vs. PBO. AMG 139 also led to decreased serum IL-22, which was typically higher in PsO vs. HVs. In the MAD study, AMG 139 accumulated between 1.51- to 2.15-fold from Dose 1 to 3. Preliminary blinded evaluations of the ongoing CD part of the study indicate PK in CD to be similar to HV. Clinical response was determined by decreases in CDAI, serum C-reactive protein, and fecal calprotectin. No ADAs, serious adverse events, or deaths have been reported in either study.
CONCLUSION: Initial assessments of available PK/PD and safety data in HV, PsO, and CD support further testing of AMG 139 in subjects with inflammatory diseases.
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Disclosure of Interest: W.-J. Pan Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, W. Rees Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, J. Towne Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, J. Gibbs Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, A. Colbert Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, T. Goletz Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, K. Newhall Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, K. Zhou Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, S. Prokop Financial support for research from: Amgen Inc., A. Umble-Romero Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, C. Krill Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, P.-C. Yi Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, N. Standifer Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, J. Lee Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee, G. Hodsman Financial support for research from: Amgen Inc., J. Lickliter Financial support for research from: Amgen Inc., J. Wishart Financial support for research from: Amgen Inc., S. Shakib Financial support for research from: Amgen Inc., C. Reid Financial support for research from: Amgen Inc., J. Marjason Financial support for research from: Amgen Inc., C. Wynne Financial support for research from: Amgen Inc., D. Hassman Financial support for research from: Amgen Inc., P. Miner Jr Financial support for research from: Amgen Inc., W. Tsuji Financial support for research from: Amgen Inc., Shareholder of: Amgen Inc., Other: Amgen Employee
Keywords: AMG 139, Anti-IL-23 Antibody, Crohn's disease, Inflammatory bowel disease (IBD), MEDI2070

P916 A MULTICENTER RANDOMIZED DOUBLE BLIND PLACEBO CONTROLLED TRIAL TO EVALUATE THE EFFICACY OF A PROBIOTIC PREPARATION AS MAINTENANCE THERAPY IN PATIENTS WITH ULCERATIVE COLITIS.

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INTRODUCTION: Probiotics are live microorganisms which when administered in appropriate amounts are expected to produce therapeutic effects in the gut. Accordingly, hitherto, we have reported that probiotics have significant therapeutic effect in the prevention of relapse of ulcerative colitis (UC), notably patients who were found not to have adequate gut microbiota cluster.
AIMS&METHODS: In a multicentre, double blind placebo controlled setting, we were interested to determine if a commercially prepared probiotic called BIO-THREE has efficacy in the prevention of UC relapse. Each tablet of BIO-THREE contained 2mg of Streptococcus faecalis T-110, 10mg Clostridium butyricum TO-A and Bacillus mesenterium TO-A. Outpatients with quiescent UC (n=251) were recruited at 4 medical institutions. Faecal samples from these 251 patients were examined by the "Terminal Restriction Fragment Length Polymorphism" (T-RFLP), which is a molecular biology technique for profiling microbial communities. Additionally, we were interested to determine if patients' faecal microbiota had a high ratio of Bifidobacterium, which was an exclusion criterion in this study. Patients were randomly assigned to two groups: receiving 9 BIO-THREE tablets per day for 12 months or 9 placebo (lactose) tablets per day for 12 months. Patients in both arms could continue with their ongoing medications if had started well in advance of entry. Patients' symptoms were evaluated at every hospital visit up to 12 months. Patients' faecal samples were again examined after 12 months.
RESULTS: Among the 251 patients who were screened for eligibility, 170 were excluded because T-RFLP showed their faecal microbiota to have a high ratio of Bifidobacterium. Eighty-one patients were available for evaluation, and 5 patients were excluded for not adhering to the treatment protocol. The overall rates of sustained clinical remission after 12 months were 74.4% in the BIO-THREE group and 70.3% in the placebo group. The Kaplan-Meier analysis did not show any significant difference between the two groups. However, when patients under 45 years of age were considered, the rates of sustained clinical remission after 12 months were an 83.3% in the BIO-THREE group and 53.6% in the placebo group (P=0.034).
CONCLUSION: In this multicenter placebo controlled trial, the probiotic BIO-THREE showed significant efficacy in the prevention of UC relapse in young patients who had their faecal microbiota not to contain a high ratio of Bifidobacterium as determined by T-RFLP.
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Disclosure of Interest: None Declared
Keywords: Faecal microflora, Probiotics, Randomised trial, Terminal Restriction Fragment Length Polymorphism, Ulcerative colitis

P917 CIRCULATING B CELL SUBSETS CORRELATE WITH CLINICAL RESPONSE TO ANTI-TNF THERAPY IN IBD

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INTRODUCTION: Various immune disorders, such as systemic lupus, Sjögren's syndrome and rheumatoid arthritis (RA), are associated with marked reductions of B-cell subtypes, notably of IgM^+CD27^+ pre-switched B cells , and anti-TNF therapy specifically upmodulates this population in RA. In active Crohn's disease(CD) and ulcerative colitis (UC) Ig M memory and $CD5^+$ B cells decrease. An increase in mucosal $CD19^+$ B cells in CD predicts long remission after Infliximab(IFX) therapy. We aimed to study the kinetics of B cell subsets during IFX therapy in patients (pts) with IBD.

AIMS&METHODS: Whole blood was taken from healthy controls (HC, n= 15) and pts with IBD (9 UC, 42 CD) before or after start of IFX (5mg/kg IV 0-2-6 and q8 wks). N=28 and 23 before therapy(BT) and after therarpy(AT). B cell subsets were assessed by flow cytometry for CD19, CD5,CD27, IgD and IgM. Assessments of symptoms, endoscopic healing and histological improvement were used to classify pts as responders (RS, n=17) or non-responders (NRS, n=6). To monitor biological response to IFX, serum C-reactive protein (CRP) was collected.
RESULTS: Active IBD pts had lower levels of circulating $CD19^+$, $CD5^+CD19^+$, total memory and pre-switched B cell subsets compared to HC (Table1). IFX therapy increased these 4 populations above and decreased post-switched memory B cells in RS. NRS had lower levels of the 4 populations than RS during after IFX therapy. CRP negatively correlated with $CD5^+$, 27^+memory, IgM^+CD27^+ pre-switchedmemory B cells(r=-0.47, p=0.01;-0.67,0.01; -0.51,0.01), and positively with 27^-naïve, IgD^+27^-naïve, $IgM^-IgD^-27^+$ post-switched B cells (r=0.32, p=0.03; 0.31,0.04; 0.30,0.04) respectively.
Table 1

Mean±SEM	HC	BT	RS	NRS	
(p value)		(p value vs. HC)	(vs. HC, BT)	(vs. HC,BT,RS)	UNIT
CD19+	0.25±0.04	0.16±0.02 (0.02)	0.25±0.04 (0.99,0.02)	0.15±0.02 (0.02,0.94,0.02)	10e9/L blood
CD19+ CD5+	6.66±0.85	2.44±0.47 (<0.001)	12.56±2.32 (0.03, <0.001)	2.03±0.69 (0.004, 0.3859,0.02)	% of CD19
Naive	67.16±2.34	72.11±3.01 (0.29)	68.43±4.56 (0.81,0.49)	73.36±3.47 (0.17, 0.85,0.55)	% of CD19
Memory	32.55±2.24	23.74±2.27 (0.01)	34.13±4.52 (0.76,0.03)	16.69±2.67 (0.0007, 0.067,0.03)	% of CD19
Pre-Switched	47.42±3.19	36.11±3.26 (0.03)	53.86±2.73 (0.13, <0.001)	41.99±5.512 (0.39, 0.44,0.04)	% of CD19+ CD27+
Post-Swtched	44.86±3.25	53.33±3.48 (0.06)	40.68±3.69 (0.42,0.02)	31.58±4.12 (0.03, 0.009,0.12)	% of CD19+ CD27+

CONCLUSION: $CD5^+$, pre-switched and total memory B cells in active IBD pts are lower than in healthy controls, and increases correlate with clinical and biological response to IFX, suggesting a role for these cells in IBD associated inflammation and in the molecular response to anti TNF therapy.
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Keywords: anti TNF therapy, IBD

TUESDAY, OCTOBER 15, 2013 9:00-17:00
OTHER LOWER GI DISORDERS II - Poster Area

P918 CHARACTERISTICS OF CMV ENTEROCOLITIS IN PATIENTS WITH OR WITHOUT INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The objective is to evaluate the differences in clinical characteristics of CMV enterocolitis with or without inflammatory bowel disease (IBD).
AIMS&METHODS: From 2003 to 2013 at Seoul National University Bundang Hospital and Seoul National University Hospital, a total of 84 patients with symptoms including hematochezia or diarrhea or abdominal pain diagnosed as CMV enterocolitis based on the pathologic findings were reviewed retrospectively.
RESULTS: Among the 84 patients, 26 had IBD [21 with ulcerative colitis (UC), 4 with Crohn's disease and 1 with Behcet's colitis] treated with steroids or other immunosuppressive agents. CMV enterocolitis in patients without IBD (n = 58) was mainly associated with immunocompromised or critically-ill non-immunosuppressed conditions. As for symptoms, hematochezia (84.6 % and 34.5 % in IBD and non-IBD groups, respectively) and weight loss (30.8 % and 5.2 %) were more common in IBD group than non-IBD group (all *P*-values < 0.01); fever was a common symptom in non-IBD group (11.5% and 50.0 %, $P < 0.001$). Non-IBD group showed a higher positivity of CMV antigenemia testing, which was not statistically significant (58.3 % and 82.4 %, $P = 0.097$). Endoscopic findings were varied, but not different between the two groups. In patients with UC (n = 21), 17 patients (80.9 %) were treated with antiviral agents, but 6 of them (35.3 %) underwent total proctocolectomy despite antiviral therapy; spontaneous remission occurred in 3 out of 4 patients who were not given antiviral agents and 1 patient had undergone total proctocolectomy. Forty-seven patients (81.0 %) in non-IBD group were treated with antiviral agents, but 19 patients (40.4 %) died of underlying disease; 7 out of 11 patients (63.6 %) who did not receive antiviral treatment recovered spontaneously.
CONCLUSION: CMV enterocolitis sometimes can cause serious illness and be associated with poor outcomes. However, it also can be cured naturally in both groups of patients who have IBD or not.
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Disclosure of Interest: None Declared
Keywords: CMV, cytomegalovirus, enterocolitis, inflammatory bowel disease

P919 PPIS ARE ASSOCIATED WITH HIGHER C. DIFFICILE INFECTION IN CRITICALLY ILL PATIENTS COMPARED TO H2RA

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INTRODUCTION: Proton pump inhibitors (PPI) and histamine-2 receptor antagonists (H2RA) are commonly prescribed for stress ulcer prophylaxis (SUP) among critically ill patients. Several studies suggested that the use of PPI is a potential risk factor for *Clostridium difficile* infection (CDI). We compared the CDI incidence of PPI treatment group and H2RA group for SUP in critically ill patients.
AIMS&METHODS: The aim of this study was to compare the CDI incidence of PPI treatment group and H2RA group for SUP in critically ill patients. From August 2005 to July 2012, the incidence of CDI were retrospectively analyzed in patients more than 18 years of age who were directly admitted and stayed more than 3 days in ICU. Patients who received gastric acid suppressants less than 3 days or crossover use were excluded. CDI was diagnosed when patients complained diarrhea with any positive results in *C. difficile* toxin assay, stool culture or endoscopy. SUP-related CDI was defined as a CDI diagnosed during SUP. Patients demographic and clinical data were analyzed to find potential risk factors for SUP-related CDI.
RESULTS: Among 1,005 patients (444 patients received PPI and 561 received H2RA) enrolled, 48 patients (4.8%) were diagnosed as a SUP-related CDI. The incidence of SUP-related CDI was higher in patients receiving PPI than in patients receiving H2RA (6.73% vs 1.82%). PPI use relative to H2RA (OR 2.67; CI95 1.25-5.72; p=0.012) and diabetes mellitus (OR 2.13; CI95 1.07-4.23; p=0.031) were independent risk factors for SUP-related CDI.
CONCLUSION: Our study showed PPIs are associated with higher risk of SUP-related CDI compared to H2RA in critically ill patients.
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Disclosure of Interest: None Declared
Keywords: Clostridium difficile infection, Critical care, H2 receptor antagonist, proton pump inhibitor

P920 EFFICACY OF RIFAXIMIN COMPARED TO CIPROFLOXACIN IN THE TREATMENT OF TRAVELER'S DIARRHEA: A META-ANALYSIS

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INTRODUCTION: Background: Flouroquinolones are the mainstay of treatment for traveler's diarrhea (TD) but its wide spread use have led to increased resistance rates especially in Asia. Rifaximin, a non-absorbable antibiotic for TD caused by noninvasive strains, has significant efficacy against placebo, good tolerability profile and with no relevant bacterial resistance.
AIMS&METHODS: Objectives: This study aims to determine the efficacy of Rifaximin compared to Ciprofloxacin in the treatment of TD by evaluating time to last unformed stools (TLUS), clinical wellness and treatment failure.
Methods: Extensive article search was done using Medline/Pubmed; Cochrane central register for Controlled trials, EMBASE, HERDIN; outcomes analyzed using Review Manager software and assessed for heterogeneity.
RESULTS: Results: Three (3) randomized, double-blind, prospective clinical trials were reviewed. A total of 610 patients were included; 354 and 256 in the rifaximin and ciprofloxacin arm. The TLUS favors ciprofloxacin (MD 3.20 95% CI [-1.58, 7.98], $I^2 = 41\%$); Clinical wellness favors rifaximin (RR=0.96, 95% CI [0.89, 1.03], $I^2 = 0\%$); and low Treatment failure favors ciprofloxacin (RR=1.28, 95% CI [0.50, 3.27], $I = 68\%$). However, the prevalence of pathogens causing TD differs between geographic locations and up to 40% of cases are of unknown etiology despite comprehensive microbiological evaluation.
CONCLUSION: Conclusion: There is a trend towards earlier time to unformed stools and less treatment failure in the ciprofloxacin arm, while there is a trend towards rifaximin in earlier clinical wellness in the setting of traveler's diarrhea. However, more studies should be done regarding geographic location, enteropathogens involved and resistance patterns.
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Disclosure of Interest: None Declared
Keywords: Ciprofloxacin, Meta-analysis, Rifaximin, Traveller's Diarrhea

P922 FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT CLOSTRIDIUM DIFFICLE IN PATIENTS WITH PROLONGED IMMUNOSUPPRESSION

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INTRODUCTION: Safety and efficacy of fecal microbiota transplantation (FMT) is not known in immunosuppressed patient. The only published prospective control trial excluded patients with immunodeficiency due to concerns of potential bacterial translocation and infectious complications. Immunodeficiency is associated with high burden of C. difficile infection (CDI).
AIMS&METHODS: Between 5/2012 and 2/2013, a total 33 patient underwent fecal microbiota transplantation for recurrent CDI using patient selected donors at our institution. Of these, 12 patients were immunosuppressed at the time of the procedure and during the follow-up period (1 month). Patients received vancomycin (125 mg po four times per day) for 14 days stopping it 48 hours before FMT. Following a bowel lavage with 4L of polyethylene glycol, emulsified fresh stool (<6 hrs.) was delivered in the terminal ileum or cecum during colonoscopy. Patient follow-up consisted of stool testing for C. difficile by PCR and recording of stool frequency, consistency, and adverse effects on days 7 and 30.
RESULTS:

Baseline characteristics of the patients	N = 12
Age – year (SD)	46 ± 17
Body mass index (SD)	27 ± 7
Female sex – N (%)	5 (42)
Use of PPI – N (%)	6 (50)
Median stool frequency (range)	5.5 (2-15)
Median CDI recurrences (range)	4 (3-7)
Previous failure of tapered vancomycin therapy (%)	11 (92)
WBC median (range)	6.9 (2.7-20.7)
Albumin –g/dl (SD)	3.7 ± 0.7

The underlying medical conditions requiring prolonged immunosuppression were the following: 3 patients with ulcerative colitis, 1 patient with ulcerative colitis and liver transplant for PSC, 3 patients with Crohn's disease, 2 patients with multivisceral transplant, 1 patient with multiple myeloma, 1 patient with lung transplant, and 1 patient with renal transplant. Immunosuppression included one of the following medications as a single therapy or in combination: azathioprine, prednisone, infliximab, tacrolimus, sirolimus, mycophenolate mofetil, and lenalidomide.
Stool test was negative for C. diff on day 7, and day 30 in 8 (75%) after 1 FMT, and in 11 (92%) patients after 2 FMTs. In comparison, the cure rate in patients without immunosuppression was higher 20/21 (95%) after 1 FMT (p=0.047). One patient became an asymptomatic carrier. One patient continued to have diarrhea despite CDI clearance. No significant adverse effects were reported.
CONCLUSION: FMT is a highly efficacious and safe therapy for recurrent CDI in immunosuppressed patients. A second stool infusion may more frequently be required in immunosuppressed patients for cure.
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Disclosure of Interest: None Declared
Keywords: Clostridium difficile infection, Fecal microbiota transplantation, Immunosuppression

P923 ADULT ACUTE DIARRHOEA: IS RACECADOTRIL EFFECTIVE? ANSWER FROM A META-ANALYSIS

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INTRODUCTION:
The efficacy of racecadotril, an intestinal antisecretory drug acting *via* an enkephalinase inhibition, was reviewed in paediatric acute diarrhoea but not yet in adults.
AIMS&METHODS:
Aims: to estimate the effectiveness of racecadotril in the symptomatic treatment of acute diarrhoea in adults.
Methods: all randomised trials performed in adults suffering from acute diarrhoea with racecadotril as the studied group, whatever the control group. All pooled analyses were based on random-effects models. The only commun efficacy criteria was the duration of diarrhoea. According to available data, hazard ratio racecadotril / control with 95% confidence interval were adjusted for baseline predictors, calculated from individual raw data or estimated from Kaplan-Meier curves.
RESULTS:
Twelve randomised trials (2619 patients) met inclusion criteria. Results are summarized in the table. The diarrhoea duration in the racecadotril groups was significantly lower as compared to placebo groups and was not different as compared as in loperamide groups. The frequency of constipation in the racecadotril groups was not different as compared as in placebo groups and was significantly lower as compared to loperamide groups.

Criteria	Studies	N	population	Ratio	95% CI	*P*
Diarrhoea duration	*versus* placebo	5	1001	1.65	1.38 to 1.97	< 0.0001
	versus loperamide	7	1618	1.08	0.95 to 1.22	0.24
Constipation frequency	*versus* placebo	5	1070	1.02	0.29 to 3.57	0.97
	versus loperamide	7	1637	0.27	0.18 to 0.40	< 0.0001

CONCLUSION:
As compared to placebo, racecadotril induced a significant 65% reduction of the diarrhoea duration among one thousand adults. As compared to loperamide, diarrhoea was not significantly shorter but secondary constipation was significantly less frequent.
Disclosure of Interest: J.-M. Vetel: None Declared, P. Baumer Consultancy for: Bioprojet Pharma, P. Lehert: None Declared
Keywords: acute diarrhoea, metaanalysis, racecadotril

P924 IN PATIENTS WITH CLOSTRIDIUM DIFFICILE ASSOCIATED DIARRHOEA: DOES STOPPING PROTON PUMP INHIBITORS REDUCE RELAPSE?

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INTRODUCTION: Hypochlorhydydria due to proton pump inhibitor (PPI) therapy is associated with increased susceptibility and propensity to relapse from infection due to *Clostridium difficile*. We have done a retrospective audit of patients with *C difficile* - Associated Disease (CDAD) examining PPI use and any benefit achieved by stopping the PPI.
AIMS&METHODS: All patients with CDAD between 2010-12 were reviewed by infection control nurses who advised the attending doctors to stop any PPI therapy where a clear indication was not obvious. We have retrospectively audited patient's relevant baseline characteristics pertaining to other risk factors for CDAD, clinical outcome, length of hospital stay and PPI prescription at hospital discharge. In addition we followed patients up post discharge recording PPI prescription and further CDAD.
RESULTS: 99 patients with CDAD identified. No difference was seen regarding CDAD risk factors; antibiotic use, co-morbidity, immunosuppression, recent surgery, enteral feeding or place of residence.

PPI status at admission	None	Taking & not stopped	Taking & stopped
Number	47	25*	20*
Age mean (st dev)	76.7 (12.4)	69.2 (21.5)	73.4 (18.4)
LHS mean (st dev)	27 (26)	26.2 (23.4)	36.4 (32.8)
Died in hospital	7	-*	-*
At discharge :Number	40	25	20
Further diarrhoea C diff +ve	6 (15%)	4 (16%)	5 (25%)
Further diarrhoea C diff -ve	5 (12.5%)	1 (4%)	1 (4%)
Died	1	0	0

*7 patients taking a PPI died, thus were not discharged
No differences were seen between those patients who never took a PPI vs those who did irrespective if the PPI was stopped.
CONCLUSION: It was possible to stop PPI prescription in 44% of patients presenting with CDAD. We found no evidence of reduced recurrence of CDAD in patients who had stopped taking their PPI or had never taken it.
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Disclosure of Interest: None Declared
Keywords: clostridium difficile infection, proton pump inhibitor

P925 TRENDS IN UPTAKE OF THE BOWEL CANCER SCREENING PROGRAMME IN THE EASTERN REGION OF ENGLAND

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INTRODUCTION: Bowel cancer is more common in men than women with age-adjusted incidence in the UK being over 50% higher in men and mortality 63% higher. However uptake of the Bowel Cancer Screening Programme in England (BCSP) has been generally about 5% lower in men[1]. We have examined whether with increasing familiarity with the BCSP there have been changes in uptake of screening invitations over the past 4 -5 years.
AIMS&METHODS: Analysis of uptake of screening invitations by sex and 2 year age bands of people invited for screening by the Eastern Hub which covers the East of England and East Midlands (total population 10.6 million) between 1 Jan 2008 and 30 June 2012 by 6 month periods.

RESULTS: Over the 4.5 years >2.8 million invitations were sent by the Eastern Hub. For those aged 60-61 years uptake by men was 9-10% lower than that by women (uptake 60%) with no evidence of any change over the 4 years. In women uptake remained over 60% for the 62-63, 64-65 and 66-67 age bands with a small increase over time reaching 65% in 2012. In men uptake showed a steady increase with age such that by age 68-69 uptake was 3% lower than in women. For those aged 70-71 uptake in men was only 2% lower than in women and for those aged 72-73 and those aged 74 uptake was around 1-2% higher in men than women. This was partly accounted for by a decline in uptake in women to below 60%. Analysis of time trends in those over 70 was unreliable because of only partial roll-out ('age extension') of the BCSP to this group in the Eastern region.

Uptake

	60-61yr	62-63yr	64-65yr	66-67yr	68-69yr	70-71yr	72-73yr	74yr
Men	**51.2%**	**53.9%**	**56.4%**	**57.6%**	**56.9%**	**60.3%**	**61.5%**	**55.7%**
Women	**60.0%**	**61.5%**	**62.9%**	**62.2%**	**60.1%**	**62.3%**	**59.9%**	**54.5%**
All	**55.6%**	**57.7%**	**59.6%**	**60.0%**	**58.5%**	**61.2%**	**60.5%**	**55.1%**

CONCLUSION: While the small decline in uptake in women >70 years is a concern the increasing uptake in men with age is encouraging and suggests that the introduction of simpler screening approaches using faecal immunochemical tests will see substantial increses in uptake of the BCSP[2].

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Disclosure of Interest: None Declared

Keywords: colorectal cancer screening, fecal occult blood test

P926 HOW OFTEN IS BOWEL CANCER DETECTED FROM A POSITIVE 3RD KIT IN THE ENGLISH BCSP?

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INTRODUCTION: In the English Bowel Cancer Screening Programme (BCSP) subjects returning a weak positive kit (1-4 of the 6 windows positive) are invited to do a 2nd kit and if none of the windows are positive they are invited to complete a 3rd kit. If any windows are then positive subjects are referred for possible investigation; if no windows are positive subjects are discharged from that screening round. This testing algorithm has been criticised for making the screening process too prolonged thereby producing anxiety and drop-outs and the Scottish BCSP has abandoned asking for a 3rd kit on the grounds that the yield was negligible.

AIMS&METHODS: We have analysed the outcomes from the 3rd kits returned to the Eastern BCSP Hub from subjects invited for screening between 1 Jan 2011 and 31 March 2012.

RESULTS: Over this period over 850,000 subjects aged 60-74 yrs were invited for screening. 4% (20,021) completed 3 kits and of these 16% (3192) had a positive 3rdkit and were referred for further investigation. Of those investigated (2830) 4.4% (125) were found to have bowel cancer compared with 17.8% (298) with cancer found after a single kit and 8.1% (483) with cancer found after completing 2 kits. A further 7% and 12% completing 3 kits were found to have high and intermediate risk adenomas. The mean time from selection for screening to obtaining a definitive result for those completing 3 kits was 63 days compared to 34 days for those completing a single kit (95% of all subjects returning kits) and 49 days for those completing 2 kits (1% of all subjects returning kits).

Patient Test Outcome according to number of kits completed

1 kit (n=1673) 2 kits (n=5939) 3 kits (n=2830)
Cancer 298 17.8% 483 8.1% 125 4.4%
High-risk Adenoma 137 8.2% 589 9.9% 199 7.0%
Intermediate-risk Adenoma 246 14.7% 978 16.5% 336 11.9%

CONCLUSION: A significant number (14%,125/906) of bowel cancers are detected in those completing 3 kits but this is at the cost of having a screening episode prolonged to almost twice that for subjects obtaining a definitive result after one kit. The intended introduction of faecal immunochemical tests to replace guaiac faecal occult blood tests should allow the use of a simpler and shorter testing algorithm.

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Disclosure of Interest: None Declared

Keywords: colorectal cancer screening, Faecal Occult Blood test (FOBt)

P927 RISK OF BOWEL CANCER INCREASES WITH NUMBER OF WINDOWS POSITIVE ON GUAIAC FAECAL OCCULT BLOOD TESTING

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INTRODUCTION: Bowel (colorectal) cancer screening programmes using a 6 window guaiac faecal occult blood test kits (gFOBt) are now in operation in the UK and in several countries in Europe and elsewhere. In the UK subjects returning kits with 5-6 windows positive are referred immediately for colonoscopy while subjects with only 1-4 windows positive are asked to repeat the gFOBt up to twice and are referred for colonoscopy only if one or more windows are positive on the repeat kits.

AIMS&METHODS: To determine the relationship between the number of positive gFOBt windows and subsequent cancer detection we have examined data collected by the Eastern Bowel Cancer Screening Hub covering the Eastern region of England (total popn. 10m) for the period Jan 2011-July 2012

RESULTS: Over this period more than 1.1million people aged 60-74yrs were sent gFOBt kits with 760,000 returning them. Of the kits returned 14020 were deemed abnormal and 12,198 subjects were investigated (>90% by colonoscopy). Overall cancer was detected in 1005 and 'high' risk adenomas in 1081. The table shows the cancer detection rate according to the number of windows positive on the *first* gFOBt kit returned.

	1 Window Positive*	2 Windows Positive*	3 Windows Positive*	4 Windows Positive*	5 Windows Positive	6 Windows Positive
Total Abnormals	4827	4202	1444	1196	1012	1339
Number investigated (n)	4310	3694	1257	1017	863	1057
Cancers Detected	191	219	128	134	123	210
%	4.4%	5.9%	10.2%	13.2%	14.3%	19.9%

*only referred for investigation if one or more windows positive on repeat gFOBt For subjects with only 1-4 windows positive on the first gFOBt kit the likelihood of returning a positive second gFOBt kit increased with the number of positive windows on the first kit and in these the cancer detection rate increased according to the total number of positive windows on both gFOBt kits.

CONCLUSION: These findings are consistent with occult blood loss from colorectal neoplasia being prolonged but variable over time. They also suggest that for bowel cancer screening programmes where the availability of colonoscopy is a major constraint a testing and investigation algorithm based on repeat testing of subjects with 'weak' positive results will result in higher cancer detection rates than a testing algorithm based on a single test for a defined colonoscopy capacity.

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Disclosure of Interest: None Declared

Keywords: colorectal cancer screening, Faecal Occult Blood test (FOBt)

P928 REDUCED 5-YEAR MORTALITY IN SCREEN-DETECTED COLO-RECTAL CANCERS DIAGNOSED AT THE 1ST BIENNIAL ROUND OF A FIT-BASED MASS SCREENING PROGRAMME IN COMPARISON WITH NON-SCREENING CANCERS IN NORTHERN ITALY.

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INTRODUCTION: Population-based colorectal cancer(CRC) screening programmes aim to reduce disease-related mortality by detection of cancers at an earlier stage and by removal of its precursors. To date, however, no study has specifically focused on the effect of a single FIT screening round with respect to a reduction in CRC-related mortality among average risk subjects.

AIMS&METHODS: We aimed to compare 5-year mortality rates of screen-detected CRCs with those of non-screening cancers diagnosed in the same northern Italian province. We determined tumour characteristics and mortality of asymptomatic CRCs detected by faecal immunochemical testing (FIT) at the 1st biennial round of mass screening programme of Lecco province addressed to 50-70 years old resident population of the province (78,083 individuals) and characterized by a FIT uptake of 50% and colonoscopy compliance of 92%. TNM stage at diagnosis, anatomical distribution of cancers along the colon and 5-year survival were compared with those of non-screening CRCs detected in the same age-range population during the screening period(January 2006-January 2008) as well as with those of CRCs diagnosed in our province in 2003-2004(pre-screening biennium), whose data were retrieved from the Regional cancer registry. Kaplan-Meyer survival estimates and Log-rank test for equality of survivor functions were used for statistical analysis.

RESULTS: Stage distribution significantly differed between screening and non-screening CRCs. Indeed, among screen-detected cancers 73% were stage A or B as compared to 43% and 40% among non-screening CRCs detected in the same or previous biennium, respectively. Cumulative 5-year CRC-related

mortality was significantly lower in screening CRC patients as compared to non-screening cancers detected in the same biennium (*19% versus 41%*, $p<0.001$) or in the biennium preceding screening implementation (44%). No significant difference in anatomical distribution of cancers nor in the presence of synchronous lesions were found between screening and non-screening CRC patients.
CONCLUSION: CRCs are detected at earlier stages in asymptomatic individuals with positive FIT compared to non-screening patients. As a consequence, the cumulative 5-year disease-related mortality rate among screened patients is significantly reduced, already from the 1st round of screening as compared to non-screening patients.
Disclosure of Interest: None Declared
Keywords: colon cancer screening, colon cancer survival, faecal immunochemical test

P929 THE POSITIVE PREDICTIVE VALUE OF FAECAL IMMUNOCHEMICAL BLOOD TEST FOR CANCER AND ADVANCED ADENOMA, BUT NOT FOR LOW-RISK ADENOMA, PROGRESSIVELY DECREASES WITH REPEATED SCREENING ROUNDS. A PILOT EXPERIENCE IN NORTHERN ITALY

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INTRODUCTION: Colorectal cancer (CRC) screening programs based on a biennial faecal immunochemical blood test (FIT) are widely adopted in many European countries. Whether the positive predictive value (PPV) for either carcinoma or advanced adenoma decreases through repeated rounds of FIT is still a matter of debate. Sharp fluctuation of this value could have a great clinical and socio-economic impact.
AIMS&METHODS: We aimed to assess variations of PPV for CRC and advanced adenoma in subjects testing positive at repeated screening rounds of a Regional FIT-based mass screening program in Northern Italy, addressed to average-risk subjects aged 50-69 years, which has been running since 2006. In particular, we analyzed data from subjects participating to the CRC screening campaign in one large metropolitan area (Milan 1 area) from 2006 to 2012. The PPV of FIT for CRC, advanced adenoma and low- risk adenoma was calculated for tests performed at the 1st round and for those performed at 2nd and 3rd rounds in subjects with one or two previous negative tests.
RESULTS: A total of 274,165 FITs were done in 150,512 subjects during the study period. 55% of these tests were performed at the first round, 30% at the 2nd round, and 13% at the 3rd round. The FIT positivity rate progressively reduced from 6% in 1st round to 4.4% in the 3th round. Colonoscopy was performed in 12,715 patients; the adherence to colonoscopy remained consistent through different rounds of FIT (82% > 86%). The diagnosis of cancer showed a downward trend (6% in the 1st, 3% in the 2nd, 2% in the 3rd round); a similar trend was demonstrated for high risk adenoma (30% > 21% > 18%); conversely, low risk adenoma diagnosis remained unchanged (15% and 16%). As a result, the PPV for carcinoma or advanced adenoma progressively decreased, from 36% for the 1st round to 24% and 20% for the 2nd and the 3rd round, respectively. Otherwise, the frequency of a negative result at colonoscopy increased after each subsequent round of screening, from 43% in the 1st round to 53% and 57% in the 2nd and the 3rd round, respectively.
CONCLUSION: A substantial and progressive decrease of the PPVs of FIT for either cancer and advanced adenoma, but not for low-risk adenoma, was observed in subjects undergoing repeated rounds of FIT. More data after the 3th biennial FIT are needed to verify the capacity of our Regional CRC screening program to reduce CRC incidence.
Disclosure of Interest: None Declared
Keywords: adenoma detection, cancer incidence, fecal immunochemical test, positive predictive value, Screening

P930 IMMUNOLOGIC FECAL OCCULT BLOOD TESTING (IFOBT) IN OPPORTUNISTIC SCREENING FOR COLORECTAL CANCER (CRC) – SINGLE CENTER EXPERIENCE IN 3571 PATIENTS

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INTRODUCTION: Based on higher sensitivity and convenience at appropriate specificity iFOBT has replaced guajac FOBT in major CRC screening guidelines. Despite intense efforts to increase acceptance for health maintainance plan based CRC screening it still takes place oftenly as socalled opportunistic screening on the occasion of hospital contacts for a variety of reasons. In this mostly older and sicker patients frequently treated with anticoagulants iFOBT has not been evaluated so far. We therefore investigated prospectively performance (cut off values at different levels, sensitivity, specificity, NPV, PPV) for CRC and precancerous lesions.
AIMS&METHODS: All consecutive iFOBT results in a 10 month period were correlated with demoscopic data, colonoscopy findings as far as available (colonoscopy was on the decision of referring phycision) and anticoagulant medication. Standard statistical methods were applied.
RESULTS: Fecal samples of 3519 patients were studied. The mean age was 63,6 ± 35,3 years. 50,8 % were female. 2717 patients (77,2%) had negative iFOBT, 802 patients tested positive (22,8%) at the lowest cut off level of 50 ng/ml. In iFOBT positive patients 232 colonoscopies (28,9%), in iFOBT negatives 356 colonoscopies (13,1%) were performed. In those 588 endoscopies 17 CRC (2,9%) and 173 precursors (29,4%) were dedected. Performance characteristics are summarized at different cut off levels below.

CutOff Levels		50 ng/ml		75 ng/ml		100 ng/ml	
%	CI	%	CI	%	CI		
Sensitivity	for CRC	88.2	64 - 98	82.4	58 - 95	82.4	58 - 95
	for Precursors	48.6	41 - 56	41.0	34 - 48	32.4	26 - 40
Specificity	for CRC	62.0	58 - 66	66.7	63 - 70	71.6	68 - 75
	for Precursors	66.6	62 - 71	70.1	65 - 74	73.6	69 - 78
NPV	for CRC	99.4	98 - 100	99.2	98 - 100	99.3	98 - 100
	for Precursors	74.4	70 - 79	72.6	68 - 77	71.1	67 - 75
PPV	for CRC	6.5	4 - 10	6.9	4 - 11	8.0	5 - 13
	for Precursor	52.7	35 - 48	41.7	35 - 49	40.4	34 - 48

Anticoagulants and antithrombotic agents increased sensitivity at all cut off levels reaching 100% at 50 ng/ml for CRC.
CONCLUSION:
iFOBT is also highly effective in opportunistic screening. A cut off level of 50 ng/ml haemoglobin is recommended in this population. The extraordinary high negative predictive value for CRC may help to reduce the burden of colonoscopies especially in older patients where early detection and not secondary prevention is the major goal of CRC screening.
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Disclosure of Interest: None Declared
Keywords: iFOBT, Screening colonoscopy

P931 SIGNIFICANT SUSCEPTIBILITY MARKERS FOR COLORECTAL CANCER (CRC) MAY INDICATE A SCREENING PRIORITY

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INTRODUCTION: Recommendations for screening for colorectal cancer (CRC) specify a colonoscopy at age 50 and if normal a repeat after 10 years. The yield of the follow-on colonoscopy in this setting is poor. There is a highly significant association between a SNP variant at the TGFBR1 (tumour growth factor beta, receptor 1) locus and CRC and we have suggested that TGFBR1 could be useful to screen for CRC (ASCO 2013, abstract e14591). We now present results on the association between variants of TGFBR1 and mutants at the GSTT1 (glutathione S-transferase theta 1) locus, and CRC and consider the implications for screening.
AIMS&METHODS: Tumour samples were obtained from 185 CRC patients and from 98 healthy control subjects, all Caucasian. After gDNA extraction, selected amplicons were amplified by PCR, followed by melting curve analysis. Samples were typed for the rs334348 SNP at the TGFBR1 locus and mutant vs. wild-type at the GSTT1 locus. Statistical significance was assessed using logistic regression. Sensitivity was calculated as the ratio of test-positive cases to total cases, and specificity as the ratio of test-negative controls to total controls.
RESULTS: The association between CRC and TGFBR1 variant was highly significant ($P<0.00005$) as was that of CRC with GSTT1 mutant ($P<0.00005$) in a multivariate analysis. For TGFBR1, contrasting homozygous variants (VV) versus heterozygotes plus homozygous normals (VN+NN) for CRC cases and controls, the sensitivity was found to be 43.2% and specificity 89.8%. Comparing TGFBR1 (VV+VN) with (NN) gave a sensitivity of 83.2% and a specificity of 45.9%. For GSTT1, the sensitivity and specificity were 49.7% and 83.7%. Contrasting TGFBR1 (VV+VN) or GSTT1 mutants with TGFBR1 (NN) and GSTT1 wild-type gave a sensitivity of 90.8% and a specificity of 35.7%.
CONCLUSION: There is a trade-off between sensitivity and specificity depending on how the TGFBR1 heterozygotes are considered. When they are combined with the homozygous normals, sensitivity is low and specificity is high; when combined with homozygous variants the sensitivity is high and specificity low. Sensitivity relates to the test's ability to identify positive results. Thus we conclude that the heterozygotes should be included with the homozygous variants in any eventual screening test. Including GSTT1 raises the sensitivity. Using a test to predict cancer risk would be cost-saving and easier on patients and could possibly, in patients at risk, call for a colonoscopy sooner and more often while increasing yield. A prospective clinical trial to prove the cost-benefit is indispensable.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, GSTT1, Screening, TGFBR1

P932 BODY MASS INDEX AS A PREDICTOR OF ADVANCED COLONIC NEOPLASIA

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INTRODUCTION: Colorectal cancer (CRC) was the third frequent cancer in Korea. There are several risk factors such as male sex, older age, smoking and family history of colon cancer. And advanced colon polyp larger than 1cm is a definite precancerous lesion of CRC. Recently, obesity is thought to be a risk factor of CRC and advanced colon polyp.

AIMS&METHODS: From this background the aim of cross-sectional study to determine the association BMI and advanced colorectal neoplasia. A total of 256 patients with advanced colorectal neoplasia who were diagnosed with colonoscopy during between May, 2004 and December, 2011 were included in this study. An advanced colorectal neoplasia is defined as large (≥1 cm) adenoma or adenocarcinoma. We compared these patients to control group consisted of 217 subjects with normal colonoscopic finding during the same period.
RESULTS: Of the 256 patients, men were 132 (51.6%) and mean age was 56.4 ± 12.3 years. The advanced colorectal neoplasia had a larger percentage of males, alcohol consumption and current smokers. Body mass index (BMI, kg/m^2) and age were significantly higher in advanced colorectal neoplasia than control group in female group. However, there was no significant difference except age in male group. Multiple logistic regression analysis identified overweight (BMI 23.0–24.9 kg/m2, odds ratios (OR) = 2.022) and obesity (BMI ≥ 25 kg/m2, OR = 2.383) as independent risk factors for advanced colorectal neoplasia.
CONCLUSION: BMI looks like to be an independent risk factor for advanced colonic neoplasia and the screening colonocoscopy could be recommended earlier in this group.
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Disclosure of Interest: None Declared
Keywords: Adenomatous polyp, Body mass index, Colorectal cancer

P933 BLEEDING-RELATED SYMPTOMS IN COLORECTAL CANCER: A 4-YEAR NATIONWIDE POPULATION-BASED STUDY

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INTRODUCTION: Little is known about the major presenting features of patients with colorectal cancer in a population-based setting, especially regarding bleeding-related symptoms.
AIMS&METHODS: We aimed to determine the proportion of colorectal cancer patients presenting with bleeding-related symptoms, compare bleeders and non-bleeders, and to explore the role of anticoagulants in bleeders. This was a nationwide, population-based, retrospective study, including all colorectal cancers diagnosed in Iceland from the year 2008-2011. Medical records were reviewed and relevant data collected. Bleeding-related symptoms were defined as overt bleeding, iron deficiency anemia or a positive fecal occult blood test. Obstructive symptoms were defined as a confirmed diagnosis of ileus and dilated intestines on imaging.
RESULTS: Data were available for 472/496 (95%) patients, males 51%, with a mean age of 69 (±13) years. In all, 348 (74%) patients had bleeding-related symptoms, and of those 348 patients 208 (60%) had overt bleeding. Bleeders were more likely to use warfarin than non-bleeders 9% vs. 3% (p = 0.031). The use of low-dose aspirin was the same (24%) in bleeders and non-bleeders. Bleeders were less likely than non-bleeders to have metastasis at diagnosis, 19% vs. 34% (OR 0.31, CI 0.15-0.64), respectively. Overt bleeders were less likely than non-bleeders to have obstructive symptoms, 2% vs. 16%, respectively, (OR 0.13, CI 0.042-0.42). Occult bleeders were more likely to have proximal cancer (69%) than overt (17%) and non-bleeders (44%) (p < 0.0001).
CONCLUSION: The majority of patients with colorectal cancer present with bleeding-related symptoms. Bleeders with colorectal cancer present earlier than non-bleeders. Warfarin use may induce bleeding in some patients, resulting in an earlier diagnosis.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, GI bleeding

P934 HIGH IMPACT REGIONAL COLORECTAL CANCER SCREENING PROGRAM OF AVERAGE RISK POPULATION IN NORTH-EASTERN ITALIAN REGION OF FRIULI-VENEZIA-GIULIA

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INTRODUCTION: Average-risk population screening for colorectal cancer (CRC) using fecal occult blood tests is aimed to detecting cancer in an early stage. We analyze data of 3 consecutive years experience of Bowel Cancer Screening Program (BCSP) of subjects from North-Eastern Italian Region of Friuli-Venezia-Giulia.
AIMS&METHODS: We evaluate data from 2009-2011 of 450.153 subjects referred for BCSP, aged 50-69 years, invited to complete one single qualitative immunochemical fecal test (FIT, cut-off level 100ng/ml) every 2 years. Only in 2009 the BCSP decided to give priority to subjects aged 60-69 (about 70% of all FIT invitations). Those positive were referred to colonoscopy in 11 regional hospitals and detected polyps were removed in most of the cases in the same session (88.4%).
RESULTS: We report the overall adherence to FIT being 147.485 subjects (32.76%), which resulted positive in 8060 cases (5.46%). The adherence to colonoscopy was 77.8%. All colonoscopies were performed with a completion rate of 96% (caecal or terminal ileum intubation). The positive finding on colonoscopy (initial adenoma, advanced adenoma and/or cancer) was reported in 68.02%. Colorectal cancer (CRC) was diagnosed in 529 subjects (8.43%), with most detected cases in the first year (265), followed by decreasing trend in 2010 and 2011 (148 and 116 CRC respectively). On a total of 3738 subjects, we detected 1074 with advanced adenomas (17.12%) and 2664 with initial adenomas (42.47%). Adenoma detection rate (ADR) was reported to be 59.6%, while advanced ADR was 17.12%. The highest advanced ADR was observed in subjects aged 60-69 years, varying from 11.4-12.8%. Most of the polyps were removed in the same session in 88.4% of subjects. The most of advanced adenomas were treated endoscopically by polypectomy and endoscopic mucosal resection (94.8%), while cancerized polyps and pT1 cancers were treated endoscopically in 5.4% cases. Regarding the T stadiation, the most frequent finding among cancers was pT3 stage (37.06%).
CONCLUSION: The extremely high rate of cancer/adenoma detected can partly be explained by: initial BCSP in our local population, higher incidence of colon cancer/adenomas in our region, relative initial older age of the involved population (most of them older than 60 years), the performance of FIT and the good bowel preparation in almost all the subjects. The initial low adherence to FIT could be explained with a low intensity public action campaign. The decreasing trend of detected CRC over years supports the strategy of screening in regions with high CRC incidence.
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Disclosure of Interest: None Declared
Keywords: Adenoma Detection Rate, colon cancer screening, colonoscopy

P935 OBESITY AND HEAVY ALCOHOL CONSUMPTION ARE INDEPENDENTLY ASSOCIATED WITH AN INCREASED RISK OF COLORECTAL CANCER : A NESTED CASE-CONTROL STUDY

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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 increases the risk for the disease because of insulin resistance and elevated circulating pro-inflammatory mediators. 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 a number of lifestyle factors including obesity, smoking, alcohol use, dyslipidemia and CRC in the population aged 50-70 years who were part of a colorectal cancer screening program in Northern Italy. One hundred seventy two colorectal cancers were diagnosed among 3819 subjects who underwent total colonoscopy, between March 2005 and January 2013, at a center participating to a region-wide screening program based on biannual immunochemical fecal occult blood test. A nested case-control study was performed on 161 eligible CRC patients and 322 age- and sex-matched negative controls (polyps were excluded as well). Adjusted conditional logistic regression was used to estimate odds ratios.
RESULTS: Obesity and drinking >35 gr/daily (drinkers) of alcohol were the only factors significantly and independently associated with an increased risk of colorectal cancer: odds ratio was 1.79 (95% CI, 1.01-3.17; *P*=0.043) for individuals with a BMI ≥ 30 kg/m^2 and 2.39 (95% CI, 1.06-5.42; *P*=0.036) for heavy alcohol drinkers, respectively. When considering cancer location, the odds ratio for obesity and right sided colon cancer was 5.51 (95% CI, 1.59-19.08; *P*=0.007), while no association was found between obesity and cancer of the left colon and rectum. Finally, the odds ratio between drinkers and cancer of the left colon and rectum was 3.60 (95% CI, 1.33-9.71; P=0.011). Smoking (OR 1.13, 95%CI 0.67-1.91; P=n.s.) and dyslipidemia (OR 1.45, 95%CI 0.83-2.52; P=n.s.) were not associated with CRC.
CONCLUSION: In our population undergoing a CRC screening program in Northern Italy, obesity is a significant risk factor for right-sided colon cancers. Heavy drinking has an independent relationship with CRC that is more significant in left colon and rectum. It is possible that in the future an earlier screening strategy should be adopted among obese subjects and advise should be given to people actively drinking alcohol.
Disclosure of Interest: None Declared
Keywords: colorectal cancer, Obesity

P936 COLORECTAL POLYP CHARACTERISTICS IN IRAN, AN AGE SPECIFIC TREND WITH HIGH RISK POLYP

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INTRODUCTION: Asian countries are experiencing a dramatic increase in colorectal cancer which is associated with rapid life style changes in specific age groups. Information about the age specific characteristic of colorectal polyp in these countries is limited. In this study we assessed the age specific trend of colorectal polyp and their baseline risk in a large sample from Iran.
AIMS&METHODS: During 2000-2012, demographic and clinical data of all colonoscopies performed in 2 university hospitals of Tabriz (Northwest of Iran) were collected. Colonoscopies were performed by 5 experienced gastroenterologists who followed a standard protocol. The collected data were checked by a questionnaire and then were analyzed.
RESULTS: In 10327 adult colonoscopies, 47% were female and median (interquartile) age was 49 (35-63) years. The main reasons for colonoscopy were GI bleeding (32%), change in bowel habit (21%), and abdominal pain (17%). The screening comprise of 1% of all colonoscopies. The frequency of polyp diagnosis was 17%, which increased from 7% in patients younger than 31 to 25% in patients 60-65 years (p<0.001), this frequency decreased to 24% in older patients. Male gender was associated with higher frequency of polyp (OR=1.2, p<0.001). Fifty percent of polyps were located in rectosigmoid followed by 12% in descending and 11% ascending colon. Five percent of polyps were multiple, and 29% were larger than 1 cm. The frequency of high risk polyp (multiple or >

1cm) increased from 28% in patient younger than 31 to 38% in 51-60 years and decreased to 33% in older patients. Frequency of high risk polyp was more in rectosigmoid (OR=1.6, p=0.038). Frequency of high risk polyps was not different between male and female. The highest frequency of high risk polyp were observed in patient who were visited for follow-up (50% vs. 33% for other reason, p=0.003). Among all polyps 49% were sessile which was higher in older age (OR=2.7, p=0.014) but not associated with gender, location or symptom.
CONCLUSION: This study reveals some identical characteristics of colorectal polyp in developing countries, including importance of sessile, high risk and rectosigmoid polyp besides importance of middle age in polyp prevalence and risk. Our results could indicate that in these countries population younger than 60 years old are more prone to high risk polyps. High risk of polyps in this population is also an alarm sign for future of colorectal cancer.
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Disclosure of Interest: None Declared
Keywords: age , colorectal, iran, polyps

P937 POSITIVE COLONOSCOPY FINDINGS FOR COLORECTAL CANCER IN RELATION WITH AGE AND GENDER

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INTRODUCTION: Colorectal cancer (CRC) is a major cause of morbidity and mortality throughout the world. It is the third most common cancer worldwide and the fourth most common cause of death. Colonoscopic screening has been recommended for all persons who have had a colorectal adenoma or carcinoma. Colonoscopy has the advantage of allowing biopsy and/or removal of lesions during the same procedure.
AIMS&METHODS: Aim: In this study we aimed to analyze the colonoscopy results of 3650 patients for CRC risk factors and find the relation of them with age and gender.
Methods: All records (n=3650) patients undergoing colonoscopy from 2008 to 2012 at Tabriz University of Medical science were analyzed. We also evaluated the age, gender, having polyp, signs and symptoms, other colonoscopy findings and relationship between them. We used t-test for descriptive variables and Chi-square tests to compare categorical variables.
RESULTS: In this study 3650 patients were enrolled and all of them underwent complete examination of the colon. From 1984 males (54.3%) and 1666 females (45.7%), mean age of our patients was 48.7±18.6 [5-100]. The risk factors most likely to be associated with a finding of colorectal cancer were rectorrhagia (34%), abdominal pain (18.4%), diarrhea (17.9%), constipation (12.6%), anemia (9.1%), history of CRC (7.3%) and positive fecal occult blood test (0.7%), respectively. From those who had rectorrhagia 52.7% were males and 47.3% were females. Polyps were detected in 545 patients (15%). From those who had polyp 326 patients were male (59.8%) and 219 patients were female (40.2%). Most common location of polyp was in rectum (26.5%). Other colonoscopy findings were hemorrhoid (78.1%), skin tag (8.7%), anal fissure (6.5%), diverticule (4.6%) and lesions (2.1%), respectively. From those who had hemorrhoid 52.6% were males and 47.4 were females. From those who had history of colorectal cancer 56.4% were males and 43.6% were females.
CONCLUSION: There was a significant relation between CRC risk factors and male gender. Most frequently associated with positive colonoscopy findings were rectorrhagia, presence of abdominal pain and history of CRC. A history to include these risk factors can serve to prioritize the need for a colonoscopic examination.
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Disclosure of Interest: None Declared
Keywords: age, colonoscopy , colorectal cancer, gender

P938 FIRST CYCLE OF NATIONAL COLORECTAL CANCER SCREENING PROGRAMME IN CROATIA-PRELIMINARY RESULTS

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INTRODUCTION: Colorectal cancer (CRC) was the second leading cause of cancer mortality in men and women respectivelly in Croatia, (n_m=1164, 49.77/100000; n_w=845, 34.89/100000). It is also on a second place of incidence among malignant neoplasms with 3068 cases in 2010. The National Colorectal Cancer (CRC) Screening Program was established by the Ministry of Health, and started at the beginning of 2008.
AIMS&METHODS: The fecal occult blood test (FOBT) was performed by guaiac Hemognost card-test. Each participant was required to fulfill the questionnaire and to send it together with the stool specimen on 3 test cards to the county public health institute for further reading. All positive persons had to be invited to colonoscopy within 6-8 weeks. A descriptive analysis of was performed.
RESULTS: A total of 1418103 individuals (100% of eligible) were invited to screening by the end of 2012. In total, 288347 (20.3%) persons returned the envelope with a completed questionnaire, and 247362 of them returned it with a correctly applied stool specimen on FOBT cards. Until now, 15516 (6.3%) FOBT positive patients have been found. Colonoscopy was performed in 10428 cases (67%), and identified colorectal cancers in 564 patients (5.4% of colonoscopied, 3.7% of FOBT-positive, and 0.23% of all screened individuals). Polyps were found and removed in 4107 (39% of colonoscopied) patients.
CONCLUSION: First cycle implementation characteristics are: relatively low FOBT compliance, higher number of FOBT-positive persons but still in the range for population-based programs, and higher number of pathologic findings (polyps and cancers). These results suggest a need for intervention strategies which include organizational changes and educational activities to improve awareness of CRC screening usefulness.
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Disclosure of Interest: None Declared
Keywords: colorectal cancer, gFOBT, national programme, screening

P939 VITAMIN D AND PARATHYROID HORMONE LEVELS IN PATIENTS WITH COLON POLYPS.

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INTRODUCTION: Calcium and Vitamin D have been shown to act against cancer by inducing differentiation, inhibiting proliferation and inducing apoptosis. Studies have revealed that serum vitamin D levels were inversely correlated with the colorectal carcinoma incidence. Similar findings have been reported from studies involving colonic polyps.
AIMS&METHODS: Patients undergoing colonoscopy between January -March 2012 were included. Serum 25 (OH) vitamin D, PTH, serum calcium, phosphorus, creatinine, albumin and hemoglobin levels were measured. Patients in whom entire colon could not be visualized, inflammatory bowel disease patients were excluded. Also patients with creatinine clerences < 50 ml/min were left out of the study. History was taken from all patients about family history of colorectal carcinoma, previous medical history about colon polyps. They were also asked about alcohol intake or smoking and whether they get nonsteroidal anti-inflammatory drugs or calcium and vitamin D supplements. All patients' body mass indexes were calculated
RESULTS: 620 colonoscopies were performed during the study period. 325 colonoscopies were excluded. Of 295 patients analysed 122 were female. Average age was 53,39±12,38 years. 98 patients had colon polyps (33,2 %). Mean vitamin D levels in polyp group were 14,30±11,10 ng/ml and PTH levels were 61,32±35,40 pg/ml while mean vitamin D levels in normal colonoscopy were 12,70±6,74, and PTH levels were 55,84±24,34 (p > 0,05). Only age was found to be moderately correlated with polyp risk. Vitamin D levels did not correlate with polyp number, diameter, localization or type. 16 colorectal carcinoma cases were identified. Vitamin D and PTH levels were not different from noncancer group. Patients with polyps were further classified as high and low risk polyp(high risk polyp: more than 3 adenomatous polyps, polyp diameter > 1 cm or presence of villous component). Only age was found to be related with the probability of having high risk polyp. Analyses failed to show any effect of NSAID intake, smoking or family history on probability of having high risk polyp.
CONCLUSION: We could not find any relationship between colorectal polyp incidence and 25 (OH) vitamin D and PTH levels. Vitamin D and PTH levels also did not affect polyp characteristics. Our study was performed during winter months in Ankara. Vitamin D levels were low in all groups. This might have prevented any relation to be detected. One measurement of serum vitamin D levels may not be reflecting long term vitamin D status . Since it was a cross sectional study long term follow up of these patients may reveal different results.
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Disclosure of Interest: None Declared
Keywords: colon polyp, PTH, vitamin D

P940 AGE RELATED INCREASE IN THE PREVALENCE OF PROXIMAL ADVANCED NEOPLASIA IN THREE ROUNDS OF A POPULATION BASED COLORECTAL CANCER SCREENING BY IMMUNOCHEMICAL FECAL OCCULT BLOOD TESTING

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INTRODUCTION: There is a growing interest about the anatomical site of screen-detected colorectal cancer (CRC). Some recent data suggested that both colonoscopy and fecal immunochemical test (FIT) might be less sensitive for cancer located in the right side of colon. Moreover right-sided CRCs seem to be diagnosed more frequently in older compared to younger age. We analysed a screened population looking for age-related differences in the colonic location of advanced neoplasia (AN) (carcinomas and advanced adenomas).
AIMS&METHODS: In Aosta Valley Region (Italy) between 2006 and 2010, about 38,000 average-risk subjects, 50–74 years old, were invited for 3 rounds of a biennial screening program for CRC, based on 1-day FIT (OC Sensor, cut-off set at 100 ng Hb/ml buffer). We estimated the cumulative detection rate (DR) of AN over 3 rounds among people who attended the initial screening invitation, stratified by two age group (50-54 years vs 65-69 years) and by two colonic site (right vs left colon) at colonoscopy in FIT positive subjects. Adenomas with at least one of the following features – size > 9 mm; villous component >20%; high-grade dysplasia – were classified as advanced.

RESULTS: About 75% out of 12,944 subjects attending the initial screening performed 2 consecutive tests and 50% had 3 consecutive FITs (average: 2.2 tests per person). In the 8,708 subjects in the younger cohort 464 (5.3%) had at least 1 positive FIT compared to 535 (12.6%) of the 4,236 subjects in the older cohort. Table I reports the results of the cumulative DR and the site distribution of CRCs and advanced adenomas in the two age groups. The relative risk in the cumulative DR for older cohort, compared to younger subjects, was 5.02 (95% CI: 3.15-8.00) for right-sided and 2.20 (CI: 1.68-2.87) for left-sided AN.

Tab I - Cumulative Detection Rate of AN over 3 FIT screening rounds **by colonic site and screenees age**

50-54 years	CRC	Advanced Adenoma	Total	65-69 years	CRC	Advanced Adenoma	Total
Distal N %	9 0,10	93 1,07	102 1,17	**Distal N %**	10 0,24	99 2,34	109 2,57
Proximal N %	3 0,03	22 0,25	25 0,29	**Proximal N %**	15 0,35	46 1,09	61 1,44
Total N %	12 0,14	115 1,32	127 1,46	**Total N %**	25 0,59	145 3,42	170 4,01

CONCLUSION: Over 3 CRC screening rounds with FIT subjects aged 65 to 69 showed a near 3 fold increased cumulative DR of AN compared to subjects aged 50 to 54. The increase was about twice as high for proximal than for distal AN. These findings would confirm a shift from left toward right side of colon of advanced neoplasia with age.

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Disclosure of Interest: None Declared

Keywords: advanced neoplasia, anatomical site , colorectal cancer screening, fecal immunochemical test

P941 SOCIOECONOMIC STATUS IS ASSOCIATED WITH INEQUALITIES IN SURGICAL TREATMENT AND SHORT-TERM OUTCOMES IN PATIENTS WITH NON-METASTATIC COLORECTAL CANCER

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INTRODUCTION: Low socioeconomic status (SES) is associated with lower survival in colorectal cancer (CRC) patients. Factors responsible for these inequalities include disease stage, access to and use of medical care and comorbidities. However, only a few studies have focused on the association between SES, surgical treatment and short-term outcomes.

AIMS&METHODS: We aim to investigate whether SES is associated with surgical treatment and short-term outcomes after surgery in patients with stage I-III CRC. All patients diagnosed with stage I-III CRC in the period 2005-2010 in the Eindhoven Cancer Registry area in the Netherlands (~2.4 million inhabitants) were included in this study. Demographic and clinical data were routinely collected from medical charts. Multivariable logistic analyses were used to estimate adjusted odds ratios (OR) for 1-year mortality, undergoing resection of the primary tumor, emergency surgery, open vs. laparoscopic surgery, residual tumor after surgery, ≥12 lymph nodes examined, and anastomotic leakage/abscess formation. Analyses were adjusted for age, gender, comorbidities, disease stage, tumor characteristics and, in case of 1-year mortality for chemo- and radiotherapy.

RESULTS: A total of 4,814 colon and 2,500 rectal cancer patients were included. Compared to low SES, high SES colon cancer patients had a lower likelihood to undergo open surgery (OR 0.61, 95% > CI 0.46-0.82), develop anastomotic leakage/abscess formation (OR 0.70, 95% > CI 0.49-0.99) and urgent stoma/stent placement (OR 0.19, 95% > CI 0.04-0.93). No associations with regard to SES and outcome of rectal cancer were observed. One year mortality risk was lower in high vs. low SES patients for both colon (OR 0.48, 95% > CI 0.38-0.61) and rectal (0.62, 95% > CI 0.43-0.90) cancer. The latter associations attenuated after adjustment for clinical characteristics and (neo)adjuvant treatment for both colon cancer (OR 0.68, 95% > CI 0.53-0.88) and rectal cancer (OR 0.78, 0.95% > CI 0.52-1.17), while further adjustment for surgical treatment characteristics and complications had no effect.

CONCLUSION: Marked SES specific differences exist with regard to type of surgical treatment (open vs. laparoscopic) and (short-term) outcomes in stage I-III CRC. However, it remains to be elucidated whether these findings can be attributed to patient- or physician-related factors that were not studied. Meanwhile, in a society where health care is available to the same extent for the whole population, low SES patients may benefit from specific attention with regard to the surgical technique used and the monitoring of post-operative complications.

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Disclosure of Interest: None Declared

Keywords: Colorectal cancer, socioeconomic status, surgery

P942 AUTOMATED WORKFLOW FOR MRNA BIOMARKER ANALYSIS OF COLORECTAL CANCER DEVELOPMENT USING BIOPSY, FRESH FROZEN AND FORMALIN-FIXED, PARAFFIN EMBEDDED (FFPE) SPECIMENS

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INTRODUCTION: Recently a colorectal cancer-specific transcript set (including COL12A1, CXCL2, IL1B, MMP3) was identified on colonic biopsy samples using whole genomic microarrays[1].

AIMS&METHODS: Our aim was to evaluate the applicability of these markers on independent biopsy and also on fresh frozen and formalin-fixed, paraffin-embedded (FFPE) tissue specimens from healthy and CRC patients by expression arrays and RT-PCR. Furthermore, automated RNA isolation was introduced and evaluated with increased sample number. Total RNA from 3 normal and 3 CRC FFPE specimens were analyzed by using Affymetrix HGU133Plus 2.0 whole genome expression arrays. Total RNA was isolated from 30 biopsy samples stored in RNALater (15 CRC, 15 normal), 20 fresh frozen surgically removed colonic tissues (10 CRC, 10 adjacent normal) and 60 FFPE (30 CRC, 30 adjacent normal using fresh (≤6 months) and archive (≥5 years) old FFPE blocks) samples with the automated MagNA Pure 96 system using MagNA Pure 96 Cellular RNA Large volume kit (Roche) and reverse transcription was done using Transcriptor First Strand cDNA Synthesis Kit (Roche). Gene expression analysis was performed with real-time PCR using RealTime ready assays and the LightCycler 480 system (Roche).

RESULTS: The FFPE specimens could be clustered correctly by the results of the microarray analysis. According to the gene expression levels of the set of 11 transcripts the biopsy, fresh frozen and fresh FFPE samples could be distinguished by 100% sensitivity and 100% specificity by RT-PCR. The discriminatory power of the marker set was proved to be high also on archive FFPE samples. The automated RNA isolation technique has not influenced the classification power of the markers, but decreased the handling time.

CONCLUSION: The analyzed set of markers in an automated environment could correctly characterize the healthy and the tumorous colonic tissue samples on biopsy, fresh frozen and also on FFPE tissue samples by microarrays and RT-PCR. On the basis of these results, FFPE samples can serve as valuable source for retrospective gene expression studies and these markers can enhance the automated, early and differential detection of colorectal cancer.

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Disclosure of Interest: None Declared

Keywords: Colorectal cancer, Gene expression , Real-time quantitative reverse transcriptase polymerase chain reaction

P943 INCREASE IN PARTICIPATION RATE IN SUCCESSIVE ROUNDS OF FIT SCREENING

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INTRODUCTION: Faecal immunochemical test (FIT) based screening for colorectal cancer requires successive screening rounds for an optimal preventive effect. However, data on multiple rounds of FIT screening are lacking until so far. We therefore conducted a third round of FIT screening in a population-based trial.

AIMS&METHODS: Average-risk subjects aged 50-75 years were approached for screening with a single FIT (OC-sensor). They were excluded from further FIT screening when they had a positive FIT in the previous screening round, when they had a previous history of CRC or inflammatory bowel disease and in case of imaging of the bowel in the former three years. Subjects with a FIT ≥50 ng/ml were referred for colonoscopy.

RESULTS: A total of 9228 subjects were invited for consecutive screening with a maximum of 3 rounds of FIT screening. Participation was 62.6% in the first, 63.2% in the second and 64.6% in the third screening round (p=0.013). In total, 2910 participants attended all screening rounds. The overall positivity rate (PR; proportion of participants with a positive FIT) was 8.4% in the first, 6.0% in the second and 5.8% in the third screening round (p<0.001). The overall detection rate (DR; proportion of participants with advanced neoplasia) was 3.3% in the first, 1.9% in the second and 1.1% in the third screening round (p<0.001). The overall positive predictive value (PPV; proportion of participants who underwent colonoscopy with advanced neoplasia) was 40.7% in the first, 33.2% in the second and 21.5% in the third screening round (p=0.007).

Table 1: FIT characteristics per screening round

	Round 1	Round 2	Round 3	*P*
Attendance	62.6%	63.2%	64.6%	0.013
Positivity rate	8.4%	6.0%	5.8%	<0.001
Detection rate	3.3%	1.9%	1.1%	<0.001
Positive predictive value	40.7%	33.2%	21.5%	0.007

CONCLUSION: The participation to FIT screening increases with successive screening rounds. This implies that repeated FIT screening is acceptable on a population level. A decline in detection rate is seen over three successive screening rounds, suggesting that consecutive FIT screening has a beneficial effect on decreasing the prevalence of advanced neoplasia. The majority of these lesions are detected in the first screening round.
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Disclosure of Interest: None Declared
Keywords: colorectal cancer screening, fecal immunochemical test

P944 COMPARISON OF TWO FAECAL OCCULT BLOOD TEST CUT-OFF VALUES IN COLORECTAL CANCER SREENING

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INTRODUCTION: Faecal immunological blood tests (FITs) are the recommended tests for colorectal cancer (CRC) screening, yet the standardization of the tests, including the cut-off values is still remaining an open issue.
Objective is to compare the positivity and lesion detection rates between two FITs with identical cut-off values.
AIMS&METHODS: Within the pilot-study conducted in Latvia two target groups aged 50-74 years were offered FIT testing; 4899 individuals were offered FOB Gold (Sentinel Diagnostics, Milan, Italy), but 4871 – OC-Sensor (Eiken Chemical Co., Tokyo, Japan) tests. Here, we report the test-positivity rates with the following cut-off values – 50, 75, 100, 150 and 200 ng Hb/ml buffer as well as advanced lesion detection rates (cancer+advanced adenoma) in each of the subgroups.
RESULTS:

Faecal immunological blood test

	Cut-off value (ng Hb/ml buffer)	50	75	100	150	200
FOB Gold	Positive tests*	305	233	198	162	134
	Adequately reported colonoscopies**	150	117	97	76	60
	Advanced lesions**	27	25	23	21	20
OC-Sensor	Positive tests*	191	136	119	96	80
	Adequately reported colonoscopies**	94	61	50	38	31
	Advanced lesions**	26	20	16	14	12

* p between tests <0.001 with all cut-off values
** p between tests >0.05 with all cut-off values

44.7% of FOB Gold and 47.4% OC-Sensor tests got returned. The positivity rate with 50 ng/ml cut-off was 13.9% for FOB Gold and 8.3% for OC-Sensor ($p<0.001$), similarly with all the other cut-off values FOB Gold showed substantially higher positivity. At the same time there was no difference in advanced lesion detection rates between the groups – 27 cases with advanced lesions were detected in the FOB Gold group, but 26 – in the OC-Sensor group. To detect these lesions 150 adequately reported colonoscopies were performed in the FOB Gold group and 94 – in the OC-Sensor group.
CONCLUSION: Similar numbers of advanced colorectal lesions were identified with identical cut-off levels with FOB Gold and OC-Sensor tests at the cost of higher test positivity rate and necessary colonoscopy number in the FOB Gold group.
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Disclosure of Interest: None Declared
Keywords: faecal immunochemical test, Screening

P945 DNA METHYLATION BIOMARKERS FOR NON-INVASIVE DIAGNOSTIC OF COLORECTAL CANCER

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INTRODUCTION: The aim of the present study was to identify a panel of methylation markers useful for diagnosis of colorectal cancer (CRC) in stool DNA. Additionally, we analyze the methylation status of selected genes as a risk marker for CRC in IBD patients.
AIMS&METHODS: For the *discovery phase* we assessed DNA methylation levels using the Illumina® GoldenGate Methylation Cancer Panel I microarray (to assay 1.505 CpG sites selected from 807 genes) in 92 sporadic CRC patients. An *in silico* validation was performed for the selected probes using public datasets GSE17648 and GSE29490 (Infinium HumanMethylation27 BeadChip array). The *biological validation* of the selected methylation biomarkers was performed by pyrosequencing in three independent groups of samples: 1) 62 tumors, 32 normal-appearing adjacent mucosa and 87 stool samples were tested from 126 sporadic CRC patients. 2) 25 FFPE biopsies from surgical resections of patients with IBD-associated neoplasia. 3) colonic biopsy specimens from 39 healthy subjects. As a reference we also evaluate two previously described methylation-based markers (*Vimentin* and *Septin 9*) in a subset of these samples.
RESULTS: After *discovery phase* and *in silico* validation, three genes (*AGTR1, WNT2* and *SLIT2*) were validated in stool DNA of affected patients with a detection sensitivity of 78% (50/64). DNA methylation of *VIM* and *SEPT9* in stool samples yield sensitivities of 55% (18/33) and 20% (7/35) respectively. In tissue 95% of sporadic carcinomas (57/60) were positive for at least one methylation marker. In IBD-associated neoplasia we found 93% of neoplastic tissues (13/14) positives. The prevalence of methylation in adjacent non-neoplastic mucosa in IBD-associated neoplasia was also higher than in mucosa from healthy controls (14/17; 82% vs 4/38; 11%; $p<0.001$).
CONCLUSION: This novel panel of specific methylation markers can be useful for diagnosis of CRC using stool DNA from CRC patients, and may help in the follow-up of high-risk IBD patients.
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Disclosure of Interest: None Declared
Keywords: Biomarkers, Colorectal Cancer, Early Detection, Inflammatory bowel disease (IBD), Methylation, Pyrosequencing

P946 PREVALENCE AND VARIABILITY OF SERRATED ADENOMA DETECTION RATES IN GREEK PATIENTS UNDERGOING SCREENING COLONOSCOPY

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INTRODUCTION: Adenoma detection rate (ADR) is a validated quality indicator of screening colonoscopy. The emerging problem of missed lesions in the right colon has prompted the study of nonhyperplastic serrated adenoma detection rates (SDR), and especially proximal serrated polyps detection rate (PDR).
AIMS&METHODS: All 1445 screening colonoscopies performed by 5 experienced endoscopists in the years 2011-2012 were retospectively reviewed, as part of an internal quality enhancement programm. Examinations with poor preparation were excluded, only if the endoscopist suggested that the examination should be repeated immediately. Colonoscopies performed by an endoscopist with less than 50 examinations per year were also excluded. Completion rates and withdrawal times were not taken into account. ADR, SDR, PSDR were assessed and Pearson linear coefficients were calculated to explore possible assosiations between them.
RESULTS: 1393 average risk patients were evaluated: mean age was 63.6 years, 57% were female. Mean adenoma detection rates were 35% in men, 23% in women, and 28% in total. SD: 5.9%, LDL (95%): 21%, UDL (95%): 36%. SDR and PSDR were 1.8% and 0.8% respectively. No correlation between ADR and SDR (r:-0.334 p:0.583) or between ADR and PSDR (r:-0.470 p:0.425) was observed.

	ADR male	ADR female	ADR total	SDR	PSDR
Endoscopist A	36/98	36/128	72/226	6/226	1/226
Endoscopist B	57/157	31/175	88/332	2/332	0/332
Endoscopist C	60/131	41/145	101/276	5/276	3/276
Endoscopist D	43/124	45/216	88/340	5/340	3/340
Endoscopist E	23/115	31/156	47/219	6/219	3/219
Total	215/599	181/794	496/1393	24/1393	10/1393

CONCLUSION: Lack of any correlation between ADR and SDR/PSDR poses limitations to the use of ADR as a sole quality indicator of screening colonoscopies in a real life setting. Further improvement in the histopathologic and endoscopic recognition of serrated lesions is required. PSDR/SDR may be an additional, more stringent marker of high quality colonoscopy.
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Disclosure of Interest: None Declared
Keywords: adenoma detection rate, serrated adenoma detection rate

P947 ANALYSIS OF THE ENDOCYTOSCOPIC IMAGE OF COLORECTAL LESION FROM THE ASPECT OF MICRO VASCULAR PATTERN

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INTRODUCTION: Endocytoscopy (EC) is an ultra-magnification technique, which can be performed to evaluate structural and cellular atypia with observation of lumens and nuclei in the surface layer of the mucosa[1,2]. EC has made it possible to diagnose living tumor cells in vivo and to obtain an ultra-magnification pathological image simply by applying the scope to the target mucosa during an endoscopic examination. On the other hands, analysis of the surface microvessels of colorectal lesions using magnifying narrow-band imaging is useful for identifying the appropriate treatment method for colorectal lesions. In addition, the surface microvessels can be analyzed using EC.
AIMS&METHODS: The aim of this study was to investigate whether the observation of surface microvessels using EC was useful in predicting the histopathology of colorectal lesions. The study included 193 patients who underwent complete colonoscopy and endoscopic or surgical treatment between April

Table: P948

	Dukes' Stage A		Dukes' Stage B		Dukes' Stage C		Dukes' Stage D	
	Screen	**Interval**	**Screen**	**Interval**	**Screen**	**Interval**	**Screen**	**Interval**
Gender	No Difference		No Difference		**More Men**	**More Women**	No Difference	
Deprivation Level	No Difference		No Difference		No Difference		No Difference	
ASA Grade	No Difference		No Difference		No Difference		No Difference	
T Stage	No Difference		**More T3**	**More T4**	No Difference		No Difference	
N Stage	N/A		N/A		**More N1**	**More N2**	No Difference	
Tumour Site	No Difference		No Difference		**More Left-Sided**	**More Right-Sided**	No Difference	
Survival Rate	No Difference		No Difference		**Better**	**Worse**	**Better**	**Worse**

2006 and January 2013. A total of 220 lesions (10 normal mucosae, 10 hyperplastic polyps, 135 adenomas, and 65 submucosally invasive cancers) were retrospectively evaluated. The colonic surface micro-vascular patterns observed using EC were classified into the following 3 groups: EC-V1, the surface microvessels were obscure ; EC-V2, the surface microvessels were clearly observed, and their caliber and arrangement were uniform; and EC-V3, the surface microvessels were thick, and their caliber and arrangement were non-homogeneous.
RESULTS: The EC-V1 group included all the normal mucosae and hyperplastic polyps, whereas 88.5% (131/148) of EC-V2 lesions were adenomas and 94.1% (48/51) of EC-V3 lesions were invasive cancers.
CONCLUSION: Vascular patterns of colorectal cancers observed by endocytoscopy were useful in predicting the histopathology of colorectal lesions.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, Endocytoscopy, narrow band imaging

P948 SCREEN-DETECTED COLORECTAL CANCERS ARE ASSOCIATED WITH AN IMPROVED OUTCOME WHEN COMPARED WITH INTERVAL CANCERS WHEN MATCHED FOR STAGE

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INTRODUCTION: Colorectal cancers detected through the NHS Bowel Cancer Screening Programme (BCSP) have been shown to have a more favourable outcome compared to non-screen detected cancers. The aim of this study was to identify whether this was solely due to the earlier stage shift of these cancers, or whether there were other factors involved.
AIMS&METHODS: A combination of a regional colorectal cancer registry (Northern Colorectal Cancer Audit Group) and the BCSP database were used to identify screen detected cancers and interval cancers (diagnosed after a negative faecal occult blood test, before the next screening round). All cancers were diagnosed between April 2007 and March 2010, within the North East of England. For each Dukes' stage, patient demographics, tumour characteristics, and survival rates were compared between the screen detected and interval cancer groups.
RESULTS: 322 screen detected cancers were compared against 192 interval cancers.
Significant differences highlighted in bold, $p < 0.05$. Mean follow-up 32 months.
CONCLUSION: With equivalent patient demographics and tumour characteristics, the improved survival of screen detected cancers over interval cancers for Stages C and D suggest that there may be a biological difference in the cancers in each group. Although lead-time bias may have a role, this may be related to a tumours propensity to bleed and therefore may reflect detection through current screening tests.
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Disclosure of Interest: None Declared
Keywords: Screening, Survival Rate

P949 EFFECT OF MEDICATION USE ON FAECAL OCCULT BLOOD TEST POSITIVITY IN THE NHS BOWEL CANCER SCREENING PROGRAMME

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INTRODUCTION: Faecal occult blood test (FOBt) positivity is linked with both tumour site and gender. Left sided cancers, and cancers in men are detected in significantly greater proportions by screening. The aim of this study was to evaluate for an association with certain medication use at time of test, with the FOBt result, in patients diagnosed with a colorectal cancer.
AIMS&METHODS: Using a regional colorectal cancer dataset (Northern Colorectal Cancer Audit Group) and Bowel Cancer Screening Programme database, all screen detected and interval cancers (diagnosed after a negative faecal occult blood test, before the next screening round) were identified. Diagnosis date was between April 2007 and March 2010. General Practitioners for each patient were asked to complete a proforma detailing use of hormone antagonists, hormone replacement therapy, anticoagulants, aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), and pre cancer diagnosis cholecystectomy. Medication use within two months of performing a FOBt was deemed positive. Chi-squared and logistic regression analyses were used.
RESULTS: Of 514 patients, 346 (67.3%) proformas were returned and suitable for analysis. 120 patients analysed were in the interval cancer group, with 226 in the screen detected cancer group. Between screen detected and interval cancers groups, no difference was found in the use of hormone antagonists, hormone replacement therapy, anticoagulants, and aspirin. Rates of cholecystectomy were equivalent. The use of non-aspirin NSAIDs within two months of test was seen in a significantly greater proportion in the screen detected cancer group (10.6% vs. 4.2%, p=0.039). For the population who used NA-NSAIDs, there was no difference between groups in gender, tumour location, or stage of tumour.
CONCLUSION: The use of NA-NSAIDs around the time of test was associated with a greater rate of positivity of the FOBt. This finding adds to our understanding of factors influencing the positivity of FOB testing, and may be useful in understanding the rates of interval colorectal cancers within the screening programme.
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Disclosure of Interest: None Declared
Keywords: medications, Screening

P950 INTEROBSERVER AGREEMENT IN THE ENDOSCOPIC CLASSIFICATION OF COLORECTAL LATERALLY SPREADING TUMORS: A MULTICENTER STUDY AMONG EXPERTS AND TRAINEES

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INTRODUCTION: The risk of cancer varies with the subtype of the colorectal laterally spreading tumors (LST). However, there are variable visual interpretations among endoscopists.
AIMS&METHODS: The aim of this study was to evaluate interobserver agreement and accuracy for endoscopic classification of LST subtypes among experts and trainees. Forty LST images were collected and independently reviewed by 14 gastroenterology experts and 10 trainees. All investigators recorded their findings as one of the four categories (homogeneous, nodular mixed, flat elevated, and pseudodepressed). Agreement was expressed by a kappa estimate (k). The accuracy was assessed by agreement with gold standard which was based on the gross morphology of resected specimen.
RESULTS: 41 (45.1%) out of the possible 91 pairwise k estimates among experts were greater than 0.75, indicating excellent agreement while only 2 (4.44%) out of the 45 pairwise k estimates among trainees were greater than 0.75. The mean kappa value was 0.73 (range 0.54–0.86) for experts and 0.56 (range 0.36–0.83) for trainees. The agreement for individual LST subtype in trainee group were significantly lower than those in the expert group, except LST subtype of flat elevated which showed similar agreement between two groups (0.96 vs. 0.94). Also, the overall accuracy of LST was higher in experts ($k = 0.811$) than in trainees ($k = 0.620$).
CONCLUSION: The interobserver agreement and accuracy for LST subtype classification were different between experts and trainees. Implementation of adequate training system is necessary for beginners to better identify colorectal LST.
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Disclosure of Interest: None Declared
Keywords: Interobserver agreement, laterally spreading tumor

P951 A COMPARISON OF ENDOSCOPIC TREATMENTS IN RECTAL CARCINOID TUMORS

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INTRODUCTION: Various endoscopic techniques for rectal carcinoid tumor have been developed recently. In this study, we compared the outcomes among conventional endoscopic mucosal resection (EMR), two-channel EMR, and EMR after circumferential precutting (EMR-P).
AIMS&METHODS: From March 2004 to January 2013, the medical records of 140 patients who were treated by endoscopic procedure for rectal carcinoid tumor in Seoul National University Bundang Hospital were investigated retrospectively. The characteristics of patients and tumors, selection of treatment method, complete resection rate and complication were analyzed retrospectively.
RESULTS: The mean age was 45.5 (range, 28-74 yrs), and the number of male patients was 88 (62.9 %). The mean tumor size was 5.1 ± 2.4 (1-14) mm and mean distance from anal verge was 7.0 ± 2.9 (1-16) cm. Forty-two patients were treated by EMR, 65 by 2 channel-EMR and 33 by EMR-P. The mean procedure time of EMR, 2 channel-EMR and EMR-P was 291.6 ± 220.0 sec, 389.4 ± 237.3 sec and 442.9 ± 179.7 sec, respectively. Post hoc analysis showed a significant difference in the mean procedure time between EMR and EMR-P ($P = 0.012$). Endoscopic complete resection was achieved in all cases. But histologic examination showed positive lateral or deep resection margins in 38 out of 140 patients (27.1 %). Multivariate analysis showed that 2-channel EMR method and EMR-P method were independent factors for the prediction of margin positive, with odds ratios of 0.11 and 0.11 with 95% confidence interval [CI], 0.04-0.32 and 0.03-0.38, respectively.
CONCLUSION: For the optimal endoscopic treatment of rectal carcinoid tumor, 2-channel EMR and EMR-P are more effective than conventional EMR in the meaning of margin status. Although EMR-P needs more time than the conventional EMR, the effectiveness of treatment offsets EMR-P's disadvantage of time consumption.
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Disclosure of Interest: None Declared
Keywords: conventional EMR, EMR after circumferential precutting, EMR-P, rectal carcinoid tumor, two-channel EMR

P952 LONG-TERM OUTCOME OF BRIDGE-TO-SURGERY COLONIC STENTING STRATEGY IN PATIENTS WITH MALIGNANT LARGE BOWEL OBSTRUCTION.

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INTRODUCTION: Bridge-to-surgery stenting (BTSS) has been advocated as a potential strategy to manage obstructing colonic cancer. Stent-related tumor-cell seeding and dissemination is the main long-term safety concern.
AIMS&METHODS: Long-term outcome and survival of patients treated with BTSS.
This is a retrospective, cohort, multicenter study. Patients operated with curative intent after BTSS from January 2003 to April 2008 in four tertiary referral centers were included. Data were extracted from medical records, updated after telephone contact with the patients, their relatives or family physician, and analyzed on an intention-to-treat basis according to the study outcomes.
RESULTS: Overall 68 consecutive patients (pt) were included (38 male; 30 female, median age at the onset of obstruction 73 years) which were followed for a median of 41 months (range 1-89). Tumor staging resulted as follows: stage I: 2 pt (2.9%); stage II: 20 pt (29.5%); stage III: 30 pt (44.1%;); stage IV: 16 pt (23.5%). Technical success of stent placement was 97.1%. Median time from stent placement to surgery was 8 days (range 1-257). Four patients (5.9%) underwent laparoscopic surgery while 94.1% pt underwent open surgery. In 4 pt (5.9%) a temporary stoma was effectuated following stent-induced perforation or incomplete relief of obstruction. Early perforation rate following BTSS was 4.4% (3/68). Six patients (8.8%) received neo-adjuvant chemotherapy whilst adjuvant therapy was administered in 39 patients (57.3%; six pt received biologic drugs). Tumor recurrence was observed in 24 patients (35.2%) after a median of 20 months (range 3-40) from surgery, sooner on the group receiving adjuvant chemotherapy (median 14 months; range 3-40). Twenty-nine patients (42.6%) had died at the end of follow-up. Of these 19 (65.5% of deaths; 27.9% of total pt) died from disease progression. Five-year overall survival was 57.4% while five-year disease-free disease was 44.1%. At multivariate analysis, only advanced stage of disease (stage III and IV) was significantly associated to tumor recurrence and fatal outcome.
CONCLUSION: To date this is the largest study reporting the 5-year outcome after bridge-to-surgery stenting. More than 50% of patients in this study were still alive at the end of follow-up. Overall survival, disease-free survival and death are comparable to literature data on patients with same stage of disease, operated in an elective manner.
Disclosure of Interest: None Declared
Keywords: Bridge to surgery stenting, Colorectal cancer

P953 CURCUMIN POTENTIATES AN ANTIPROLIFERATIVE EFFECT OF 5-AZA-CDR WITHOUT INTERFERING WITH ITS DNA HYPOMETHYLATING EFFECT

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INTRODUCTION: Colorectal cancer (CRC) is the result of multiple genetic and epigenetic alterations. Accumulating evidence indicates that epigenetic-modifying drugs may be useful in cancer prevention and treatment of malignant conditions. DNMT inhibitors, such as 5-aza-2'-deoxycytidine (5-aza-CdR) induce reactivation of the silenced genes through promoter DNA hypomethylation, however are associated with dose-dependent toxicity. Curcumin is one of the most effective dietary polyphenols and has been also shown to modify DNA methylation in CRC. Yet, concurrent application of both compounds has not been studied before.
AIMS&METHODS: The aim of our study was to evaluate the interaction of 5-aza-CdR and curcumin treatment on proliferation and on the DNA methylation in the CRC. Two CRC cell lines (RKO and HCT116) were treated with different concentrations of curcumin and 5-aza-CdR and alone and in combination. Proliferation analyses were performed using MTT assay. Global (LINE-1), and gene-specific methylation analysis was carried out using quantitative bisulfite pyrosequencing. The functional validation of the methylation-dependent gene expression changes was determined by quantitative RT-PCR (ex. miR-137, MLH1, UCHL1).
RESULTS: Both 5-aza-CdR and curcumin inhibited proliferation of CRC cells in concentration-dependent manner in vitro. However, the combination of both drugs in comparison to single drug treatment, resulted in stronger inhibition of proliferation (60% and 45% vs. 32% for RKO and 42% and 49% vs. 26% for HCT116, $p<0.001$, for 5-aza-CdR and Curcumin vs. combination, respectively). As expected, 5-aza-CdR, but not curcumin, lead to global (LINE-1) and gene-specific hypomethylation and subsequently to re-expression of genes (ex. miR-137, MLH1 etc.). The simultaneous treatment of CRC cells with 5-aza-CdR and curcumin was associated with similar or stronger induction of DNA hypomethylation and corresponding gene expression changes, but not when curcumin was given 24h prior to the 5-aza-CdR treatment.
CONCLUSION: Our results provide valuable information on the interaction of 5-aza-CdR and curcumin in CRC cells in vitro supporting concurrent use of those drugs. Simultaneous application of 5-aza-CdR and curcumin leads to a stronger inhibition of tumor cell proliferation without affecting the effectiveness of 5-aza-CdR to induce promoter DNA hypomethylation and gene expression. This study provides rational for the further systematic analyses in vivo.
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Disclosure of Interest: None Declared
Keywords: 5-aza-CdR, Colorectal Cancer, Curcumin, DNA methylation, LINE-1

P954 DEPTH OF INVASION IS A SIGNIFICANT PROGNOSTICATOR IN STAGE II COLORECTAL CANCER.

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INTRODUCTION: The clinicopathological factors of recurrence in stage II colon cancer have been investigated.
AIMS&METHODS: This study aimed at investigating the factors which affect recurrence and survival in patients with stage II colorectal cancer. Our study comprised 206 stage II colorectal cancer patients that were surgically resected at our center from January 2005 to December 2009. Median observation period was 44 months. The patients were divided into 2 groups: recurrence group and non-recurrence group. Further, the following clinicopathological factors were retrospectively compared between two groups: lymphatic invasion, venous invasion, tumor size, depth of invasion, histological type, the number of dissected lymph node, tumor location and adjuvant chemotherapy.
RESULTS: See the table. Multivariate logistic regression analysis revealed that depth of invasion was related to a higher incidence of recurrence.
Table: Univariate analysis of factors

	Recurrence group (n=25)	Non-recurrence group (n=181)	P value
Lymphatic invasion	22 (88%)	133 (71%)	0.142
Venous invasion	21 (84%)	150 (83%)	0.999
Tumor size (more than 39mm)	16 (64%)	102 (56%)	0.469
Depth of invasion (pT4)	7 (28%)	16 (9%)	0.004
Histological type (muc, por)	1 (4%)	9 (5%)	0.999
Preoperative CEA level (more than 5.0 ng/ml)	3 (12%)	34 (19%)	0.999
The number of dissected lymph node (more than 11)	18 (72%)	131 (72%)	0.935
Tumor location (Rectum)	7 (32%)	35 (19%)	0.174
Adjuvant chemotherapy	5 (20%)	38 (21%)	0.908

CONCLUSION: Depth of invasion is a significant prognosticator in stage II colorectal cancer.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, Stage II

P955 SENSITIZATION OF COLON CANCER STEM CELLS TO CHEMOTHERAPY BY ER STRESS INDUCED DIFFERENTIATION

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INTRODUCTION: In cancer, a small subpopulation of cells, is responsible for tumor-initation and -growth. These so called cancer stem cells (CSCs) are more resistant to chemotherapy than differentiated tumor cells, that represent the bulk of the tumor. We recently showed that normal intestinal epithelial stem cells experience very low levels of Er stress and that ER stress induces the earliest steps in stem cell differentiation (Heijmans et al Cell Rep. 2013). We hypothesized that induction of ER stress may force CSCs into a more differentiated state, which could sensitize them to the effects of chemotherapy.
AIMS&METHODS: We used a previously described cancer stem cell culture (Vermeulen et al Nat Cell Biol 2010) with a TCF/LEF driven GFP reporter for Wnt signaling activity. This allowed us to compare cancer stem cells (GFP-high) with more differentiated cancer cells (GFP-low) within the same experiment. ER stress was induced with SubAB (1000ng/μl), a toxin that specifically depletes GRP78, the major ER chaperone. Stemness of the GFP-high cells was determined using gene arrays to examine expression of a previously published colon cancer gene set (De Souza Cell Stem Cell 2011), qPCR, a matrigel differentiation assay and a limiting dilution assay. Sensitivity to oxaliplatin (50 uM) induced apoptosis was determined using a FACS based cleaved Caspase-3 assay.
RESULTS: Induction of ER stress revealed loss of stem cell markers OLFM4 and LGR5 and downregulation of the previously described colon cancer stem cell gene set, NES -1.54, $P<0.001$. When treated with subAB for 24 hours, clonogenic capacity of GFP-high cells was markedly reduced (1.3% vs 20.8% sphere initiating cells). In matrigel 3D culture SubAB treatment dramatically increased the percentage of differentiated spheres (90% vs 11%, $p<0.001$). GFP-high cells where more resistant to oxaliplatin induced apoptosis that GFP-low cells (23% vs 47% respectively). Treatment for 24 hours with SubAB alone did not induce apoptosis in GFP-high cells but increased their sensitivity to oxaliplatin induced apoptosis to that observed in GFP-low cells (42% vs 51%).
CONCLUSION: ER-stress forces colon cancer stem cells into differentiation and sensitizes CSCs to oxaliplatin induced apoptosis. ER stress inducing agents may be developed as adjuvants in chemotherapy of colorectal cancer.
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Disclosure of Interest: None Declared
Keywords: chemoresistance, chemosensitivity, colon cancer, ER stress, Stem Cells, Wnt

P956 SURGICAL OUTCOME OF SCREEN-DETECTED ENDOSCOPICALLY-TREATED MALIGNANT POLYPS: DATA FROM A NORTHERN ITALIAN REGISTER

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INTRODUCTION: Although more and more experience is being gained and published concerning indications to surgical radicalization after endoscopic resection of colo-rectal polyps or flat lesions considered at high risk, the issue still relies on clinical experience with no prospective controlled trials available. Residual disease at surgery in such patients has been recently reported in the region of 18% (Gill, Scotland, 2012) and 15% (Kim-Kwang, South Korea, 2013).
AIMS&METHODS: We have collected and evaluated data on endoscopically-resected malignant polyps coming from the first round of colo-rectal screening series of a few centres of Northern Italy, with the aim of creating a common register, analysing endoscopic and surgical results and the future intent to homogenize histological reports and clinical behaviours.
RESULTS: Six centres have so far participated to the study: Trento/Rovereto, Padova (Ospedale Sant'Antonio), Bussolengo (Verona), Torino (Ospedale Molinette), Bassano (Vicenza) e Feltre (Belluno).
251 malignant polyps have been treated endoscopically during the first round of respective screening campaigns.
133 have been sent to radicalization surgery, according to high risk attribution (53%).
Their site distribution was the following: rectum 24.2%, left colon 56.1%, right colon 19.7%.
The mean number of resected lymph-nodes at surgery was 7.8 (range 0-37)
At surgical intervention the Dukes' classification was the following: A: 91.7%; B1: 1.5%; C1: 6.8%.
CONCLUSION: In this multicentre northern Italian screening series, site distribution and rate of surgical radicalization in endoscopically-resected colo-rectal malignant polyps is in keeping with most international data. The number of lymph-node removed at surgery is sub-optimal according to published guidelines, which suggest to resect and send to pathologist at least 12 nodes. The rate of residual disease at surgery in high-risk malignant polyps turned out to be lower than reported in recently published series.
These last data deserve particular attention in a screening environment and – in this regard - a multicentre histological re-evaluation of endoscopic samples prior to risk attribution is in progress.
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Disclosure of Interest: None Declared
Keywords: Endoscopically-treated malignant polyps, Radicalization surgery

P957 FAMILIAL ADENOMATOUS POLYPOSIS: WHICH SURGICAL OPTION?

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INTRODUCTION: Prophylactic surgery in patients with Familial Adenomatous Polyposis (FAP) comprises two approaches: total colectomy with ileo-rectal anastomosis (IRA) and total proctocolectomy with ileo-pouch anal anastomosis (IPAA). The choice can be determined by the experience of the center, as well as the age, phenotype and the wish of the patient to have children.
AIMS&METHODS: Our objective was to evaluate surgical option (IPAA vs IRA) in FAP patients in a specialized center and relate preoperative variables to postoperative outcomes. Demographic and clinical data on patients with FAP submited to surgical treatment and followed in regular consultation were retrospectivelycollected.
RESULTS: Of 67 patients with a mean age of 47.3 years (20-83), 58.2% were female and in 83.6% of cases APC gene mutation was identified. In 16.4% desmoid tumors were recognized and 26.9% had duodenal adenomas. With an mean age of 34.2 years-old, 77.6% (n=52) underwent total colectomy with IRA and 22.4%(n=15) underwent total proctocolectomy with IPAA. Among patients submitted to IRA or IPAA, there were no differences related to sex, age, identification of APC mutation, severity of colonic polyposis, rectal polyposis and postoperative follow-up polyps. IRA patients had less desmoid tumors when compared to patients with IPAA (9.3% vs. 40.0%, $p = 0.012$), less duodenal adenomas (15.4% vs. 67.7%, $p < 0.001$), had fewer complications related to surgery (5.8% vs 46.7%, $p = 0.001$), fewer surgical reinterventions (11.5% vs. 40.0%, $p = 0.020$), needed more endoscopic surveillance (12.5 vs 4.3 exams, $p < 0.001$) and did not have lower birth rates (7.7% vs 40.0%, $p = 0.006$). Only one patient submited to IRA required reoperation for rectum adenocarcinoma.
CONCLUSION: We didńt verify a clear association with some classic factors related to IRA and IPAA indication. IPAA patients had more complications related to the pouch, higher need for surgical reintervention, but not a lower birth rate. Similar long-term results are achieved with both options.
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Disclosure of Interest: None Declared
Keywords: Familial adenomatous polyposis (FAP), surgical treatment

P958 CZECH NATIONAL COLORECTAL CANCER SCREENING PROGRAM: QUALITY CONTROL OF 107,876 PREVENTIVE COLONOSCOPIES

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INTRODUCTION: The National Colorectal Cancer Screening Programme in the Czech Republic has been introduced in 2000, focused on asymptomatic individuals. Since the beginning of 2013, only immunochemical fecal occult blood tests (FIT) and preventive colonoscopies are recommended. In age 50 – 54, annual FIT is offered, followed by FOBT+ colonoscopy, if positive. In age of 55, there is a choice of either FIT biannually or screening colonoscopy in 10 years interval.
AIMS&METHODS: Three main indicators have been used to assess the quality control of screening colonoscopies – adenoma detection rate (ADR), advanced adenoma detection rate (aADR) and cecal intubation rate (CIR). These indicators have been compared to European guidelines (published in 2010). Other quality indicators of all preventive colonoscopies (positive predictive value, endoscopic complications) have been measured.
RESULTS: Between January 2006 and April 2013, there have been 107,876 preventive colonoscopies performed: 92,449 FOBT+ colonoscopies (86.7%) and 15,457 screening colonoscopies (14.3%). Adenomas have been diagnosed in 31,497 patients within FOBT+ colonoscopy (34.0%; 48.1% of them with advanced adenomas) and in 3,874 patients within screening colonoscopy (25.1%; 29.4% of them with advanced adenomas). In all preventive colonoscopies 4,227 cancers have been registered. The overall cecal intubation rate has reached 96.2%. In years 2006 – 2012, there were 92 cases of perforations

(0.09% of all examinations) and 361 cases of bleeding during endoscopic polypectomies (0.76% of all therapeutic procedures) reported.
Table: Quality indicators of screening colonoscopies: comparison of Czech CRC Screening Program and European Guidelines

	Adenoma detection rate (ADR)	Advanced adenoma detection rate (aADR)	Cecal intubation rate
European Guidelines	14.9 – 37.5%	4.9 – 8.6%	90.0%
Czech Republic	25.1%	7.4%	97.7%

CONCLUSION: Preventive colonoscopies performed within the Czech National Colorectal Cancer Screening Program are safe diagnostic and therapeutic procedures. All of three main quality indicators of screening colonoscopies are comparable to European guidelines.
This project has been supported by the Czech Ministry of Health grant No. NT 13673
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Disclosure of Interest: None Declared
Keywords: colorectal cancer, Czech Republic, immunochemical fecal occult blood test, quality control, screening colonoscopy

P959 EICOSAPENTAENOIC ACID (EPA) EFFICACY FOR COLORECTAL ABERRANT CRYPT FOCI (ACF): A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL

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INTRODUCTION: Colorectal cancer (CRC) is one of the most commonly occurring neoplasms and a leading cause of cancer death worldwide, and new preventive strategies are needed to lower the burden of this disease. Eicosapentaenoic acid (EPA), the omega-3 polyunsaturated fatty acid that is widely used in the treatment of hyperlipidemia and prevention of cardiovascular disease, has recently been suggested to have a suppressive effect on tumorigenesis and cancer cell growth. Aberrant crypt foci (ACF), defined as lesions containing crypts that are larger in diameter and stain more darkly with methylene blue than normal crypts, are considered as a reliable surrogate biomarker of CRC. We conducted a prospective randomized controlled trial as a preliminary study prior to a CRC chemoprevention trial to evaluate the chemopreventive effect of EPA against colorectal ACF formation and the safety of this drug.
AIMS&METHODS: This study is a multicenter, double-blind, placebo-controlled, randomized controlled trial to be conducted in patients with both colorectal ACF and colorectal polyps scheduled for polypectomy. Twenty-four eligible patients were recruited for the study and the number of ACF in the rectum counted at the baseline colonoscopy. Then, the participants were allocated randomly to either one of two groups, the EPA group and the placebo group. Twelve patients in the EPA group received oral 900 mg EPA capsules thrice daily (total daily dose, 2.7 g per day), and 12 patients in the placebo group received oral placebo capsules thrice daily. After one month's treatment with EPA/placebo, colonoscopic examination and polypectomy were performed to evaluate the formation of ACF, and the cell-proliferative activity and cell-apoptotic activity in normal colorectal mucosa and colorectal polyps.
RESULTS: At polypectomy, the EPA group had a significant decrease in the mean number of ACF per patient (8.9 ± 4.5 before treatment versus 4.8 ± 2.3 at 1 month, $P = 0.003$), whereas the mean ACF number did not change significantly in the placebo group (7.7 ± 5.2 versus 8.9 ± 8.0, $P = 0.347$). The proliferating cell nuclear antigen index was significantly decreased and the apoptotic cell index was significantly increased in both normal rectal epithelium and polyps in EPA group patients.
CONCLUSION: This is the first study proposed to explore the chemoprevention effect of EPA against colorectal ACF formation in humans. For the future, we plan to conduct a long-term chemoprevention trial of EPA for colorectal adenoma or cancer.
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Disclosure of Interest: None Declared
Keywords: Aberrant crypt foci, chemoprevention, Eicosapentaenoic acid, RCT

P960 FROM THE POPLAR MECHANO-PERCEPTION TO VISCERAL SENSITIVITY IN MICE: ROLE OF UBIQUITOUS TRANSCRIPTION FACTOR EGR-4?

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INTRODUCTION: In a pathophysiological context such as inflammatory bowel disease or irritable bowel syndrome, perception of mechanical stimuli may be impaired in the colon, leading to colonic hypersensitivity. The perception of mechanical stimuli is common to many species whether animal or plant. Initially, works done on poplar by the MECA team of UMR PIAF identified a transcription factor involved in mechano-perception in plants. Bioinformatics analysis has then highlighted a homologous gene in mice, named EGR-4. The encoded protein has been described as a transcription factor which appeared to be involved in early perception of mechanical stimuli.
AIMS&METHODS: The aim of this study is to determine the EGR-4 localization and its involvement in the mouse colon sensitivity to a mechanical stimulus. For that purpose, wild-type and healthy mice were subjected or not to a colorectal distension (mechanical stimulus) for 10 seconds *via* inflation of a balloon inserted at 1cm from the anal margin. Then, we analyzed the expression of EGR-4 at different time points after the distension at the mRNA level in the colon, dorsal root ganglia (DRG) and spinal cord by quantitative RT-PCR and its cellular localization in DRG, and in colon after whole-mount dissection, by immunohistochemistry. We also identified targeted genes of this transcription factor in mouse colonic epithelial cells transfected by an EGR-4 expressing vector after microarray analysis.
RESULTS: EGR-4 transcription factor is localized in the colon, DRG and spinal cord cells. In addition, its expression is modified after colorectal distension in a time dependent manner. In the sub-mucosal plexus and myenteric plexus EGR-4 is co-localized with PgP9.5, a neuronal marker.
CONCLUSION: Our study indicates that EGR-4 is involved in colonic mechano-sensitivity and suggests its contribution to colonic hypersensibility, mainly associated to visceral chronic pain. Its co-localization with nervous fibers suggests a role in nervous transmission of mechanical perception and hypersensibility. This study opened new avenues in treatment of abdominal pain, by proposing new therapeutic targets to correct mechanical sensitivity disturbance.
Disclosure of Interest: None Declared
Keywords: EGR-4, Mechano-perception, Visceral hypersensitivity

P961 ABNORMAL INTESTINAL PERSISTENCE OF CD-ASSOCIATED ADHERENT-INVASIVE ESCHERICHIA COLI ENHANCES SPONTANEOUS VISCERAL HYPERSENSITIVITY

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INTRODUCTION: Crohn's disease is characterized by acute phases with moderate to severe intestinal inflammation, and chronic phases with colonic hypersensitivity and abdominal pain. This intestinal disease is believed to result from breakdown of homeostasis between intestinal microbiota and the mucosal immune system, with both environmental and genetic influencing factors. A number of studies of IBD in humans have described a functional class of *Escherichia coli* referred to as adherent invasive *E. coli* (AIEC) to be abnormally present in the ileum and associated with overexpression of the bacterial colonizing receptor CEACAM6.
AIMS&METHODS: We hypothesized that, depending on the level of intestinal AIEC colonization, mice will spontaneously develop a visceral hypersensitivity which will persist even after bacterial clearance and intestinal inflammation alleviation.
Transgenic mice overexpressing the human form of CEACAM6 protein and their wild-type littermates were orally infected by CD-associated AIEC bacteria (reference strain LF82) or by a non-pathogenic *E. coli* (MG1655). At 3, 9 and 21 days after infection, visceral hypersensitivity was assessed using a technique based on measuring electromyographic abdominal contractions induced by colorectal distension. This test is to induce, by progressive inflation of a balloon inserted into the colon, abdominal cramps whose amplitude is proportional to the colon sensitivity. Moreover, mice were euthanized and were assayed for intestinal inflammation level. Inflammation was monitored using anatomical indicators of colitis such as spleen and colon weight, and assessed by determination of the colonic myeloperoxidase activity and expression of systemic pro-inflammatory cytokines.
RESULTS: Human CEACAM6 overexpression in mice induced a significant decrease of the visceral hypersensitivity in comparison to their housekeeping WT mice. Otherwise, CD-associated AIEC LF82, but not non-pathogenic *E. coli* MG1655, infection dramatically quickly (D3) increased levels of visceral hypersensitivity in comparison to their housekeeping WT. Such visceral hypersensitivity persisted in mice overexpressing CEACAM6 receptor after bacterial clearance and did not match with intestinal inflammation.
CONCLUSION: Direct involvement of CD-associated AIEC LF82 infection in colonic hypersensitivity has been demonstrated. Thus, due to abnormal expression of their intestinal colonization receptor CEACAM6, increased intestinal persistence of such AIEC bacteria in CD patients may impact on colonic sensitivity.
Disclosure of Interest: None Declared
Keywords: Adherent-invasive E. coli, CEACAM6, IBD remissions, P2X receptors, Post-infectious IBS model

P962 INCREASED COLONIC BILE ACID EXPOSURE: A RELEVANT FACTOR FOR SYMPTOMS AND TREATMENT IN IRRITABLE BOWEL SYNDROME (IBS).

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INTRODUCTION: Bile acids may play a role in the pathophysiology of irritable bowel syndrome (IBS). Bile acid malabsorption (BAM) is commonly diagnosed by use of the ^{75}SeHCAT retention test or by measurement of the ratio between plasma C4 and cholesterol (C4/chol) as an expression of bile acid synthesis.
AIMS&METHODS: The aims of this study were to investigate if any GI symptoms (GSRS-IBS and bowel habits) in patients with IBS (Rome II criteria) correlated with ^{75}SeHCAT retention values or C4/chol ratio. Results were compared with healthy controls (^{75}SeHCAT n=29, C4/chol n=419). Stool frequency

and form (Bristol Stool Form Scale) was registered and oro-anal transit time (OATT) measured with radio-opaque markers. We also offered 8 weeks open label treatment with colestipol to patients with a ^{75}SeHCAT retention value <20%. Registration of IBS symptom severity (IBS-SSS) at baseline and every other week and a weekly question about adequate relief of IBS symptoms (yes/no) was done for evaluation.

RESULTS: We included 141 patients (102 females; mean age 35.3 (range 17-71) years) where 18.5% had ^{75}SeHCAT retention <10% and 16% had high C4/chol ratio. Patients had lower ^{75}SeHCAT retention and higher C4/chol ratio (p=.0001 for both) compared to controls. ^{75}SeHCAT retention was lower in IBS-D and IBS-A compared to IBS-C and healthy controls (p<.0001). There were no differences between IBS subtypes regarding C4/chol ratio. Positive correlations were seen between ^{75}SeHCAT retention and stool frequency (r=0.27; p=.001), stool form (r=0.19; p=.03) and OATT (r=0.496; p=.001), but not with any of the GSRS-IBS parameters. C4/chol ratio did not show any relevant correlations to bowel habits or other GI symptoms. Fifteen of the 27 patients who agreed to participate in the colestipol treatment were responders (55%) defined by adequate relief of IBS symptoms at week 7 and/or 8. IBS Symptom severity was reduced at the end of the last treatment week compared to baseline (IBS-SSS 220±109 vs. 277±106 (mean±SD); p<.0001).

CONCLUSION: Increased colonic bile acid exposure measured by ^{75}SeHCAT retention influence bowel habits and OATT in patients with IBS. Symptom reduction and a high response rate to open label treatment with colestipol supports this, but placebo-controlled studies are warranted.

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Keywords: bile acid binders, bile acid malabsorption, C4, FGF 19, IBS, Oroanal transit time

P963 A REGIONAL STUDY IN THE HUNT FOR ENTERIC NEURAL STEM CELLS

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INTRODUCTION: Enteric neuropathies remain a challenging group of diseases. Current management is mainly palliative driving research towards enteric nervous system (ENS) cell replenishment therapies using enteric neural stem cells (ENSCs). Human ENSCs have been isolated from colonic full thickness and mucosal biopsies, while mouse ENSCs have been derived from entire gut. It remains unclear as to which gut region should be targeted in order to best harvest ENSCs for transplantation.

AIMS&METHODS: The aim of this study was to determine the optimal region of the gut for the harvesting of ENSCs. The study used both wild-type as well as transgenic mice (Rosa26YFPstop:TgWnt1Cre), in which all the neural crest cells (NCCs) and their derivatives constitutively express yellow fluorescent protein (YFP). The presence and relative proportion of ENSCs was compared between Oesophagus, Stomach, Small intestine,Colon and Caecum. Methods used to determine this were,1. Fluorescence-activated cell sorting (FACS), which calculated the % of YFP+ cells per region (therefore % of NCC as a total of all cells derived from each region);2. Immunohistochemistry on gut sections and entire gut to characterise and calculate the proportion of NCC cells that were presumptive ENSCs (based on a Sox10+/S100- immunostaining profile; Sox 10 is a transcription factor expressed by neural crest cells and S100 a glial marker) and to count cells per high power field in each region.

RESULTS: The study revealed qualitative and quantitative differences in ENS across the regions. Gut wholemount and section immunochemistry revealed the most YFP, p75^{NTR} (NCC marker), Tuj1 (neuronal marker), Sox10 and S100 stained cells in the colon and caecum followed by small intestine then stomach and oesophagus. In all regions more immunostained cells (all markers) were noted in the myenteric rather than submucosal plexus. FACS sorting (n=3) demonstrated the highest percentage of YFP+ cells in the large intestine (colon - 6.33% and caecum - 7.96%) and lowest in the stomach (2.21%). Counting of Sox10 only cells from Sox10/S100 double-labelled sections in each region of gut also revealed that the caecum contained the highest number of progenitor cells (7.6%) followed by colon (2.2%) and the least in the stomach (0.7%) and oesophagus (0.4%).

CONCLUSION: Although present in all regions, ENSCs have the greatest density within caecum, followed by colon, progressively decreasing more proximally in the gut. Considering these findings and the balance between which region are likely to contain more progenitors as well as be easily accessible to harvest tissue, we suggest that future ENSCs studies should focus on the colonic region, including the appendix, which may be a potential niche for ENSCs.

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Disclosure of Interest: None Declared

Keywords: enteric nervous system, enteric neural stem cells

P964 DOES SHIFT WORK AFFECT COLONIC MOTILITY? A STUDY PERFORMED IN THE OCTODON DEGUS.

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INTRODUCTION: Recent evidences suggest that the circadian rhythm disruption that occurs in aging also plays a role in cellular senescence. Modern life is increasing the gap between personal habits and natural synchronizers, as people increasingly adopt nocturnal life modes. Premature aging in these conditions could be responsible for several digestive disturbances and associated pathologies. Contrary to humans, most rodents have nocturnal habits. *Octodon degus*, which mainly shows diurnal rythms, represents a valuable tool in order to make circadian cycle studies translational to human research.

AIMS&METHODS: To study whether lighting simulating rotating shift work causes changes in colonic.

18 *Octodon degus,* split into two groups, were used in this study. In order to emulate shift work, the chronodisrupted group was under weekly shifting illumination for three weeks, going back to standard light during the weekends. Control group received a standard 12h-light pattern. The physical activity and internal temperature of the animals were continuously recorded in order to determine their biological rhythms. Colonic motility was studied using isometric contractile recordings from proximal and distal colonic strips without the mucosal layer and spatiotemporal mapping of distal colonic segments.

RESULTS: Animal activity and internal body temperature were uncoupled from the light/dark cycle due to the weekly changes in the illumination. This circadian alteration translates into changes in the contractility of colonic strips. Thus, distal colon strips showed lower spontaneous activity in the chronodisrupted animals. In addition, the contractile response to depolarization induced by KCl was differentially affected depending on the region: proximal response decreased by 68% whereas distal strips showed an increase of 125%. Similar results were obtained with muscarinic agonist bethanechol. Regarding the response to electrical field stimulation (EFS), chronodisruption induced an overall decrease for all the frequencies tested. Pharmacological dissection suggests that circadian alteration predominantly affects the adrenergic and cholinergic components of the neural response. Finally, spatiotemporal mapping of distal colonic segments revealed that motility patterns remained mainly unaffected in the chronodisrupted animals.

CONCLUSION: Chronodisruption alters contractility in colonic muscular strips; however these changes do not necessary translate into colonic motility alterations. It could be possible that functional redundancy counteracts the effects observed in the strips, preventing alterations at colonic function levels.

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Disclosure of Interest: None Declared

Keywords: Chronodisruption, Colonic motility, Octodon degus

P965 LINACLOTIDE INDUCES SECRETION OF CGMP FROM MOUSE COLONIC EPITHELIUM

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INTRODUCTION: Linaclotide is a novel receptor guanylyl cyclase C (GC-C) agonist approved for treatment of abdominal pain and constipation in patients with irritable bowel syndrome with constipation (IBS-C). Linaclotide effects on bowel movements are mediated by intracellular cGMP produced upon activation of GC-C. It is hypothesized that the effects of linaclotide on abdominal pain are mediated by extracellular cGMP, which was shown to decrease the activity of pain-sensing nerves [1].

AIMS&METHODS: We used an *ex vivo* Ussing chamber assay to measure cGMP secretion from the mouse colonic mucosa in response to linaclotide treatment. Linaclotide-induced ion transport and epithelial barrier function were monitored by measuring short-circuit current (I_{sc}) and trans-epithelial electrical resistance (TEER).

RESULTS: Stimulation with linaclotide (1 uM) elicited a robust short-circuit current across mouse colonic epithelium. I_{sc} reached a maximum within ten minutes following stimulation with linaclotide and remained steady during the duration of the study (60 min). Treatment of colonic mucosa with linaclotide induced release of cGMP from the apical as well as the basolateral side of the epithelium. The time course of cGMP accumulation in the basolateral bath of the Ussing chamber was linear with an estimated cGMP secretion rate equal to 23 fmol/mińcm^2. The trans-epithelial electrical resistance of the colonic mucosa did not change over the course of the study indicating that the cGMP measured in the basolateral compartment after linaclotide stimulation is not diffusing from the apical compartment.

CONCLUSION: These findings demonstrate that linaclotide-stimulated mouse colonic epithelium secretes cGMP from both the apical and basolateral sides and that cGMP is present in the submucosal space to inhibit colonic nociceptors.

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Keywords: abdominal pain, cGMP, Guanylate Cyclase-C, linaclotide

P966 RADIAL STRETCH TO HUMAN COLONIC SEGMENT IN VITRO IDENTIFIES DIFFERENT FUNCTION BETWEEN THE RIGHT AND LEFT COLON

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INTRODUCTION: We previously demonstrated that the propagation patterns of contractions were different between the right and left colon in human. Since stretch is an important stimulus to evoke contractions in colon, we intended to determine whether there are any differences between the right and left colon with regards to the stretch reflex in human.
AIMS&METHODS: Colon segments of 5x3cm in size were obtained from the specimen of elective colon resections. Four steel clips were attached to each lateral margin of the colon in a direction that was orthogonal to the segment so as to record the activity of muscular contractions. Radial stretch was applied by intraluminal balloon distension of 9 Fr Foley catheters. Frequency (/min), amplitude (mN), and area under the curve (AUC, sec×mN/min) of muscle contractions were recorded before and after stretch intervention at the proximal and distal side of colon. Conventional microelectrode recordings for membrane potentials were performed using sharp microelectrodes.
RESULTS: Tension recordings on colonic segments were analyzed in tissues obtained from 50 patients (21 from the right and 29 from the left colon). Frequency (/min), amplitude (mN), and AUC (AUC, sec×mN/min) of contraction were 0.5±0.2, 13.9±7.0, and 263.2±128.5 in the right colon and 0.4±0.2, 21.9±16.3, and 357.5±225.5 in left colon, respectively. After radial stretch in the right colon, these variables increased to 0.6±0.2 (p=0.02), 22.5±16.6 (p=0.01), 387.4±129.5 ($p<0.001$) at the proximal side, and 0.6±0.2 (p=0.39), 19.6±10.1 ($p<0.001$), 369.0±197.7 ($p<0.001$) at the distal side, respectively. In the left colon, excitation of contractility after radial stretch was also observed at the proximal side, 0.6±0.2 ($p<0.001$), 23.1±16.1 (p=0.001), and 388.9±241.6 ($p<0.001$), but on the contrary, at the distal side, inhibition of contractions were recorded as follows, 0.4±0.1 (p=0.007), 17.5±11.0 ($p<0.001$), and 293.3±162.4 ($p<0.001$). The pattern of the contractility changes at the distal side were also significantly different between right and left colon segment (all $p<0.05$). In intracellular recordings after stretch intervention from the circular muscles, hyperpolarization (from -54.8±12.0 to -55±3.1mV) was noted at the distal side of the left colon, in contrast to depolarization at all other sites.
CONCLUSION: Our results indicate that radial stretch in human colon *in vitro* evoke excitatory contractions at both proximal and distal sides in the right colon and proximal side of left colon, but inhibits contractions in the distal side of the left colon. This may reflect the differences in functions between the right and the left colon.
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Disclosure of Interest: None Declared
Keywords: Colonic motility, Contraction, Radial stretch

P967 DEPLETION OF MURINE INTESTINAL MICROBIOTA BY ANTIBIOTICS: EFFECTS ON GUT TRANSIT AND TOLL-LIKE RECEPTORS EXPRESSION.

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INTRODUCTION: Alteration of intestinal microbiota, induced by infection, diet or antibiotics, is involved in intestinal disorders like Irritable Bowel Syndrome. In fact, disruption of the intestinal microbiota by antibiotics induces changes in gut sensory-motor function and immune activity[1]. Toll-like receptors (TLRs) play a pivotal role in sensing both pathogenic and commensal microorganisms. Thus, TLRs are critical for the initiation of inflammatory and innate immune responses.
AIMS&METHODS: The aim was to investigate the effects of the alteration of murine intestinal microbiota induced by antibiotics on gut transit. We also examined the expression of TLRs (1, 2, 3, 4, 5, 6, 7, 9 and 11) in the intestine from mice treated with antibiotics.
Female C57BL/10 mice of 5-8 weeks old were divided into two groups: control and treated with antibiotics (n=8). Mice were gavaged for 7 days with water (controls) or a combination of antibiotics (bacitracin 20 mg and neomycin 20 mg) and the antifungal substance pimaricin 5 μg per mouse and day (treated mice). Alteration of the gut microbiota was confirmed by measuring the load of bacterial DNA in feces by 16S rRNA gene quantitative PCR. The colonic transit was studied in mice fasted for 14 h and anesthetized with isoflurane before a glass bead was inserted 2 cm intrarectally. The latency to the expulsion of the bead was recorded. Afterwards, mice were individually housed and gavaged with an Evans blue marker and the latency to the detection of Evans blue in the droppings was recorded to determine the whole gut transit. TLRs gene expression (mRNA) was determined in ileum and colon by quantitative RT-PCR.
RESULTS: Mice treated with antibiotics had 370 fold less bacterial DNA in feces than controls, demonstrating depletion of the colonic microbiota. The treatment with antibiotics delayed the colonic (711.2 ± 147.6 s vs. 329.2 ± 90.2 s; $P \leq 0.05$) and whole gut transit (341.4 ± 13.9 min vs. 177.4 ± 21.08 min; $P \leq 0.001$) respect to controls. Mice treated with antibiotics showed a reduced expression of TLR2, TLR3 and TLR6 in ileum and TLR2 and TLR9 in colon. On the contrary, these animals showed an increased expression of TLR4, TLR5 and TLR9 in ileum and TLR3, TLR4, TLR6 and TLR7 in colon.
CONCLUSION: The treatment with antibiotics depletes the murine colonic microbiota and induces delay in gut transit. These functional changes are accompanied by downregulation or upregulation of TLRs mRNAs, depending on the segment of the gut.
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Disclosure of Interest: None Declared
Keywords: Antibiotics, intestinal motility, Microbiota, Toll like receptor

P968 IN CONSTIPATED IRRITABLE BOWEL SYNDROME (IBS-C) RESPONSE TO PRUCALOPRIDE IS ASSOCIATED TO A NORMALIZATION OF POSTPRANDIAL MODIFICATION OF RECTOSIGMOID TONE: PRELIMINARY DATA

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INTRODUCTION: Increased postprandial rectal tone is related to the occurrence of postprandial defecation (1): when contractions of the sigmoid colon present stool to the rectum in a high tone status (2), an increase in parietal tension occurs, heightening sensation, and providing the call to stool. In IBS, we have previously shown that postprandial recto-sigmoid tone modification is impaired, due to an altered activation of neural pathways (3). Moreover, in IBS-C patients, we have shown that the administration of serotoninergic agents improves this abnormality (4).
AIMS&METHODS: The aim of this work was to verify if responder patients to prucalopride treatment show an improvement of intestinal tone regulation. Eight female patients (mean age 33 years, range 25-38) with constipation-predominant IBS (IBS-C), diagnosed according to Rome III criteria, were studied. In all subjects, presence and severity of symptoms, number and consistency of daily evacuations (Bristol Stool Form Scale) and recto-sigmoid barostat test were evaluated. After an overnight fast, a double lumen polyvinyl tube with an adherent, infinitely compliant plastic bag (1200 ml capacity), finely folded, was inserted through the anus as far as the recto-sigmoid junction. The perception and discomfort thresholds were investigated during fasting and the postprandial period (200 Kcal, 200 ml liquid meal) by a series of isobaric distentions; at the end of each distention, patients were asked to assess the sensation using a standardized scale from 0 (no sensation) to 6 (pain), were 1=perception and 5=discomfort. During the test, we evaluated modification of rectosigmoid tone, as the difference between mean 60-min post-prandial volume and mean 30-min fasting volume. After prucalopride 2 mg/day for 4 weeks, a second evaluation of symptom assessment and recto-sigmoid tone was performed. A patient was considered as a responder if ≥3SCBM/week were achieved.
RESULTS: Four out of 8 patients showed a clinical response to prucalopride. In all, postprandial modification of recto-sigmoid tone improved at the end of the treatment (postprandial modification tone from +8±35% to -64±22%). No modification of sensitivity thresholds was evident after treatment. In the 4 non responder patients, no modification of postprandial rectosigmoid tone nor of sensitivity thresholds was evident.
CONCLUSION: These preliminary data show that in IBS-C, in responder patients to prucalopride treatment, the improvement of symptom severity is accompanied by an improvement of regulation of intestinal tone.
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Disclosure of Interest: None Declared
Keywords: IBS-C, prucalopride, RECTOSIGMOID TONE

P969 RECIPROCAL MYENTERIC NEUROTRANSMISSION IN THE CIRCULAR AND LONGITUDINAL MUSCLE LAYERS IN AGED HUMAN SIGMOID COLON

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INTRODUCTION: The postprandial propulsion of intestinal contents depends on the coordinated activity of circular and longitudinal smooth muscle brought about by the peristaltic reflex. The role of neuromuscular function in the contractility of the circular muscle layer has been extensively studied, but studies in the control of the human longitudinal one are lacking, specially in humans.
AIMS&METHODS: To unveil possible differences in the myenteric neurotransmission between both muscular layers of human sigmoid colon.
Macroscopically normal samples of human sigmoid colon were obtained from 6 patients (aged 60-87 yrs) who underwent surgery for rectal cancer. After removing mucosa and submucosal layers, circular muscle strips (10 x 4 mm) were cut with the long axis lying in the direction of the muscle fibres. Longitudinally orientated strips were taken after removing the circular muscle. *In vitro* contractility was recorded under basal conditions and electrical field stimulation (EFS, 0.3 ms, 350 mA, 0.2-10 Hz, for 60 s every 9 min). Statistical differences were determined by two-way ANOVA, followed by Bonferroni post-hoc test.
RESULTS: Isolated strips contracted rhythmically in the absence of stimuli, but circular strips had spontaneous contractions of higher frequency and amplitude than the longitudinal ones. The longitudinal muscle presented long-lasting giant contraction every 5 min. In the longitudinal muscle, EFS-induced responses at all tested frequencies but in the circular layer 2, 5 and 10 Hz had an inhibitory character, indicating a predominant inhibitory myenteric neurotransmission to the circular muscle. In keeping with this, after EFS a significant decrease in the basal tone and spontaneous activity was present only in the circular muscle. Blockade of excitatory cholinergic and adrenergic innervations caused a strong reduction in EFS-induced responses of the longitudinal layer, and the residual contraction was abolished by GR94800, a substance P blocker . However, in the circular layer these inhibitors had little effects and EFS-induced responses were reverted by blockade of nitrergic and purinergic inhibitory nerves that present mutual inhibition.
CONCLUSION: Activation of myenteric plexus of aged human sigmoid colon causes relaxation of the circular muscle but contraction of the longitudinal layer, which will favor peristaltic reflexes. The giant contractions that appear in the longitudinal layer could contribute to the progression of colonic content or act as a braking mechanism.
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Disclosure of Interest: None Declared
Keywords: ageing, circular muscle, longitudinal muscle, neurotransmission

P970 INHALED METHANE IS PREVENTING AN INCREASE IN NITRERGIC MYENTERIC NEURON DENSITY AND ENHANCED OXIDATIVE AND NITROSATIVE STRESS AFTER MESENTERIC ISCHEMIA-REPERFUSION IN RATS

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INTRODUCTION: The gastrointestinal tract is highly susceptible to hypoxic insults; therefore, the intestinal vascular failures are often accompanied by enteric neuropathy. We recently demonstrated that inhaled methane (CH_4) has potent anti-inflammatory effects in experimental mesenteric ischemia-reperfusion (IR), however, the impacts of exogenous CH_4 on the IR-induced enteric neuropathy has not been studied yet.
AIMS&METHODS: Therefore, we aimed to investigate the neuroprotective potential of inhaled CH_4 and to determine the parallel biochemical signs of reactive oxygen and nitrogen species generation in a rat model of mesenteric IR. Anesthetized rats were randomly divided into sham-operated control, IR and CH_4 treated IR groups. Superior mesenteric artery occlusion was maintained for 30 min and the subsequent reperfusion was monitored for 120 min. The animals inhaled normoxic artificial air (21% O_2) with or without 2.5% CH_4 during the last 10 min of ischemia and in the first 5 min of reperfusion. At the end of reperfusion, segments of the duodenum, ileum and colon were processed for quantitative histochemical and biochemical studies. The nitrergic and total neuronal density and the number of neurons containing neuronal and endothelial nitric oxide synthase (nNOS and eNOS, respectively) were evaluated by single and double-labelling immunohistochemistry on whole-mounts from different gut segments. The tissue content of nitrite/nitrate (NO_x) and nitrotyrosine (NTyr), and xanthine oxidoreductase (XOR) activity were determined, from small intestinal biopsies.
RESULTS: As a consequence of IR the density of nitrergic myenteric neurons, nNOS and eNOS immunoreactive neurons was significantly elevated in the duodenum only, while the number of total myenteric neurons did not change. The levels of NO_x, NTyr and XOR were significantly increased in the intestinal biopsies as compared to control samples. The inhalation of CH_4 kept the nitrergic neuronal density as well as the levels of oxidative and nitrosative stress markers at the control level.
CONCLUSION: These results demonstrate that CH_4 inhalation can neutralize the reactive oxygen and nitrogen species during the early phase of reperfusion, and therefore may contribute to the resetting of nitrergic myenteric neuronal density and restore the nitrergic function in gut motility after mesenteric IR.
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Disclosure of Interest: None Declared
Keywords: mesenteric ischemia-reperfusion, methane inhalation, nitrergic myenteric neurons, oxidative and nitrosative stress

P971 CELLULAR ALTERATIONS INDUCED BY ENTEROGLIAL S100B ON HUMAN COLONIC SMOOTH MUSCLE CELLS.

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INTRODUCTION: S100B, a Ca^{2+}-binding protein, is predominantly expressed and secreted by enteroglia in inflammatory conditions. As an extracellular factor, S100B engages RAGE (Receptor for Advanced Glycation End-products) with different outcomes (i.e. beneficial or detrimental, pro-proliferative or pro-differentiative) depending on the concentration attained. At micromolar concentrations, S100B exerts toxic effects on neurons via activation of the NADPH oxidase complex that, through theoverproduction of reactive oxygen species (ROS), induces inflammatory cytokines production and apoptosis. The expression of enteroglial-derived S100B and its possible contribution to inflammatory motor disorders has been poorly investigated
AIMS&METHODS: Aim of this study is to evaluate the effects induced by S100B on nearby gut smooth muscle. A primary highly pure human colonic smooth muscle cells (HSMC) culture was exposed to 1μM of S100B up to 24h. Total RNA was isolated and expression of S100B, RAGE and proinflammatory cytokines IL-6 and MCP-1 were determined by q-PCR. ROS (Hydrogen peroxide) (H_2O_2), cytoskeleton and apoptosis were measured by cytofluorometry and biological activity by scanning micrometry. Results are expressed as mean±SE and analysed by ANOVA, $p<0.05$ considered statistically significant.
RESULTS: HSMC presented a resting length of 75.06 ± 2.66 μm and a maximal contractile response to the muscarinic agonist acetylcholine of $24.94 \pm 1.27\%$. qPCR analysis showed that HSMC constitutively express mRNA encoding for RAGE and S100B. Exposure to S100B for 24h induced a dose dependent decrease in cell length (21.46±2.01% $p<0.05$) and contraction (64,02±7.08% $p<0.005$). In addition quantitative flow cytometry analysis indicated that S100B induced an increase of ROS generation, in particular an over-production of hydrogen peroxide (437.00±4.01, $p<0.0005$) without concomitant increase in the apoptosis factor caspase-3 activity. Moreover, S100B induced a peculiar dose-dependent rearrangement and redistribution of the contractile filament actin (23.30±0.12, $p<0.05$), and an increase of pro-inflammatory cytokines MCP-1 and IL-6 expression. The effects of S100B were abolished in the presence of Ab antiRage (1:10000) or of the NADPH oxidase inibhitor apocynin (60μM).
CONCLUSION: S100B can induce HSMC dysfunction through interaction with Rage coupled to the NADPH oxidase transduction signalling. Taken together, these results increase our understanding of the molecular mechanisms of RAGE signaling in muscle cells and could lead to the identification of novel therapeutic targets for motor disorders.
Disclosure of Interest: None Declared
Keywords: enteroglia, inflammation, S100B PROTEIN, smooth muscle cells

P973 THE SHORT HEALTH SCALE QUESTIONNAIRE VALIDATION IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Subjective health assessment is central when treating patients with irritable bowel syndrome (IBS). The "Short Health Scale" (SHS) is a simple 4-item questionnaire covering most aspects of subjective health that has been validated for inflammatory bowel disease.
AIMS&METHODS: to evaluate validity, reliability and responsiveness of the SHS in IBS patients. To test validity, 451 patients with IBS (mean age 38 years; 81% females) completed the SHS and questionnaires assessing IBS symptom severity (IBS-SSS), gastrointestinal (GI)-specific anxiety (VSI) and quality of life (IBSQOL). To evaluate reliability and responsiveness to changes, the questionnaires were repeated after 2 weeks in 18 patients, and after 12 weeks in 212 patients who had completed a patient education program.
RESULTS: Validity was documented with 1) gradually increasing mean scores for all four SHS items with increasing IBS symptom severity, ($P<0.0001$), and 2) positive correlations between the four SHS item and the corresponding items from the other subjective health assessment tools (item 1 rho= 0.67, item 2 rho=-0.44;-0.46, item 2 rho=-0.51;0.57, item 4=-0.34;-0.46, $P<0.0001$). Reliability was confirmed (Spearman's rho >0.7, and intraclass correlations >0.7). Responsiveness was good with patients defined as being responders after the patient education (reduction of IBS-SSS≥50 points) having significant reductions in three of the SHS items ($P<0.05$), and borderline change for the fourth SHS item ($P=0.06$).
CONCLUSION: The SHS is a valid, reliable, and responsive health measure in IBS patients. It can be rapidly completed and evaluated, which supports its usefulness in clinical practice and clinical trials.

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Disclosure of Interest: None Declared
Keywords: Irritable bowel syndrome, questionnaire, reliability, responsiveness, subjective health assessment, validation

P974 ADEQUATE RELIEF ASSESSMENT: MEASUREMENTS OF SUBJECTIVE HEALTH IN PATIENTS WITH IRRITABLE BOWEL SYNDROME AND RELATIONSHIP TO OTHER VALIDATED QUESTIONNAIRE OUTCOMES

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INTRODUCTION: Subjective health assessment is necessary when treating patients with irritable bowl syndrome (IBS). The simple 2-item questionnaire "IBS Adequate Relief" (IBS-AR) has been proposed as standard for primary outcome assessment in IBS trials. It has been proposed that the baseline results of IBS-AR may confound treatment results[1].
AIMS&METHODS: The aim of this study was to compare the IBS-AR outcomes with outcomes using other validated IBS questionnaires. Before and after treatment 584 IBS patients (mean age 40 years; 79% females) completed IBS-AR, "IBS Severity Scoring System" (IBS-SSS), IBS specific Gastrointestinal Symptom Rating Scale (GSRS-IBS), "IBS disease-specific Quality Of Life" (IBSQOL), and "Gastrointestinal-Specific Anxiety" (VSI).
RESULTS: At baseline 19.3% of the 579 patients completing IBS-AR reported adequate relief (*baseline responders*). They had a higher distribution of women (87% versus 77%, P=0.01), milder IBS severity (6.6% versus16.1%, P=<0.01), lower symptom scores (261.7 versus 311.7, P>0.001) and better quality of life (domains; sleep, energy, physical role and function, all P<0.05) compared to *baseline non-responders*. After treatment the 253 (43.7%) IBS-AR responders had improvement in IBS-SSS severity, (-86.6 ± 83 versus -1.4 ±112, P<0.001), and in several of the GSRS and IBS-QOL scores (P<0.02). When excluding IBS-AR *baseline responders* these differences were even more pronounced. Only when excluding IBS-AR *baseline responders* did the proportion of IBS-AR *responders* follow the IBS-SSS severity scores (P=0.004 versus P=0.3). There were no strong agreement between treatment *responders* defined by IBS-AR versus IBS-SSS and GSRS (Kappa 0.13-0.45, all P<0.05).
CONCLUSION: IBS-AR *baseline responders* differ significantly from *baseline non-responders* and this may confound treatment results if *baseline responders* are not excluded. Different commonly used IBS treatment endpoints do not strongly agree on definitions of *responders*.
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Disclosure of Interest: None Declared
Keywords: adequate relief, Irritable bowel syndrome, questionnaire, subjective health assessment, trial end point

P975 IRRITABLE BOWEL SYNDROME PATIENTS DIAGNOSED IN PRIMARY AND SECONDARY CARE; WHAT EXPLAINS THE DIFFERENCE IN HEALTH CARE COSTS?

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INTRODUCTION: Irritable Bowel Syndrome (IBS) is a chronic condition that is often accompanied by other chronic or functional comorbidities. IBS is reported to initiate substantial health care expenditure, but the background of these costs is unknown.
AIMS&METHODS: The aims of this study were to compare the costs of healthcare consumption of patients diagnosed with IBS in primary and secondary care before and after diagnosis and to specify the origin of additional costs in further detail. All patients diagnosed with IBS by a general practitioner or specialist between 2006 and 2009 and a control group of individuals without IBS, matched for age and gender, were extracted from the database of a Dutch health insurance company, with over 2 million members. Direct medical costs for general practitioner consultations, drug prescription and hospital care were compared between the two groups. Hospital costs were further divided into costs for IBS, for other chronic diseases, for other functional disorders and for all other disorders.
RESULTS: Data of 326 primary care IBS patients, 9274 IBS patients diagnosed in secondary care and 652 respectively 18548 non IBS control patients were included in the analysis. For primary care IBS patients the mean (± SD) total annual health care costs were 1648 (± 2898) € in the two years before diagnosis and 2134 (± 3258) € annually in the three years after the diagnosis was made, as compared to 1320 (± 2840) and 1492 (± 3120) € for control patients. For secondary care IBS patients mean annual costs in the three years before diagnosis were 2003 (± 3863) and 4331 (± 6958) € in the three years after diagnosis; costs for control patients were 1951(± 6002) respectively 1976 (± 5692) €. For primary care patients the increase after diagnosis could be mainly attributed to costs for 'non-IBS'-medication, to specialist costs for 'all other disorders' and to the increase in general practitioners' consultations. For secondary care patients the increase in costs after IBS was diagnosed was almost completely caused by additional costs for specialist care for 'all other disorders'.
CONCLUSION: Mean annual health care costs per patient increase with 30% after the diagnosis of IBS in primary care and over 100% for patients diagnosed in secondary care. Costs of control patients are higher in secondary care than in primary care, but do not change in time. The increase in costs after the IBS diagnosis is mainly due to non IBS related health care expenditure.
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Disclosure of Interest: None Declared
Keywords: health care costs, Irritable bowel syndrome, primary care, secondary care

P976 EFFECT OF TRANSCRANIAL MAGNETIC STIMULATION ON RECTAL SENSITIVITY IN IRRITABLE BOWEL SYNDROME: A RANDOMIZED, PLACEBO-CONTROLLED PILOT STUDY

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INTRODUCTION: Repetitive transcranial magnetic stimulation (rTMS) applied to the motor cortex can induce analgesic effects in patients with chronic pain syndromes through its effect on central pain modulatory systems. Our aim was to evaluate the effect of rTMS on rectal sensitivity in irritable bowel syndrome (IBS) patients.
AIMS&METHODS: In this randomized, sham-controlled trial, 21 IBS patients (11 women, 10 men, mean age 44 ± 12.6 years) were randomized using a double-blind crossover protocol to active or sham rTMS for five days of treatment. The primary outcome measure was the increase in the pressure pain threshold after rTMS. Secondary outcomes were the changes in maximum tolerated rectal volume, rectal compliance, and average pain intensity between baseline and the end of the treatments.
RESULTS: There were no statistically significant differences between active and sham rTMS in terms of an increase in the pressure pain threshold, maximum tolerated volume, and rectal compliance at the end of the treatments compared to baseline. However, in the subgroup of patients with the most marked rectal hypersensitivity, the volume threshold was significantly improved by active but not by sham rTMS (p=0.03). Patients experienced a significant improvement in pain regardless of the type of stimulation.
CONCLUSION: This pilot study failed to demonstrate any benefit of rTMS on our primary endpoint. However, the effect of rTMS on rectal tolerated volume in the most hypersensitive patients was encouraging enough to plan more powered studies.
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Disclosure of Interest: None Declared
Keywords: Irritable bowel syndrome, rectal barostat, rectal sensitivity, transcranial magnetic stimulation

P977 CALCIUM ANTAGONISTIC EFFECTS OF ETHANOLIC MYRRH EXTRACT IN INFLAMED INTESTINAL SMOOTH MUSCLE PREPARATIONS

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INTRODUCTION: Myrrh is the oleo-gum resin of mainly *Commiphora molmol* ENGLER (Burseraceae) and as powdered substance one compound in the traditional medicinal product Myrrhinil-INTEST®, which has been used for the treatment of unspecific and inflammatory intestinal disorders. To date only limited data is available regarding its mechanism of action. Besides antimykotic and antiphlogistic properties calcium antagonistic and antidiarrhoic effects have been discussed [1].
AIMS&METHODS: The aim of the present study was to evaluate the calcium antagonistic effect of myrrh. Therefore, an ethanolic myrrh extract (MY) was tested for its effects on muscle tone and acetylcholine (ACh)-induced contractions in untreated and inflamed rat ileum/jejunum preparations. Inflammation was experimentally induced by 2,4,6-trinitrobenzene sulfonic acid (TNBS, 10 mM, 30min). Additionally, the effect of the calcium channel agonist Bay K8644 in presence of varying MY concentrations was examined to confirm the calcium antagonistic effect.
RESULTS: MY suppressed the ACh-induced contraction down to 25,75 % (0,99 mg/ml MY). MY (0,15; 0,25 and 0,35 mg/ml) induced a concentration-dependent right-ward shift of the Bay K8644 concentration-response curve in untreated and inflamed preparations with a significant EC50 shift. Schild analyses resulted in a pA2 value of 0,93 for untreated preparations. Increasing MY concentrations induced a concentration-dependent decrease of the agonistic maximum effect in untreated and inflamed preparations down to 15,84% and 25,78% respectively for the highest concentration leading to a pD2 value of 0,58.
CONCLUSION: MY reduced intestinal muscle tone and ACh-induced contraction of untreated and inflamed ileum/jejunum preparations based on dual calcium antagonism characterised by a right-shift of the agonistic dose-response curve and a depression of maximum effect. The resulting reduction of intestinal motility and spasmolytic effects provide a rationale for the treatment of intestinal disorders.
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Keywords: calcium antagonism, herbal substance, Motility Disorders, myrrh

P978 IRRITABLE BOWEL SYNDROME AND PSYCHOLOGICAL COMORBIDITY – LONG-TERM SUCCESS OF GUT-DIRECTED GROUP HYPNOSIS

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INTRODUCTION: A recent long-term study (Moser et al., Am J Gastroenterol 2013) has shown gut-directed group-hypnosis (GGH) to have a positive effect on refractory irritable bowel syndrome (IBS). Patients with severe psychological disorders were excluded from that study. However, IBS is frequently associated with psychological co-morbidity.
AIMS&METHODS: Aim of this study was to examine a) if patients with psychiatric diagnoses do also profit by GGH, and b) if GGH can lead to higher resilience. **Methods:** nA=37 Gastroenterology outpatients with IBS (Rome III criteria), 26 (70%) of which had psychiatric co-morbidity and participated in 7 to 10 GGH-sessions were included. Quality of life, physical and psychological wellbeing (visual analogue scales; 0="extremely bad", 100="excellent") as well as anxiety and depression (HADs) were measured before first, fifth, last GGH-session, and at follow-up (after 10,3 months averagely). Additionally, at follow-up, IBS-severity and factors of resilience were measured. The same data was collected for a control group of nB=37 IBS patients not undergoing GGH-treatment.
RESULTS: Comparison between begin of GGH and follow-up revealed significant improvement in physical wellbeing (mean: 33.8 vs. 57.3; $p<.001$), psychological wellbeing (43.0 vs. 57.0; $p<.01$), quality of life (38.3 vs. 58.9; $p<.001$), and showed reduction in anxiety (HADs: 9.8 vs. 7.45; $p<.001$) and depression (6.6 vs. 5.0; $p<.01$). Thirty patients (81%) indicated considerable improvement after GGH-treatment. This responder-subgroup showed lower IBS-severity and higher resilience ($p<.001$ respectively) than the control group.
CONCLUSION: GGH presents a valuable therapy even for IBS-patients with psychological co-morbidity. Lower IBS-severity and higher resilience after treatment indicate better coping.
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Disclosure of Interest: None Declared
Keywords: hypnosis, Irritable bowel syndrome, psychological comorbidity

P979 EFFECT OF LINACLOTIDE ON IBS-QOL SEXUAL SUBSCALE SCORES IN PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH CONSTIPATION: RESULTS FROM 2 PHASE 3 TRIALS

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INTRODUCTION: Linaclotide (LIN) is a minimally absorbed guanylate cyclase-C agonist approved for treatment of IBS with constipation (IBS-C). IBS often results in diminished quality of life (QOL), including decreased sexual desire and activity. This post hoc analysis aimed to determine if LIN treatment improved IBS-QOL sexual subscale scores in IBS-C patients, compared to placebo (PBO).
AIMS&METHODS: Data from 2 randomised, double-blind Phase 3 trials of LIN in IBS-C were pooled. The IBS-QOL was administered at baseline and Week 12. The sexual subscale includes items on difficult sexual activity and reduced sexual desire, both rated on a 5-point scale (1=not at all, 2=slightly, 3=moderately, 4=quite a bit, 5=extremely/a great deal), with the sum of both items scaled to 0 (worst) to 100 (best). Scores for LIN- vs PBO-treated patients in the intent-to-treat (ITT) population and the Impaired Sexuality (IS) subgroup (patients with baseline sexual subscale scores $\leq$50) at Week 12 were compared to baseline.
RESULTS: Of 1598 ITT patients with baseline sexual subscale scores, 522 (33%) had a score $\leq$50 indicating IBS significantly impacted their sexual desire and activity (34% of females [484/1439] and 24% of males [38/159]). LIN significantly improved change-from-baseline sexual subscale scores at Week 12 vs PBO in both the ITT population and the IS subgroup (Table, $P<0.001$ for both). Although baseline scores for males were higher (better) than those of females, improvement vs PBO for males compared to females was similar in the ITT population and greater for the IS subgroup. However, the sample size for males was too small to establish statistical significance.
IBS-QOL Sexual Subscale Results

	PBO (ITT)	LIN (ITT)	Change from baseline Δ	P-value (ITT)	PBO (IS)	LIN (IS)	Change from baseline Δ	P-value (IS)
Overall (n)	795	803	5.2	<0.0001[a]	249	273	7.2	0.0007[a]
Baseline	68.9 (31.9)	66.9 (30.9)			27.2 (17.8)	29.5 (17.7)		
Week 12	79.7 (25.9)	83.1 (23.6)			57.8 (29.9)	67.9 (28.1)		
Females (n)	706	733	5.2	<0.0001[a]	228	256	6.7	0.0016[a]
Baseline	68.0 (32.3)	66.1 (31.1)			26.6 (17.8)	29.5 (17.8)		
Week 12	79.8 (25.8)	83.2 (23.4)			58.5 (30.2)	68.6 (27.7)		
Males (n)	89	70	4.2	0.3129[a]	21	17	10.2	0.2389[a]
Baseline	76.3 (28.1)	74.5 (28.7)			32.7 (16.5)	30.1 (17.7)		
Week 12	78.9 (26.7)	81.5 (26.0)			50.0 (25.7)	57.8 (33.2)		

Data are mean (SD)
[a]P values based on change-from-baseline treatment difference for LIN vs PBO in an ANCOVA model
CONCLUSION: LIN treatment significantly improves IBS-QOL sexual subscale scores in IBS-C patients, compared with PBO in both the total population and in patients with impaired sexuality at baseline.
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Disclosure of Interest: M. Currie Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals, S. Shiff Shareholder of: Forest Research Institute, Other: Employee of Forest Research Institute, X. Hao Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals, R. Carson Shareholder of: Forest Research Institute, Other: Employee of Forest Research Institute, M. Baird Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals, J. Johnston Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals
Keywords: IBS-C, quality of life, sexual activity, sexual desire, treatment

P980 IS RESPONSE TO LINACLOTIDE AFTER 4 WEEKS OF TREATMENT PREDICTIVE OF 12-WEEK IMPROVEMENT?

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INTRODUCTION: Linaclotide (LIN) is a minimally absorbed guanylate cyclase C agonist approved in the US and EU for irritable bowel syndrome with constipation (IBS-C). A question for prescribing physicians is whether to continue LIN in patients who do not improve during early weeks of therapy. This post hoc analysis assessed if response to LIN at Week 4 predicts Week 12 improvement, and if LIN should be continued in IBS-C patients not responding by Week 4.
AIMS&METHODS: Pooled data from 2 Phase 3 IBS-C trials of LIN were analysed. For Degree of Relief of IBS Symptoms, Degree of Relief of Abdominal Pain, and Spontaneous Bowel Movement [SBM] frequency, a patient's Week 4 clinical response was used to predict improvement at Week 12. For the purposes of determining a patient's Week 4 response, the 7-point balanced Degree of Relief scale was collapsed into 3 categories: Improved (completely, considerably, or somewhat relieved), Unchanged, and Worse (somewhat worse, considerably worse, or as bad as I can imagine) compared to baseline. For SBM frequency, a dichotomous end point was used: SBMs increased by $\geq$2/week or not increased by $\geq$2/week from baseline.
RESULTS: The proportion of patients who had response at Week 4 was significantly greater for LIN- vs placebo (PBO)-treated patients: 72% vs 47% for Degree of Relief of IBS Symptoms, 70% vs 47% for Degree of Relief of Abdominal Pain, and 59% vs 33% for SBM frequency (all comparisons: $P<0.0001$). For all parameters, most LIN-treated patients ($\geq$70%) who had response at Week 4 were improved at Week 12. For LIN-treated patients whose symptoms were unchanged at Week 4 for Degree of Relief of IBS Symptoms and Degree of Relief of Abdominal Pain, 36% and 39% were improved at Week 12, compared with 19% and 21% of the PBO group, respectively ($P<0.05$). For SBM frequency, 30% of LIN-treated patients vs 17% of PBO-treated patients without response at Week 4 were improved (SBMs $\geq$2) at Week 12 ($P<0.05$).
CONCLUSION: Patients whose IBS symptoms improved with LIN after 4 weeks were likely to maintain improvement. At least 30% of LIN patients who were unchanged at Week 4 experienced symptom improvement by Week 12. The significant differences between LIN and PBO in the percentage of patients improved at Week 12 who were unchanged at Week 4 indicates that $\geq$1 month of LIN therapy may be required for improvement in some patients. As such, an initial course of LIN therapy in IBS-C patients should be >4 weeks.
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Disclosure of Interest: W. Chey Consultancy for: Ironwood Pharmaceuticals and Forest Research Institute, B. Lavins Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals, S. Shiff Shareholder of: Forest Laboratories, Other: Employee of Forest Laboratories, J. MacDougall Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals, C. Kurtz Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals, M. Currie Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals, J. Johnston Shareholder of: Ironwood Pharmaceuticals, Other: Employee of Ironwood Pharmaceuticals
Keywords: Abdominal symptoms, Bowel symptoms, IBS-C, Treatment

P981 A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED STUDY: EFFECTS OF THE ENZYME ALPHA-GALACTOSIDASE ON GASTROINTESTINAL SYMPTOMS IN IBS PATIENTS.

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INTRODUCTION: IBS is a functional gastrointestinal (GI) disorder. Gas-related symptoms, e.g. abdominal distension and bloating are common. Certain foods that contain large amounts of incompletely absorbed carbohydrates (IAC) enhance gas-formation. α-Galactosidase (αG) is an enzyme that is able to digest IAC to smaller entities, thereby facilitating uptake and minimizing the bacterial fermentation in the colon. αG has been shown to reduce GI symptoms when combined with meals in healthy subjects, but has not been evaluated in IBS.
AIMS&METHODS: The aim of the study was to assess if αG is superior to placebo in reducing GI symptoms and production of hydrogen and methane gas in IBS patients after ingestion of meals rich in IAC. The patients were served breakfast and lunch together with capsules containing either αG or placebo according to a randomization schedule with a two weeks washout period in-between. A breath test measuring hydrogen and methane was performed at baseline and every 30 min during 7.5 h. The patient completed a questionnaire assessing GI symptom severity (gas, bloating, discomfort, distension, nausea, rumbling, urgency, abdominal pain) and general well-being, ranging from 0= no symptoms to 20= worst imaginable symptoms at baseline and after every breath test. Area under the curve (AUC) was calculated for hydrogen, methane and GI symptoms. Abdominal pain, bloating/distension and dissatisfaction with bowel habits were assessed on a visual analogue scale in the morning at each visit and in the morning the day after.
RESULTS: Twenty IBS patients (19 women, age 50 years (20-75) (median (range)) were included. There were no significant differences between AUC concerning hydrogen (ppm) (5543 (2085-29040) vs. 8198 (2700-20280); p=0.47) or methane (ppm) (1823 (750-17265) vs. 1815 (660-16560); p=0.64) between αG or placebo. Furthermore, no differences regarding AUC for GI symptoms or general well-being were noted between the study days. There was a significant reduction in the severity of bloating/distension the morning after intake of αG compared with placebo (z=1.94, p=0.05, *r*=0.31), but not for abdominal pain or satisfaction with bowel habits.
CONCLUSION: Based on this study, α-Galactosidase cannot be recommended to IBS patients in order to alleviate GI symptoms caused by meals rich in IAC. However, a positive effect on bloating/distension the following day was noted, which need to be further evaluated in long-term studies.
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Disclosure of Interest: None Declared
Keywords: bloating, Distension, Gastrointestinal disorders, IBS, treatment

P982 ROLLING OUT FODMAP DIET –SYMPTOM IMPROVEMENT IN TERTIARY REFERRAL AND SELF-REFERRAL POPULATION

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INTRODUCTION: Low FODMAP dietary approach which minimizes consumption of dietary factors that distend the intestine, has been recommended as a useful strategy in the management of patients with functional GI disease.
AIMS&METHODS: The aim of this study is to review the outcomes of Irish patient cohort instructed re low FODMAP diet over 17month period. Individually tailored instruction in low FODMAP diet was provided by 2 trained dieticians. Patients completed questionnaire scoring symptom severity at baseline assesment and at 8 weeks after FODMAP elimination
RESULTS: 54 patients received instruction re low FOD MAP diet over study period; 31/54 were referred by consultant gastroenterologist, 6/54 by primary care physican and 17/54 self-referred. After 8 weeks dietary intervention 87%(39/45) patients self reported score improved for symptoms of bloating symptoms, 76%(35/46) reported an improvement in abdominal pain and 69%(11/16) of patients with >4 BO daily noted reduction in bowel frequency. There was no significant difference in outcomes between tertiary referral and self referral /GP referral patients. 40%(20/50) patients considered diet difficult but 76%(38/50) patients advised that they would definitely recommend diet to other IBS patients
CONCLUSION: Our study confirms the benefit of FODMAP elimination for functional GI symptoms in unselected Irish population.
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Disclosure of Interest: None Declared
Keywords: abdominal pain, bloating, dietary intervention, fodmap diet, Irritable bowel syndrome

P983 TARGETING MECHANISMS OF IRRITABLE BOWEL SYNDROME: EFFECTS OF LACTOBACILLUS REUTERI ON EPITHELIAL BARRIER DYSFUNCTION

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INTRODUCTION: The irritable bowel syndrome (IBS) is a complex disorder characterized by abdominal symptoms including chronic abdominal pain or discomfort and alteration of bowel habit. Increasing evidence demonstrates a central role of intestinal epithelial barrier (IEB) dysfunction, and especially increased paracellular permeability, in the pathophysiology of IBS. Therefore, enhancing the IEB may become a valuable therapeutic option in IBS.
AIMS&METHODS: The purpose of this study was to investigate the effects of the probiotic strain *Lactobacillus reuteri* (DSM 17938; NOOS S.r.l., Italy) upon intestinal paracellular permeability using an *in vitro* model of IEB induced dysfunction. Caco-2 cell monolayers were incubated with *L.reuteri* (live; dead or supernatant of bacteria culture) for 8h (10^6 or 10^7CFU/100 µl) prior to treatment with a PAR-2 agonist (SLIGRL 100µM) for 24h. At the end of this period, Caco-2 monolayer paracellular permeability was measured using fluorescein sulfonic acid (FSA). Finally, Caco-2 monolayers were processed for quantitative PCR, Western blot or ELISA analysis of key tight junctions protein (ZO-1) and/or cytokines (IL-8).
RESULTS: Treatment of Caco-2 monolayers with PAR-2 agonist significantly increased paracellular permeability. Pre-incubation of Caco-2 with live, heat inactivated and supernatant of *L. reuteri* prevented PAR-2 agonist-induced increase in paracellular permeability. Incubation of Caco-2 monolayer with PAR-2 agonist caused a significant increase and decrease in the expression of ZO-1 mRNA and protein expression, respectively. Pre-incubation of Caco-2 monolayers with *L. reuteri* (10^7 CFU/100 µl) prevented PAR-2 induced reduction in ZO-1 protein expression. Incubation of Caco-2 monolayer with PAR-2 agonist increased apical and baso-lateral IL-8 secretion. Pre-incubation of Caco-2 with live bacteria (but not heat inactivated and bacteria supernatant) prevented PAR-2 agonist-induced increase in IL-8 levels.
CONCLUSION: Our study demonstrates that *L.reuteri* is able to prevent barrier dysfunction induced by PAR-2 agonists probably in part via a mechanism involving modulation of tight junction protein expression. Additional studies need to be performed to validate its putative therapeutical use in the treatment of IBS associated symptoms.
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Disclosure of Interest: None Declared
Keywords: Intestinal epithelial barrier, PAR-2 receptors, Probiotics

P984 THE EFFECTIVENESS OF GUIDED AFFECTIVE IMAGERY FOR TREATMENT OF IRRITABLE BOWEL SYNDROME

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INTRODUCTION: Methods of guided affective imagery (GAI) have been suggested to be effective in the treatment of irritable bowel syndrome (IBS). GAI is a form of psychotherapy yet to be fully researched in the treatment of IBS.
AIMS&METHODS: To compare the efficacy of combined GAI with standard medical treatment versus standard medical treatment only in patients with IBS. 32 IBS patients, age- and gender-matched, were randomly assigned to two treatment groups for 9 weekly appointments. The first group (N= 19) received standard dietary consultation and medical treatment and served as the control group. The second group (N= 13) received the same basic treatment in addition to GAI therapy from the same trained medical psychologist. All patients completed a demographic questionnaire as well as the Irritable Bowel Syndrome Quality of Life (IBS QOL) and the SF-36 at entry and at the last treatment for the assessment of their quality of life. We used the Welch two sample t-test (testing the hypothesis of equality of means) to compare results of IBS QOL and SF-36 between first and last meeting and then between groups.
RESULTS: At the end of treatment, IBS patients that were treated with standard medical care and GAI scored higher than controls on 3 domains of SF-36: physical functioning (p=0.04), general health perceptions (p= 0.001) and social role functioning (p=0.04). However, no significant differences between the groups were found for the IBS QOL domains. erun:yes'> All patients completed a demographic questionnaire as well as the Irritable Bowel Syndrome Quality of Life (IBS QOL) and the SF-36 at entry and at the last treatment for the assessment of their quality of life. We used the Welch two sample t-test (testing the hypothesis of equality of means) to compare results of IBS QOL and SF-36 between first and last meeting and then between groups.
CONCLUSION: Guided affective imagery improved several domains of quality of life and may become a promising therapeutic option in patients suffering from IBS. A larger study will be required to confirm our findings.
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Disclosure of Interest: None Declared
Keywords: Guided Affective Imagery , Irritable Bowel Syndrome

P985 THE ANTI-INFLAMMATORY COMMENSAL BACTERIUM FAECALIBACTERIUM PRAUSNITZII ALSO EXHIBIT ANTI-NOCICEPTIVE EFFECT IN A NON-INFLAMMATORY VISCERAL IBS-LIKE PAIN MODEL

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INTRODUCTION: Visceral pain is a diffuse and stabbing sensation which may be associated with functional gastrointestinal disorders, such as IBS, or with direct inflammation of a visceral organ as in IBD. This common complaint is a crucial feature because of its significant impact on patients' quality of life and lack of efficient therapies. In IBS, as in IBD, patients, dysbiosis have been recently detected suggesting a long term impact of the intestinal microbiota on inflammation, but also on colonic hypersensitivity (CHS). Diminished prevalence and abundance of *F. prausnitzii*, an extremely oxygen sensitive (EOS) Firmicute, have been reported in intestinal disorders as IBD, IBS and colorectal cancer. This bacterium was the first anti-inflammatory commensal bacterium identified on the

basis of human clinical data. The aim of this study was to determine if *F. prausnitzii* could also have a direct impact on CHS, independently to its anti-inflammatory properties.
AIMS&METHODS: We assessed the effect of *F. prausnitzii* in Neonatal Maternal Separation (NMS) CHS mouse model. After birth, wild-type C57Bl/6J pups were isolated from their mother from D2 to D14, three hours per day. At eight-week old age, male mice were orally treated each day with 10^{10} *F. prausnitzii* (A2-165 reference strain) bacteria for nine days. Visceral pain due to CHS was assessed using a technique based on measure of electromyographic abdominal contractions induced by colorectal distension. In this test, abdominal contractions (whose amplitude is proportional to the colon sensitivity) are induced by progressive inflation of a balloon inserted into the colon. These data were expressed as visceromotor response (VMR) reflecting CHS. After euthanasia, inflammation was monitored using anatomical indicators of colitis and assessed by expression of the colonic myeloperoxidase activity or colonic pro-inflammatory cytokines.
RESULTS: NMS treatment induced an increased VMR in the absence of any significant alteration in gut wall macroscopic integrity or colonic mucosa inflammation. Only a slight increase of colonic permeability has been measured after this stress-induced CHS. *F. prausnitzii* treatment significantly decreased VMR in NMS model, without affecting the VMR in non NMS control mice.
CONCLUSION: All of these results suggested a specific protective role of this commensal bacterium on CHS in a non-inflammatory NMS model. This study could facilitate and optimize the potential future use of *F. prausnitzii* as a novel probiotic to treat abdominal pains observed in IBS patients.
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Disclosure of Interest: None Declared
Keywords: Faecalibacterium prausnitzii, Neonatal maternal separation , Non-inflammatory IBS model, Visceral hypersensitivity

P986 THE EFFICACY OF A MULTISPECIES PROBIOTICS MIXTURE ON THE IBS SYMPTOMS AND CORRELATION BETWEEN CHANGE OF FECAL FLORA AND IBS SYMPTOMS

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INTRODUCTION: Some clinical trials tried to reveal the efficacy of probiotics in irritable bowel syndrome (IBS), but the use of probiotics in IBS is still contentious. According to previous report multispecies probiotic mixture had an effect on the symptoms in diarrhea-dominant IBS patients.
AIMS&METHODS: We tried to evaluate the effects of probiotics mixture on IBS symptoms and the relation between IBS symptoms and change of fecal micorbiota. 100 patients were enrolled and 11 patients were dropped out during screening and trial period. 89 patients were randomized into placebo (n=42) or probiotic mixture (n=39) (*Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus rhamnosus, Bifidobactrium breve, Bifidobactrium actis, Bifidobactrium longum, and Stretococcus thermophius* 1.0 x 10^{10} CFU) groups. Probiotics and placebo were taken daily for 4 weeks. The primary outcome was relief of overall IBS symptoms assessed after 4 weeks treatment. Relief of symptoms was defined as a patient who experienced adequate relief at least half of IBS symptoms during study period. Secondary outcomes included the effects on individual symptoms, stool parameter, change of fecal flora and relations between change of symptoms and fecal flora. The fecal floras were quantized by polymerase chain reaction denaturing gradient gel electrophoresis (DGGE).
RESULTS: The proportion of symptom relief seemed to be higher in probiotics group than placebo group (72.7% vs 60.5%, p=0.278). Percent changes on individual IBS symptom scores were not different in both groups. The mean score on the Bristol Stool Scale has decreased in probiotics group whereas increased in placebo group (-0.14 vs 0.09, p=0.245). Denaturing gradient gel electrophoresis profiles of fecal flora showed that *B. bifidum, B. lactis, L. rhamnosus, L. acidophilus* increased significantly in probiotics group comparing to placebo group. Analyzing probiotics group separately, the *Lactobacillus* species increased higher in patients experienced with relief of symptoms than the patients without relief of symptoms (n=24 vs 9, p=0.027).
CONCLUSION: The probiotic mixture might be effective in providing relief of overall IBS symptoms and make the Bristol Stool Score decreased in IBS patients, even if it had no significant effect on individual IBS symptoms. And in the patients with relief of IBS symptoms of probiotics group, *Lactobacillus* species has increased higher than the patients without relief of IBS symptoms in fecal flora analysis. The therapeutic effect of probiotics could be expected in subgroup IBS patients whom probiotics might settle down well in their intestine.
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Disclosure of Interest: None Declared
Keywords: Fecal flora, Irritable bowel syndrome, Probiotics

P987 LONG TERM MANAGEMENT OF PATIENTS WITH MESENTERIC INFARCTION: A 10 YEAR EXPERIENCE

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INTRODUCTION: Morbidity and mortality from mesenteric infarction is still high despite advances in diagnostic and therapeutic measures. The management of patients who survive their initial emergency operation has not been extensively investigated. The aim of this study was to review our experience in long term management of patients with mesenteric infarction.
AIMS&METHODS: A retrospective review of hospital database of patients treated with mesenteric infarction from 2000 to 2010.
RESULTS: 115 patients (61 females, median age 54) were referred to our institution following emergency resection in the referring institution. Aetiology breakdown: superior mesenteric artery thrombosis (SMA) in 40 (34%), SMA embolism in 36 (31%), superior mesenteric vein thrombosis in 25 (21%) and unknown in 10 (8%). Of the 115 patients, 57 (49%) were suitable for restoration of bowel continuity. 25 (43%) of these patients stopped their parenteral nutrition within a month after restoration of bowel continuity. Multivariate analysis did not show any factors that would alter survival in this group.
CONCLUSION: In this cohort of patients with mesenteric infarction, careful patient selection for consideration of bowel continuity following an emergency resection is a feasible option that reduces parenteral nutrition requirements and may improve quality of life.
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Disclosure of Interest: None Declared
Keywords: mesenteric infarction, parenteral nutrition, restoration of bowel continuity

P988 A SIMPLE SCORE FOR PREDICTING MORTALITY IN PATIENTS WITH PNEUMATOSIS INTESTINALIS

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INTRODUCTION: This study was conducted to identify simple computerized tomography (CT)and clinical predictors of mortality in patients with pneumatosis intestinalis (PI). We tried todefine the clinical characteristics and outcomes of PI and to identify the predictors thatassociate with mortality retrospectively.
AIMS&METHODS: The medical records of 123 patients with PI were reviewed. Multivariate logisticregression models were constructed to determine independent predictors of mortality. Thesedata were used to develop a simple score that would predict mortality on the first and seventhday after diagnosis.
RESULTS: The median age at diagnosis was 62 years (range, 20–91). The most common causeof PI was mesenteric vascular ischemia (n=43, 35.0%). Twenty-nine (23.6%) disease-relateddeaths occurred during the index admission. The presence of peritoneal irritation signs onphysical examination (HR: 4.57, 95% CI: 1.99–10.39, P = 0.0003) and decreased or absentenhancement of the bowel wall on CT (HR: 9.43, 95% CI: 3.18-27.98, P <0.001) were bothassociated with increased mortality. If both factors were absent, the in-hospital mortality wasless than 5% on the first and seventh days after the diagnosis of PI. However, if both factorswere present, the in-hospital mortality was 57% on the first day and 59% on the seventh day.
CONCLUSION: A simple and novel risk score that predicts mortality in patients with PI wasproposed. Patients with both peritoneal irritation and decreased or absent enhancement ofbowel wall on CT should be observed vigilantly and early intervention should be instituted.
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Disclosure of Interest: None Declared
Keywords: Pneumatosis intestinalis, wall enhancement

P989 CLINICAL FEATURES AND ENDOSCOPIC FINDINGS OF PATIENTS WITH ACTIVE BLEEDING COLONIC ANGIODYSPLASIA

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INTRODUCTION: Colonic angiodysplasia (AGD) is an important cause of lower gastrointestinal bleeding. However, most of bleeding from colonic AGD stops spontaneously. To date few data are available on the endoscopic findings of bleeding colonic angiodysplasia.
AIMS&METHODS: To clarify the clinical features and endoscopic findings of active bleeding colonic AGD, we conducted a retrospective study of colonoscopies undertaken at our hospital. From November 2006 to March 2013 inclusive, 32,586 colonoscopies were undertaken at this hospital. Thirteen patients with bleeding colonic AGD were enrolled in the study. Criteria to define bleeding from colonic AGD were, active bleeding from AGD without any other major colonic lesion or the bleeding site being identified on colonoscopy.
RESULTS: The mean age was 84 years (range 69-90 years), and eight patients were women (62%). The mean follow-up period was eight months (range 1-52 months). All patients had chronic heart disease. Other coexisting diseases were

chronic uremia undergoing dialysis for two patients and liver cirrhosis in one patient. All patients were using anticoagulant and/or antiplatelet drugs.
Bleeding AGD was localized in the left colon of two patients (15%) and in the right colon of the remaining patients (85%). 77% of lesions (10/13) were 2 mm, and two lesions were 4 mm. Only one lesion was larger than 5 mm.
Endoscopic treatment by argon plasma coagulation and/or hemoclip had a therapeutic success rate of 100%. In 85% of patients (11/13), bleeding did not reoccur after treatment. During the study period, two patients presented with bleeding from residual AGD and underwent endoscopic treatment.
CONCLUSION: In most instances, the size of the bleeding colonic AGD was smaller in our study compared to previous reports. Targeted colonoscopic treatment for active bleeding AGD was effective and safe. It is essential that physicians consider active bleeding colonic AGD when performing colonoscopy in elderly patients with a history of cardiovascular disease, and anticoagulant and/or antiplatelet therapy.
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Disclosure of Interest: None Declared
Keywords: angiodysplasia , Bleeding, colon

TUESDAY, OCTOBER 15, 2013 9:00–17:00
OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS II – Poster Area

P990 PREDICTIVE FACTORS FOR REBLEEDING AND MORTALITY IN NON-VARICEAL UPPER DIGESTIVE BLEEDING

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INTRODUCTION: Non-variceal upper digestive bleeding represents an important cause of morbidity and mortality.
AIMS&METHODS: To assess the predictive factors for rebleeding and mortality in patients with non-variceal upper digestive bleeding (UDB).
We have performed a retrospective study including 1842 patients with non-variceal UDB (644 women and 1198 men), mean age 61±15 years admitted in the Department of Gastroenterology and Hepatology, Emergency County Hospital Timisoara during 2003-2012. We have analyzed the variables that might influence the rebleeding and mortality rate of these patients: demographic characteristics, pre-endoscopic aspects of severity-haemorrhagic shock (tachycardia, hypotension), consumption of NSAIDs or anticoagulants, severity of anemia, Forrest classification (for the 1293 patients with UDB of ulcerous etiology), as well as Rockall, Baylor (pre-endoscopic, endoscopic and total) and Cedar-Sinai scores used for stratifying the risk in patients with UDB. For the statistical analysis we have used the method of multivariate regression.
RESULTS: Of the 1842 patients, a number of 151 have rebled (8.2%), and 115 died (6.2%). The rebleeding rate was not influenced by the consumption of NSAIDs/anticoagulants ($p>0.05$). The presence of active bleeding during endoscopy was significantly correlated with the risk of rebleeding, and it was noticed in 73/151 patients that have rebled (48.3%) vs. 231/1407 patients without rebleeding (16.4%) ($p<0.0001$). The independent variables that presented a statistically significant correlation with the death of the patients were the following: Aspirine consumption ($p=0.03$), tachycardia ($p=0.01$), rebleeding ($p=0.04$), hypotension ($p<0.0001$). The consumption of other AINS, anticoagulants, the level of haemoglobin and the age didn't influence the survival ($p>0.05$). By comparing the three risk scores, the Rockall score proved to be statistically significant more useful regarding the prediction of mortality ($p=0.004$). For the subgroup of patients with UDB of ulcerous etiology, the presence of active bleeding/sitgns of recent bleeding at endoscopy (Forrest classification I and II) was correlated significantly with the risk of death: active bleeding was noticed in 64% of the patients that died (48/75 patients) vs. 51,7% of the patients that survived (630/1218 patients) ($p=0.03$).
CONCLUSION: The factors that were correlated significantly with death in patients with non-variceal UDB are represented by the Aspirine consumption, the presence of haemorrhagic shock and rebleeding. The Rockall score proved to be the most reliable in predicting mortality. The presence of active bleeding at endoscopy was correlated with an increased risk of rebleeding and death.
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Disclosure of Interest: None Declared
Keywords: mortality, non-variceal upper gastrointestinal bleeding, Predictive factors, Rebleeding

P991 MORTALITY IN HIGH-RISK PATIENTS WITH BLEEDING MALLORY-WEISS SYNDROME IS SIMILAR TO THAT OF PEPTIC ULCER BLEEDING - RESULTS OF A PROSPECTIVE DATABASE STUDY

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INTRODUCTION: Mallory-Weiss syndrome and peptic ulcer disease remains an important cause of nonvariceal gastrointestinal bleeding.
AIMS&METHODS: The aim of this study was to identify the predictive factors influencing mortality in patients with bleeding Mallory-Weiss syndrome in comparison with peptic ulcer bleeding.
Between January 2005 and December 2009, 281 patients with endoscopically confirmed Mallory-Weiss syndrome and 1530 patients with peptic ulcer bleeding were consecutively evaluated. The 30-day mortality and clinical outcome were related to patient's demographic data, endoscopic and clinical characteristics.
RESULTS: The one-year cumulative incidence for bleeding Mallory-Weiss syndrome was 7.3 cases/100,000 people and for peptic ulcer bleeding 40.4 cases/100,000 people. The age-standardized incidence for both bleeding Mallory-Weiss syndrome and peptic ulcer bleeding remained unchanged during the observational five-year period. The majority of patients with bleeding Mallory-Weiss syndrome were male patients with significant overall comorbidities (ASA class 3-4). Overall 30-day mortality rate was 5.3% for patients with bleeding Mallory-Weiss bleeding and 4.6% for patients with peptic ulcer bleeding ($p = 0.578$). In both patients with bleeding Mallory-Weiss syndrome and peptic ulcer bleeding, mortality was significantly higher in patients over 65 years of age and those with significant overall comorbidities (ASA class 3-4).
CONCLUSION: The incidence of bleeding Mallory-Weiss syndrome and peptic ulcer bleeding has not changed over a five-year observational period. The overall 30-day mortality was almost equal for both bleeding Mallory-Weiss syndrome and peptic ulcer bleeding and was positively correlated to older age and underlying comorbid illnesses.
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Disclosure of Interest: None Declared
Keywords: Bleeding, Clinical outcome, Mallory-Weiss syndrome, Peptic ulcer

P992 POTENTIATION BY CO-ADMINISTRATION OF ANTIPLATELET DRUGS OF ASPIRIN-INDUCED GASTRIC BLEEDING AND ULCEROGENIC RESPONSES IN RATS: COMPARISON WITH CLOPIDOGREL, TICROPIDINE AND CILOSTAZOL

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INTRODUCTION: Although antithrombotic therapy plays a central role in the treatment of apoplexy, cardiac disorders and peripheral arterial diseases, recent studies suggest that the risk of upper gastrointestinal bleeding is increased by the concomitant use of anti-platelet drugs with low-dose aspirin (ASA). We recently reported that an antiplatelet drug clopidogrel, the $P2Y_{12}$ receptor antagonist, increased gastric bleeding induced by intraluminal perfusion with acidified low dose ASA in the rat stomach.
AIMS&METHODS: We examined the effects of other antiplatelet drugs, such as ticlopidine and cilostazol, on gastric bleeding and lesion formation induced by

intraluminal perfusion with low-dose ASA in rats, in comparison with those of clopidogrel.
Under urethane anesthesia, a catheter was inserted into the rat stomach through an incision in the esophagus and another cannula was provided in the stomach through the pylorus. Then, the gastric lumen was perfused with saline through a catheter, and the perfusate was collected. After an equilibration period with saline perfusion, the stomach was perfused with acidified ASA (25 mM in 50 mM HCl) for 60 min. Gastric bleeding was evaluated as the hemoglobin concentration in the perfusate. Clopidogrel (10-100 mg/kg, PO), ticlopidine (10-300 mg/kg, PO) or cilostazol (3-30 mg/kg, IP) was given twice, 24 h and 0.5 h before ASA perfusion.
RESULTS: Perfusion of the stomach with acidified ASA alone caused slight bleeding and lesions in the stomach. Pretreatment of the animal with clopidogrel, despite provoking by itself neither bleeding nor damage, dose-dependently increased gastric bleeding and damage after intraluminal perfusion with acidified ASA, and these responses were significantly prevented by PGE_2. Likewise, ticlopidine also dose-dependently aggravated the severity of damage with an increase of gastric bleeding, the effects at 300 mg/kg being equivalent to those of clopidogrel at 100 mg/kg. On the other hand, cilostazol, unlike other two antiplatelet drugs, dose-dependently decreased gastric bleeding and lesions in response to acidified ASA, the inhibition of hemoglobin output and lesion score at 30 mg/kg being 68.2% and 46.8%, respectively.
CONCLUSION: These results suggest that the antiplatelet drug ticlopidine increases gastric bleeding and ulcerogenic responses to low-dose ASA, similar to clopidogrel, while ciloztazol suppresses these responses, yet the mechanism for the protective action remains unknown. It is assumed that cilostazol may be safely used as a dual antiplatelet therapy combined with low-dose ASA, without increase of the risk of gastric bleeding.
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Keywords: antiplatelets, Bleeding, gastric injury

P993 EFFECT OF SURGICEL® (FIBRILLAR) ON PREVENTING DELAYED BLEEDING AFTER ESD FOR GASTRIC EPITHELIAL TUMORS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) provides larger gastric epithelial tumors to be completely resected, compared endoscopic mucosal resection (EMR). However, ulcer bleeding after ESD can occur more frequently. Proton pump inhibitor (PPI) has used to prevent bleeding from the post-ESD ulcer. Surgicel® (Fibrillar) is oxidized regenerated cellulose and absorbable hemostats, and has used to control of oozing bleeding. We assessed the effect of Surgicel® on preventing bleeding after ESD.
AIMS&METHODS: From January through September 2012, patients scheduled for ESD to treat the gastric epithelial tumors were prospectively enrolled in this study. Patients were assigned to combination therapy with Surgicel® and H2RA or monotherapy with PPI after ESD procedure. Bleeding rate and change of hemoglobin (Hb) were assessed to evaluate the effect on preventing ulcer bleeding after ESD.
RESULTS: A total of 116 patients (87 male, 29 female) were enrolled in this study. Fifty-nine patients were assigned to combination therapy with Surgicel® and H2RA and 57 patients to monotherapy with PPI. There were no significant differences between the two groups in terms of age, sex, underlying disease, antiplatelet medication, location of lesion, and histological result from ESD. There was no significant difference in major bleeding including active bleeding on follow-up endoscopy, unstable vital sign, decreasing Hb of more than 2 g/dL, or need for transfusion (combination therapy 5.1%, monotherapy 3.6%, P=1.000). However, the laboratory result showed there was significant change of Hb (7 days after ESD) between two groups (-0.6±1.3 in combination therapy, -1.2±1.3 in monotherapy , P=0.013).
CONCLUSION: Combination therapy with Surgicel® and H2RA had similar effect on preventing major ulcer bleeding after ESD for gastric epithelial tumors, compared to monotherapy with PPI. Moreover, Surgicel® enables oozing bleeding to be discontinued, resulting in preventing reduction of Hb.
Disclosure of Interest: None Declared
Keywords: Delayed bleeding, Endoscopic submucosal dissection, Gastric epithelial tumor, Surgicel

P994 CLINICAL MARKERS INDICATING THE NEED FOR EMERGENCY ENDOSCOPY FOR UPPER GASTROINTESTINAL BLEEDING ARE USEFUL TO REDUCE MEDICAL EXPENSES: A PROSPECTIVE COHORT STUDY IN JAPAN

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INTRODUCTION: Upper gastrointestinal bleeding (UGIB) is frequently indicative for an emergency endoscopy (EE) and hospital admission. Indeed, it has been estimated that the prevalence of gastric ulcers is 353.9/100,000, and the incidence of bleeding is 3.3% in Japan. However, EE is associated with disadvantages including the labor of the medical staff and is time-consuming, particularly after office hours. The Glasgow-Blatchford Score (GBS) was introduced for UGIB to help avoid unnecessary EE and admission. However, the patients with UGIB usually show high GBS scores in Japan, thus resulting in it having a lower impact for decreasing the rate of EE. We have proposed that a high blood urea nitrogen (BUN) level and low blood pressure (BP) were significant markers as an indication for EE in UGIB.
AIMS&METHODS: The aim of this prospective cohort study was to investigate the medical expenses associated with EE, and to determine the efficacy of using clinical markers to provide the indications for EE with regard to decreasing the medical expenses. From January 2011 to August 2012, 83 patients with hematemesis, melena and/or anemia who underwent EE were enrolled in this study. Clinical factors and the results of blood examinations were investigated to determine whether they are associated with the need for endoscopic treatment. The medical expenses included the costs of the devices and agents used and the personnel expenses, which were estimated from mean staff salaries.
RESULTS: Endoscopic treatments were needed in 32 cases (38.5%) because of the hemostasis (Forrest I or IIa), but were not needed in 51 cases (61.5%) (Forrest IIb or III). The average time of all EE was 24.8 minutes, and the hospital stay was 4.1 days. A high BUN level and a low BP were significantly associated with the need for intervention, whereas the other clinical factors were not. The average costs of EE during overtime and normal office hours were calculated to be 272 and 239 dollars, respectively. If only patients with a high BUN level and/or low BP were considered to be indicated for EE, 42% patients with UGIB would not undergo EE. If the indications for EE had been limited to UGIB patients with a high BUN level and/or low BP, it is estimated that more than 4,600,000 dollars would have been saved in a year.
CONCLUSION: In the Japanese population, the average cost to treat the patents with EE was estimated to be 1040 dollars. The cost of EE was higher after hours than during office hours. If only the patients with a high BUN level and/or low BP are considered to be indicated for EE, then the medical expenses for EE will be greatly reduced.
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Disclosure of Interest: None Declared
Keywords: emergency colonoscopy, UGIB

P995 DOES PROTON PUMP INHIBITORS ARE SUFFICIANT FOR GASTROPROTECTION DURING ANTIPLATELET THERAPY WITH CLOPIDOGREL AND ACETYLSALICYLIC ACID?

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INTRODUCTION: The dual antiplatelet therapy may increase the risk of damage to the mucous membrane of the stomach with the development of complications such as bleeding. For gastroprotection during dual antiplatelet therapy widely used proton pump inhibitors. However, remains little studied gastroprotective properties of proton pump inhibitors with dual antiplatelet therapy.
AIMS&METHODS: To study in rats gastro protective properties of pantoprazole with a double (acetylsalicylic acid + clopidogrel) antiplatelet therapy. The study was conducted on 30 white male rats. Control group received no medication, group #1 received clopidogrel 6.8 mg/kg body weight (recalculated 75 mg for an adult human) + acetylsalicylic acid 6.8 mg/kg body weight (75 mg allocation adult), group #2 received clopidogrel 6.8 mg/kg body weight + acetylsalicylic acid 6.8 mg/kg body weight + pantoprazole 3.6 mg kg (40 mg allocation for an adult). Drugs were administered intragastrically once a day. On the 14th day of the study degree of destruction of the gastric mucosa was studied in rats. For this purpose gastric mucosa was homogenated to determinate the level of malondialdehyde (MDA) and phospholipids. Study was conducted according to the rules of humane treatment of experimental animals.
RESULTS: The level of MDA in the gastric mucosa homogenate was significantly greater ($p < 0.001$) in the group #1 as compared to control (8,73 ± 0,43 nmol/mg against LCA b e 6,26 ± 0,42 nmol/mg b e LCA), and level of phospholipids in group #1 was significantly lower ($p < 0.01$) compared with control (57,96 ± 6,03 mkg/mg b e LCA vs. 77,06 ± 6,61 mkg / mg b e LCA). In group #2 MDA level in homogenates of gastric mucosa did not differ significantly ($p > 0.05$) from the control group (6,84 ± 0,34 nmol/mg b e LCA vs. 6,26 ± 0,42 nmol/mg b e LCA). When the level of phospholipids in gastric mucosa group #2 was significantly lower ($p < 0.01$) compared to controls (45,19 ± 3,83 mkg / mg against b e LCA 77,06 ± 6,61 mkg/mg b e LCA). In group #2 level of MDA in homogenates of gastric mucosa was significantly lower ($p < 0.01$) compared with the group #1 (6,84 ± 0,34 nmol/mg b e LCA vs. 8,73 ± 0,43 nmol/mg b e LCA), and the level of phospholipids in group #2 and group #1did not differ ($P > 0.05$) between them (45,19 ± 3,83 mkg / mg b e LCA vs. 57,96 ± 6,03 mkg/mg b e LCA).
CONCLUSION: We found that taking dual antiplatelet therapy leads to the destruction of the gastric mucosa of rats. Adding pantoprazole to therapy partially fulfills gastroprotective properties. Experimental data can help in the further development of new schemes for the prevention of gastro protective gastropathies with dual antiplatelet therapy.
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Disclosure of Interest: None Declared
Keywords: antiplatelet therapy, gastric mucosa, pantoprazole, rats

P996 HER2 HETEROGENEITY IN GASTRIC CANCER: THE COMPARISON BETWEEN BIOPSY AND RESECTED SPECIMENS

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INTRODUCTION: The importance of human epidermal growth factor receptor 2 (HER2) in the tumor is well established in breast cancer (BC). According to the ToGA trial in gastric cancer (GC), molecular-targeted drugs, such as traszumab, are recognized to prolong overall survival and progression-free survival in patients with HER2-positive gastric cancer. However, it is well known that the

HER2 overexpression in GC in is different from that BC and that the heterogeneity is GC is high. In this study, we investigated the HER2 overexpression between biopsy and resected specimens in GC.
AIMS&METHODS: This retrospective study was conducted in 87 patients with GC between April 2009 and May 2012. These specimens were obtained from biopsy and resected specimens. The clinicopathlogical features and HER2 imunohistochemistry (IHC) were investigated in these gastric cancers. We divided the specimens into two groups: the HER2 0/1+ group and the HER2 2+/3+ group. In the HER2 score, the intratumoral heterogeneity of 2+/3+ resected specimens was assessed from the viewpoint of the distribution in the resected specimen. To study the heretogenity in detail, we added 11 GC cases with HER2+/3+. The heterogeneity was defined as those positive in at least 5% and under 50% of nuclei overexpression.
RESULTS: Eighty seven patients with GC (male 56/ female 31, median age 65.0) were enrolled in this study. There were 15 early and 72 advanced GCs; 42 were intestinal type and 45 diffuse type. Seventy-one fell into the HER2 0/1+ group, and 16 into the HER2 2+/3+ group. The ratio of the intestinal / diffuse type in the HER2 0/1+ group was lower than that in the HER2 2+/3+ group. Even in early gastric cancer, HER2 2+/3+ overexpression was observed. The concordance of HER2 score was 89.7% (78/87) between biopsies and resected specimens. In 27 gastric cancers with HER2+/3+, the heterogeneity was investigated as the distribution of HER2 overexpression. Seventeen were diffuse type and 11 were focal type. The four patterns of HER2 overexpression observed were: diffuse / complete, diffuse / incomplete, focal patchy, and focal localized. False negative cases were observed in focal positive cases.
CONCLUSION: The HER2 score in biopsy specimens was almost equal to that in resected specimens. However we have to recognize the intratumoral heterogeneity of HER2 overexpression and take care of the site and numbers of biopsy.
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Disclosure of Interest: None Declared
Keywords: Gastric cancer, HER2, heterogeneity, histology

P997 OBESITY CAUSES ALTERATIONS OF GASTRIC HUMAN SMOOTH MUSCLE CELLS

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INTRODUCTION: In obese patients motor alterations have a higher prevalence than in normal-weight controls likely through an increased production and secretion of pro-inflammatory molecules by inflamed adipose tissue. These cytokines cause morpho-functional alterations of smooth muscle cells (SMC) *in vitro* and affect G protein–coupled receptors transmembrane signaling regulation. This has been reported for the cAMP-dependent transduction pathway in human airway smooth muscle cells which is the main pathway involved in relaxation of human smooth gastric antrum through activation of VIP_2 receptors
AIMS&METHODS: Aim of this study was to evaluate morpho-functional and molecular alterations in gastric muscle tissue in obese. Smooth muscle cells (SMC) were isolated from muscle specimen of terminal antrum obtained from 5 normoglycemic-normocholesterolemic morbid obese patients (BMI$\geq$40 Kg/m^2) submitted to bariatric surgery and 5 patients submitted to gastrectomy for gastric cancer (19$\leq$BMI$\geq$25 Kg/m^2)(control). Analysis of morpho-functional parameters (length and biological response to contractile and relaxant neurotransmitters) and mRNA expression encoding for VIP_2, inflammatory (IL-1β, TNFα, COX2) and anti-inflammatory (IL-10) molecules were performed on isolated SMC. Data are expressed as mean±SE, $p<0.05$ considered significant.
RESULTS: Obese and control SMC presented similar resting lengths (75.8±0.6 μm and 72.7±1.6 μm respectively) and maximal contractile responses to the muscarinic agonist carbachol (24.2±1.8% and 26.0±1.4% respectively). In turn, differences were found in VIP-induced relaxation, the effect of which was tested on maximal carbachol induced-contraction. While 1μM VIP induced a 70.6±8.5%relaxation in control SMC, no effects were observed in obese SMC. RT-PCR analysis and densitometric comparison of amplified cDNA, showed however a similar distribution of mRNA expression for VIP_2 between obese and control SMC. Relaxation induced by the 2nd messenger cAMP (1mM) instead was similar between obese and control SMC (86.10±0.1 and 71.7±8.2 respectively). Finally the qPCR analysis for inflammatory molecules showed a 5-fold increase in expression of cyclooxygenase 2 in obese SMC in respect to control ($p<0.05$). No difference were instead observed in mRNA expression of TNFα, IL-1 β or IL-10.
CONCLUSION: During obesity gastric muscle present an uncoupling in relaxant transmembrane signaling and an over-expression in COX-2. These myogenic cellular alterations might contribute to the genesis of motor alterations observed in obese patients
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Disclosure of Interest: None Declared
Keywords: inflammation, motility, MOTILITY DISORDERS, OBESITY

P998 EFFECT OF DIFFERENT VOLUME CHALLENGE ON THE GASTRIC MYOELECTRIC ACTIVITY IN EXPERIMENTAL PIGS

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INTRODUCTION: Surface electrogastrography (EGG) is a non-invasive method for the assessment of gastric myoelectrical activity. Porcine EGG is fully comparable with that recorded in healthy humans with normal rhythm of 3 cycles per minute (3-cpm) (1). There were no data on EGG with water load test in experimental pigs so far.
AIMS&METHODS: The aim was to evaluate the effect of different volume challenge on the gastric myoelectric activity. Five mature female experimental pigs (*Sus scrofa f. domestica*, mean weight 30.9±1.6 kg) entered the study three-times within 3 weeks. After a 15-minute baseline EGG was recorded, tap water (23 °C) was administrated into the stomach by a gastric tube: 500 mL (part A) or 1000 mL (part B) or 1500 mL (part C). A total of twenty 15-minute intervals were recorded afterwards. Surface cutaneous EGG was recorded under general anaesthesia using an Electrogastrography System (MMS, Enschede, the Netherlands). The results were expressed as running spectrum percent activity and the dominant frequency and amplitudes of slow waves were set.
RESULTS: The dominant frequency of slow waves decreased from baseline values (3.34±0.69; 3.25±0.72; 3.30±0.68 cpm) to 2.97±0.52 (part A; p=0.004) or 3.16±0.48 (part B; p=0.116) or 3.09±0.28 (part C; p=0.013) 15 min. after intragastric water administration. Dominant frequency returned back to baseline values within 30 to 60 min. In the part A, the amplitudes of waves increased from basal values (2611±3726 μV^2) to their maximum after 15 min. (7733±1246; p=0.001), subsequently decreased to their minimum after 90 min. (312±283; $p<0.001$) and finally equalised after 160 min. In the part B, the amplitudes of waves increased from basal values (1851±2795) to their maximum after 30 min. (12450±1428; $p<0.001$), subsequently decreased to their minimum after 90 min. (554±460; NS) and finally equalised after 210 min. In the part C, the amplitudes of waves increased from basal values (1991±2713) to their maximum after 60 min. (9070±1258; $p<0.001$), subsequently decreased to their minimum after 180 min. (1154±1177 μV^2; $p<0.001$) and finally equalised after 255 min.
CONCLUSION: Water load test is feasible in experimental pigs. The EGG rhythm remained in a 3-cpm pattern after the water load. After the administration of water, there were 3-cpm EGG waves with initially increased amplitudes, subsequently decreased values and with their final equalisation.
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1. BMC Gastroenterol 2013; 13: 48
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Keywords: electrogastrography, experimental pigs, gastric myoelectric activity, volume challenge, water load test

P999 MODALITY SPECIFIC ALTERATIONS OF ESOPHAGEAL SENSITIVITY CAUSED BY LONGSTANDING DIABETES MELLITUS

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INTRODUCTION: A substantial proportion of patients with diabetes mellitus (DM) suffer from diabetic autonomic neuropathy (DAN), which involves upper and lower GI symptoms. The enteric nervous system (ENS) is not easily accessible and this has called upon new techniques to study the pathophysiology, such as *multimodal pain stimulation* (MMPS) (e.g. mechanical, electrical, thermal) in the oesophagus.
AIMS&METHODS: To further explore ENS alterations in patients with DAN, we compared 30 healthy volunteers (11 M) and 26 patients (8M) with longstanding DM and gastrointestinal (GI) symptoms refractory to medical treatment. Subjects underwent MMPS and HOLTER-ECG, as a measure of ANS function. We used the Gastrointestinal Cardinal Symptom Index to reflect GI symptom severity, and the Short Form-36, (SF-36) to assess quality of life.
RESULTS:

Multimodal Pain Stimulation (MMPS) in the oesophagus

	Electrical (mA)		**Mechanical** (mmHg)		**Mechanical** (bag vol. ml)		**Heat** (sec x °C)	
VAS	**Patients**	**Healthy**	**Patients**	**Healthy**	**Patients**	**Healthy**	**Patients**	**Healthy**
1(SD)	21(12)	16(6)	14(13)	25(29)	16(9)	23(14)	107(164)	178(161)
3	27(13)	21(5)	21(17)	33(32)	27(13)	35(17)	172(197)	268(207)
5	32(13)	29(5)	31(20)	33(33)	38(20)	48(20)	353(233)	473(289)
7	35(13)	36(6)	44(29)	42(36)	52(25)	58(27)	554(297)	602(450)
P	P=0.02		P=0.02		P<0.001		P<0.001	

The patients were more sensitive to heat and mechanical stimulation than controls, but less sensitive to electrical stimulation (see table). There was a positive correlation between heat stimulation and RR(beat-to-beat)-interval (measure of parasympathetic tone) (P=0.04), and physical health (SF-36) (P=0.03). Furthermore patients reported reduced physical (median: 33 vs. 54; $P<0.001$) and mental health (median 34 vs. 54; $P<0.001$) according to SF-36, and reported more severe nausea and vomiting ($P<0.001$), post prandial fullness ($P<0.001$) and bloating ($P<0.001$).

CONCLUSION: Patients with diabetic autonomic neuropathy demonstrate signs of altered oesophageal sensitivity, which may be of relevance for their upper GI symptoms. The complex pattern with *hyper*sensitivity to mechanical and heat stimulation, but *hypo*sensitivity to electrical stimulation implicates that different receptors may respond differently under the influence of long-standing diabetes mellitus.

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Keywords: autonomic nervous system, diabetes mellitus, Diabetic complications, Neuropathy, Pain

P1000 NEUROTICISM & ANXIETY RETARDS AUTONOMIC NERVOUS SYSTEM RECOVERY FOLLOWING ESOPHAGEAL INTUBATION

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INTRODUCTION: Esophageal intubation activates a complex stress response, mediated in part by the Autonomic Nervous System (ANS) (1). Measurement of ANS tone at intubation is thus a useful method of assessing the duration of the physiological stress response which may influence any measurements of esophageal sensory-motor function. For instance, it is known that both ANS tone and psychological factors such as the personality trait of neuroticism and anxiety levels, influence esophageal sensitivity to distension (1). However, factors that influence recovery of ANS tone following intubation are incompletely understood.
AIMS&METHODS: To evaluate the ANS response to esophageal intubation and to identify whether personality traits influence its recovery to baseline. 50 healthy subjects (25 male, mean age 38.1 years, range 21-59 years) had personality traits, using the validated Big-Five Inventory (BFI), and anxiety levels, using the validated Spielberger State/Trait Anxiety Inventory (STAI). ANS tone was assessed using cardiac vagal tone (CVT) which is a measure of brain stem mediated parasympathetic (PNS) efferent tone at baseline (10 minutes) & continuously thereafter in addition to heart rate (HR) and mean arterial blood pressure (MBP) which are mixed measures of PNS and sympathetic tone. Subjects were then intubated with a naso-esophageal catheter, without the aid of local anaesthetic, and monitored for a further 20 minutes.
RESULTS: All subjects tolerated the study well. The mean BFI neuroticism score (BFI-N) was 2.86 (range 1-5). The mean baseline HR, MBP and CVT was 65 beats per minute (range 48-88), 87 mmHg (range 68-104) and 7.8 (range 2.2-14.1) respectively. As expected, naso-esophageal intubation caused a significant elevation in HR ($p<0.0001$) and MBP ($p<0.0001$) with associated CVT withdrawal ($p=0.001$). The mean recovery time of CVT to baseline was 4.5 minutes (range 1.1 – 14.9). BFI-N, state STAI and trait STAI were positively correlated with recovery time (r=0.86, $p<0.0001$; r=0.48, $p<0.0001$; r=0.58, $p<0.0001$).
CONCLUSION: Naso-esophageal intubation results in the withdrawal of PNS tone and an increase in HR and MBP and the speed of recovery to baseline of PNS tone is correlated with neuroticism. Future studies should allow for at least 15 minutes of recovery time after intubation before any physiological assessments are made and consideration should be given to psychological trait measures as these can influence the recovery of stress response to intubation.

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Keywords: autonomic nervous system, intubation, personality

P1001 NORMAL VALUES AND REPRODUCIBILITY OF THE REAL TIME BEAT-TO-BEAT INDEX OF CARDIAC VAGAL TONE IN HEALTHY HUMANS

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INTRODUCTION: The vagus nerve is the primary neuroanatomical substrate within the brain gut axis (1). Vagal dysfunction is considered to be a central pathophysiological feature in many functional gastrointestinal (GI) disorders (2). In humans, surrogate measures of vagal tone are most commonly evaluated using heart rate variability (HRV) albeit with considerable methodological limitations, particularly with respect to temporal resolution. However, recent advances have allowed the measurement of a novel non-invasive validated measure of efferent vagal activity from the brainstem, known as cardiac vagal tone (CVT). CVT is measured on a linear vagal scale (LVS) where 0 represents full atropinization and has improved temporal resolution compared to HRV. CVT is increasingly being utilised in a diverse array of GI research (3,4,5).
AIMS&METHODS: The aim of this study was to define the normal range of CVT and to assess its reproducibility. 120 healthy subjects (68 males, median age 29 years, range 19-55 years) were studied in a temperature controlled, constantly lit, quiet laboratory. After attachment of CVT recording equipment (Neuroscope), 20 minutes of CVT data (resting/no stimulation) was acquired. 30 subjects, selected at random, were restudied after 1 year. Reproducibility was assessed using a two-way, random effects, single measure intra-class correlational coefficients (ICC) model and Bland Altman plots.
RESULTS: All subjects completed the study. The mean CVT was 8.2 LVS with a standard deviation of 3.0. Thus, the normal range (mean +/- 2 standard deviations (SD)) for CVT based on this data is therefore 2.2 LVS to 14.2 LVS. Age correlated negatively with CVT (r=-0.36, $p<0.0001$) but there was no discernable effect of gender, body mass index or ethnicity. The ICC for CVT was 0.81 (95% confidence interval 0.64-0.91), indicating excellent reproducibility. Figure 1 shows the Bland-Altman plot that demonstrate that 29 out of the 30 measurements lie within +/- 2 SDs of the differences between measurements suggesting that there was no bias or systematic error and that the parameter of CVT is reproducible at a period of 1 year.
CONCLUSION: The normal range for CVT should be considered to be 2.2 – 14.2 LVS. CVT is a reproducible measure over the period of 1 year. Future research utilising CVT should refer to these values.

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Keywords: autonomic nervous system, cardiac vagal tone

P1002 A PROSPECTIVE STUDY OF COGNITIVE PERFORMANCE IN IRRITABLE BOWEL SYNDROME: VISUOSPATIAL MEMORY DEFICITS AS A STABLE FEATURE

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INTRODUCTION: The cognitive neurobiological model of irritable bowel syndrome (Kennedy et al., 2012a) proposes that key pathophysiological features, such as altered hypothalamic-pituitary-adrenal (HPA) axis function, may lead to impaired cognitive performance. Recently IBS patients were found to exhibit visuospatial memory deficits (Kennedy et al., 2012b). However, a prospective assessment is essential to confirm if cognitive dysfunction is a stable feature of IBS.
AIMS&METHODS: Aim: To prospectively assess visuospatial memory performance in participants with IBS, in comparison to disease controls [Crohn's disease (CD)] and healthy controls (HC).
Method: Age and IQ-matched participants were assessed at baseline and 6-month follow-up. IBS patients (baseline n = 39), CD patients (baseline n = 18), and HC (baseline n = 40), were assessed using a selection of cognitive tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) and Stroop test. Abdominal pain severity at time of testing was reported by IBS patients on a scale ranging from 0-100. Cortisol awakening response was taken as a measure of activity in the hypothalamic-pituitary-adrenal axis.
RESULTS: At both baseline and follow-up, IBS patients displayed visuospatial memory deficits [assessed using the Paired Associates Learning (PAL) test]. IBS patients made more errors at the 6 pattern recall stage (baseline: $p < 0.05$), which also approached significance across baseline and follow-up ($p = 0.05$), and they required a greater number of trials to complete the PAL [baseline and follow-up ($p < 0.05$)]. Both patients with IBS and those with CD displayed reduced morning cortisol. However, pain severity did not correlate with PAL performance ($p > 0.05$).
CONCLUSION: Visuospatial memory dysfunction is a stable feature of IBS. These results may inform future management of this debilitating disorder in which there is a great unmet medical need.

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Keywords: abdominal pain, cognitive performance, corticosteroid, Inflammatory bowel disease, Irritable bowel syndrome

P1003 THE ESOPHAGEAL MULTIMODAL PAIN MODEL: EXPLORATION OF GENDER DIFFERENCES IN PAIN THRESHOLDS IN THE NORMAL AND SENSITIZED STATE OF HEALTHY VOLUNTEERS

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INTRODUCTION: Clinical data suggests gender differences in gastrointestinal pain, but very little experimental data exists. With the esophageal multimodal pain model gender differences in pain perception to distension, heat, cold, electric current and acid can be measured.
AIMS&METHODS: Using the esophageal pain model, the aim was to measure the effect of gender and mild esophagitis on esophageal pain perception. 35

healthy volunteers (19 males, median age 29 (22-56 years)) underwent gastroscopy, 24h pH metry, and esophageal multimodal pain stimulation. Stimulus intensities at painful thresholds were measured.
RESULTS: Men had a higher pain detection threshold (PDT) to distension (mean volume: men 20.9 ± 10 ml versus women 15.2 ± 6.8 ml, P=0.02. There were no differences between the PDT for men and women to 1) thermal stimulation (mean stimulation time (men, women): heat; 20±5 sec versus 21±6 sec or cold; 33.3 ± 20.1 sec versus 20.7 ± 21.4 sec, $P>0.2$), 2) electrical current (mean current: men 17.6±9.2 mA versus women 12.9±3.7 mA, P=0.11), or 3) tolerated volume acid (median volume: men 200 (20;200) ml versus women 133 (40;200) ml, P=0.2). However, more men compared to women tolerated the maximum volume of acid, P=0.03. Fifteen asymptomatic subjects had mild esophagitis (10 men, all Los Angeles grade A). There were no differences in any esophageal PDT between subjects with normal endoscopy or subjects with mild esophagitis (all $P>0.3$)
CONCLUSION: Esophageal pain thresholds for young men and women have been compared. The results suggest that gender but not mild esophagitis tend to influence esophageal pain perception.
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Keywords: Esophagus, Gender, Human, Pain, Sensation, Sex

P1004 THE EFFECT OF SILDENAFIL CITRATE ON GASTRIC MOTILITY AND SATIATION IN HEALTHY VOLUNTEERS.

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INTRODUCTION: Sildenafil induces an intense and prolonged relaxation of smooth muscle cells by blocking phosphodiesterase type 5, which inactivates the nitric oxide-stimulated cyclic guanosine monophosphate. Studies have shown that dyspepsia is one of sildenafil most frequent reported adverse event next to headache and flushing. Therefore, sildenafil might have important effects on gastric motility.
AIMS&METHODS: The **aim** of this study was to examine the effect of sildenafil on gastric accommodation and gastric emptying in humans. **Methods:** Sildenafil (50 mg) or placebo was orally administered to 20 fasted healthy volunteers (HVs) in a single-blind manner. After a manometry probe and an infusion catheter were positioned in the proximal stomach, the intragastric pressure (IGP) was measured before and during nutrient drink infusion (60 ml per minute). Volunteers were asked to fill in a visual analogue scale for hunger and satiation and 6 epigastric symptoms (fullness, nausea, belching of air, cramps in the abdomen, bloating and pain) at 5-minute intervals. The experiment ended when the volunteers scored maximal satiation at 1-minute intervals by using a graphic rating scale that combines verbal descriptors on a scale graded from 0–5 (1, threshold; 5, maximum satiety). Additionally, a breath test was used to measure gastric emptying rate. The volunteers ingested a standardized solid meal consisting of one non-radioactive ^{13}C-octanoic acid labeled pancake. Breath samples were collected every 15 minutes for 6 hours after the meal.
RESULTS: Nutrient drink infusion induced a rapid drop in proximal stomach IGP, which was suppressed by sildenafil compared to placebo. The average AUC change from baseline was -34.7±8.2 mmHg after sildenafil compared to -81.3±17.1 mmHg after placebo (p=0.001) (see Figure 1). Sildenafil-treated volunteers scored maximal satiation at a significantly lower volume compared to placebo treated subjects (837±86.6 vs. 663±64.8 mL, p=0.002). Finally, gastric half emptying time was significantly slower after sildenafil (76.8±6.1 vs. 90.1±5.9 minutes, p=0.04).
CONCLUSION: Sildenafil inhibits gastric accommodation, leading to significantly decreased nutrient tolerance, and slightly delays gastric emptying rate in man.
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Disclosure of Interest: None Declared
Keywords: gastric accommodation, gastric emptying, intragastric pressure, sildenafil

P1005 OESOPHAGEAL BIOFEEDBACK USING BALLOON DISTENSION OF THE OESOPHAGUS AND SWALLOWING-RELATED VISUAL, OLFACTORY, AND GUSTATORY STIMULI IN THE TREATMENT OF SEVERE DYSPHAGIA WITH TUBE FEEDING

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INTRODUCTION: Tactile, gustatory and visual biofeedback stimuli modulate neural substrates of deglutition (1). Sacral nerve stimulation activates a region of the frontal cortex, which is normally active during focused attention, while subsequent stimuli activate the caudate nucleus, which is involved in learning and reward processing (2). The purpose of this pilot study was to modulate the altered neuronal substrate of swallowing through the stimulation of tensoreceptors with esophageal balloon distension combined with visual, olfactory, and gustatory stimuli in patients with severe dysphagia and feeding tube.
AIMS&METHODS: Seventeen patients with severe dysphagia (Castell dysphagia severity scale = 6±2) after unsuccessful prior therapies were studied [clinical, radiology, endoscopy, and esophageal manometry (MMS, Netherlands)] and compared with 12 healthy subjects for manometry studies. Biofeedback: 1) Inflation of the balloon in the mid esophagus was performed three times in a single session. 2) The patients received a graphic description of how a normal person swallowing mechanism functions. 3) On waking, they rinsed out their mouths with water. 4) Patients were asked to look at, smell, chew and then discharge the food. 5) Then they were asked to try and swallow food while bearing in mind the working of the swallowing system that had been explained to them. Steps 3-4-5 were followed at home, every morning until healing. Mean±SD, binominal 95% confidence interval, and nonpaired Student two-tailed t test with alpha=0.05.
RESULTS: All patients recovered completely the mechanism of swallowing in 36.9±25 (CI: 24-49) days. The 3 patients who were initially feeding tube dependent progressed to total oral intake after 13±10.5 (CI: -1.6-27.6) days of treatment. Patients with dysphagia compared with healthy subjects showed impaired peristalsis (p=0.008), lesser esophageal medial amplitude [47±21 (CI: 35-59) Vs. 88±54 (CI: 57-119) mmHg, respectively; p=0.022), and lesser esophageal upper duration [3±0.7 (CI: 2.5-3.4) Vs. 3.6±0.5 (CI: 3.3-3.9) s, respectively; p=0.034). Lower esophageal sphincter pressure was not different between patients with dysphagia (14±6 (CI: 10.2-17.7) mmHg and healthy subjects (20.8±11.2 (CI: 14.4-27.2) mmHg, p=0.082.
CONCLUSION: This successful outcome with our innovative Dysphagia Therapy Program suggests that the stimulation of oesophageal tensoreceptors combined with visual, olfactory, and gustatory biofeedback stimuli, can modulate the neural substrates of swallowing reprogramming the physiological mechanism of swallowing in patients with severe dysphagia.
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Disclosure of Interest: None Declared
Keywords: dysphagia, Oesophageal biofeedback, oesophageal tensoreceptors, swallowing, visual, olfactory, and gustatory biofeedback stimuli

P1006 OUTCOMES OF INTRAPYLORIC BOTULINUM TOXIN INJECTION FOR REFRACTORY GASTROPARESIS - A SINGLE CENTER EXPERIENCE.

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INTRODUCTION: Refractory gastroparesis (GP) constitutes a major therapeutic challenge. Drug therapy for GP is often ineffective and intolerance to drugs is common. Two small controlled studies suggested a limited value of endoscopic intrapyloric Botox (BTX) injections. In clinical practice we found that some patients noticed significant improvement in symptoms and quality of life. With limited treatment options, Botox injections can still be considered for treatment of refractory GP when drug therapy failed.
AIMS&METHODS: The aim of this study was to evaluate the long-term outcomes of intrapyloric Botulinum toxin injection for patients with proven GP by gastric emptying study. Retrospective medical records review was performed. Patients with GP who received intrapyloric BTX injection from 1/2008-7/2012 were included. Demographics, comorbidities, diagnosis, past surgical history, amount of BTX injected, intraprocedural complications, and medication were collected. The questionnaire was sent to all patients. Symptoms, the overall improvement after procedure, gastric stimulator placement, complications related to BTX injection and number of visits to ER/hospitalizations were analyzed. BTX was injected into 4 quadrants into the pyloric channel.
RESULTS: 25 of 32 pts. were included (refused participation 1, no response 6) 19 females (♂), 6 males (♀). Mean age: 46.1 (range 21-71). Causes of GP: idiopathic (IGP) 17 (13F, 4M), Diabetes (DGP) 6 (4F, 2M), postsurgical (PGP) 2F. Number of BTX injections: 1-15 pts. (13F, 2M), 2-5 pts.(4F, 1M); 3-3 pts. (1F, 2M), 4-2 pts. (1F, 1M). The mean follow up: 31months. Overall symptom improvement: 0% (2F), 25% (5F), 50% (8F, 2M), 75% (3F, 4M), 100% (1F). Improvement (>50%) based on Dx: IGP 82% (14/17); DGP: 67% (4/6), PGP 0% (0/2). Reduced ER/hospital visits: 24% pts. (6/19). Gastric stimulator placement: 28% pts. (7/25).
Symptom Improvement with BTX injections (GCSI).

Response	Bloating		Abdominal distention	Early satiety	Nausea*	Vomiting*
No improvement	(♂)	9	10	11	6	4
	(♀)			1	1	
Partial improvement	(♂)	9	8	6	10	9
	(♀)	4	3	2	2	3
Complete	(♂)	1	1	2	2	5
	(♀)	2	3	3	3	3
improvement						

*1 patient no nausea/vomiting
CONCLUSION: Approximately 72% of our GP patients noticed significant (>50%) symptom improvement. This response rate does not exclude BTX therapy from the armamentarium for treatment of refractory GP. There may be a role for BTX therapy in properly selected GP patients. The subgroup of GP patients who benefited the most were males and those with IGP. Further studies with a larger sample size are needed.
Disclosure of Interest: None Declared
Keywords: botox, gastroparesis, therapy

P1007 FACTORS THAT EFFECT THE DISRUPTION OF OESOPHAGOGASTRIC JUNCTION AND ITS RELATION WITH HIGH RESOLUTION MANOMETRY ALTERATIONS AND ACIDIC REFLUX

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INTRODUCTION: The oesophagogastric junction (OGJ) is a mobile structure and several factors contribute to its disruption. High resolution manometry (HRM) facilitates the investigation of the OGJ and its progressive disruption which favors gastroesophageal reflux (GOR).
AIMS&METHODS: To evaluate the risk factors associated with OGJ disruption and the relationship between OGJ type, manometric alterations and acid reflux. 115 patients with GOR symptoms included. HRM (Manoscan; Given) and 24 hour pH-metry were performed on all. They were classified according to the OGJ type based on the axial separation between the lower oesophageal sphincter (LOS) and crural diaphragm (CD) (type I: normal; type II: 1-2 cm LOS-CD separation; type III or hiatus hernia: LOS-CD separation > 2 cm). Statistical analysis: regression logistic models; Kruskal-Wallis; Chi-Square.
RESULTS: Epidemiological data, HRM and pH-metry parameters are expressed in the table. Age (Odd Ratio (OR) 1.03 [1.01-1.06]; p=0,016), body mass index (BMI) (OR 1.09 [1.02-1.17]; p=0,01) and abdominal perimeter (AP) (OR 1.03 [1.01-1.06]; p=0,021) were independent risk factors for OGJ type III (area under the curve 0.70). OGJ disruption is associated with lower pressure (p=0,006), greater length (p < 0.001) and oesophageal body (OB) shortening (p<0.001), noting that the increase of one unit in the length of the hernia decreases the length of the oesophagus in 0.963 (p=0,013). Higher acid exposure was found in OGJ type II and III with respect to type I (p =0,015).

	OGJ I (n=56)	OGJ II (n=44)	OGJ III (n=15)	P value
	Epidemiological data			
Age	49,3 [45,4-53,2]	54,3 [49,6-58,9]	64,9 [58,5-66]	**0,001**
Sex (F)	33 (58,9%)	28 (63,6%)	10 (66,7%)	0,815
BMI (kg/m2)	25,2 [23,9-26,4]	27,9 [26,3-29,7]	31,4 [25,4-37,4]	**0,001**
AP (cm)	88,5 [84,8-92,2]	95,6 [91,5-99,6]	98,4[92,6-104,2]	**0,003**
	HRM parameters			
OGJ pressure	16,3 [13,8-18,8]	10,6 [9-12,3]	13,9 [9,8-18,1]	**0,006**
IRP-4s	8,7 [7,4-9,9]	7,5 [5,8-9,3]	11,3 [7,9-14,7]	0,133
OGJ length (cm)	4 [3,9-4,2]	4,7 [4,5-4,9]	8,5 [6,9-10,2]	**<0,001**
OB length (cm)	24,6[24,1-25,1]	23,6[23-24,1]	20,5[18,5-22,4]	**<0,001**
DCI(mmHg.cm.s	2525,5	1981,4	1865,4	0,204
VFC (cm/s)	4,9 [3,1-6,7]	4,1[3,1-5,1]	2,9 [2,5-3,4]	**0,027**
Latency (s)	6,3 [5,7-6,9]	6,9[5,6-8,3]	5,8 [2,4-14,1]	0,577
	pH-metry			
% pH < 4 total	2,3[1,6-2,9]	4,9[3,6-6,4]	8,1[3,4-12,8]	**0,015**
% pH < 4 upright	2,6[1,9-3,4]	5,9[4,3-7,6]	7,2[3,2-11,3]	**0,022**
% pH< 4 supine	1,3[0,6-2,1]	3,8[1,8-5,8]	8,9[2,5-15,2]	**0,001**
DeMeester score	9,8[6,6-13]	19,8[14,2-25,3]	30,9[13,6-48,3]	**0,014**

CONCLUSION: Age, overweight and central obesity pose a greater risk for hiatus hernia. The greater OGJ disruption is associated with lower pressure, oesophageal shortening, and higher acid exposure in pH-metry.
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Disclosure of Interest: None Declared
Keywords: ACID REFLUX, high resolution manometry, oesophagogastric juntion

P1008 INTEGRATED RELAXATION PRESSURE IN ACHALASIA IN SITTING POSITION

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INTRODUCTION: One of the criteria used to diagnose achalasia by means of high resolution manometry is an Integrated relaxation pressure >15 mmHg of the esophago-gastric junction measured in supine position. Normal values in upright position have been published but by now there is not a cut-off value in order to diagnose achalasia.
AIMS&METHODS: The aim of the study was to determine the usefulness of the 15 mm. Hg. integrated relaxation pressure (IRP) value of the esophago-gastric junction (EGJ) in patients with achalasia studied by High Resolution Manometry (HRM) in the sitting position.
MATERIAL AND METHODS: The HRM (ManoScan A100, Given / Sierra Scientific Instruments Inc.) records of consecutive patients diagnosed with achalasia from december 2007 to december 2012 in our unit were retrospectively analyzed. All of the studies were done with the patient in the sitting position in fasting state. After a 5 min adaptation period, subjects were provided with ten swallows of 5 mL water. The proximal and distal esophageal margins of the EGJ were adjusted manually to ensure accuracy for every swallow. A descriptive analysis of the data was made.
RESULTS: The records of 97 patients were analyzed. 29 records were excluded because of poor quality studies (artifacts, impossibility to get a gastric record), history of associated disease that can affect esophageal motility, previous treatment of achalasia, esophageal or gastric surgery, and those in whom a secondary achalasia could not be ruled out.
The final group was composed of 68 patients (39 M (57%): 29 F, with a mean age of 49 years (range: 15-92). The mean age of male was 45 years (range: 17-83) and 54 years in female (range: 15-92).
The average value of the IRP in the 68 patients was 26.4 (SD 10.65) mm. Hg. In 9 patients (13.2%) the IRP was <15 mm. Hg, of which 6 were men, and none had an IRP <10 mm. Hg.
The IRP patients >15 mm. Hg. had a higher mean resting pressure (32.2 (11.7 to 88.8) mm. Hg.) than those with an IRP <15 mm. Hg. (16.9 (6.7 to 40.9) mm. Hg.).
CONCLUSION: Our results show that using IRP values >15 mm.Hg. in diagnosing patients with achalasia by HRM in the sitting position may produce up to 13% false negatives.
With the limitations imposed by the small number of patients with achalasia and IRP <15 mm.Hg, there is a significant relationship between resting pressure and IRP values. Although further studies will be necessary to confirm our data to formally establish the cutoff point, we consider that values of IRP ≥ 10 mm.Hg. would be more appropriate.
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Disclosure of Interest: None Declared
Keywords: achalasia,, esophagogastric junction, Integrated Relaxation Pressure

P1009 PNEUMATIC DILATION IN ACHALASIA: 30 YEARS EXPERIENCE

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INTRODUCTION: The success rate, of pneumatic balloon dilatation (PD) in achalasia varies.
AIMS&METHODS: This longitudinal cohort study investigated the long term clinical after pneumatic dilatation, with a focus on possible predictors for the time of recurrence. Between 1982-2012, 99 patients with a mean age of 49.7 ± 16 years were treated with PD and followed-up at regular intervals for a median of 13 years. Remission was determined with the use of a structured interview and the Eckardt score. Patient's characteristics, manometry, barium swallow results and PD characteristics were evaluated as predictors for the need of a second treatment.
RESULTS: One perforation occurred with no mortality, and 84 (84.4%) of the 99 patients were symptom-free 12 weeks after dilation. The mean time of remission was 87 months. However, later on, 51 (51.5%) patients required a second treatment (39 PD, 12 cardiomyotomy). Lower esophageal sphincter pressure (LES) (mean 21.2 mmHg vs. 15.5 mmHg; *P*=.001), width of esophageal corpus (mean 4.2cm vs. 3.4cm; *P*=.007) post PD and young age at presentation are predictive factors of recurrence. Neither clinical, manometric or radiological findings, nor gender determined the need for a second treatment.
CONCLUSION: Single pneumatic dilation in achalasia is a safe and effective therapy. However, half of the patients will need a second treatment in the long term. Young age at presentation, a high LES pressure and a wide esophageal corpus 3 months after PD are predictive factors for the need for repeated treatment.
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Disclosure of Interest: None Declared
Keywords: Achalasia, dysphagia, pneumatic dilatation

P1010 ACUPUNCTURE FOR DIABETIC GASTROPARESIS - A FEASIBILITY COMPARATIVE STUDY

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INTRODUCTION: Available medical treatments for diabetic gastroparesis (DG) are less than satisfactory. Acupuncture treatment has been used for various gastrointestinal conditions with effects noted on gastrointestinal motility.
AIMS&METHODS: To compare the degree of symptoms, gastric emptying rate (GER) and glucose control improvement before and after domperidone followed by acupuncture treatment.
Eight patients with long-standing, uncontrolled diabetes mellitus and gastroparesis were enrolled in this pilot, prospective case-crossover study. All patients received domperidone (20 mg QID) for 12 weeks and after a wash-out period of 2-3 weeks, received acupuncture treatments for 16 weeks. All patients completed a demographic questionnaire as well as the Gastroparesis Cardinal Symptom Index (GCSI), Satisfaction with Life Scale (SWLS) and the 36-item short-form (SF-36) at entry and at the end of each treatment period. Gastric emptying rate (GER) measurement, glucose level and HbA1C were performed at entry and at the end of each treatment period as well.
RESULTS: Mean age, M/F ratio and mean BMI (kg/m^2) were 57.1 ± 9.9 yrs, 1/7 and 25.2, respectively. Treatment with domperidone did not improve symptoms, GER or glucose control. Acupuncture treatment was associated with improvement of almost all cardinal symptoms scores of GCSI, SWLS (p=0.002) Social Functioning (SF) score (p=0.054) but not with GER or glucose control.
CONCLUSION: Acupuncture was associated with improvement in symptoms related to gastroparesis. A larger trial is warranted for the evaluation of acupuncture in patients with diabetic gastroparesis.
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Disclosure of Interest: None Declared
Keywords: Acupuncture, Diabetic Gastroparesis

P1011 ROLE OF GASTROESOPHAGEAL REFLUX IN PROTON PUMP INHIBITORS-REFRACTORY NON-EROSIVE REFLUX DISEASE PATIENTS WITH ESOPHAGEAL MOTILITY DISORDERS

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INTRODUCTION: A high proportion of non-erosive reflux disease (NERD) patients do not respond to proton pump inhibitors (PPI) therapy. Various underlying mechanisms have been shown to contribute to the failure of PPI treatment. Although esophageal motility disorders (EMD) are considered to be one of the most important factors causing PPI-refractory NERD, there is no report of EMD related with the frequency, classification, symptom and gastroesophageal reflux in patients with NERD.
AIMS&METHODS: The aim in this study is to evaluate the relationship between symptoms of PPI-refractory NERD patients with EMD and their gastroesophageal reflux. Seventy six patients (44 males and 32 females) whose heartburn symptoms did not improve despite taking PPI at the standard dose for at least 8 weeks (PPI-refractory NERD patients) underwent intraesophageal pressure test and were divide into 2 groups; normal esophageal motility and EMD. Twenty-four -hour multichannel intraluminal impedance-pH (MII-pH) monitoring examination and medical interview such as reflux symptoms were assessed using the Questionnaire for the Frequency Scale for the Symptoms of GERD (FSSG) were performed in all patients to analyze patient's backgrounds, gastroesophageal reflux and their symptoms between the groups.
RESULTS: Of 76 PPI-refractory NERD patients, 19 patients (25%) had EMD. In 17 patients except 2 patients with achalasia, there were 6 patients with ineffective esophageal motility (IME), 9 patients with non-specific esophageal motility disorder (NEMD) and 2 patients with hypertensive lower esophageal sphincter (HLES). Fifty seven patients had no esophageal motility disorders. There were no significant differences related with gender, age, BMI, duration of 24-hour esophageal pH < 4, mean frequency of gastroesophageal and proximal reflux between the 2 groups. The MII-pH monitoring examination revealed that symptom index (S.I.≧50%) exactly coincided with reflux of gastric contents in 12 patients (70.5%) with EMD and 43 patients (75.0%) with normal esophageal motility. The FSSG scores of normal esophageal motility and EMD were 17.8±8.9 and 17.0±2.1, respectively, and there was no significant difference. Of patients with EMD the questionnaire No.10 of FSSG was significantly related with the rate of gastric reflux (r=0.58, p=0.02) and proximal reflux (r=0.63, p=0.02). The questionnaire No.9 of FSSG was also related with the rate of gastric reflux (r=0.44, p=0.06).
CONCLUSION: PPI-refractory NERD involved some prevalence of EMD, and symptoms of patients with EMD were considered to be caused by gastroesophageal reflux.
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Disclosure of Interest: None Declared
Keywords: esophageal motility disorders, non-erosive reflux disease, proton pump inhibitor

P1012 CORRELATION OF NOVEL ESOPHAGEAL PRESSURE-FLOW METRICS WITH BOLUS TRANSPORT AND ESOPHAGO-GASTRIC JUNCTION FLOW DURING BARIUM SWALLOW

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INTRODUCTION: Esophageal pressure-flow analysis derives metrics that better describe the interactions between bolus transport and pressure generation. Pressure-flow metrics detect abnormal bolus pressurisation in dysphagia patients with apparently normal peristalsis (1-4). To date there are no data correlating esophageal pressure-flow metrics with videofluroscopic (VF) measures. To address this knowledge gap we undertook a pilot study in dysphagia patients undergoing VF + impedance-pressure assessment of swallowing.
AIMS&METHODS: We analysed simultaneous VF + impedance-pressure recordings in 9 dysphagia patients (62-82y, 7m) during liquid barium swallows. A 3.2mm catheter with 25 1cm pressure/12 2cm impedance was used (Solar GI system, MMS). We derived metrics of bolus pressurisation (Pressure Flow Index, PFI), bolus clearance (Impedance Ratio, IR) and bolus flow timing relative to pressure generation (time from nadir impedance to peak pressure, TZnPp). Peristaltic break size (20mmHg iso-contour defect, ICD) and 4 sec integrated relaxation pressure (IRP4s) were also measured. Bolus transport was assessed by 7-point VF scale (5); high score = abnormal. The cumulative time of flow across the EGJ was also measured (bolus flow time, BFT). Age-match control swallows were used as a normal comparator for pressure-impedance derived variables.
RESULTS: Patients compared to controls had larger peristaltic breaks, higher Impedance Ratio and reduced EGJ relaxation (ICD 8 [2, 13] vs. 2 [0, 2] cm, p = 0.027; IR 0.5 ± 0.1 vs. 0.3 ± 0.0, p=0.019; IRP4s 11 ± 2 vs. 6 ± 1 mmHg, p = 0.070). In patients, a higher VF score correlated with larger ICD (Spearman r = 0.895, p<0.001) and a higher IR (r = 0.661, p<0.05). Diminished EGJ BFT correlated with a shorter TZnPp (r = -0.733, p<0.05) and a higher IR (r = -0.750, p<0.05). IRP4s did not correlate with either VF score or BFT. Patients could be separated into three distinct groups on grounds of abnormal bolus pressurisation (high pressure flow index) and/or clearance (high Impedance ratio); Grp1 normal PFI/normal IR (n=4), Grp2 abnormal PFI/normal IR (n=2) and Grp3 normal PFI/abnormal IR (n=3). Comparisons among these groups showed that VF scores were most abnormal for Group 3 (ANOVA p = 0.014) and BFT shortest in Groups 2 and 3 (ANOVA p=0.04).
CONCLUSION: Peristaltic breaks (large ICD) and incomplete clearance (high IR) correlate with bolus transport abnormalities on VF, however PFI in combination with IR, may better discriminate abnormalities due to over-pressurisation of the bolus when bolus transport is nomal. The metric TZnPp appears to be an indirect marker of EGJ flow time.
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Keywords: Diagnosis, dysphagia, esophageal manometry

P1013 DELAYED GASTRIC EMPTYING IS THE REASON OF EARLY GASTRO-ESOPHAGEAL REFLUX DISEASE RELAPSE.

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INTRODUCTION: Gastro-esophageal reflux disease (GERD) relapses occur commonly and call for maintenance therapy (1). Early relapse possibly caused by hiatal hernia or rebound of acid hypersecretion after PPI-treatment stopping, other reasons have to be investigated (1,2,3). Searching and correction of possible individual factors causing the reflux could be beneficial for long remission of GERD symptoms. Delayed gastric emptying (DGE) is known as possible reason of GERD, but gastric emptying time is not measured routinely. Use of 13C-octanoate breath test (13C-OBT) (4) could be reasonable for this topic in part of GERD patients.
AIMS&METHODS: Our aims were to detect DGE in GERD patients as a possible reason of early symptoms relapse and to define appropriate treatment regimen using 13C-OBT with infrared stable isotope spectrometer (IRIS,Wagner-Analysen-Technik) for measure the gastric emptying half-time ($T_{1/2}$) in those patients. 42 (27 male, 15 female) patients with erosive GERD and without hiatal hernia were examined and treated. Egg-13C-OBT $T_{1/2}$ was previously validated in 18 healthy volunteers. Gastric emptying half-time was measured with egg-13C-OBT before treatment with single dose of PPI (esomeprasole 40 mg) and after 8 weeks. Those patients, who have DGE after 8 weeks divided to 2 groups. Group 1 patients received prokinetic drug itopride hydrochloride 50 mg 3 times a day during 2 weeks, group 2 were informed untreated controls. Symptoms frequency and severity (0 to 5 points) were assessed in groups after 2 and 6 weeks from itopride start. ''Statsoft 7,0'' was used for statistics.
RESULTS: Median $T_{1/2}$ in healthy volunteers was 74,5 minutes (95% CI=67-85). 32 patients had grade A of esophagitis, 10 – grade B. DGE was revealed in 33 of 42 (78,6%) patients at start. After 8 weeks esophagitis was healed in 40 pts (95,2%±3,3%), 22 of 40 successfully treated patients (55,0%) had DGE. Healing influences on $T_{1/2}$ improving: OR (0,6 95% CI=0,4-0,9). Heartburn relapsed in 1 patient of 11 during 2 weeks period of itopride treatment in group 1 and in 3 of 11 patients in group 2, p=0,09. After 1 month from treatment stop in group 1 were 2 patients, who noticed heartburn, in group 2 – 8 patients had heartburn. Impact of itopride on early (within 6 weeks) relapse prevention was significant: OR 3,0 (95%CI=1,0-5,0). Long-term observation is continued.
CONCLUSION: 13C-ODT is good tool for gastric emptying time measure, an it is beneficial for GERD patients. DGE is highly prevalent among erosive GERD patients. The probability of early symptomatic relapses is dependent on impaired gastric emptying speed. Search for individual reason of DGE is needed. Additional prokinetic treatment is useful in part of GERD patients.
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Disclosure of Interest: None Declared
Keywords: 13C octanoate breath test, delayed gastric emptying, GERD relapse

P1014 DURATION OF UNTREATED INFLAMMATION REPRESENTS THE MAIN RISK FACTOR FOR STRICTURE DEVELOPMENT IN EOSINOPHILIC ESOPHAGITIS

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INTRODUCTION: Eosinophilic Esophagitis (EoE) is a chronic-inflammatory condition presenting either as inflammatory-phenotype (IP), as stenosing-phenotype (SP) or as an overlap form. The IP is endoscopically characterized by whitish exudates, furrows and edema, whereas the SP shows signs reflecting tissue remodeling, such as rings and strictures. There is some evidence that SP develops over time, but the precise evolution of stricture formation during the disease course remains largely unknown.
AIMS&METHODS: We aimed to correlate the prevalence of esophageal strictures with the duration of untreated disease and to evaluate risk factors for stricture formation. We analyzed data from the Swiss EoE Database (SEED), extended by a review of patients charts, endoscopy and pathology records. Strictures were assessed endoscopically at first diagnosis of EoE and defined as a narrowing leading to problems passing a standard adult upper endoscope (outer diameter 9mm). Diagnostic delay was defined as period from onset of EoE symptoms to diagnosis.
RESULTS: Two hundred EoE patients were analyzed (153 males, mean age at index visit 39 ± 15 years, all Caucasians). All patients were symptomatic; dysphagia was present in 94% and chest pain in 35% of patients. Allergies were identified in 132 (66%) of patients. An endoscopic bolus removal was performed in 56 patients (28%), whereof 28 prior and 28 at the time of EoE diagnosis. Median diagnostic delay was 6 years (IQR 2-12, range 0-36 years). We observed the following stricture prevalence at EoE diagnosis according to the following intervals of disease duration: 0-2 years (n=58) 17.2%, 3-5 years (n=39) 30.8%, 6-8 years (n=18) 38.9%, 9-11 years (n=29) 37.9%, 12-14 years (n=12) 41.7%, 15-17 years (n=14) 64,3%, 18-20 (n=6) 66.7%, >20 years (n=24) 70.8% ($p < 0.001$). Logistic regression modeling detected a long duration of untreated disease (defined as diagnostic delay ≥ 7 years) to be strongly associated with the presence of strictures at the index visit (Odds Ratio 3.24, 95% confidence interval 1.75-5.97, $p < 0.001$). No association of strictures at the index visit was found with gender, presence of allergies, age at EoE diagnosis, positive family history of EoE, blood eosinophilia, elevated serum IgE, and peak eosinophil count at index histology.
CONCLUSION: Strictures in EoE develop over time. The frequency of stricture formation is proportional to the duration of the untreated disease. These findings underscore the need to reduce the diagnostic delay in EoE and to control the underlying inflammation in order to prevent esophageal remodeling.
Disclosure of Interest: None Declared
Keywords: Eosinophilic esophagitis, esophageal stictures, natural history

P1015 PATIENTS WITH EOSINOPHILIC ESOPHAGITIS TRIGGERED BY NATIVE PROTEINS TOLERATE COW'S MILK-BASED HYDROLYZED FORMULA

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INTRODUCTION: Eosinophilic esophagitis (EoE) is an emerging gastrointestinal disorder characterized that usually persists from childhood to adulthood. Its high response rate to food-elimination diets implies that the disease involves allergic sensitization to commonly consumed foods. Cow's milk protein is the main food trigger for EoE in both children and adults and should be continuously avoided once identified as such.
AIMS&METHODS: We aim to evaluate tolerance of a cow's milk-based extensively hydrolyzed formula (eHF) with regard to disease remission maintenance in adult patients with milk-triggered EoE. Seventeen adult patients in whom cow's milk was consecutively demonstrated to trigger EoE after an empiric six-food elimination diet-based study protocol and who subsequently maintained disease remission were prospectively recruited. They were given 400 mL of a cow's milk-based eHF daily for 8 weeks. Intraepithelial peak eosinophil and blood esosionophil counts, esophageal related symptoms, serum total and specific IgE to major milk proteins, and eosinophil cationic protein were monitored before and after eHF intake.
RESULTS: Thirteen male and 4 female patients aged 17 to 56 completed the study protocol. 15 patients (88.24%) achieved and maintained EoE remission, while an infiltration >15 eosinophils/hfp reappeared in the remaining two patients. No differences in age, gender, symptoms and endoscopic appearance at baseline conditions, or personal/family allergic background were observed between those patients who tolerated the eHF and those who did not. Symptom scores did not significantly change after eHF intake and were significantly lower than those documented at baseline conditions or after cow's milk challenge. No differences were documented in blood eosinophil counts or serum markers after eHF intake.
CONCLUSION: Most adult patients with EoE triggered by cow's milk tolerate a cow's milk-based eHF, thus providing them with a safe, economical alternative to cow's milk.
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Disclosure of Interest: None Declared
Keywords: Eosinophilic esophagitis, food allergy, hydrolyzed formula, milk allergy, milk proteins

P1016 OESOPHAGEAL BASELINE IMPEDANCE VALUES ARE DECREASED IN PATIENTS WITH EOSINOPHILIC OESOPHAGITIS

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INTRODUCTION: Gastro-oesophageal reflux has been suggested to play a role in eosinophilic oesophagitis (EoO). Oesophageal acid exposure decreases baseline impedance, a marker of mucosal integrity, in patients with gastro-oesophageal reflux disease.
AIMS&METHODS: The aim of this study was to assess oesophageal baseline impedance levels in EoO patients and to investigate their relationship with oesophageal acid exposure in EoO.
Ambulatory 24-h pH-impedance monitoring was performed in 11 EoO patients and in 11 healthy controls with matched oesophageal acid exposure. We assessed baseline impedance levels in the distal, mid and proximal oesophageal impedance channels every 2 hours during a 30-second time window. The median baseline impedance level during all 2-hour periods was considered to be the baseline impedance level for the measurement.
RESULTS: Patients did not differ from controls with regard to acid exposure time (4.7 (2.0-9.2)% vs 4.8 (4.4-5.6)%, $p = 0.693$), the total number of reflux episodes (50 (21-74) vs 56 (41-71), $p = 0.622$) and the number of proximal reflux episodes (13 (1-21) vs 31 (22-58), $p = 0.148$). Baseline impedance levels in EoO patients were markedly lower compared to healthy controls in the distal oesophagus (988 (757-1978) Ω vs 2259 (1767-2896) Ω, $p = 0.015$), mid oesophagus (1420 (836-2164) Ω vs 2614 (2374-3879) Ω, $p = 0.003$), and proximal oesophagus (1856 (1006-2625) Ω vs 2868 (2397-3439) Ω, $p = 0.005$). In EoO patients, distal, mid and proximal oesophageal baseline impedance values were not correlated with acid exposure at these levels ($r = 0.427$, $p = 0.190$, $r = 0.136$, $p = 0.689$, and $r = 0.027$, $p = 0.937$, respectively). Whereas baseline impedance decreased from proximal to distal in healthy subjects ($p = 0.037$), no such gradient was seen in EoO patients ($p = 0.123$).
CONCLUSION: Throughout the oesophagus baseline impedance values are decreased in EoO patients, indicating impaired mucosal integrity. Our findings suggest that factors other than acid reflux are the cause of low baseline impedance in EoO.
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Disclosure of Interest: None Declared
Keywords: Baseline impedance, Eosinophilic esophagitis, gastro-esophageal reflux disease, impedance-pH monitoring, pathophysiology, Reflux

P1017 SWALLOWED FLUTICASONE RESTORES OESOPHAGEAL MUCOSAL INTEGRITY BY REDUCING EOSINOPHILIC INFLAMMATION IN ADULTS WITH EOSINOPHILIC OESOPHAGITIS

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INTRODUCTION: It has been shown that the oesophageal mucosal integrity is impaired in patients with eosinophilic oesophagitis (EoO). It is unknown whether this is the cause or a result of eosinophilic inflammation. Inflammatory cytokines and degranulation products of eosinophilic inflammation may impair the mucosal integrity. However, the latter may also facilitate transmucosal allergen flux leading to inflammation. An improvement of the mucosal barrier function with the anti-inflammatory drug fluticasone would suggest that barrier dysfunction is a result and not the cause of eosinophilic inflammation.
AIMS&METHODS: To evaluate the effect of swallowed fluticasone on the mucosal integrity in EoO, we included 8 adult EoO patients (>15 eosinophils/hpf, no response to PPI). Patients underwent upper endoscopy at baseline and after 8 wks of swallowed fluticasone 500 μg BID. As a measure of mucosal integrity *in vivo*, electrical tissue impedance spectroscopy (ETIS) measurements 5 cm proximal to the LOS were performed during endoscopy. Four biopsies taken at the same level were transferred to Ussing chambers to measure transepithelial electrical resistance (TER) and transmucosal flux of small fluorescein and large rhodamine molecules during a 1-hour period. Intercellular spaces were measured with electron microscopy.
RESULTS: Eosinophil and mast cell counts decreased after fluticasone (table 1). The mucosal integrity was substantially improved after fluticasone, as shown by increased extracellular impedance and TER. In line, transmucosal flux of fluorescein and rhodamine molecules decreased, however significance was not reached. Intercellular spaces were not affected by fluticasone(p=.263). Dysphagia and endoscopic signs were decreased by fluticasone (both $p<.05$). After fluticasone, the peak eosinophil count correlated with the extracellular impedance (r=-.778, $p<.05$), TER (r=-.874, $p<.01$), and transepithelial flux of rhodamine molecules (r=.741, $p<.05$).
Table 1

	Baseline, median (IQR)	After fluticasone, median (IQR)	p
Extracellular impedance (Ω•m)	2057 (1715-3971)	5852 (4973-9510)	.036
TER (Ω•cm^2)	31.6 (26.2-45.7)	68.9 (50.1-102.0)	.017
Fluorescein flux (μmol/cm^2/h)	2419 (834-2826)	157 (0-2132)	.093
Rhodamine flux (μmol/cm^2/h)	69 (25-83)	0 (0-26)	.310
Peak eosinophilia (n/hpf)	70.0 (30.0-78.8)	6.5 (1.0-32.0)	.069
Peak mastocytosis (n/hpf)	21.5 (11.5-46.3)	6.0 (3.5-17.3)	.036

CONCLUSION: Fluticasone treatment decreases eosinophilic inflammation and improves mucosal integrity in EoO. Our study suggests that esophageal mucosal barrier dysfunction is a consequence and not the cause of eosinophilic inflammation in EoO.
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Disclosure of Interest: None Declared
Keywords: Eosinophilic esophagitis, epithelial barrier dysfunction, Glucocorticoids, Mucosal integrity, pathophysiology, therapy

P1018 SAFETY OF PROPOFOL ADMINISTRATION IN ADULT EOSINOPHILIC OESOPHAGITIS PATIENTS SENSITIZED TO EGG, SOY OR PEANUT

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INTRODUCTION: Propofol administration in a fatty emulsified formulation containing egg lecithin and soybean oil is often contraindicated in patients with allergies to egg and/or soy. However, Intralipid, a fat emulsion prepared for intravenous administration, which contains soybean oil and egg lecithin as well, can be safely administered in egg- or soy-allergic patients.
AIMS&METHODS: To investigate the safety of propofol for procedural sedation in adult eosinophilic oesophagitis (EoE) patients sensitised to egg, soy or other foods showing cross-reactivity with them. A prospective cohort study of the safety of propofol for procedural sedation during upper endoscopies in consecutive adult EoE patients was conducted in two secondary referral hospitals between January 1, 2007 and March 1, 2013. Propofol was administered by an endoscopist in all procedures excepting two 14-yrs old male with food impaction who underwent general anesthesia. Food-specific serum IgE measurements and skin prick/prick prick tests for egg, chicken, soy, peanut and other legumes (including lentils, chickpeas, beans and peas) were carried out.
RESULTS: Sixty consecutive EoE adult patients, mostly on empirical six-food elimination diet, were evaluated. Mean age was 28 years-old (14-56), with a clear male predominance (54/6, 90%). Atopy was present in 52/60 (87%) of patients, being the most prevalent allergic comorbidities rhinoconjunctivitis (75%) and seasonal asthma (61%). The rate of food sensitisation in the cohort, measured by either blood or skin testing, was egg (41%), soy (41%), chicken (23%), peanut (52%), lentils (64%), chickpea (17%) and pea (17%). A total of 404 upper endoscopies (mean 6.78 (3-17)) were performed under propofol sedation (mean dose 175 mg (90-282)), including 7 stricture dilations. No anaphylactic or allergic adverse events were reported in the entire cohort excepting a transient bronchospasm episode after orotracheal intubation in one of the 14-yrs old male undergoing anesthesia. This patient, who suffered from severe asthma, received as well ketamine and midazolam for anesthesia induction and further allergic work-up ruled out sensitisation neither to propofol nor to Intralipid.
CONCLUSION: Propofol was safely administered for procedural sedation in a large series of adult EoE patients sensitised to egg, soy or cross-reactant foods. These findings may warrant further reconsideration of warning labels regarding propofol administration in egg or soy-allergic patients
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Disclosure of Interest: None Declared
Keywords: Egg, Eosinophilic oesophagitis, Propofol, sedation, soy

P1019 TOPICAL CORTICOSTEROIDS DO NOT RESTORE A HEALTHY BLOOD EOSINOPHIL PHENOTYPE IN PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

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INTRODUCTION: Eosinophilic esophagitis (EoE) is an allergic disorder in which eosinophilic granulocytes invade the esophagus. Patients typically suffer from dysphagia and food bolus impaction. Swallowed corticosteroids are the standard therapy. Eosinophils in the circulation of untreated patients display a particular pattern of surface molecules.
AIMS&METHODS: The objectives of this study were to examine if topical corticosteroid therapy restores the phenotype of eosinophils to a healthy phenotype.
Blood eosinophils from adult EoE patients before (n=13) and following a 2-month course of topical corticosteroids (n=7) were investigated, and compared to healthy controls (n=10). Eosinophilic surface molecule expression was determined by 4-color flow cytometry. Data was processed by multivariate pattern recognition methods to reveal specific patterns.
RESULTS: Eosinophils from all EoE patients, independent of treatment, had decreased expression of CD44 and CCR3, and enhanced expression of CD23, CD40 and CD54 relative to control persons. Corticosteroids decreased the expression of CD18 on eosinophils, but did not otherwise alter the phenotype of blood eosinophils in EoE patients.
CONCLUSION: Topical corticosteroids did not reverse the phenotype of blood eosinophils to a healthy profile. The diminished expression of CD18 on blood eosinophils may explain the reduced entry of eosinophils into the esophagus following corticosteroid treatment of EoE patients.
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Keywords: corticosteroids, eosinophil, esophagus

P1020 STEROID THERAPY FOR EOSINOPHILIC ESOPHAGITIS: A META-ANALYSIS AND SYSTEMIC REVIEW

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INTRODUCTION: Eosinophilic esophagitis (EoE) is an inflammatory disorder of the esophagus causing upper gastrointestinal symptoms with distinctive endoscopic and histologic features. Although many therapies are advocated, there is currently no consensus on its appropriate treatment protocol.
AIMS&METHODS: To clarify the benefits and harms of steroid therapy for EoE, we performed a meta-analysis and systemic review with the published literatures. PubMed, EMBASE, Medline, ISI Wed of Science were searched to obtain relevant randomized controlled trials (RCTs) with comparison of steroid therapy vs. non-steroid therapy, retrospective and prospective trails on steroid therapy for EoE till March 2013. Two reviewers independently screened the trials and extracted the related information from the included studies, and RevMan 5.2 was used.
RESULTS: Six RCTs fulfilled inclusion criteria of meta-analysis, with 193 subjects (55 children); And 3 RCTs, 2 prospective and 5 retrospective trials fulfilled criteria of systemic review. All of them were of high quality evaluated via Cochrane collaboration's tool for assessing risk of bias or Newcastle-Ottawa Scale. Meta-analysis showed topical steroids significantly decreased the mean and peak values of the esophageal eosinophils (eos) count (MD_{mean}= -23.41, 95%CI_{mean} -42.08~ -4.73, P=0.01 and MD_{peak}= -51.27, 95%CI_{peak} -78.62~ -23.92, P=0.0002 respectively), compared to the non-steroid therapy. The decease of mean value of eos was more pronounced in the adult group and when compared to the placebo group (P=0.02 and P= 0.002 respectively). And the decrease of peak value of eos remained significant independent of patient age, types of steroids (both $P<0.05$). There were 14 trials showing the effectiveness of steroids on decreasing eos count, 10 trials showing improvement of symptoms, and 5 trials showing endoscopic improvement after steroids therapy. Only mild adverse effects (esophageal or oral candidiasis) were reported for topical steroids, but severe systemic side effects for systemic steroids.
CONCLUSION: This meta-analysis and systemic review demonstrated the effectiveness of steroids on decreasing the mean and/ or peak value of eos count for EoE, especially among the adult patients and when compared to the placebo group, but regardless of the types of steroids. As lack of unified standards, we yet couldn't determine its value of improving symptoms and endoscopic changes.
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Disclosure of Interest: None Declared

Keywords: treatment or therapy, eosinophilia, eosinophilic esophagitis, meta-analysis, steroid, systemic review

P1021 INFLUENCE OF LONG-TERM TREATMENT WITH TOPICAL CORTICOSTEROIDS ON NATURAL COURSE OF EOSINOPHILIC ESOPHAGITIS AND CORRELATION BETWEEN SYMPTOMS AND ENDOSCOPY, HISTOLOGY, AND BLOOD EOSINOPHILS

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INTRODUCTION: Natural history studies on Eosinophilic Esophagitis (EoE) have shown that the disease remains clinically, endoscopically and histologically active over years. However, whether this course can be altered by treatment with swallowed topical corticosteroids (TCS) is completely unclear. Furthermore, the association between clinical, endoscopic, histologic, and biochemical features of EoE needs further elucidation.

AIMS&METHODS: We aimed to assess the influence of treatment with TCS on disease activity and to determine the association between clinical and endoscopical, histological and biochemical activity in the long term run in a well characterized cohort of adult EoE patients. Patients from the Swiss EoE Database (SEED) were analyzed.

RESULTS: Hundred fifty two patients with a total of 511 visits were analyzed (115 males, mean age at EoE diagnosis 39 ± 14 years). The median follow-up time was 5 years (IQR 2-6), patients had on average 3.4 follow-up visits. In the follow-up period, patients were during 424 (83%) of visits clinically active (94% dysphagia, 22% thoracic pain) and in 87 (17%) of visits inactive. The following risk factors for clinical activity were evaluated: peripheral eosinophilia (OR 2.49, 95%>CI 0.69-8.94, p=0.16), presence of whitish exudates and/or furrows (OR 6.23, 95%>CI 3.79-10.26, p<0.001), presence of rings and/or strictures (OR 4.32, 95%>CI 2.66-7.01, p<0.001), histologic activity (OR 5.93, 95%>CI 2.65-13.29, p<0.001), therapy with topical steroids (OR 0.30, 95%>CI 0.17-0.54, p<0.001), and endoscopic dilation (OR 1.58, 95%>CI 0.80-3.11, p=0.185). In the multivariate logistic regression model (factors entered if p<0.1) clinical activity was significantly associated with active endoscopic and fibrotic activity (OR 4.01, 95%>CI 2.15-7.49, p<0.001 and OR 4.37, 95%>CI 2.42-7.90, p<0.001, respectively), and histologic activity (OR 0.25, 95%>CI 0.11-0.54, p<0.001), while therapy with topical steroids was significantly negatively associated (OR 0.25, 95%>CI 0.11-0.54, p<0.001) with clinical activity.

CONCLUSION: This is the first study demonstrating that long-term use of TCS in EoE is associated with symptom resolution. In addition, a good correlation between symptoms and endoscopic and histologic activity was found, but not with peripheral blood eosinophilia.

Disclosure of Interest: None Declared

Keywords: Eosinophilic esophagitis, natural history, swallowed topical corticosteroids

P1022 TOPICAL STEROID THERAPY EFFICIENTLY REDUCES THE RISK FOR LONG LASTING FOOD IMPACTIONS REQUIRING ENDOSCOPIC REMOVAL IN EOSINOPHILIC ESOPHAGITIS

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INTRODUCTION: Long lasting food impactions requiring endoscopic bolus removal occurs frequently in Eosinophilic Esophagitis (EoE) and are risky and frightening for patients. So far it is unknown whether the risk of impaction can be reduced by therapy with swallowed topical steroids (TCS).
AIMS&METHODS: To assess the frequency of impactions requiring endoscopic bolus removal in EoE patients under therapy with topical corticosteroids compared to a group of untreated EoE patients. In addition, we aimed to identify other risk factors for bolus removal. We analyzed retrospectively data of the Swiss EoE Database (SEED).
RESULTS: Hundred fifty two patients with a total of 511 visits were analyzed (115 males, mean age at EoE diagnosis 39 ± 14 years). The median follow-up time was 5 years (IQR 2-6), patients had on average 3.3 follow-up visits. In the follow-up period, 32 (6.3% of all endoscopies) episodes with endoscopic bolus removal were observed in 25 patients (16.4% of the cohort). Therapy with topical swallowed steroids reduced the risk for bolus removals (OR 0.53, 95% > CI 0.27-1.05, p=0.069). The following risk factors for bolus removal were further evaluated by univariate logistic regression modeling: clinical activity (OR 1.07, 95% > CI 0.43-2.65, p=0.880), esophageal stricture (OR 2.66, 95% > CI 1.41-5.03, p=0.003), peak eosinophil count > 20 eosinophils/HPF (OR 0.62, 95% > CI 0.29-1.28, p=0.193), blood eosinophilia (OR 0.62, 95% > CI 0.29-1.28, p=0.193), adherence to steroid therapy 3 months before bolus removal (OR 1.14, 95% > CI 0.40-3.25, p=0.805), and esophageal dilation (OR 2.36, 95% > CI 1.16-4.79, p=0.018). Factors with $p < 0.1$ were entered into the multivariate logistic regression model. In the multivariate model therapy with topical steroids was signicantly negatively associated with the risk for endoscopic bolus removal (OR 0.34, 95% > CI 0.16-0.73, p=0.006), whereas the presence of esophageal strictures was positively associated with endoscopic bolus removal (OR 2.56, 95% > CI 1.12-5.84, p=0.025). Dilation was no longer associated with endoscopic bolus removal (OR 1.79, 95% > CI 0.75-4.28, p=0.190).
CONCLUSION: Treatment with swallowed topical steroids efficiently reduces long lasting bolus impactions requiring endoscopic intervention. A reduced esophageal diameter is associated with an increased risk for bolus impactions. Of note, clinical activity is clearly insufficient to predict the risk of bolus impactions.
Disclosure of Interest: None Declared
Keywords: bolus removal, Eosinophilic esophagitis, esophageal strictures, food impaction, swallowed topical corticosteroids

P1023 DIFFERENCE OF SYMPTOM-RELIEF TO PROTON PUMP INHIBITOR BETWEEN NEW-ONSET OR RECURRENT GASTROESOPHAGEAL REFLUX DISEASE DURING THE ON-DEMAND VERSUS CONTINUOUS MAINTENANCE THERAPY IN JAPAN- A POST HOC ANALYSIS

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INTRODUCTION: Gastroesophageal reflux disease (GERD) is considered as liable to show recurrence. Although a number of studies describe the clinical importance of maintenance therapy, no study focused on the difference of efficacy during maintenance therapy between patients with new-onset and recurrent GERD.
AIMS&METHODS: The aim of this study is to reveal whether there is any difference in symptom-relief between new-onset or recurrent GERD during the on-demand versus continuous maintenance therapy. Endoscopically proven GERD patients who completed 8-week initial therapy were sequentially randomized to continuous arm (Omeprazole 20mg od) or on-demand arm (Omeprazole 20mg on-demand). Patients filled in daily symptom and tablet usages on the daily chart for 24 weeks. Symptom relief was defined as no-symptom on >6 days during a week. Patients were divided into new-onset GERD and recurrent GERD. In this subgroup, the number of patients who achieved symptom-relief was compared between continuous and on-demand arm during a maintenance therapy. This study was approved by the ethical committee.
RESULTS: A total of 118 patients, 82 were new-onset GERD (mean age 59.6 years, men/women 53/29) consisting of 42 continuous and 40 on-demand arm, and 36 were recurrent GERD (mean age 57.6 years, men/women 22/14) consisting of 17 continuous and 19 on-demand arm. Among new-onset GERD, more patients in contentious arm achieved symptom-relief than on-demand arm only at 4,5,6 and 17week whereas among recurrent GERD, contentious arm achieved superior effect at 1,2,3,4,5,7,8,17 and 18 week respectively. For instance, percentages of symptom-relief in continuous/on-demand in new-onset GERD were 62.5%43.2% at 1week, 78.1%/54.1% at 4week, 78.1%/59.5% at 8week, 80.6%/67.6% at 16week and 76.7%/83.3% at 24week, respectively. In continuous/on-demand in recurrent GERD, percentages of symptom-relief were 84.6%31.2% at 1week, 84.6%/40.0% at 4week, 92.3%/46.7% at 8week, 83.3%/56.3% at 16week and91.7%/73.3% at 24week, respectively. The mean tablet consumption showed no difference between new-onset and recurrent GERD in on-demand therapy in each week.
CONCLUSION: In patients with recurrent GERD comparing to new-onset GERD, continuous therapy provided more satisfying symptom-relief than on-demand therapy during a maintenance therapy.
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Disclosure of Interest: None Declared
Keywords: GERD, maintenance treatment, recurrent

P1024 A PILOT STUDY OF AN ENDOSCOPIC SURGICAL STAPLER FOR THE TREATMENT OF GERD – FIVE YEAR FOLLOW UP RESULTS

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INTRODUCTION: From May - Oct 2007, an IRB approved pilot study of a new endoscopic stapling device (Medigus SRS^{TM} device) for GERD treatment was conducted on 13 subjects. Inclusion - h/o PPI use > 2y for pH-metry proven GERD & no co-morbidity. The device is a flexible endoscopic surgical stapler with ultrasonic sight & range finder. It fires a staggered quintuplet of standard titanium B shaped 4.8mm surgical staples. It is guided into the stomach through the esophagus like a standard gastroscope. Cartridge is positioned in esophagus 2-3 cm above GE junction. Distal 21 cm is flexed in fundus, pushing it toward cartridge in esophagus. Ultrasonic sight is used to align cartridge in esophagus, measure intervening gap & allow compression to optimize firing range. Procedure repeated after replacing cartridge for 2nd or 3rd stapling. Result is an anterolateral true fundoplication functionally similar to Dor-Thal operation. A single operator did all procedures under general anesthesia.
AIMS&METHODS: Aim: To evaluate the 5-year follow up results of Medigus SRS^{TM} fundoplication. As per original informed consent, subjects were contacted annually for 5 yrs, the final telephone interviews conducted in early October 2012. Following data were collected: Velanovich GERD-HRQL scores, PPI use, symptoms, satisfaction with the procedure & willingness to repeat procedure again. This data and the trends were compared to the 6-month & annual follow up data of these same subjects.
RESULTS: Each year, 11 / 13 subjects could be reached by phone (but not the same subjects each year). GERD-HRQL scores were reduced > 50% in all subjects but one. This subject had an initial score - 29, & had reported scores of 15 or 14 in different years. All subjects agreed to undergo the procedure again if required in future. Mean satisfaction score was 7.7 (6-10) on a scale 1-10 (1 – not satisfied, 10 – fully satisfied). None had dysphagia or gas bloat. In 1st 3 years, slight increase in PPI reuse was seen. 3 resumed daily PPI's (compared to 2 at 2y follow up), 3 need reduced dose PPI (<50%), 1 takes PPI only after large meal & 4 are off PPI. No deterioration of results was seen after 3rd year.
CONCLUSION: At 5 years, the SRS procedure remained effective to improve QOL in moderate to severe GERD without causing dysphagia. PPI use was eliminated / reduced > 50% in 73% subjects. All subjects remain satisfied with the procedure & would do it all over again. There was no deterioration of results after 3rd year. This study suggests that at 5-years, results of SRS fundoplication are similar to laparoscopic fundoplication in terms of PPI use & QOL improvement.
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Keywords: endoscopic fundoplication, Fundoplication, GERD, GERD-HRQL, long term follow up

P1025 GAVISCON DOUBLE ACTION (ANTACID + ALGINATE) IS MORE EFFECTIVE THAN ANTACID ALONE IN CONTROLLING POST-PRANDIAL ACID REFLUX IN GERD PATIENTS; A DOUBLE-BLIND CROSSOVER STUDY

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INTRODUCTION: Recent studies have shown that Gaviscon (an alginate containing antacid) administered after a meal localizes in the postprandial acid pocket suggesting a targeted mechanism of action in GERD.
AIMS&METHODS: The aim of this study was to compare the effectiveness of Gaviscon to an equivalent strength non-alginate antacid on postprandial distal esophageal acid exposure in GERD patients. 14 GERD patients (LA A or B esophagitis or >5% distal esophageal acid exposure on BRAVO pH monitoring) not taking antisecretory medications were recruited for two 3.5-hour pH-impedance recording periods. After being instrumented with a high resolution manometry (Given Imaging) and a pH-impedance electrode (Sandhill Scientific) participants consumed a standardized meal (MacDonald's double quarter-pounder with cheese and small fries). In a double-blinded randomized crossover design they then received Gaviscon Double Action (alginate, sodium bicarbonate, calcium carbonate) or CVS Antacid Liquid Supreme (calcium carbonate, magnesium hydroxide), each at a volume containing ~20mEq acid neutralizing capacity. The recording was continued for 3 hours with patients scoring their symptoms q30 min with the GERDQ instrument. The primary outcome was the % time that the distal esophageal pH was <4; secondary outcomes were number of reflux events, proximal extent of reflux, and nadir pH of the refluxate. A paired t-test was used to compare the data.
RESULTS: 11 patients completed the study (mean age 47.3, 6 female); 9 had esophagitis and 2 had abnormal pH-metry. Mean baseline GERDQ scores were 9.5 (SD 1.20) and 7.3 (SD 1.70) on study days 1 and 2 respectively. Gaviscon studies had significantly less distal esophageal acid exposure and greater mean

pH of refluxate than CVS antacid studies (Table). There were no statistically significant differences between the total number of reflux events or the proximal extent of reflux.

	Antacid	Gaviscon	*p*
% time pH <4.0 median (IQR)	11.2 (5.9 - 17.85)	0.8 (0 - 8.95)	0.002
Total number of reflux median (IQR)	21 (16 - 31.5)	19 (14 - 32.5)	0.705
Nadir pH mean +/- SD	1.44 +/- 0.52	2.07 +/- 1.14	0.049
% reaching 17cm from LES median (IQR)	0.19 (0.12 - 0.33)	0.08 (0.026 - 0.17)	0.222

CONCLUSION: Gaviscon Double Action was more effective than antacid alone in controlling postprandial acid reflux. However, the number of reflux events and the spatial distribution of reflux within the esophagus were similar. This suggests that Gaviscon's effectiveness was related to its co-localization with and neutralization of the post-prandial acid pocket rather than by creating a barrier (raft) that prevents reflux.

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Keywords: alginates, antacid, esophagus, GERD, pH monitoring, treatment

P1026 EFFECT OF PROTON PUMP INHIBITORS IN ASTHMATICS WITH GASTROESOPHAGEAL REFLUX DISEASE

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INTRODUCTION: Prevalence of Gastroesophageal Reflux Disease (GERD) among patients with asthma has varied, according to different studies, from 33% to 90%[1]. Treatment with Proton Pump Inhibitors (PPIs) seems to improve asthma symptoms in some patients with asthma and GERD[2].

AIMS&METHODS: The objectives of this study was to investigate the presence of esophagitis in patients with asthma and GERD and to assess the effect of PPIs on pulmonary function. 51 patients with asthma and typical esophageal GERD symptoms (heartburn and/or regurgitation), according to the Montreal Consensus for GERD definition[3], were enrolled. All patients were submitted to upper gastrointestinal endoscopy, so that the presence of esophagitis could be recorded (according to Los Angeles classification). Patients were classified in two groups, according to the presence or absence of reflux esophagitis. Peak Expiratory Flow Rate (PEFR) was measured and then all patients began treatment with a double dose of PPI (omeprazole 20mg bid) for three months. PEFR was measured again at the end of the 3-month period. Response to treatment was defined a priori as positive if PEFR increased at least by >20%[4].

RESULTS: 44 patients (mean age 46±12 years, 24 women, 20 men) were finally investigated. 19 out of 44 patients (43.18%) had endoscopic findings of reflux esophagitis (grade A: 10, grade B: 5, grade C: 3, grade D: 1) and the rest 25 patients (56.82%) did not have reflux esophagitis. Among the esophagitis group, 4 out of 19 patients (21.05%) responded positively at the end of the 3-month treatment with the PPIs (PEFR increase >20%). Among the non-esophagitis group, 5 out of 25 patients (20%), improved their PEFR>20%. The difference between the two groups regarding positive response to PPI treatment was non significant (NS).

CONCLUSION: PPI treatment may improve pulmonary function in some patients with asthma and typical esophageal GERD symptoms. The presence or absence of reflux esophagitis does not seem to influence this response.

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Disclosure of Interest: None Declared

Keywords: asthma, Reflux disease

P1027 COMPARISON OF COMBINED THERAPY OF PROTON POMP INHIBITOR AND ALGINATES AND A MONOTHERAPY OF PROTON POMP INHIBITOR IN TREATMENT OF PATIENTS WITH EROSIVE ESOPHAGITIS AFTER USAGE OF NON-STEROID ANTI-INFLAMMATORY DRUGS

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INTRODUCTION: The serious medical problem is an esophagus pathology after usage of non-steroid anti-inflammatory drugs (NSAID). It is known that usage of NSAID (including low doses of the aspirin) is a risk factor of developing of damages of the esophageal mucous.

AIMS&METHODS: The aim: to evaluate the efficacy of proton pomp inhibitors (PPI) and combined treatment of PPI and alginates ("Gaviskon-Forte") in the treatment of erosive esophagitis after receiving NSAIDs. 68 patients with erosive esophagitis were observed. All of these patients use NSAIDs at least 1 month and have heartburn. These patients were divided into 2 groups: the 1st group (n=30) received PPI (pantoprasol) 40 mg once a day and "Gaviskon-Forte" 10 ml after a meal 3 times a day and 10 ml before sleeping within 14 days, the 2nd group (n=38) - PPI (pantoprasol) in the dose of 40 mg once a day. All patients responded to daily questionnaire for consideration of complaints; esophagogastroscopy and pH monitoring before and after the treatment were carried out.

RESULTS: Combination of PPI and "Gaviskon-forte" noted more persistent symptom control (heartburn to the 7th day disappeared in 53.3% of patients, to the 14th day - in 90.0% ($p<0.05$ in comparison to 2nd group)) compared with an isolated application of PPI (heartburn to the 7th day disappeared in 42.1% of patients, to the 14th day - in 68.4%). More pronounced positive dynamics of the endoscopic picture was observed in the group of patients receiving combination therapy (on 14th day full healing of erosion was observed in 73.3% in the 1st group and the 60.5% in the 2nd group ($p<0.05$)). Combined treatment of PPI and "Gaviskon-forte" improved results of pH monitoring (24 hours) and significantly reduces the period percent with intragastral pH less 4 during a day (from 23.5% to 7%), total reflux number decreased from 161 to 52.2 within 24h ($p<0.05$ in comparison to 2nd group). In the group of patients receiving only PPI the period percent with intragastral pH less 4 during a day reduced from 21.7% to 10.1%, total reflux number decreased from 143 to 72.2 within 24h. For a treatment period the side effects and allergic reactions were not registered.

CONCLUSION: Combination of PPI and «Gaviskon-Forte» showed the higher clinical and endoscopic efficiency in the treatment of the erosive esophagitis after usage of NSAID compared with monotherapy PPI. Also combination of PPI and "Gaviskon-forte" quite safety to consume. So we can recommend this combination to use in such patients

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Disclosure of Interest: None Declared

Keywords: alginates, erosive esophagitis, non-steroid anti-inflammatory drugs, proton pomp inhibitor

P1028 IMPROVEMENT IN SYMPTOM RELIEF WITH PANTOPRAZOLE MAGNESIUM 40MG VERSUS ESOMEPRAZOLE 40MG IN PATIENTS WITH EROSIVE ESOPHAGITIS AFTER 8 WEEKS

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INTRODUCTION: The proton pump inhibitor (PPI), pantoprazole-Mg, has a prolonged elimination half-life, which may translate into extended inhibition of the proton pump with the potential for improved symptom relief.

AIMS&METHODS: Pantoprazole-Mg was compared with esomeprazole over 4 and 8 weeks for symptom relief in a multicentre (14 Brazilian sites), phase III, randomised, double-blind, controlled study in patients with erosive gastroesophageal reflux disease (GERD; Los Angeles grades A–D). Patients received pantoprazole-Mg (n=290) or esomeprazole (n=288), administered as 40 mg once daily for 8 weeks. GERD-related symptoms were assessed at baseline (BL) and after 4 and 8 weeks using ReQuest^{T}-GI, which includes acid-related complaints, upper abdominal/stomach complaints, lower abdomen/digestive tract complaints and nausea.

RESULTS: Symptom relief rates were significantly higher at Week 8 with pantoprazole-Mg (n=275) than with esomeprazole (n=264) (91.6% vs. 86.0%, p=0.0370). Significant improvements were seen in mean ReQuest^{T}-GI scores from BL to Weeks 4 and 8 (both $p<0.0001$), and from Week 4 to Week 8 (p=0.0206), in pantoprazole-Mg recipients. ReQuest^{T}-GI scores significantly improved from BL to Weeks 4 and 8 (both $p<0.0001$) with esomeprazole, but not from Week 4 to Week 8. A similar trend was seen for all individual ReQuest^{TM}-GI sub-scores (Table). This correlated with improvements in general well-being from BL to Weeks 4 and 8 for both pantoprazole-Mg (both $p<0.0001$) and esomeprazole (both $p<0.0001$), and improvements from Week 4 to Week 8 for pantoprazole-Mg (1.42 to 1.06) but not esomeprazole (1.42 to 1.36).

Table. Individual ReQuest^{TM}-GI dimension mean scores after 4 and 8 weeks' treatment (intent-to-treat efficacy population).

	Acid complaints			Upper abdominal/ stomach complaints			Upper abdominal/ stomach complaints			Nausea		
	BL	Wk 4	Wk 8	BL	Wk 4	Wk 8	BL	Wk 4	Wk 8	BL	Wk 4	Wk 8
Pantoprazole-Mg												
Frequency	2.24	0.54	0.36	2.30	0.75	0.50	1.30	0.69	0.44	1.03	0.39	0.27
Intensity	2.61	0.70	0.47	2.75	0.96	0.68	1.76	0.89	0.59	1.30	0.54	0.41
Esomeprazole												
Frequency	2.15	0.49	0.44	2.36	0.81	0.71	1.60	0.80	0.74	1.16	0.39	0.36
Intensity	2.53	0.59	0.56	2.74	0.96	0.90	1.96	0.96	0.88	1.54	0.58	0.62

$p<0.0001$ for Baseline (BL) to Week (Wk) 4 and Week 8 for all dimensions for both drugs.

CONCLUSION: CONCLUSION: Symptom relief with pantoprazole-Mg continued to improve from 4 to 8 weeks and was greater than that with esomeprazole at Week 8, suggesting an extended period of treatment effect.

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Keywords: Esomeprazole, GERD, Pantoprazole, Symptom relief

P1029 EVALUATING THE CONTROL OF DAYTIME INTRAGASTRIC PH BY ESOMEPRAZOLE 20 MG (ESO 20): NEW COMPARATIVE ANALYSES WITH OTHER PROTON PUMP INHIBITORS OMEPRAZOLE 20 MG (OME 20), LANSOPRAZOLE 15 MG (LAN 15) AND PANTOPRAZOLE 20 MG (PAN 20)

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INTRODUCTION: It is well established that the oesophageal mucosal inflammatory component of the gastric refluxate and the associated symptoms of gastro-oesophageal reflux disease (GORD) are pH-dependent.[1] In untreated patients, the major burden of high rates of acid reflux and frequent heartburn symptoms occurs during waking hours.[2,3] Control of daytime pH provides relief of nighttime symptoms, presumably by making the oesophagus less sensitive to nighttime reflux.[4] Published studies have evaluated the 24-hour control of intragastric pH by ESO 20 and the OTC doses of other proton-pump inhibitors (PPIs).[5-8] Here we report new analyses of these studies, focusing on intragastric pH in the 14-hour awake period.
AIMS&METHODS: In one double-blind[5] and three open-label,[6-8] randomized, crossover studies, intragastric pH was monitored for 24 hours on Day 5 of treatment. Acid control was reassessed for the 14-hour daytime period. Mean percent times with pH > 4 were estimated using a linear mixed-effect model that included factors for treatment, treatment period, and treatment sequence as fixed effects and a factor of subject nested with treatment sequence as a random effect. Using the same model, geometric mean ratios were estimated based on log-transformed individual values.
RESULTS: The results are presented in Table 1.
Table 1. Mean time with pH > 4 during the 14-hour daytime period, and geometric mean ratios

Treatment	Mean (95% CI) time with pH > 4 (%)	Geometric mean (95% CI) ratio, ESO 20 / comparator
ESO 20 vs OME 20, N=36[a,5]	61.9 (53.9-69.9)** vs 51.7 (43.7-59.7)	1.45 (1.14-1.85)**
ESO 20 vs PAN 20, N=38[b,8]	55.2 (48.2-62.1)*** vs 27.5 (20.5-34.5)	2.57 (2.09-3.16)***
ESO 20 vs LAN 15, N=37[a,7]	51.2 (45.6-56.8)*** vs 31.5 (25.9-37.0)	1.69 (1.46-1.97)***
ESO 20 vs LAN 15, N=26[b,6]	55.8 (43.5-68.0)* vs 45.2 (33.0-57.5)	1.89 (1.05-3.37)*

[a]Patients with GORD; [b]Healthy subjects; *p < 0.05; **p < 0.01; ***p < 0.0001 vs comparator
CONCLUSION: During the period of daytime food-stimulated acid secretion and postprandial reflux, ESO 20 provides acid control for a significantly greater average portion of the time vs other PPIs at OTC doses. As the majority of reflux occurs during the day, we postulate that better control of daytime intragastric pH should translate to improved treatment of acid-related inflammation and sensitization of the oesophagus and thereby better directed symptomatic control of frequent heartburn.
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Keywords: Acid control, esomeprazole, intragastric pH, proton-pump inhibitor, reflux

P1031 THE EVALUATION OF THE EFFICACY OF WEIGHT LOSS IN CONTROLLING SYMPTOMS IN PATIENTS WITH GASTROESOPHAGEAL REFLUX SYMPTOMS .

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INTRODUCTION: An association between obesity and gastroesophageal reflux (GERD) symptoms has been reported in a large number of studies. A recent meta-analysis have concluded that individuals with BMI > 30 have an approximately twofold risk of GERD compared with individuals who have a normal BMI. Weight loss is commonly recommended as part of first-line management of GERD despite the paucity of published clinical trials.
AIMS&METHODS: The aim of the study was to evaluate the effect of weight loss in controlling symptoms in a group of patients with GERD. The secondary aim was to evaluate the progressive reduction of proton pump inhibitors (PPI) therapy after the weight loss.
We enrolled a group of 50 overweight and obese patients with typical and atypical GERD symptoms with previous erosive esophagitis endoscopically proven. These patients were evaluated with two validated questionnaires (QOLRAD and VAS) to detect the prevalence of GERD related symptoms and the ongoing PPI therapy. All patients underwent an anthropometric evaluation (BMI, height, weight, abdominal circumference) and received a personalized hypo-caloric diet with 1200–1500 kcal for women and 1500–1800 kcal for men. All patients were invited to perform a daily aerobic activity auto-evaluated by mean of a pedometer. It was considered effective if the step number was higher than 10 thousand. The hypocaloric diet was considered effective if at least of 10% weight loss was obtained in each patient. The hypocaloric diet was completed within 6 months. The same anthropometric evaluation and questionnaires were performed at the end of treatment. The PPI dosage per day was also evaluated. The results were evaluated with a Student paired t-test and considered statistically significant when p value was < 0.05.
RESULTS: Male/female ratio was 0.78 (22/28). Mean age was 49.3 (±11.8). Mean BMI decreased from 30.3 (sd ±4.1) to 25.7 (±3.1) ($p < 0.05$) and the mean weight loss from 82.1 (±16.9) to 69.9 (±14.4) after hypocaloric diet ($p < 0.05$). Symptoms perception decreased both with QUOLRAD and VAS scale ($p < 0.05$). In particular, heartburn decreased from 3.68 (±1.9) to 0.28 (±0.4) in QUOLRAD scale and from 5.7 (±1.8) to 0.6 (±0.6) in VAS scale ($p < 0.05$). PPI therapy was completely discontinued in 27/50 (54%) patients, was halved in 16/50 (32%) patients. Only 7/50 (14%) continued the same PPI dosage.
CONCLUSION: We can conclude that a 10% of weight loss is recommended in all patients with GERD-related symptoms. This weight reduction could be able to reduce not only symptoms perception but also the dose of PPI therapy.
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Disclosure of Interest: None Declared
Keywords: GERD, Obesity, weight loss

P1032 PREDICTORS OF RAPID HEALING AND REFRACTORY REFLUX ESOPHAGITIS WITH POTENT ACID SUPPRESSION

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INTRODUCTION: Potent acid suppression heals reflux esophagitis (RE), but little is known about how patient characteristics affect the rapidity of healing.
AIMS&METHODS: We performed a *post hoc* analysis of a large, randomized trial of AZD0865 (a potassium-competitive acid blocker) 25–75 mg/day vs esomeprazole 40 mg/day for the treatment of RE.[1] Group A (n=732) were treated for up to 4 weeks (therapy stopped at 2 weeks if healed). Group B (n=747) were treated for up to 8 weeks (therapy stopped at 4 weeks if healed). All patients had frequent heartburn at baseline. Patients completed the RDQ e-diary during treatment, and the Quality Of Life in Reflux Disease and Dyspepsia (QOLRAD) questionnaire at baseline and at 2 and 4 weeks. Data from all treatment groups were pooled as there was no difference between treatments in symptom response or RE healing.
RESULTS: In group A, RE healed in 495/732 (68%) patients by 2 weeks (rapid healers). Rapid healers were more likely to have Los Angeles (LA) grade A–B RE at baseline vs those with unhealed RE at 2 weeks (Table). In group B, of those with unhealed RE at 4 weeks, 49/127 (39%) had unhealed RE at 8 weeks (refractory). Refractory patients were more likely to have LA grade C–D RE (Table), frequent (≥4 days/week) regurgitation (81% vs 63%) and lower mean QOLRAD scores (at baseline vs those healed by 8 weeks but not at 4 weeks (slow healers). However, the 95% confidence intervals for all mean QOLRAD scores overlapped. Age, *Helicobacter pylori* status and baseline heartburn or dyspeptic symptoms did not predict the rapidity of RE healing.
Table: Baseline demographics of patients with rapid and refractory healing of RE.

Baseline demographics	Group A (n=732) Rapid healers: RE healed at 2 weeks (n=495)	Group A (n=732) RE not healed at 2 weeks (n=237)	Group B (n=747) Slow healers: RE healed at 8 weeks (n=78)	Group B (n=747) Refractory: RE not healed at 8 weeks (n=49)
Mean age in years (standard deviation)	46.7 (13.2)	47.3 (11.8)	44.4 (12.2)	43.9 (12.3)
Men Women	290 (58.6) 205 (41.4)	160 (67.5) 77 (32.5)	60 (76.9) 18 (23.1)	32 (65.3) 17 (34.7)
LA grade A B C D	192 (38.8) 222 (44.8) 77 (15.6) 4 (0.8)	52 (21.9) 96 (40.5) 62 (26.2) 27 (11.4)	22 (28.2) 26 (33.3) 17 (21.8) 13 (16.7)	7 (14.3) 17 (34.7) 19 (38.7) 6 (12.2)
Hiatal hernia	316 (63.8)	171 (72.2)	54 (69.2)	25 (51.0)
H. pylori	66 (13.5)	34 (14.4)	9 (11.5)	4 (8.2)

Results are numbers and percentages unless stated otherwise.
RE, reflux esophagitis.
CONCLUSION: Rapid healers are more likely to have LA grade A–B at baseline. Patients with refractory RE are more likely to have LA grade C–D, frequent regurgitation and lower HRQoL at baseline than slow healers.
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Keywords: acid suppression, proton pump inhibitors, reflux esophagitis

P1033 ELECTRICAL STIMULATION THERAPY (EST) OF THE LOWER ESOPHAGEAL SPHINCTER (LES) – AN EFFECTIVE THERAPY FOR REFRACTORY GERD – INTERIM RESULTS OF AN INTERNATIONAL MULTICENTER TRIAL

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INTRODUCTION: A previous single-center trial showed that LOS-EST significantly improves esophageal acid and symptoms in GORD patients long-term.
AIMS&METHODS: The aim of this international multicenter trial was to evaluate the safety and efficacy of LOS-EST in refractory GORD patients.
We studied GORD patients partially responsive to PPI with off-PPI GORD HRQL >20, LOS end-expiratory pressures of >5 mmHg, % 24 hour oesophageal pH<4 for >5%, hiatal hernia < 3cm and oesophagitis < LA Grade C. Bipolar stitch electrodes and a pulse generator (EndoStim BV, Hague, Netherland) were implanted laparoscopically. EST at 20 Hz, 220usec, 5-8mAmp in 6-12, 30 minutes sessions was initiated post-implant. Patients are evaluated using GORD-HRQL, symptom diaries, SF-12, oesophageal pH and manometry at regular intervals. Stimulation sessions are optimized based on residual symptoms and oesophageal pH.
RESULTS: Twenty-four patients (median age 51; men=14) have been enrolled and implanted with the LOS stimulator. One patient suffered a trocar perforation of small bowel during the implant successfully repaired on POD#1 and device prophylactically explanted. The remaining 23 patients are continuing with LOS-EST; 18 patients have completed their 3 month and 14 their 6 month evaluation. The median (IQR) off-PPI GERD-HRQL scores at baseline were 31 (25-37), which improved to 4 (2-11) on EST at months 3, ($p<0.001$) and 5 (4-9) at month 6 ($p<0.01$). There was improvement compared to the on-PPI GORD-HRQL scores of 14 (8-22) at baseline. Patients median oesophageal pH was 11.3% (9-15.5) at baseline and improved to 3.3% (2.5-9.1, $p<0.01$) at 3 months and 2.6% (1.8-5.4, $p<0.01$) at 6 months. Thirty-six AEs including 2 SAE were reported in 14 patients. Nine were non-serious events, not device or procedure related. Fourteen were probable or definite device or procedure related, including pain at the implant site and post-op nausea.
CONCLUSION: Interim results show that LOS-EST can be effective in treating refractory GORD. There was a significant improvement in patients' symptom, PPI usage and trend in improvement in their oesophageal acid exposure. LOS-EST was safe with no GI or cardiac side-effects. Long-term results in a larger group of patients are being collected to establish safety and efficacy of LOS-EST in refractory GORD.
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Keywords: electrical stimulation, reflux disease

P1034 REFLUX-RELATED COUGH AND RESPONSE TO PPI TREATMENT: DIFFERENCE BETWEEN PRIMARY CARE EXPERIENCE AND TERTIARY CARE CLINICAL TRIAL OUTCOMES?

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INTRODUCTION: Gastro-oesophageal reflux disease (GORD) has long been considered a cause of chronic unexplained cough. Despite this, multiple trials of proton pump inhibitor (PPI) in cough have consistently failed to show a significant therapeutic response. A possible reason for this is the tertiary care location (in either gastroenterology or respiratory departments) of many of these studies, where many patients will have already failed PPI treatment by family practitioners.
AIMS&METHODS: We **aimed** to evaluate the experience of UK primary care doctors in treating chronic cough with PPI.
A web-based questionnaire was sent to UK-wide general practitioners with an interest in gastroenterological or respiratory disease. The questionnaire asked for information including experience of PPI use for chronic cough, symptoms associated with a higher probability of cough resolution, PPI dose given, and perceived proportion of PPI-response.
RESULTS: 294 general practitioners (200 with interest in gastroenterology and 94 with interest in respiratory medicine) responded to the questionnaire. 88% regularly treated cough empirically with PPI. The strongest factor associated with decision to treat was the presence of accompanying heartburn (92% respondents) and regurgitation (83%). 54% used PPI when all other treatments for cough had failed. Most (65%) practitioners treated with once-daily PPI, and the most common duration of trial of therapy was one month (64%). 98% of responders considered a satisfactory PPI response to be a 50% or greater improvement in cough. Two thirds of respondents considered that a satisfactory response was seen in 40% or more of treated patients, with accompanying typical reflux symptoms being considered most associated with good response (88% of responders agreed).
CONCLUSION: Treatment of chronic cough with PPI therapy is common in UK primary practice in spite of lack of evidence based in clinical trial results. Most practitioners treat empirically with once daily PPI for one month. Perceived PPI-response rate was high, with most respondents agreeing that accompanying typical GORD symptoms are the best predictor of satisfactory response. These results suggest successful PPI outcome studies may best be performed in primary care.
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Keywords: Cough, extra-esophageal manifestations, gastroesophageal reflux, proton pump inhibitor

P1035 SYSTEMATIC REVIEW: OBSERVATIONAL STUDIES ASSESSING THE ASSOCIATION BETWEEN CARDIOVASCULAR OUTCOMES AND THE CO-PRESCRIPTION OF PROTON PUMP INHIBITORS WITH CLOPIDOGREL

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INTRODUCTION: Proton pump inhibitors (PPIs) are often co-prescribed with the antiplatelet agent clopidogrel to reduce the risk of gastrointestinal bleeding. Although some pharmacokinetic and pharmacodynamic studies have reported that PPIs, in particular omeprazole and esomeprazole, reduce the activity of clopidogrel by inhibiting its conversion from a pro-drug to an active metabolite, the results of studies assessing clinical outcomes in patients receiving both drugs are inconsistent. We conducted a systematic review of observational studies reporting cardiovascular (CV) outcomes in patients receiving clopidogrel with or without a PPI, focusing in particular on the differences between omeprazole and esomeprazole and other PPIs.
AIMS&METHODS: The Embase and Medline literature databases were searched for articles published before 9 July 2012. Studies identified through regular drug safety surveillance carried out by AstraZeneca were also included. Non-observational studies (including clinical trials, clinical pharmacology studies and guidelines) and reviews were excluded, as were congress abstracts when the study was also published as a full paper.

RESULTS: The final review comprised 68 observational studies. Overall, 31 (45.6%) reported a statistically significant increase in the risk of CV events in patients receiving clopidogrel with a PPI, compared with those receiving clopidogrel without a PPI. The remaining 37 studies (54.4%) reported no such increase. A total of 21 studies reported the results for different PPIs separately, 11 of which presented hazard ratios (HRs) for CV events in patients receiving clopidogrel with a PPI compared with those receiving clopidogrel without a PPI. HRs were 0.3–1.8 for esomeprazole, 0.8–4.2 for omeprazole, 0.4–1.4 for lansoprazole, 1.0–2.5 for pantoprazole and 0.5–1.8 for rabeprazole. All studies that showed a significant association between omeprazole or esomeprazole co-prescription with clopidogrel and an increased risk of CV events also showed an association of comparable magnitude (with overlapping 95% confidence intervals) for other PPIs.
CONCLUSION: In the 68 observational studies analysed, considerable variability was seen in their conclusions regarding the clinical outcomes associated with co-prescribing a PPI with clopidogrel. There was no consistent evidence of there being a greater likelihood of CV events in patients receiving both drugs. No evidence was found that omeprazole or esomeprazole are more likely than other PPIs to affect clinical outcomes in patients receiving clopidogrel.
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Keywords: Adverse events, Clinical outcomes, Clopidogrel, Drug interactions, Proton pump inhibitors

P1036 LONG-TERM TREATMENT OF GASTRO-ESOPHAGEAL REFLUX DISEASE: DOES CARDIA-LIKE METAPLASIA OF THE DISTAL ESOPHAGUS MATTER?

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INTRODUCTION: Our previous study has established that patients with gastroesophageal reflux disease (GERD) and cardia-like metaplasia of the distal esophagus have a higher relative risk (3.2) in the development of the erosive esophagitis than patients with GERD and squamous epithelium in the distal esophagus [1].
AIMS&METHODS: The aim of our study was to assess the effectiveness of different types of long-term PPI therapy among patients with GERD who had cardia-like metaplasia of the distal esophagus and patients with GERD who had squamous epithelium in the distal esophagus. To assess the effectiveness of treatment the rate of endoscopically confirmed erosive esophagitis was estimated at the end of one year of follow up.
Prospective, comparative study was conducted. The first study group included 35 patients with GERD and cardia-like metaplasia of the distal esophagus (the mean age 56.2±13.7 years). The second group included 34 patients with GERD and squamous epithelium in the distal esophagus (the mean age 58.2±11.3 years). At the end of one year of follow-up all patients were endoscopically examined in order to assess the condition of the distal esophagus. The patients were randomly assigned to receive omeprazole 20 mg on-demand (14 patients in the first group and 17 patients in the second group) and omeprazole 20 mg 'weekend' therapy: on Friday, Saturday and Sunday (21 patients in the first group and 17 patients in the second group).
RESULTS: Among patients with GERD and cardia-like metaplasia of the distal esophagus the rate of erosive esophagitis was significantly ($\chi 2 = 11.81$, $P = 0.0006$) higher in on-demand group (64.3%, 95% CI: 39.1 – 89.5%) than in the group treated only on week-ends (4.7%, 95% CI: - 0-13.9%). Among patients with GERD and squamous epithelium in the distal esophagus there were no reliable differences ($\chi 2 = 0.06$, $P = 0.8$) among two treatment strategies (11.8%, 95% CI: 0 – 27.3% and 7.7%, 95% CI: 0 – 22.5% respectively).
CONCLUSION: The 'weekend' therapy is more effective treatment strategy for patients with GERD and cardia-like metaplasia of the distal esophagus than on-demand one. For patients with GERD and squamous epithelium in the distal esophagus on-demand treatment and 'week-end' treatment are both equally effective.
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Keywords: Gastroesophageal reflux disease(GERD), metaplasia

P1037 EVALUATION OF EFFICACY OF PROTON PUMP INIHIBITORS IN REFRACTORY GASTROESOPHAGEAL REFLUX DISEASE

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INTRODUCTION: Many patients with gastroesophageal reflux disease (GERD) have persistent reflux despite treatment with proton pump inhibitors (PPIs). Treatment in clinical practice has been primarily focused on doubling the PPI dose or switching to another PPI. The purpose of this study was to assess whether PPI is effective in refractory GERD or not.
AIMS&METHODS: Forty-five patients with clinical reflux symptoms (heartburn, chest pain, and/or regurgitation) and a history of ineffective response to PPIs were enrolled in this study. At admission, patients performed ambulatory 24-h pH impedance monitoring to identify the reflux pattern. They received doubling the PPI or switching to another PPI. Clinical outcome was defined as responder (≤ 2 symptoms/week) or nonresponder (≥ 3 symptoms/week).
RESULTS: Demographic analysis of the refractory GERD group revealed a mean age of 50.4 years (19-75 years) with 42.5% males. The rates of hernia, alcohol intake, smoking and weight loss was not different between two groups, responder (n = 21) vs. nonresponder (n = 24). In univariate and multivariate analysis, doubling the PPI or switching to another PPI was not related to symptom relief. The causes of refractory GERD might be the weakly acidic reflux. In ambulatory 24-h pH impedance monitoring, there were fewer acid reflux episodes in refractory GERD group to control group (19.3 ± 15.2 vs. 4.4 ± 5.3) while more weakly acidic reflux episodes were identified (21.7 ± 14.6 vs. 28.0 ± 17.3).
CONCLUSION: PPIs do not affect the total number of reflux episodes. PPIs only decrease the acidity of refluxate. In refractory GERD patients, the treatment of weakly acid and weakly alkaline reflux is more effective to PPI treatment.
Disclosure of Interest: None Declared
Keywords: GERD, PPI

P1038 THE EFFECT OF ACID SUPPRESSION FOR CHRONIC COUGH: A PROSPECTIVE RANDOMIZED STUDY, PRELIMINARY RESULTS

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INTRODUCTION: Gastroesophageal reflux disease (GERD) is one of the causes of chronic cough. Some studies suggest an association between chronic cough and GERD, but the effectiveness of acid suppression with proton pump inhibitors (PPI) in chronic cough is controversy.
AIMS&METHODS: The aim of our study was to investigate prospectively the effect of PPI in the patients with chronic cough. Subjects with chronic cough for 8 weeks were evaluated. Subjects underwent a chest x-ray, PNS view, pulmonary function test, methacholine challenge test, and empiric trial of postnasal drip (PND) therapy. After excluding other causes of cough such as asthma, PND, or lung cancer, the remaining patients measured GERDQ questionnaire and underwent endoscopy with 24-h pH/impedance study to investigate the combination of typical GERD. Subjects were randomized to 3 groups; standard dose of PPI daily, high dose of PPI daily or placebo for 8 weeks. Therapeutic effect was measured by the Cough visual analogue scores (VAS) and Leicester cough questionnaire (LCQ) after 4 weeks and 8 weeks of treatment.
RESULTS: A total of 31 patients were enrolled and randomized. Seventeen patients (9 subjects with typical GERD and 8 without typical GERD) completed 8-week treatment. Nineteen patients (10 subjects with typical GERD and 9 without typical GERD) only completed 4-week treatment. Cough VAS and LCQ score improved in patients with typical GERD symptoms in 4-, 8-week treatment periods. This improvement was not statistically different between high dose and standard dose of PPIs. Patients without typical GERD also responded to PPI therapy for cough. Both Cough VAS and LCQ score improved in patients without typical GERD in 4-, 8-week treatment periods. This improvement was also not statistically different between high dose and standard dose of PPIs.
CONCLUSION: Acid suppression by PPI improved cough-related quality of life and symptoms in patients with chronic cough regardless of combined typical GERD or the dose of PPI. The final results of our study may be helpful for establishment of guidelines for PPI therapy in chronic cough.
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Disclosure of Interest: None Declared
Keywords: chronic cough, GERD, proton pump inhibitor

P1039 CLINICAL STUDY OF ESOPHAGITIS INDUCED BY DABIGATRAN

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INTRODUCTION: Dabigatran is an anticoagulant drug for atrial fibrillation. Compared with warfarin, dabigatran does not have interactions with many foods and does not require frequent laboratory monitoring, and has been shown to have at least the same efficacy in reducing stroke for patients with atrial fibrillation. It was reported that dyspepsia was the adverse effect that was more common with dabigatran (11.5%) than with warfarin (5.8%). There are some case reports of esophagitis induced by dabigatran, and we also have experienced many cases of esophagitis after administration of dabigatran.
AIMS&METHODS: The aim of this study was to determine the prevalence and clinical characteristics of esophagitis induced by dabigatran. First, a total of 112 patients prescribed dabigatran in 2012 were retrospectively analyzed. We investigated the prevalence of esophagitis symptoms (dysphagia, heartburn, regurgitation), and evaluated clinical characteristics such as age, sex, dose of dabigatran, and cotreatment with proton pump inhibitors (PPI). Second, a total of 35 patients prescribed dabigatran and 124 patients prescribed warfarin who underwent esophagogastroduodenoscopy (EGD) in 2012 were retrospectively analyzed. We have compared the prevalence, region and form of erosive esophagitis.
RESULTS: Esophagitis symptoms were observed in 25.9% (29/112), and medication was discontinued in 12.5% (14/112). Esophagitis symptoms were associated with the dose of dabigatran (4/5, 80% in 300mg/day, and 25/107, 23.4% in 220mg/day, p=0.015), but not with the other factors. The prevalence of erosive esophagitis at EGD was 20.0% (7/35) in the dabigatran group and 11.3% (14/124) in the warfarin group (p=0.144). Erosive esophagitis in the middle esophagus and in the lower esophagus were found in 5 and 4 cases in the dabigatoran

group, and 0 and 14 cases in the warfarin group, respectively. Linear erosions were found in 5/35 cases (14.3%) in the dabigatran group and in 14/124 cases (11.3%) in the warfarin group (p=0.851), and round erosions were found in 3/35 cases (8.6%) in the dabigatran group and in 0/124 cases (0%) in the warfarin group (p=0.009).
CONCLUSION: The prevalence of esophagitis symptoms after administration of dabigatran was 25.9%. We considered that round erosion in the middle esophagus is the characteristics of erosive esophagitis induced by dabigatran.
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Disclosure of Interest: None Declared
Keywords: dabigatran, esophagitis

P1040 NON-CONJUGATED BILE ACIDS CAN MODIFY THE ACID-BASE TRANSPORTER FUNCTION OF THE METAPLASTIC HUMAN ESOPHAGEAL EPITHELIAL CELLS

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INTRODUCTION: Barrett's esophagus (BE) is the most severe complication of gastro-esophageal reflux disease (GERD). Exposure of gastric and/or bile acids during reflux episodes play a critical role in the pathogenesis of BE. The acid extruding mechanims of esophageal epithelial cells (EECs) are not completely understood, although the acid-base transporters may play an important role against these toxic agents.
AIMS&METHODS: The **aim** of our study was to investigate the effects of bile acids on human EECs.
Methods: CP-A esophageal epithelial cell line was derived from a region of non-dysplastic metaplasia of BE and grown to confluent monolayers. To monitor changes in intracellular pH (pH_i) cells were loaded with the fluorescent dye, BCECF-AM NH_4Cl pulse technique and RT-PCR were used to measure the activity and expression of the acid-base transporters.
RESULTS: Chenodeoxycholate (CDC; 0.1 mM, 0.5 mM and 1 mM) caused reversible and dose-dependent decrease in pH_i. CDC significantly increased the activity of Na^+/H^+ exchanger (NHE) while decreased the activity of Na^+/HCO_3^- cotransporter (NBC). It had no significant effect on Cl^-/HCO_3^- anion exchanger (AE). Twenty-four hour incubation of CP-A cells with 0.1 mM CDC significantly increased the expression of NHE-2 and decreased the expression of NBC, but had no effect on the expression of AE.
CONCLUSION: CDC reversibly decreased the pH_i and increased the activity and the expression of NHE indicating the activation of the defensive pH_i regulating mechanisms on the epithelial cells. The role of the decreased activity and expression of NBC in the development of gastroesophageal reflux related esophageal complications needs further investigation.
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Disclosure of Interest: None Declared
Keywords: BARRETŕS ESOPHAGUS, Biliary reflux, epithelial function, GERD

P1041 MONITORING OF BARRETT'S ESOPHAGUS IN ELDERLY PATIENTS: RESULTS OF FIVE-YEAR PROSPECTIVE STUDY

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INTRODUCTION: Barrett's esophagus (BE) is a disease, which increases significantly the probability of esophageal cancer [1]. In this regard great attention is paid to diagnostics and treatment of this pathology [2].
AIMS&METHODS: Aim. To study the frequency of transformation of GERD to BE in elderly patients based on the results of five-year prospective study.
Methods. We performed a prospective five-year observation of 891 elderly GERD patients (569 females, 322 males, median age 78,1 years). GERD was diagnosed on the basis of the Montreal Consensus (Vakil N et al., 2006). The presence of erosive esophagitis was defined based on the Los Angeles classification (Lundell LR et al., 1999). For endoscopic verification of Barrett's esophagus chromoendoscopy and five quadrant biopsy were used. During the five-year follow-up clinical examination and endoscopy of the esophagus were performed twice a year. Morphological examinations of the esophagus to determine BE were done in the beginning and the end of study.
RESULTS: A five-year prospective study in elderly patients showed an increase of frequency of BE and erosive esophagitis (Table 1). The risk factors for BE development in elderly patients were obesity (OR = 3,27, CI 1,53-4,90; p <0,001), smoking more than 20 cigarettes per day for more than 10 years (OR = 8,0, CI 3,65-9,66; p <0,001) and the lack of maintenance proton pomp inhibitors therapy (OR = 6,1, CI 4,0-9,2; p <0,001).

Table. Five-year dynamics of GERD structure.

	NERD		Erosive esophagitis		BE	
Pathology	Abs.	%	Abs.	%	Abs.	%
Beginning of the study	472	52,9	357	40,1	61	7,0
In 5 years	335	37,6	471	52,9	85	9,5
OR; CI; p	1,87; 1,56-2,26; <0,001		0,60; 0,49-0,72; <0,001		0,71; 0,51-1,0; 0,058	

CONCLUSION: GERD is a progressive disease in elderly patients, which is attended by increasing of BE frequency.
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Disclosure of Interest: None Declared
Keywords: Barrett's esophagus, GERD

P1042 JUMBO BIOPSY FORCEPS IMPROVES ADEQUATE TISSUE SAMPLING IN PATIENTS WITH BARRETŕS ESOPHAGUS: FINAL RESULTS OF A RANDOMIZED STUDY

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INTRODUCTION: Good quality of biopsy specimen is required for reliable diagnosis of early neoplasia in patients with Barretís esophagus (BE). It remains controversial whether the use of jumbo forceps provides an advantage compared to large capacity forceps. The aim of this study was to assess sampling quality of 4 different forceps in patients with BE. We hypothesized that jumbo forceps if used with a standard diagnostic endoscope provides a better quality of biopsy specimen as compared to large capacity forceps.
AIMS&METHODS: A single center, randomized, prospective and single blind study. Thirty seven patients with BE (6 women, 31 men) were enrolled. The following forceps (with spike) were tested: **A:** disposable large capacity biopsy forceps FB-240K (Olympus), outer diameter 2.45 mm; **B.** disposable large capacity biopsy forceps BI01-D3-23 (Medwork), outer diameter 2.3 mm; **C.** single-use large capacity biopsy forceps (Medi-Globe), outer diameter 2.3 mm. **D.** single-use biopsy forceps Radial Jaw 4 (Boston Scientific), outer diameter 2.8 mm (jumbo). Targeted and random biopsies with all 4 forceps (in a random order) were obtained from every patient during a single endoscopy using a diagnostic endoscope (with a standard channel of 2.8 mm). The samples were analyzed by a blinded experienced pathologist. Main outcome measurement was specimen adequacy (defined as a well oriented biopsy sample 2 mm or greater with muscularis mucosa present).
RESULTS: A total of 436 biopsy samples were analyzed (**forceps A**: 121, **forceps B**: 115, **forceps C**: 108, **forceps D**: 92). Compared to all other forceps, a significantly higher proportion of biopsy samples with jumbo forceps (D) were adequate (A: 26%, B: 17%, C: 18%, D: 71%; p<0.001 D vs. other forceps). Biopsies with jumbo forceps (D) had the largest diameter (median 2.4 mm vs. 2 mm (A), 1.6 mm (B) and 2 mm (C); p<0.001 D vs. other forceps). Muscularis mucosae was detected in 45% of specimen with forceps A, in 23% with forceps B, in 82% with forceps C and in 52% with forceps D (p<0.001 C vs. other forceps). Excellent or good specimen orientation was present in 61% of samples with forceps A, in 44% with forceps B, in 66% with forceps C and in 77% with forceps D. There was a trend for a higher diagnostic yield with Jumbo biopsy forceps.
CONCLUSION: Jumbo biopsy forceps provides more adequate specimen as compared to three types of large capacity forceps. This might lead to an increased diagnostic yield regarding both the detection of intestinal metaplasia and early neoplasia.
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Disclosure of Interest: None Declared
Keywords: BARRETŕS ESOPHAGUS, BIOPSY FORCEPS

P1043 LOW PREVALENCE OF BARRETT'S ESOPHAGUS AND ESOPHAGEAL ADENOCARCINOMA OVER A 10-YEAR PERIOD

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INTRODUCTION: Barrett's esophagus (BE) is prevalent in the Western world, however the majority of patients with BE will never develop esophageal adenocarcinoma (EAC). Few data are available on risk factors for progression to neoplasia. Identifying predictors of high-grade dysplasia (HGD) and EAC would be useful for risk stratification.

AIMS&METHODS: Clinical, endoscopic and histologic data were reviewed for patients with a new BE diagnosis between 2002 and 2011. Patients were classified as having specialized intestinal metaplasia, low grade dysplasia (LGD), HGD and EAC. Gender, age, presence of hiatal hernia, segment length of BE and Helicobacter pylori (H. pylori) status were evaluated for their association with dysplasia severity and presence of EAC.
RESULTS: Over a 10-year period 26.984 patients underwent upper gastrointestinal endoscopy. Erosive reflux esophagitis (ERD) was diagnosed in 53% (n=14322) of all patients. In all, 358 patients (61% men and 39% women, mean age: 58) were newly diagnosed with BE (1.33% of all patients and 2.5% of ERD patients). Among them 74 patients had LGD (0.52% of ERD and 20.7% of BE patients) and 17 patients HGD/EAC (0.06 of all investigated patients, 0.12% of ERD and 4.7% of BE patients). The presence of hiatal hernia was significantly more frequent in more severe ERD (Los Angeles classification C/D versus A/B, 55% and 37%, respectively, $p<0.05$). The presence of hiatal hernia ($P<0.001$), longer Barrett segment length ($P<0.001$), male gender ($P<0.05$) and absence of *H. pylori* infection ($P<0.05$) were significantly associated with higher pathological grade and presence of EAC.
CONCLUSION: We demonstrate a low prevalence of BE and EAC over a 10-year period. We confirm that only a minority of BE patients will develop EAC. Presence of hiatal hernia, segment length of Barrett, male gender and *H. pylori* negative status were strong predictors of risk for development of HGD and EAC.
Disclosure of Interest: None Declared
Keywords: Barrett's esophagus, esophageal adenocarcinoma, prevalence

P1044 DYSPLASIA IN BARRETŕS ESOPHAGUS. EXPERIENCE IN A TERTIARY CARE CENTER IN SOUTH EUROPE

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INTRODUCTION: Barretś esophagus (BE), as a premalignant condition, constitutes the principal risk factor for the development of esophageal adenocarcinoma (EAC).
AIMS&METHODS: To analyze prospectively patients with BE between 2009-2013. To analyze retrospectively the previous natural course of their disease. To evaluate epidemiological characteristics, development of dysplasia or EAC and natural course of BE.
We studied 179 patients, excluding 8 patients in whom BE was not confirmed. Thus, we included 171 patients (male 133, 77,8%). 38% of them presented a long BE and 62% a short BE. Median length of BE was 3 cm (1-20 cm). Median age of first BE detection: 54 years (23-84). Median time of follow up: 6 years (1-27). The endoscopic follow up was performed with a High Definition-NBI endoscope (H-180, Olympus). Patients were classified in four groups: intestinal metaplasia (IM), low-grade dysplasia (LGD), high-grade dysplasia (HGD), adenocarcinoma (EAC). Patients with confirmed HGD, were treated with HALO Radiofrequency.
RESULTS: According to the most severe histological grade presented during their course: 8 patients presented EAC (4,7%), 13 HGD (7,6 %), 54 LGD (31,6%) and 94 IM (56,1%). In relation to the follow up: 8 patients (4,7%), all of them men, presented EAC. 6 of them had a long BE. 50% at the same time of the diagnosis, and the other half during the follow up (median time 8,8 years). Six patients were treated surgically. 14 patients (8,2%) presented HGD at any time of their disease. 79% were male and 71% had long BE. 50% at the same time of diagnosis. Ten patients were treated with Radiofrequency. One patient rejected the endoscopic follow up, who developed a stenotic EAC after five years. Two patients, dysplasia resolved completely. 61 patients (35.6%) presented LGD at any time of their disease. 77% were male and 50% had a long BE. Almost half of the patients at the same time of diagnosis. (44,8%). In 49%, there has been a resolution of dysplasia. In the 11.5% there has been progression to HGD/ADC and in the rest of them (39.3%) LGD persisted. 133 patients (75.4%) presented IM. The 76% were male, with short BE predominatly. There has been a progression in 27,8% of them (24% to LGD, 3% to HGD and 0,8 to ADC).
CONCLUSION: Our patients with BE had similar epidemiological characteristics as published elsewhere. The HGD/ADC are more frequent in males with long BE. In our cohort, the presence of dysplasia in patients with BE is high, although LGD has a low rate progression. It is necessary a longer follow up in these patients.
Disclosure of Interest: None Declared
Keywords: Adenocarcinoma of the oesophagus, Barrett's esophagus, Dysplasia

P1045 OUTCOMES OF ENDOSCOPIC AND SURGICAL THERAPY FOR HIGH GRADE DYSPLASIA IN BARRETT'S OESOPHAGUS AND EARLY OESOPHAGEAL ADENOCARCINOMA: SINGLE CENTRE EXPERIENCE

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INTRODUCTION: Surgical therapy has long been considered standard of care for early Barrett's neoplasia. Recent evidence showed that endoscopic therapy is safer and equally effective compared to surgery. While neoplasia eradication in clinical trials can be as high as 95%, this is lower in routine clinical practice (1,2).
AIMS&METHODS: In this retrospective study, we report the outcomes of surgical and endoscopic treatment in a single tertiary referral centre. All patients with histological evidence of high grade dysplasia (HGD) or intramucosal carcinoma (IMC) on biopsies taken from the oesophagus or gastro-oesophageal junction were identified. Patients receiving photodynamic therapy were excluded. Patient with flat HGD received primary radiofrequency ablation (RFA), whereas patients with visible neoplasia underwent endoscopic resection (ER), followed by RFA. Surgical therapy consisted of minimally invasive oesophagectomy, results were assessed for complete remission of neoplasia (CR-N), disease recurrence and procedural complication. CR-N was defined as eradication of HGD or cancer based on follow up endoscopic biopsies.
RESULTS: Between January 2002 to March 2013, 72 patients were identified. Average age was 72.6, 53 patients had IMC and 19 patients had HGD. Median follow up was 23.8 months (range 1.4 - 134.5). 10 patients had primary oesophagectomy which led to 100% CR-N. 4 (40.0%) patients developed 5 post-operative complications (2 oesophageal strictures, 1 anastomotic leak, 1 dumping syndrome and 1 conduit dysfunction) which were all successfully managed. 62 patients underwent primary endoscopic treatment. 9 were excluded from analysis as they were upstaged to T1b following initial ER. Among the 53 patients with disease stage <T1b, 44 (83.1%) achieved CR-N. 5 (9.4%) went on to have successful rescue surgery. There were 5 (5.2%) complications following ER (3 perforation, 2 significant gastrointestinal bleed) and 8 (13.5%) complications following RFA (3 arrhythmias, 4 chest pain, 2 strictures). There were no disease related deaths.
CONCLUSION: Endoscopic therapy is safe and effective in high grade dysplasia and early oesophageal adenocarcinoma. Failure to achieve disease remission can be successfully managed with surgery. Endoscopic therapy alone achieved complete remission in 83.1%.
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Disclosure of Interest: None Declared
Keywords: Barrett's esophagus, Barrett's neoplasia, endoscopic resection, high grade dysplasia, intramucosal carcinoma, radiofrequency ablation

P1046 GASTRIC INTESTINAL METAPLASIA: A RETROSPECTIVE ANALYSIS IN A DISTRICT GENERAL HOSPITAL IN UNITED KINGDOM

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INTRODUCTION: Gastric intestinal metaplasia (IM) is part of a carcinogenesis sequence leading to gastric cancer. Recent evidence-based European Society of Gastrointestinal Endoscopy (ESGE) guidelines have highlighted additional risk factors, such as the extensive intragastric distribution of IM and the presence of *Helicobacter pylori*. The former is identified with ≥2 antral and ≥2 corpus biopsies, involving the greater and lesser curvature, and warrants three-yearly surveillance endoscopies. The latter should be eradicated to slow the progression of carcinogenesis.
AIMS&METHODS: Using the keywords ''intestinal metaplasia'', the histology database for the Queen Elizabeth Hospital, South East London, was reviewed over 2000-11 to identify patients with IM on gastric biopsy. Gastro-oesophageal junctional IM was excluded. The number and site of biopsies taken and the presence of *H.pylori* was identified. The terminology used, with regards to ''extensive'' and ''focal'' IM, was compared with the suggestions from the ESGE guidelines. To investigate the development of cancer in patients with IM, histology and upper gastrointestinal cancer databases were compared.
RESULTS: 175 patients with gastric intestinal metaplasia were identified. Only one patient with gastric intestinal metaplasia developed gastric cancer. *Helicobacter pylori* was associated with 20/175 (11.4%) of gastric IM biopsies. After review of pathology reports, in 37/175 (21.1%) of cases with gastric IM, the pathologist did not receive sufficient clinical information specifying the site of the biopsies. Of those where the biopsy site was specified, only 10/138 (7.2%) had sufficient biopsies. The term ''extensive'' was used in 27/175 (15.4%) pathology reports despite either insufficient number or unspecified location of biopsies.
CONCLUSION: This study identified 175 patients with gastric intestinal metaplasia over 2000-2011. One patient developed gastric adenocarcinoma after 8 years. Since surveillance endoscopy is not routine practice in the Trust, all biopsies were incidental findings. This study suggests that, where biopsy site details were provided, only 7.2% of patients were adequately biopsied. Remaining cases should have a repeat endoscopy with ample biopsies to decide on surveillance. ''Extensive metaplasia'' refers to a wide intragastric distribution of IM to include the antrum and corpus. We identified discrepant use of nomenclature in pathology reporting in 15.4%. *Helicobacter pylori* was associated in 11.4%, where ESGE advocates its eradication. This study reveals further work is needed to risk stratify and survey this important pre-cancerous condition.

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P1047 AGE DISTRIBUTION OF GASTRIC CANCER PATIENTS ACCORDING TO THE FAMILY HISTORY

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INTRODUCTION: The risk of gastric cancer (GC) is higher in patients having family members with the disease.
AIMS&METHODS: The aim of our study was to evaluate whether gastric cancer patients having family history has young onset age. A total of 4282 patients diagnosed with GC in National Cancer Center Hospital from October 2002 to December 2012 were enrolled. Among them, 924 patients (21.6%) had the first- degree family member with GC. Information about the age of GC detection in the family members was obtained by questionnaire.
RESULTS: The mean onset age of patients with and without the first-degree family member diagnosed as GC were 58.0±10.7 and 58.1±12.0 years, respectively and showed no difference (p-value 0.897). Patient's age having GC family history in their father, mother and siblings were 54.4±10.4, 57.2±10.0 and 62.2±9.9 years, respectively. Patients having GC family history in their father showed 3.7 years earlier onset age than those without family history on average (p-value <0.001). Patients having GC family history in their mother showed no difference (p-value 0.222) and those having that in sibling showed 4.2 years later onset age than those without family history (p-value <0.001). Patient's age having father, mother or siblings with GC diagnosed before age of 50 years were 47.7±10.3, 48.6±10.4 or 57.4±11.5 years, respectively. Patients having father or mother with GC diagnosed before age of 50 years showed 10.4 or 9.5 years earlier onset age than those without family history (p-value both <0.001), respectively. But, patients having siblings with GC diagnosed before age of 50 years showed no difference than those without family history (p-value 0.603).
CONCLUSION: The patients having GC family history in their father or having parents with GC diagnosed before age of 50 years showed young onset age than those without family history.
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Disclosure of Interest: None Declared
Keywords: family history, gastric cancer, onset age

P1048 THERAPEUTIC OUTCOMES OF ENDOSCOPIC PAPILLECTOMY FOR AMPULLARY NEOPLASMS: RETROSPECTIVE ANALYSIS OF A MULTICENTER STUDY

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INTRODUCTION: Endoscopic papillectomy (EP) is reported to be relatively safe and reliable procedure for complete resection of ampullary neoplasms. There were no large-scale studies concerning the effectiveness and complications related to EP.
AIMS&METHODS: This study was aimed to evaluate the therapeutic outcomes and complications of EP for ampullary neoplasms. A retrospective multicenter study was done with 5 participating centers from January 2007 to August 2012. A total of 84 patients who underwent EP for ampullary neoplasms were retrospectively reviewed. EP was performed by snare resection with or without saline lifting of the lesion.
RESULTS: The mean age of the84 patients was 60.2±12.5 years, and the male-to-female ratio was 2:1. A biliary and pancreatic stent was placed in 32 patients and in 44 patients, respectively. En bloc resection was possible in 75 patients (89.3%). Histology of resected specimen was as follows: low grade adenoma (42.7%), high grade adenoma (17.1%), adenocarcinoma (18.3%), hyperplastic polyp (9.8%), and others (12.1%). A pathologically incomplete resection was noted in 10 cases (11.9%). Of the 56 cases with low grade adenoma on biopsy specimen, 25% turned out to have high grade adenoma (12.5%) or adenocarcinoma (12.5%). After papillectomy, five patients with adenocarcinoma, one with high grade adenoma and one with carcinoid tumor underwent surgery due to positive resection margin. Procedure-related complications occurred in 28 patients (33.4%); bleeding (15 cases, 17.9%), pancreatitis (13 cases, 15.5%), and perforation (7 cases, 8.3%). Pancreatic duct stenting significantly increased the risk of pancreatitis by univariate and multivariate analysis. Pre EP endoscopic retrograde cholangiopancreatography (ERCP), saline lifting, sphincterotomy, biliary stenting, specimen size, and cauterization were not related with increased risk of complications. During follow-up endoscopy, remnant tumors were found in 7 patients, of whom one patient underwent surgery and the others six patients were treated with EP with and without argon plasma coagulation (APC).
CONCLUSION: EP seems to be a safe and effective treatment for ampullary neoplasms and can be considered as an alternative to surgery. However, risk of the procedure-related complications is a problem that must be considered.

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P1049 THE ASSOCIATION OF ATROPHIC CHANGES OF BACKGROUND MUCOSA AND GHRELIN EXPRESSION WITH THE PREVALENCE AND ENLARGEMENT OF GASTROINTESTINAL STROMAL TUMORS OF THE STOMACH

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INTRODUCTION: The clinical predictor for enlargement potential of gastrointestinal stromal tumors (GISTs) of the stomach has not been identified. Ghrelin correlated with atrophic changes of the gastric mucosa is occasionally expressed and associated with the pathophysiology of tumor growth.
AIMS&METHODS: The aim of this study was to investigate background atrophy in patients with gastric GISTs (N = 74, 37 men and 37 women; mean age, 65.1 years) and their association with the enlargement of the tumors between April 2004 and April 2011. For age- and sex-matched analysis, we recruited 355 patients without gastric submucosal tumor (SMT) in our hospital between and 205 workers without gastric SMT in a health management center. *The tumor proliferation index*: the changes in tumor volume/follow-up days (mm^3/day).
RESULTS: After 1:3 matching for sex and age between patients with GISTs (n = 74) and patients without GISTs (n = 222), there was a significant difference in the prevalence of open-type atrophy (30.2% vs. 53.1%, $P = .009$, odds ratio (OR) = 2.62, 95% confidence interval (CI): 1.27-5.38). After 1:2 matching for sex and age for the GISTs (n = 44) and workers groups (n = 88), there were significant differences in the presence of gastric atrophy (53.8% vs. 86.0%, $P < .001$, OR = 5.29; 95% CI: 2.20-12.66) and prevalence of open-type atrophy (19.0% vs. 29.7%). The tumor proliferation index indicated the increased (n = 19, 20.2%) and unchanged growth groups (n = 75, 79.8%). The prevalence of severe atrophic changes of the gastric mucosa was lower in the increased growth group than in the other group (10.4% vs. 32.4%, $P = .061$). Histological ghrelin expression (found in approximately 50% of patients) was not associated with the tumor growth.
CONCLUSION: The severity of atrophic changes of the gastric mucosa may be partly associated with tumor enlargement of gastric GISTs.
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Keywords: atorphy, GIST, growth

P1050 OCCURRENCE OF TYPE 1 GASTRIC CARCINOID IN PATIENTS WITH AUTOIMMUNE CHRONIC ATROPHIC GASTRITIS

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INTRODUCTION: The incidence of gastric carcinoids type 1 (GC1) has markedly increased over the last 50 years, although studies assessing long-term incidence of GC1 in patients with chronic autoimmune atrophic gastritis (CAAG) are scanty.
AIMS&METHODS: Aim of the study was to evaluate the incidence and prevalence of GC1 in a cohort of patients with CAAG.
From 2000 to 2012, 101 patients [83 women, median age 63 (21-80) years] were diagnosed as having CAAG, based on histological examination of gastric mucosa, presence of parietal cell antibodies, and elevated pH gastric levels. Active Helicobacter Pylori infection was excluded. They underwent regular clinical and endoscopic follow-up (median time of follow up 36 months, range 3-180). ECL cell status has been classified according to Solcia et al. in: no cell hyperplasia, simple, linear, micronodular hyperplasia, and GC1. Plasma chromogranin A (CgA) and gastrin levels were measured in all patients. During follow up the risk of developing GC1 was evaluated and expressed as person-time incidence rate.
RESULTS: At baseline, among 101 patients, 30 patients had no cell hyperplasia, 11 had simple, 5 linear, 32 micronodular hyperplasia, and in 23 patients GC1 were already present at the time of recruitment (single in 10 patients and multiple in 13, of variable sizes, diameter 0.2-3 cm), with a prevalence of 23%. Out of them, 13 were successfully endoscopically treated, whereas the remaining ten showed the persistence or recurrence of GC1 during the study period. After 321 person-years, one patient was newly diagnosed as having GC1, with a resulting annual incidence rate (person-year) of 0.3%. Patients with GC1 had significantly higher gastrin [median 1400 vs. 886 ng/L, $p < 0.001$] and chromogranin A [median 58 vs. 32 U/L, $p < 0.001$] levels compared with CAAG patients without GC1.
CONCLUSION: This cohort study confirms that GC1 is a possible complication in patients with CAAG due to the trophic effect of gastrin on the gastric wall mucosa. Despite an high prevalence observed in our study, the actual incidence is quite low and elevated level of CgA are strongly associated with the presence of GC1.
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Disclosure of Interest: None Declared
Keywords: autoimmune atrophic gastritis, epidemiology, neuroendocrine tumour, type I gastric carcinoid

P1051 PREOPERATIVE PROGNOSTIC VALUE OF POSITRON EMISSION TOMOGRAPHY-COMPUTED TOMOGRAPHY(PET-CT) IN SURGICALLY RESECTED GASTRIC CANCER.

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INTRODUCTION: Apart from the diagnostic value of Positron Emission Tomography-Computed Tomography(PET-CT), the prognostic value of pre-treatment PET-CT was not commonly evaluated in gastric cancer, so we investigated its preoperative prognostic value.
AIMS&METHODS: Retrospectively we collected 107 cases of gastric cancer patients who had underwent surgical treatment after being observed FDG uptake by preoperative PET-CT at a Dong-A University Medical Center from April 2007 to December 2010. Among firstly enrolled 107 patients, cases of follow up losses(13), palliative resection(5), neoadjuvant chemotherapy(1), unrelated death(1) were excluded and finally total 87 patients were evaluated. Follow up duration was defined as period from operation to date that patients were examined last imaging study such as PET-CT or CT, and the median follow up duration was 34.2 ± 14.8 months until June 2012. FDG uptake values were observed based on maximal standardized uptake value(SUVmax) varied by patients' weight. In order to find correlation of SUVmax with recurrence, Kaplan Meier's survival analysis with log rank test and cox proportional hazard model were performed with using SUVmax cutoff value defined from ROC curve.
RESULTS: Significant difference of T staging($p < 0.001$) and N staging($p < 0.001$) were observed between recurrence group and non-recurrence group in patients' baseline characteristics, but SUVmax was not showed strong difference between two groups(p-value 0.116). Significant statistical difference was observed in Kaplan Meier's survival analysis with log rank test(p-value:0.035) between high SUVmax group and low SUVmax group which separated by SUVmax cutoff value 5.6. However, in multivariate analysis with cox proportional hazard model revised for age, sex, T-staging, N-staging, the SUVmax did not showed statistical significance in correlation with recurrence(SUVmax : p-value 0.893, SUVmax classification by cutoff value : p-value 0.436).
CONCLUSION: High SUVmax on PET-CT is not independent risk factors to predict poor outcomes of surgically resected gastric cancer.
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Disclosure of Interest: None Declared
Keywords: Gastric Cancer, PET-CT, Prognostic Value

P1052 CHANGE OF THERAPEUTIC APPROACH FOR GASTRIC CANCERS PICKED UP BY X RAY SCREENING IN SAGA.

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INTRODUCTION: The medical treatment of the gastric cancer in Saga prefecture in Japan has changed dramatically in recent ten years.
AIMS&METHODS: We aim to report trends and therapeutic approaches in gastric cancers which were picked up X ray screening performed in the total number of 327,903 people in Saga prefecture from 2002 to 2010 in this study. Gastric cancers were detected in the 554 patients out of 327,903 series of X ray screening (detection rate: 0.17%) in Saga prefecture from 2002 to 2010. These cancers were categorized into three groups with the 3 year period; Period I: 2002-2004, Period II: 2005-2007, Period III: 2008-2010.
RESULTS: In Period I, stomach cancers were detected in 216 patients out of 130,286 screenings; Period II: 185 out of 108,261; Period III: 153 out of 89,396. The ratio of early gastric cancer/advanced gastric cancers in each period was Period I: 156/48 (undetected 12), Period II: 123/62, and Period III: 118/30 (undetected 5). We divided early gastric cancers into two groups of subjects who received and not received the X ray screening in every year. Period I: received 81, not received 75; Period II: received 83, not received 40; Period III: received 74, not received 44.
Locations of gastric cancer in each period were as follows (upper /middle/lower) Period I: 49/94/65; Period II: 37/85/ 61, Period III: 35/62/55. Pathological examination revealed as follows (differentiated type/ undifferentiated/ others/ unknown); Period I: 132/69/0/17; Period II: 123/54/2/6; Period III: 103/43/2/0. These data indicated the locations and pathological features of the stomach cancer in this survey were not changed in recent 10 years.
Regarding therapeutic approach to gastric cancer, open laparotomy was mainly applied to the gastric cancer in period I as 159 out of 216 patients. Endoscopic treatment was performed in 38 patients, whereas only 4 patients were treated under laparoscopy. In Period II, the ratio endoscopic treatment increased significantly (24.3%). The ratio of laparoscopic surgery increased form 1.9% to 13.0% (24/153), although the number of gastric cancer patients treated by open laparotomy was decreased (58.9%). In Period III, the ratio of laparoscopic surgery (32.0%) was markedly increased compared to Periods I & II, while increase in the ratio of endoscopic treatment was limited (34.0%).
CONCLUSION: This study showed that early gastric cancer was more often detected in the group which underwent repeated screening by X ray.

Therapeutic approach to the gastric cancer was replaced open laparotomy with endoscopic treatment and laparoscopic surgery in recent 10 years, although backgrounds of the gastric cancer were not changed.
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Disclosure of Interest: None Declared
Keywords: Gastric cancer, X ray screening

P1053 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR EARLY GASTRIC CANCER WITH POST-ESD OR ENDOSCOPIC MUCOSAL RESECTION (EMR) SCAR

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INTRODUCTION: Fibrotic changes are one of factors correlating with the technical difficulty of endoscopic submucosal dissection (ESD). We conducted a clinicopathological analysis on ESD for lesions with scar of post-ESD or post-endoscopic mucosal resection (EMR).
AIMS&METHODS: Between June 2002 and November 2012, we carried out ESD in 803 cases in our department, including 34 cases with post-ESD or post-EMR scar. We defined the case with fibrosis in a part of submucosal layer as Grade1 (G1), and that with fibrosis in all submucosal layer as Grade2 (G2). We examined the degree of fibrosis about site, post-ESD or post-EMR, and the period since the last ESD procedure in the post-ESD group with scar.
RESULTS: We recognized 10 cases with post-EMR scar and 24 cases with post-ESD scar. We combined with snare in 8.8% (3/34). The en bloc resection rate was 97.1% (33/34). The mean tumor size was 18 (4-75) mm. The procedure time was 84.8 (20-233) minute. The delayed bleeding rate of ESD was 11.8% (4/34). Perforation did not occur. The rate of G2 was 57.1% (4/7) in upper portion location, 63.2% (12/19) in middle portion location, and 25% (2/8) in lower portion location. The rate of G2 in lesser curvature lesions was 65% (13/20), and the other site was 35.7% (5/14). The G2 rate of post-ESD and post-EMR was 30% (3/10) and 62.5% (15/24). They did not produce significant difference. But in lower portion location, in the site other than lesser curvature and in post-EMR, the tendency with lower rates of G2 was recognized. After the last ESD procedure, the average period to re-ESD was 527.2 (4-1932) days. The time to re-ESD procedure of the G2 group was significantly shorter compared to the G1 group ($P < 0.05$). The rate of G2 on less than the 527days after the last ESD procedure and on 527 day or later was 80% (12/15) and 33.3% (3/9), respectively ($P < 0.05$).
CONCLUSION: The cases with strong fibrosis increases, if the time period from the last ESD is short. When performing ESD at the first time, it is necessary to observe the circumference carefully. ESD was possible safely by appropriate procedure and device even for lesions with post-EMR or post-ESD scar.
Disclosure of Interest: None Declared
Keywords: ESD, post-EMR, post-ESD, scar

P1054 CLINICOPATHOLOGICAL AND MOLECULAR ANALYSIS OF EPSTEIN–BARR VIRUS POSITIVE GASTRIC CARCINOMA

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INTRODUCTION: Epstein–Barr virus (EBV) infection is involved in a subset of gastric carcinomas (GCs), providing distinct clinical and molecular features.
AIMS&METHODS: We performed prevalence screening of EBV using surgically or endoscopically resected GC specimens in our hospital and correlated the result with clinical and molecular characteristics. In total of 217 GC cases were examined for the presence of EBV genome. The specimens were first screened for the presence of the EBV genome by PCR with primers specific the EBV BamHI W region. Then, the result was confirmed by real-time quantitative PCRs with dual-labeled fluorogenic hybridization probes (one toward the BamHI-W region; and the other toward the EBNA-1 region). For EBV positive (EBV+) cases, mutations of *TP53*, *KRAS*, *PIK3CA* were examined. The status of CpG island methylator phenotype (CIMP) was also examined using 13 panels of genes (*MINT1, 2, 12, 25* and *31, RORA, GDNF, ADAM23, MLF1, PRDM5, RASSF1A, ATP2B4* and *MLH1*).
RESULTS: Among the 217 GC cases, presence of EBV was confirmed in ten cases (4.6%). These ten cases consisted of nine males and one female and the mean age was 57 years old. Histologically, the cases consisted of 3 well, 2 moderate, 3 poorly differentiated and 2 mixed type adenocarcinomas. Four cases of superficial cancer (pM and pSM1) were diagnosed as either well or moderate differentiated type adenocarcinomas. Nine out of ten lesions located in middle and upper body having multiple lesions in three cases. All lesions presented depressed type (or with ulceration) morphology. Eight out of ten cases were CIMP showing dense methylation in all markers examined, except for *MLH1*. Two CIMP-positive cases presented missense mutation in *TP53*, one was within hot-spot lesion in DNA-binding domain (R175H) and the other was in the novel position in DNA-binding domain (D259Y), resulting in truncating protein predicted by SHIFT. One CIMP-positive case also presented *PIK3CA* missense mutation affecting helical domain (E545A).
CONCLUSION: Prevalence, clinical and molecular features of EBV-positive GCs (male dominance, multiple lesions in middle and upper body, CIMP positivity) were in line with previous report, while it was also revealed that subset of EBV+ cases show inactivating mutations in *TP53* and oncogenic mutation in *PIK3CA*. Moreover, the fact that pathologically superficial cancer presented differentiated histologic type suggests that majority of the EBV+ cases may have originally developed as differentiated type histopathology.
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Disclosure of Interest: None Declared
Keywords: EB virus, Gastric cancer

P1055 CLINICOPATHOLOGICAL FEATURES RELATING TO LYMPH NODES METASTASIS AND IMPACT OF THE EXTENT OF LYMPHADENECTOMY ON PROGNOSIS IN EARLY GASTRIC CANCER

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INTRODUCTION: Despite current treatment guidelines recommend endoscopic resection or D1 / D1+ lymphadenectomy for cases of early gastric cancer without lymph nodes metastasis, and D2 lymphadenectomy for cases with lymph nodes metastasis. Currently, information of lymph nodes metastasis in early gastric cancer mainly relies on ultrasonography, however, it's accuracy is not satisfied. Therefore, it is difficult to select a reasonable extent of lymphadenectomy for the case of early gastric cancer with unclear lymph nodes metastasis.
AIMS&METHODS: To explore the clinicopathological features relating to lymph nodes(LN) metastasis and the impact of the extent of lymphadenectomy on prognosis in early gastric cancer. A total of 142 cases of early gastric cancer undergoing radical dissection screened from data base of Gastric Cancer Center of Sun Yat-sen University, from Aug. 1994 to Jan. 2008, were divided into negative and positive group according to LN metastasis. The clinicopathological features and impact of extent of lymphadenectomy on prognosis were compared between two groups.
RESULTS: There had no significant differences in age, gender, tumor size and location, Borrmann type, WHO type, histological type, CEA level between two groups($P > 0.05$). In negative and positive group, the ratio of TNM stage IA, IB, II were 100% vs. 0.0%, 0.0% vs. 88.5%, 0.0% vs. 11.5% respectively ($P < 0.001$). No significant difference existed in postoperative hospital day(d), blood transfusion volume(ml), operation time(min), postoperative complication between cases received D1 and D2 dissection ($P > 0.05$). The number of LN dissected was significant higher in case received D2 than that in D1(P=0.000), but no significant difference existed in the number of positive LN between 2 groups (P=0.502). COX regression analysis showed LN metastasis and the extent of lymphadectomy were independent prognostic factors for total cases. The prognosis of negative group was better than that of positive group (P=0.010), and D2 dissection prolonged survival time significantly as compared with D1 dissection(P=0.0022). In negative group, no significant difference in the prognosis was found between cases received D1 and D2 dissection (P=0.502), whereas D2 dissection prolonged survival time significantly when compared with D1 dissection in positive group(27 vs. 96 months)(P=0.001).
CONCLUSION: The status of LN metastasis could not be assessed accurately preoperatively based on patients' clinicopathological features. For the cases with unclear LN metastasis, D2 dissection should be carried out due to similar mortality and complication rates but prolonged survival time when compared with D1 dissection.
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Disclosure of Interest: None Declared

Keywords: Early Gastric Cancer, Lymph Nodes Metastasis, Lymphadenectomy, Prognosis

P1056 CHARACTERISTICS OF SECOND PRIMARY CANCER IN PATIENTS WITH EARLY GASTRIC CANCER AFTER ENDOSCOPIC RESECTION

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INTRODUCTION: Second primary cancer influences the prognosis of gastric cancer patients. Increment in diagnosis of early gastric cancer (EGC) and improvement of the prognosis for gastric cancer has led to increased incidence of second primary cancer. Endoscopic resection (ER) of EGC is widely performed in Korea. The aim of this study is to analyze the incidence rate, clinico-pathologic features and risk factors of second primary cancer in patients with EGC having history of ER and those with AGC, and compare the results between the two groups.

AIMS&METHODS: We retrospectively reviewed medical information of 716 adult patients with gastric cancer, between January 2006 and December 2010 at a single center, Kyung Hee University Hospital, Seoul, South Korea. The patients who underwent operation for EGC, those with history of previous malignancy and those lost to follow up within 12 months were excluded, and 461 patients were enrolled for the study. We defined synchronous cancers as those occurring within 6 months after diagnosis of the first primary cancer, and metachronous cancers as those occurring more than 6 months later. We collected the demographic data of patients, the incidence rates of synchronous and metachronous cancers and the clinico-pathologic features in EGC with ER and AGC, respectively.

RESULTS: Out of 461 patients, 232 patients (232/461, 50.3%) underwent ER for EGC, and 229 patients (229/461, 49.7%) were diagnosed with AGC. There were no significant differences between the two groups with regard to mean follow-up period (32.9±14.9 months vs. 33.4±16.7 months, P=0.679) and mean age (<60 vs. >60, P= 0.850). Synchronous cancers were diagnosed in 9(3.9%) patients of EGC with ER group and in 10 (4.4%) patients of AGC group. Metachronous cancers were diagnosed in 10(4.3%) patients of EGC with ER group and in 11(4.8%) patients of AGC group. There was no difference in overall incidence of synchronous and metachronous cancers between the two groups (3.9% and 4.3% vs 4.4% and 4.8%, P=0.819 and P=0.828). The most common site of second primary cancer occurrence in EGC with ESD group was the lung (21%), followed by colorectum (16%) and esophagus (16%). The most frequent site of second primary cancer occurrence in AGC group was the colorectum (14%), lung (14%) and esophagus (14%). Logistic regression analyses showed no meaningful risk factors in either group.

CONCLUSION: There was no significant differences in the incidence rate of synchronous and metachronous cancers between EGC with ER and AGC group. Therefore, careful evaluation and close surveillance for detecting synchronous and metachronous cancer is strongly recommended in patients who underwent ESD for ER.

Disclosure of Interest: None Declared

Keywords: Early gastric cancer, Endoscopic resection, Gastric cancer, Metachronous, Synchronous

P1057 CLINICAL BEHAVIORS OF GASTRIC CARCINOID TUMORS ACCORDING TO THE WHO 2010 CLASSIFICATION

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INTRODUCTION: There have been several classifications defining the clinical characteristics of gastric neuroendocrine tumors (NETs) including gastric carcinoid tumors (GCTs). The World Health Organization (WHO) updated its previous classifications in 2010 and classified GCTs as NET G1 and NET G2. However, the clinical behaviors of these newly classified tumors has not been fully evaluated.

AIMS&METHODS: The aim of this study was to clarify the clinical behaviors of GCTs according to the WHO 2010 classification so we reviewed cases involving 23 GCTs at our institution between 1997 and 2012 and retrospectively assessed their clinical behaviors according to the WHO 2010 and the TNM classifications (UICC 7th).

RESULTS: GCTs were treated based on Rindi's classification with surgical resections performed in six cases, endoscopic resections performed in 12 cases and observation without treatment conducted in five cases. Among the 23 GCTs, 15 were classified as NET G1 and eight as NET G2 according to the WHO 2010 classification. Based on the TNM classification, 19 GCTs were classified as T1N0M0 Stage I, three as T2N0M0 Stage IIA and one as T2N1M0 Stage IIIB. There were no cases involving local recurrence, lymph-node (LN) metastasis, distant metastasis or tumor-related death during the median follow-up period of 57 months (range, 2-180 months) except for one patient who died of liver metastasis 78 months after surgical resection whose GCT was classified as NET G2 (Ki-67 index of 12%) and T1. There were four cases involving lymphovascular invasion including one NET G2/T1 case, one NET G2/T2 case and two NET G1/T2 cases as well as two cases involving metastasis including one NET G1/T2 case of regional LN metastasis and the previously mentioned NET G2/T1 case in which the patient died of liver metastasis. Cases involving lymphovascular invasion or metastasis occurred in three of the eight (37.5 %) NET G2 cases and three of the 15 (20%) NET G1 cases (p=0.63). Lymphovascular invasion or metastasis in six of 11 (55%) NET G2 or T2 cases was significantly higher than the total absence of such characteristics in 12 (0%) NET G1/T1 cases ($p<0.05$).

CONCLUSION: The results of this study suggest a comprehensive evaluation using both the WHO 2010 classifications and the T category of the TNM classifications may be useful in predicting the risks of lymphovascular invasion and metastasis in cases involving GCTs.

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Disclosure of Interest: None Declared

Keywords: gastric carcinoid, gastric neuroendocrine tumor, WHO 2010 classification

P1058 THE THERAPEUTIC POTENTIAL OF IRREVERSIBLE ELECTROPORATION IN GASTRIC CANCER: EXPERIMENTAL STUDY IN RAT STOMACH

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INTRODUCTION: Irreversible electroporation (IRE) is a novel, non-thermal method of tissue ablation using short pulses of high-voltage pulse current. IRE induces the breakdown of cell homeostasis and thereby cell death. Studies regarding the clinical application of IRE have been performed in humans, as well as in animals, for organs such as the liver, kidney, pancreas, prostate, brain, etc. and IRE has been tried as a novel anti-cancer ablation modality. This is the first study about the effect of IRE on stomach. The aim of this study was to evaluate the therapeutic potential of IRE in rat gastric tissue according to different electric energy.

AIMS&METHODS: Twenty-six 8-weeks-old Sprague-Dawley rats were used throughout this study. A 3-cm midline abdominal incision was made, exposing the stomach. Small incision was done on greater curvature of stomach, a set of needle electrodes were gently applies on both side of the stomach. From 50 to 160 pulses of 1000, 1500, 2000, 2500, 3000V/cm were delivered for each ablation. All samples for histologic analysis and tunnel assay were got at 0hours, 10 hours, 24 hours and 48 hours after IRE application. The aim of this study was to evaluate the therapeutic potential of IRE in rat gastric tissue according to different electric energy.

RESULTS: All animals survived for their designated times of 10 hrs, 24 hrs and 48 hrs respectively. H-E staining showed extensive areas and severe cell death, which were proved by a pyknotic nucleus and eosinophilic cytoplasm near absence of cell at 10 hours after IRE ablation. Positive results of TUNEL assay were found in the ablated zone at gross assessment, indicating involvement of apoptotic cell death. After 24 and 48 hours, mucosa becomes much thinner by shedding of dead cells in the mucosa. Similar to 10 hours finding, viable cells were rarely observed. Instead, neutrophil infiltration was much increased. And this result shows a morphologically intact endothelium of vessel on submucosal layer after IRE irrespective of time, indicating sparing of connective tissue. The apoptotic area and signals were increased according to applied voltages and pulse in H & E stain and tunnel assay.

CONCLUSION: This study showed that IRE ablated stomach tissue very effectively through the induction of cellular apoptosis. And apoptotic area was increased according to amplified IRE electric energy to 3000V/cm without damage to adjacent structure. This study suggests the potentiality of IRE application in the treatment of gastric cancer without metastasis.

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Disclosure of Interest: None Declared

Keywords: gastric cancer, irreversible electroporation

P1059 THE ROLE OF NDP KINASE–A IN GASTRIC LYMPHOMA: AS A METASTATIC SUPPRESSOR

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INTRODUCTION: The *nm23-H1* gene encodes the NDPK-A (nucleoside diphosphate kinase A) that contributes variably to the migration of cancer cell.

AIMS&METHODS: Aim: To investigate the role of the NDPK-A in gastric lymphoma, we examined the expression of NDPK-A in two different cancer cell lines of the same gastric lymphoma patient.

Methods: The primary cell line of gastric lymphoma, RF-1, was cultured from the primary gastric lymphoma site, and the other cell line RF-48 was metastasized to the peritoneum of the same patient after 6 months. We have generated stable gastric lymphoma transfectants, pIRES-NDPKA-GFP-neo, that constitutively over-express transfected and vector form of NDPK-A, in addition to a reporter, green fluorescent protein(GFP). The transfected gastric lymphoma cell migration

assay was performed 24-well modified chemotaxis chambers with FluroBloc membrane.
RESULTS: In regard to the migration rate of the gastric lymphoma cell lines, RF-1 vector was 75.8±7.5%, RF-1 transfected was 54.4±12.3%, RF-48 vector was 84.7±15.4%, RF-48 transfected type was 62.3±9.2%, RF-48 migrated better than RF-1, and the vector type migrated better than the transfected type. NDPK-A was presented more in RF-1 than RF-48, and presented more in the transfected type than the vector type, and concerning the migration rate, RF-48 migrated better than RF-1, and the vector type migrated better than the transfected type.
CONCLUSION: Concerning NDPK-A in gastric lymphomas, more abundant was NDPK-A, poorer was migration, and thus it played a role of the suppressor of migration. We concluded that NDPK-A acts as a migration suppressor in gastric lymphoma
Disclosure of Interest: None Declared
Keywords: Gastric lymphoma, NDP kinase-A

P1060 GENE-EXPRESSION OF THE WNT-MODULATOR RACGAP1 CORRELATES INVERSELY WITH CDKN1A (P21) IN PATIENTS WITH GASTRIC CANCER.

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INTRODUCTION: RACGAP1 has been recently identified as regulatory gene involved in gastric carcinogenesis by in silico gene-gene co-expression network analysis. RACGAP1 is suggested as downstream modulator of the Wnt-signalling pathway. Up to date, there are no data on RACGAP1 expression in human gastric cancer.
AIMS&METHODS: Here, we investigated the interaction of RACGAP1 with the p21 gene (CDKN1A) and Wnt-dependent signalling (DKK2, β-catenin) pathways in gastric cancer.
Biopsy samples of gastric cancer tissue and adjacent non-malignant gastric mucosa were prospectively collected (n=48; intestinal type n=28; diffuse type n=20). Antrum and corpus biopsies from subjects without any pathology of the upper gastrointestinal tract have been used as a control (n=30). Transcript levels of RACGAP1, CDKN1A, DKK2 and β-catenin were quantified by quantitative real-time PCR. For statistical analysis, non-parametric tests were applied with $p<0.05$ regarded as significant.
RESULTS: The expression of RACGAP1 in the tumour correlated inversely with CDKN1A expression (r=-0.359, p=0.011), but showed a positive association to both β-catenin and DKK2 in tumour tissue (β-catenin: r=0,300; p=0,036; DKK2: r=0,373; p=0,008). Pairwise comparison revealed no difference in the RACGAP1 or CDKN1A gene expression between samples from tumour, tumour-adjacent and tumour-distant mucosa.
However, the expression of RACGAP1 was significantly lower in samples (tumour and non-tumorous tissue) from gastric cancer patients compared to controls (2.8e-03 vs 8.3e-03, $p<0.001$), whereas CDKN1A expression was higher in tumour patients (1.4e-04 vs 7.3e-05, p=0.003). Interestingly, differential expression of RACGAP1 in tumours could be confirmed for both antrum and corpus (p=0.008, $p<0.001$, resp.). CDKN1A expression difference was observed only for corpus mucosa of the controls, but not antrum (p=0.008).
Subgroup comparison revealed no significant difference of the gene expression of neither RACGAP1 nor CDKN1A if stratified by Laurén type (58% intestinal), localisation of the main tumour mass (20% proximal GC), as well as *H. pylori* status (74% positive).
CONCLUSION: RACGAP1 expression is downregulated in gastric cancer and is associated with the expression of target genes of Wnt-dependent signalling. RACGAP1 correlates inversely with CDKN1A gene expression, therefore its role as prognostic indicator needs further assessment.
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Disclosure of Interest: None Declared
Keywords: CDKN1A, gastric cancer, p21, RACGAP1, Wnt

P1061 THE EFFECTS OF DNA METHYLTRANSFERASE INHIBITOR DECITABINE ON HOXD10-CASPASE3-MEDIATED APOPTOSIS AND PROLIFERATION OF GASTRIC CANCER CELL LINE MKN45

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INTRODUCTION: Gastric cancer is the second most common cancer with the incidence of 69 cases per 100,000 people per year in China. Epigenetic alterations such as promoter hypermethylation of tumor suppressor genes (TSGs), which lead to the silence of TSGs, has been demonstrated to contribute to gastric cancer progression.
DNA methylation is controlled by DNA methyltransferases (DNMTs). DNMTs inhibitor decitabine is a kind of cytidine nucleoside analogues. It depletes cells of functional methyltransferase activity through forming a irreversible covalent bond with DNMTs. Inhibition of DNA methylation with decitabine has been shown to reactivate the expression of genes silenced by hypermethylation in tumor cells in vitro or in vivo. In 2006, decitabine was approved by the US FDA for the treatment of patients with myelodysplastic syndrome (MDS).
AIMS&METHODS: This study was designed to investigate the relationship between the dose-time and anti-tumor effect of DNA methyltransferases (DNMTs) inhibitor decitabine in human gastric cancer cell line MKN45. Human gastric cancer cell line MKN45 was treated with a dose range (0-20 μmol/L) of decitabine for 48,72 and 96 hours, respectively. Flow cytometric analysis of Annexin V-FITC/PI staining and CCK8 assays were used to study apoptosis and proliferation in MKN45 cells. RT-PCR and Real-Time PCR were used to examine the expression of Homeobox D10(HoxD10) at the mRNA levels. Cleaved-caspase3 expression was determined by Western blot.
RESULTS: (1) Annexin V-FITC/PI staining showed that decitabine induced apoptosis of MKN45 in a time-dependent manner. The maximal amount of proapoptosis effect 17.37±1.10% was detected at 96h with 20μmol/L decitabine. (2) Decitabine was an effective inhibitor of MKN45 proliferation and the effect was time-dependent. A decitabine concentration of 20μmol/L accounted for the inhibition of cell proliferation of 59.96±4.28% at 96 hours.(3)The mRNA expression of HoxD10 in gastric cell line MKN45 was markedly downregulated than that in normal gastric epithelial cell line GES1. Decitabine could induce HoxD10 reexpression in a time-dependent manner through demethylation effect in MKN45 cells.(4)Cleaved-caspase3 was activated significantly with decitabine treatment comparing to the controls.
CONCLUSION: Our results demonstrated that decitabine exert proapoptotic and growth inhibition effects in human gastric cancer cell line MKN45 in a time-dependent manner. Reexpression of tumor suppressor gene HoxD10 and cleaved-caspase3 activation contributed to the apoptosis of MKN45 cells. DNA methylation plays an important role in gastric cancer progression.
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Disclosure of Interest: None Declared
Keywords: Apoptosis, Decitabine, Gastric cancer, HoxD10, Methylation, Proliferation

P1062 COMMON FUNCTIONAL GENETIC POLYMORPHISMS ASSOCIATED WITH SURVIVAL OF GASTRIC CANCER PATIENTS

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INTRODUCTION: So far, a number of association studies have focused on the effect of common functional SNPs on the susceptibility to gastric cancer (GC).
AIMS&METHODS: Here, we evaluated the possible association between common functional SNPs in pro-inflammatory cytokines, DNA repair and xenobiotic molecules, and pre-miRNAs with the overall survival in GC patients. 12 candidate SNPs (IL-1β gene -31T>C and -511C>T, TNF-α-857C>T, XRCC1 Arg399Gln and Arg194Trp, GSTP1 Ile104Val, GSTT1, GSTM1, Cyclin D1 G870A, miR-196a2, miR-146a and miR-499) were determined in 130 GC patients in relation to the overall survival, defined as the time from the date of surgery for respectable cases and the date of initial chemotherapy for unrespectable cases. Survival among different genotypes was assessed using the Kaplan–Meier method and compared using the log-rank test.
RESULTS: The median follow-up period of patients was 30.0 months. TNF-α-857T carrier showed significantly better overall survival than patients with CC genotype (p=0.01). GC patients who have either of IL-1β-31 CC or IL-1β-511 TT or TNF-α-857 T carrier genotypes showed also better survival than the other genotypes (p=0.02). The patients with the GSTT1 null genotype also presented better overall survival than the GSTT1 present genotype (p=0.019). When the subjects were divided according to age group, the miR-196a2 rs11614913 T carrier tended to be associated with worse overall survival than the CC genotype in patients younger than 65 years of age (p=0.05).
CONCLUSION: TNF-α-857T carrier and GSTT1 null genotype seems to be associated with better overall survival of GC patients. miR-196a2 rs11614913 T carrier might be associated with worse overall survival in younger cases.
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Disclosure of Interest: None Declared
Keywords: gastric cancer, genetic polymorphisms

P1063 THE DYNAMICS OF PEPSINOGEN LEVELS IN A CAUCASIAN POPULATION WITHIN A 3-YEAR PERIOD

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INTRODUCTION: Pepsinogen (PgI) and the ratio between PgI and pepsinogen II (PgI/PgII) detection is used as an indirect marker for atrophy in the corpus of the stomach mucosa.
AIMS&METHODS: The aim of the study was to evaluate the dynamics of pepsinogen test results within a 3-year period in a Caucasian population.
Patients that were reported to have decreased Pg levels at the time of initial sampling, were invited to undergo repeated plasma sampling and upper endoscopy with biopsy work-up according to updated Sydney system in average 3 years after the initial blood sample. PgI and PgII were measured in plasma simultaneously in the initial sample and the follow-up sample (Eiken Chemical Co., Tokyo, Japan). The initial selection of the cases was made based on a cross-sectional population-based study in Latvia.
RESULTS: Plasma samples from 107 cases were available for the analysis (45 men; the mean age was 62).

The mean PgI level was 33.1 in the initial sample and 32.2 in the follow -up sample, no statistical difference was revealed (p=0.61). The mean PgI/PgII was 2.0 and 2.2, respectively (p=0.06).
In the group of patients with moderate to severe corpus atrophy and/or intestinal metaplasia (according to histology; 11 patients altogether) the mean PgI was 19.4 initially and 16.8 at the control (p=0.28); mean PgI/II was 1.0 initially, and 0.99 at the control (p=0.85)
Altogether 11 patients had undergone *H.pylori* eradication therapy during the study period. In those having undergone eradication the mean PgI was 35.0 initially and 35.1 at the control (p=0.97); mean PgI/II was 2.1 and 2.7, respectively (p=0.11).
In the group of 45 men the mean PgI level was 33.1 in the initial sample and 32.7 in the follow - up sample (p=0.86); mean PgI/II was 1.9 initially, and 2.1 - in the follow -up sample (p=0.04).
CONCLUSION: Our data show that initially PgI or PgI/PgII levels are relatively stable and do not change substantially during a three year period neither in the entire patient sample nor in patients with *H.pylori* eradication therapy as well as in patients with moderate to severe corpus atrophy and/or intestinal metaplasia. Slight increase of PgI/II in men during a 3-year period was observed.
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Disclosure of Interest: None Declared
Keywords: dynamics, levels, pepsinogens

P1064 ALPHA1 ACID GLYCOPROTEIN BINDS TO PACLITAXEL AND SUBSTANTIALLY ALTERS ITS ANTICANCER EFFECTS WHICH COULD BE RESTORED BY ERYTHROMYCIN

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INTRODUCTION: Paclitaxel (PTX) is widely used for gastric cancer treatment, especially as low dose weekly administration. Intravenously administrated PTX elutes into ascites, which concentration is about 10 nM, and shows anticancer effects directly in peritoneal cavity. It is well known that according to cancer progression, the level of Alpha1 acid glycoprotein (AGP) in serum and ascites often increase.
AIMS&METHODS: The aim of the present study was to clarify whether AGP binds to PTX and alters its anticancer effects. For the establishment of experimental dosage, the concentration of AGP in serum and ascites of gastric cancer patients with peritoneal carcinomatosis (PC) was measured by radial immunodiffusion assay. The inhibitory effects of AGP to PTX *in vitro* were evaluated by MTT assay using gastric cancer cell line; OCUM-2MD3. We also examined the combined effects of erythromycin (EM) with AGP *in vitro* and *in vivo*.
RESULTS: The mean levels of AGP were 1.524 mg/ml in serum and 0.834 mg/ml in ascites. Addition of AGP disturbed cell growth inhibition of PTX on dose dependent manner (0.2 to 1.2 mg/ml). However, combination with EM restored anticancer effects of PTX. The elevated level of AGP was detected in ascites of mice PC model inoculated OCUM2MD3 and reached a plateau on Day 17. PTX (5mg/kg/iv) alone did not diminished PC remarkably when PTX was administrated Day 7 and 14, whereas co-administration of PTX and EM (5 mg/kg/D7-17) significantly reduced PC *in vivo* (p=0.011).
CONCLUSION: AGP is an important regulatory factor modulating the ability of intravenous PTX, and combined therapy with PTX and EM might be useful for treatment of PC in gastric cancer.
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Disclosure of Interest: None Declared
Keywords: alpha 1 acid glycoprotein, erythromycin, Gastric cancer, paclitaxel, peritoneal carcinomatosis

P1065 ENDOSONOGRAPHY-GUIDED FINE-NEEDLE ASPIRATION VERSUS KEY-HOLE BIOPSY IN DIAGNOSTICS OF GASTRIC SUBMUCOSAL TUMORS – A RANDOMIZED STUDY

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INTRODUCTION: Gastric submucosal tumors (g-SMTs) are tumors arising from subepithelial layers of the gastric wall, mostly from submucosa and muscular layer. They usually have an intact mucosa lining on the inner surface. Prognosis and treatment of g-SMTs depend on its correct diagnosis which consists in the cytohistological and immunohistochemical examination. A standard forceps biopsy of mucosa is usually not helpful due to their location. Therefore, biopsy techniques capable of reaching deeper layer of gastric wall are needed.
AIMS&METHODS: Compare the yield and success of Endosonography-Guided Fine-Needle Aspiration (EUS-FNA) and Key- Hole Biopsy (KHB) in cytohistological and immunohistochemical diagnostics of g-SMTs.
Patients with endoscopically detected g-SMTs with diameter $\geq$ 2cm were randomly allocated to undergo either EUS-FNA by 22G needle or KHB (consisting of forceps biopsy through mucosal incision by a needle knife), both with subsequent histological/cytological and imunohistochemical evaluation of the specimen. In case of failure of the initial method, the other method was performed (cross-over).
RESULTS: Up to now, a total of 24 subjects (37,5% men, mean age 65,7 years), twelve in each group, with g- SMTs were enrolled in the study .
Primary tissue diagnosis was obtained in 83,3% (10/12) of patients in each group. The final diagnosis was established by the initial sampling in 20 (80%) and in 3 patients after cross-over. In the whole study population the final tissue diagnosis was: GIST (n = 15, 62,5%), leiomyoma (n = 4, 16,7%), lipoma (n = 2, 8,3%), MALT lymphoma (n = 1, 4,16%), adenocarcinoma (n = 1, 4,16%). In one case (4,16%) no diagnosis was obtained. In the population with final diagnosis GIST, ten patients were in the EUS-FNA group. Of 15 patients with a diagnosis of GIST, some MA could be evaluated only in 5 patients (2 in the EUS-FNA group). A number of mitoses in the required 50 high power fields was approximately specified only in 3 patients . In the trial population, twelve patients (five in tke KHB group, ten with diagnosis GIST and two with diagnosis Leiomyoma) were operated. The post-operative tissue diagnosis corresponded in 4/5 (80%) patients in the KHB group and 7/7 (100%) in FNA group.
CONCLUSION: 1) According to our study Gastrointestinal Stromal Tumors are the most common Gastric Submucosal Tumors (in 62,5%).
2) Endosonography-Guided Fine-Needle Aspiration and Key-Hole biopsy enable diagnosis Gastrointestinal Stromal Tumors.
3) Neither Endosonography-guided Fine-Needle Aspiration nor Key-Hole Biposy is able to provide adequate tissue sample to determine prognostic mitotic activity.
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Disclosure of Interest: None Declared
Keywords: EUS-FNA, KHB

TUESDAY, OCTOBER 15, 2013 9:00–17:00
***H. PYLORI* II – Poster Area**

P1066 CHANGES OF ESOPHAGUS IN PATIENTS INFECTED WITH CAGA(-) AND CAGA(+) STRAINS OF HELICOBACTER PYLORI

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INTRODUCTION: Data about association between *Helicobacter pylori* infection and gastro-esophageal reflux disease (GERD) are controversial. Some studies have shown that *H. pylori* may protect against GERD and *H. pylori* eradication may be a risk factor of development of inflammation and erosive changes in esophagus. But other studies did not confirm it.
AIMS&METHODS: Aim: To estimate changes of esophagus in patient infected with *cagA(+)* and *cagA(-)* strains of *H. pylori.*
Materials and methods: 41 persons infected with *H. pylori* were under supervision. For all the surveyed patients analysis of complains and esophagogastroduodenoscopy were performed to estimate clinical and endoscopic signs of changes in esophagus. Also for all patients a biopsy from a stomach antrum was performed for verification of *H. pylori* infection by means of rapid urease test and polymerase chain reaction (PCR) with detection of genes of *H. pylori* pathogenicity island: *ureC, cagA, cagC, cagE, cagH* (Research laboratory "Diagnostics"). The choice of the genes selected for the analysis was based on the fact that these genes encode for several cytotoxins - the most important pathogenecity factors of *H. pylori.* All the surveyed patients have been divided into two groups: Patients from the 1st group (12 patients) were infected with *cagA(-)* strains. Patients from the 2nd group (29 patients) were infected with *cagA(+).* Statistical estimation was performed in programs Excel and Statistica 6.0 for Windows XP.
RESULTS: heartburn was in 75% in patients from 1st group and 79.3% in 2nd group. Hyperemia of esophagus (distal esophagitis) was in 41.7% of patients in 1st group and in 24.1% of patients in 2nd group ($p<0.05$). Erosions of esophagus were no in 1st group patients and were in 3.4% of patients in 2nd group ($p<0.05$). At the analysis of features of *cag*-status of *H. pylori* in these groups of patients it has been revealed that in patients from 1st group a frequency of occurrence of other investigated genes of *cag*-group (except *cagA*) of *H. pylori* pathogenicity islands was significantly lower than in patients from 2nd group: *cagC* gene – 8.3% and 55% ($p<0.05$), *cagE* gene – 22.2% and 33.3%, *cagH* gene – 25% and 80% ($p<0.05$) correspondingly.
CONCLUSION: Changes of esophagus are common in patients infected with as highly and lower virulence strains of *H. pylori. CagA(+)* status is associated with erosive changes of esophagus. Heartburn without hyperemia or erosions of esophagus can be sign of functional dyspepsia or endoscopic negative GERD.
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Disclosure of Interest: None Declared
Keywords: cagA gene, Esophagus, Helicobacter pylori

P1067 VARIATION IN HELICOBACTER PYLORI CAGA PROMOTER REGION IS ASSOCIATED WITH CAGA EXPRESSION AND INFLUENCES INTERLEUKIN-8 SECRETION

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INTRODUCTION: *Helicobacter pylori* CagA is a main virulence factor that is present in about 70% of the strains from Western countries, and is a major contributor for peptic ulcer disease and gastric carcinoma. Recently, four motifs have been identified that exhibit sequence heterogeneity in the promoter region of *cagA*, located at positions -344, -53, -10 and +59 bp from the transcription start site. The presence of the +59 motif has been defined as determinant of enhanced CagA protein expression, and both the presence of the +59 motif and high CagA expression have been associated with worse histopathological scores in a population of Colombia at high risk for gastric carcinoma (1).
AIMS&METHODS: The aim of this study was to characterize the *H. pylori cagA* promoter region, to assess the relationship between variation in this region and CagA expression, and to investigate the influence of *cagA* promoter variation and CagA expression on IL-8 secretion.
The *cagA* promoter region was sequenced in 46 *cagA*-positive clinical isolates and two reference strains (26695 and 60190). The CagA expression levels were assessed by western blot, and IL-8 secretion was evaluated by ELISA in culture supernatants of the gastric cell line AGS infected with *H. pylori*.
RESULTS: Nucleotide sequences of the *cagA* promoter region showed high heterogeneity among *H. pylori* strains. The differences included variation in sequence and copy number of the -344 and -54 motifs. The -10 motif only showed sequence variation, being TATAATGA the most common sequence found (54.6%). The +59 motif was either absent (23.9%), or present as one (73.9%) or two (2.2%) copies in the clinical *H. pylori* strains analysed.
CagA protein expression was associated with the -10 TATAATGA sequence ($p = 0.012$) and with the presence of the +59 motif ($p = 0.003$). Moreover, the levels of IL-8 secreted by AGS cells were correlated with the levels of CagA expression ($r_p = 0.391$; $p = 0.009$), as well as with the presence of the +59 motif in the *cagA* promoter ($p < 0.001$). No relationships were found between CagA expression ($p = 0.237$) or IL-8 secretion ($p = 0.403$) and the number of CagA EPIYA C motifs present in the *H. pylori* strains.
CONCLUSION: Variation in the *cagA* promoter region is associated with CagA expression and influences IL-8 secretion by gastric cells. Further studies are needed to confirm the usefulness of specific regions on the *cagA* promoter as markers to predict disease risk.
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Disclosure of Interest: None Declared
Keywords: cagA gene, Interleukin-8

P1068 PRIMARY CLARITHROMYCIN RESISTANCE IN H. PYLORI ISOLATES IN ITALY IS ASSOCIATED WITH NEW POINT MUTATIONS IN THE RRNA.

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INTRODUCTION: Phenotypic clarithromycin resistance in *H. pylori* strains is associated with different genotypic point mutations in the bacterial rRNA. The A2143G, A2142G, A2142C are the point mutations involved in more than 90% of clarithromycin resistant in Western countries.
AIMS&METHODS: Aim: To assess the prevalence of different genotypic mutations in *H. pylori* strains with phenotypic clarithromycin resistance isolated in Italy.
Methods: Paraffin-embedded biopsies of consecutive patients with *H. pylori* strains harbouring primary clarithromycin resistance assessed by culture (MIC $\geq$0.5 mg/L) were retrieved. A TaqMan-PCR was performed to search for different point mutations.
RESULTS: A total of 42 isolates were evaluated, and a genotypic mutation in the rRNA was identified in 37 (88%). In detail, the presence of at least 1 of the most frequent point mutation was detected in only 23 (54.8%) cases, including 13 A2143G, 8 A2142G, and 2 A2143G plus A2142G. A different point mutation was detected in further 14 (33.3%) of phenotypic resistant isolates, including 6 G2141G, 4 A2144T, 3 A2115; G, and 1 A2115G plus A2144G. None of tested mutations was present in the remaining 5 isolates.
CONCLUSION: The prevalence of the 3 most frequently detected point mutations of clarithromycin resistance is declining, whilst other point mutations are emerging in *H. pylori* isolates in Italy. This observation should be considered when assessing clarithromycin resistance by using only a PCR-based tool.
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Disclosure of Interest: None Declared
Keywords: H. pylori, resistance, rRNA mutations

P1069 RECOVERY OF GASTRIC FUNCTION AFTER HELICOBACTER PYLORI ERADICATION AND ACETIUM ADMINISTRATION: A 6 YEARS STUDY IN ATROPHIC GASTRITIS SUBJECTS.

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INTRODUCTION: The relationship between *H.pylori* eradication and atrophic changes in the gastric mucosa has not yet been fully defined. Athough studies report a partial restoration of serum pepsinogenI(sPGI)after eradication, it is not clear if this finding reflects gastric mucosal ealing on a morphological level. Recently a new compound(L-cystein Acetium, Biohit, Fin) has been proposed for prevention of gastric carcinogenesis in patients with atrophic gastritis, by reducing acetaldehyde production after food intake.
AIMS&METHODS: To assess alteration in gastric function after *H.pylori* eradication on moderate-severe body atrophiv gastritis by determination of sPGI levels and Gastrin 17 (sG-17). 74 dyspeptic pts, selected from 738 consecutive *H.pylori* + patients, with histological features of moderate-severe body atrophic gastritis and sPGI <25microg/L (34men, mean age 58, range 26-83yrs), underwent an upper gastrointestinal endoscopy with gastric biopsies and sPGI and sG-17determination at baseline. All patients underwent eradication therapy. Serum sPGI and sG-17 were measured again after 6 months, and at 1,2,3,5 and 6yrs after eradication.
RESULTS: Mean sPGI levels prior to eradication were 13,4microgr/L(range:1,5-24microgr/L). 6 months after eradication therapy, mean sPGI levels significantly increase to 16,6 microgr/L (p=0.05). At the completion of the study, 6yrs after eradication, sPGI levels increased to 27,3microgr/L (p=0.01). Conversely, the sG 17 dropped out from 84,8 at baseline to 67,6pmol/L after the 6 yrs follow up period($p<0.01$).21 patients(16 fem, mean age 44, range 27-61 yrs) out of the 74 sample atrophic gastritis subjects experienced a 3 month period of treatment with Acetium 100 mg at dosage of 3 capsules daily before eating. In all, both sPGI and sG 17 were reduced at baseline and after 3 months period of treatment. The mean levels of sPGI increases from 7,9microgr/L at baseline to 11,4 after 90 days of Acetium intake as well as sG-17 drop out from30,3 to 25,5pmol/L.
CONCLUSION: After H. Pylori eradication subjects with body atrophic gastritis showed long-lasting improvement of physiological gastric function, reflected by significantly and stabile increasing of sPGi levels and a parallel decreased of sG 17 over a 6-year period of follow up. L-cysteine seem to be usefull in restoring gastric secretion in subjects with chronic atrophic gastritis, but other studies are required to confirm and clarify this finding.
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Disclosure of Interest: None Declared
Keywords: atrophic gastritis, Gastrin

P1070 DIFFERENT BIOLOGICAL IMPLICATION OF INHIBITORY TGF-β SIGNALING, SMAD7, IN GASTRIC MUCOSAL DAMAGES ACCORDING TO HELICOBACTER PYLORI INFECTION AND NSAID ADMINISTRATION

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INTRODUCTION: *Smad7* has been known as inhibitory signaling molecule of transforming growth factor (TGF)-β superfamily, leading to block TGF-β–induced cell apoptosis and immune suppression. Since inflammation, apoptosis, endoplasmic reticulum-stress, and autophagic cell death have been identified as key cytotoxic mechanisms implicated in either *H. pylori*- or NSAIDs-induced gastric damages, we have the curiosity how *smad7* can influence *H. pylori*- and NSAID-induced gastritis.
AIMS&METHODS: To investigate the biological role of TGF-β1 or its antagonist, *Smad7*, in *H pylori*- and NSAIDs-induced gastric damages, respectively, we generated *Smad7* overexpressed RGM1 cells. Using these cells, we compared the different gene expression between MOCK transfected cells and overexpressed-*Smad7* cells after *H. pylori* and NSAIDs by high throughput analysis of cDNA microarray. We validated the findings by detecting the protein expression of inflammation-, proliferation-, apoptosis-, and autophagy- related mediators.
RESULTS: *Smad7* overexpression significantly increased *H. pylori*-induced inflammation and apoptotic actions, whereas *Smad7* overexpression suppressed indomethacin-induced apoptosis and autophagic cell death, quite contrary implications of *Smad7* according to kind of irritant. Furthermore, indomethacin treatment significantly decreased the expression of *Smad7* and induced gastric damage by *Smad7* degradation as confirmed by *Smad7* knockdown. cDNA microarray revealed these contrary implications of *smad7* in gastric epithelial damages were based on different transcriptional regulation of inflammatory and cytotoxic mediators as well as autophagy.
CONCLUSION: Our novel findings suggest that the maintenance of *Smad7* expression may have different possible therapeutic actions in *H. pylori*- and NSAIDs-induced gastric injury, rendering dual sword implication of *Smad7* in gastric damages.
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Disclosure of Interest: None Declared
Keywords: helicobacter pylori, NSAID, smad7

P1071 ACTIVATION-INDUCED CYTIDINE DEAMINASE (AID) EXPRESSION IS CORRELATED WITH OLGA AND OLGIM STAGING IN HELICOBACTER PYLORI-INFECTED MUCOSA

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INTRODUCTION: Recent studies have shown the important roles played by activation-induced cytidine deaminase (AID), an intrinsic genome mutator, in *Helicobacter pylori*-associated gastric cancer development.
AIMS&METHODS: Our aim was to evaluate the relationship between OLGA/OLGIM (Operative Link on Gastritis/Intestinal Metaplasia Assessment) staging and AID expression. A total of 109 patients with functional dyspepsia who had undergone endoscopy were selected. Histological staging of OLGA and OLGIM was assessed according to the updated Sydney system (USS). *H. pylori* infection was diagnosed by serological testing, the ^{13}C urea breath test, and histological examination. Immunohistochemical AID and p53 expression in the biopsy specimens was scored.
RESULTS: Of the 109 patients, 60 (55%) were *H. pylori*-positive and 49 (45%) were *H. pylori*-negative. AID expression was significantly higher in *H. pylori*-positive patients than in *H. pylori*-negative patients (median AID score, 14 vs 3, $p<0.01$). AID expression correlated significantly with OLGA staging (Spearman's rho, 0.51, $p<0.01$), and OLGIM staging (Spearman's rho, 0.55, $p<0.01$). In addition, AID expression correlated strongly with p53 expression (Spearman's rho, 0.71, $p<0.01$).
CONCLUSION: AID was found in the gastric epithelium of biopsy specimens, especially in association with *H. pylori* infection. Both OLGA and OLGIM staging correlated with AID and p53 expression, suggesting a significant role in atrophic change with intestinalization accompanying the development of gastric cancer.
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Disclosure of Interest: None Declared
Keywords: AID, OLGA staging, OLGIM staging

P1072 THE EFFECT OF H. PYLORI ON THE EGFR-INDUCED SIGNAL TRANSDUCTION AND PREVENTIVE EFFECT OF CELECOXIB IN THE GASTRIC CANCER CELLS

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INTRODUCTION: Epithelial growth factor receptor (EGFR) downstream targets phosphatidyl inositol 3-OH kinase (PI3K)-Akt-glycogen synthase kinase-3 (GSK3) pathways, thus regulates cell survival and migration. *Helicobacter pylori* (*H. pylori*) infection induces cyclooxygenase-2 (COX-2) over-expression, and previous study showed that selective COX-2 inhibitor, celecoxib, blocked Akt signaling pathway. COX-2 and EGFR may cross talk through Akt-signaling pathways.
AIMS&METHODS: Aim: To evaluate the effect of *H. pylori* on EGFR signaling pathways and to find out whether celecoxib has inhibitory effect on the EGFR signaling pathway or not.
Methods: AGS gastric epithelial cell lines were co-cultured with *H. pylori cagA+*, *vacA+* G27 and the *cagE-* mutant of G27. The expressions of COX-2, EGFR and TGF-ß were measured by real-time PCR. In the next, Western blot analyses of COX-2, EGFR, total Akt (tAkt), phosphorylated Akt (pAkt) and pGSK3ß were carried out at various concentrations of celecoxib (0, 10, 20, 30 μmol/L) for 24 hours in *H. pylori* treated AGS cell lines.
RESULTS: *H. pylori* infection significantly up-regulated the mRNA levels of COX-2, EGFR, HB-EGF and TGF-ß by RT-PCR. However, AGS cells treated with *cagE-* mutants, which have a defective type IV secretion system, did not show EGFR up-regulation. Celecoxib had inhibitory effects on *H. pylori*-induced over-expression of COX-2 (p=0.015), EGFR (p=0.025), pAkt (p=0.025) and pGSK3ß (p=0.029) in AGS cell lines by Western blot analysis.
CONCLUSION: *H. pylori* activated COX-2-Akt-GSK pathway, and EGFR signal pathways in AGS cell lines, which was dependent on type IV secretion system. As celecoxib showed inhibitory effects not only on COX-2-Akt-GSK pathway but also on EGFR signal pathway, it looks like that COX-2 and EGFR cross talk, mediating the *H. pylori*-induced gastric cancer.
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Disclosure of Interest: None Declared
Keywords: AGS cell line, Gastric cancer, Helicobacter pylori

P1073 ENHANCED EXPRESSION OF INDOLEAMINE 2,3-DIOXYGENASE (IDO) IN HELICOBACTER PYLORI-INFECTED HUMAN GASTRIC MUCOSA DOWNREGULATES INTERLEUKIN (IL)-17 AND UPREGULATES IL-4 PRODUCTION

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INTRODUCTION: The activation of IDO results in depletion of tryptophan (Trp) and production of its catabolites from kynurenine-metabolism pathway which are directely toxic to effector T-cells and promote the differentiation of regulatory T cells. Data from animal models propose that IDO may play a role in self-limiting Th1 response and promoting Th2 cytokine profile. IL-17, a Th17-derived cytokine up-regulated in *H. pylori*-infected human gastric mucosa, plays a role in the host response against the bacterium and, possibly, in its clearance/persistence.
AIMS&METHODS: Five antral biopsies were taken from 20 patients (10 M, median age 41 yrs, range 25-70) who underwent upper gastrointestinal endoscopy for dyspeptic symptoms: 1 for urease quick test (Yamanouchi Pharma, Milan, Italy), 2 for histology (Giemsa staining for *H. pylori* and modified Sydney System for gastritis score), and 2 for protein extraction. 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). In a subgroup of patients, further antral biopsies were taken, immediately placed in an organ culture chamber, and treated for 24 hours with and without IDO inhibitor 1-methyl-L-Trp (Sigma, St. Louis, MO). The expression of IDO protein and that of IL-17 and IL-4 was determined by Western blotting in total proteins extracted from freshly obtained gastric biopsies and gastric biopsy cultures, respectively. The ratio of IDO, IL-17, and IL-4 with beta-actin was calculated by densitometry and values expressed as means ± SD arbitrary units (a.u.).
RESULTS: IDO expression was found enhanced in gastric biopsies from *H. pylori*-infected (n=10) compared to uninfected (n=10) patients (1.28±0.20 a.u. *vs* 0.98±0.35 a.u., P=0.037, respectively). Higher levels of IDO were fairly associated with higher grade of gastritis score in all patients (r=0.409, P=0.07) but not in the *H. pylori*-infected subgroup (r=-0.262, P=0.46). In gastric biopsy cultures, IDO inhibition significantly ($P<0.05$) increased IL-17 while decreased IL-4 expression, particularly in *H. pylori*-infected compared to uninfected samples.
CONCLUSION: This study demonstrates, for the first time, that an enhanced expression of IDO takes place in *H. pylori*-infected human gastric mucosa. This is capable of downregulating IL-17 and upregulating IL-4 production and, possibly, of favouring the persistence of *H. pylori*. Targeting IDO pathway may be a new strategy for modulating *H. pylori*-induced mucosal immune response.
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Disclosure of Interest: None Declared
Keywords: Gastritis, IDO, IL-17, IL-4

P1074 EFFECT OF COMMON FUNCTIONAL GENETIC POLYMORPHISMS ON CPG ISLAND METHYLATION IN NON-NEOPLASTIC GASTRIC MUCOSA

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INTRODUCTION: CpG island hyper methylation (CIHM) is also closely associated with *H. pylori* infection, degree of gastritis, suggesting that this epigenetic change seems to be an early step in carcinogenesis in the stomach.
AIMS&METHODS: To evaluate the influence of host genetic factors on methylation related carcinogenesis, we investigated the association between common functional SNPs in pro-inflammatory cytokines, DNA repair and xenobiotic molecules, and pre-miRNAs with DNA methylation status in non-neoplastic gastric mucosa. Eleven candidatete SNPs (IL-1β gene -31T>C and -511C>T, TNF-α-857C>T, XRCC1 Arg399Gln and Arg194Trp, GSTP1 Ile104Val, GSTT1, GSTM1, miR-196a2, miR-146a and miR-499) were determined in 415 cancer free subjects, in relation to four candidate CpG (p14, p16, DAP-kinase and CDH1) loci, assessed by Methylation-Specific-Polymerase Chain Reaction (MSP). CIHM high was defined as two or more CpG islands methylated.
RESULTS: Methylation of all four genes and CIHM high were significantly associated with *Helicobacter pylori* infection. In over all, significant association was found between IL-1β-511 TT, XRCC1 codon 399 Gln/Gln genotypes and DAP-kinase methylation (adjusted OR=0.48, 95%CI=0.29-0.78 and OR=0.30, 95%CI=0.13-0.71, respectively) and CIHM high (OR=0.53, 95%CI=0.32-0.86, and OR=0.42, 95%CI=0.19-0.97, respectively). Also, significant associations were found between miR-196a2 and miR-146a SNPs and methylation of p16 (miR-196a2 rs11614913 CT vs. CC, OR=0.52, 95%CI=0.28-0.99, miR-146a rs2910164 CC vs. GG, OR=0.42, 95%CI=0.22-0.82 and CC vs. GG+GC, OR=0.54, 95%CI=0.33-0.89). When subjects were divided according to age, an association was also found between GSTM1 null genotype and to CIHM high in the 50 years and older generations (OR=1.63, 95%CI=1.01-2.62, p=0.045).
CONCLUSION: Host genetic factors, related to pro-inflammatory cytokines, DNA repair and xenobiotic molecules, and pre-miRNAs may have a role in methylation related gastric carcinogenesis.
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Disclosure of Interest: None Declared
Keywords: gastric mucosa, genetic polymorphisms, methylation

P1075 SEQUENTIAL VS. CONCOMITANT THERAPY FOR THE FIRST-LINE HELICOBACTER PYLORI ERADICATION TREATMENT.

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INTRODUCTION: Whenever resistance to metronidazole and clarithromycin surpasses 20% triple eradication regimens have a poor effectiveness.
AIMS&METHODS: Aim: A prospective study to compare the efficacy of the first-line pantoprazole-based sequential therapy and concomitant therapy (pantoprazole, amoxicillin, clarithromycin and metronidazole) to eradicate Helicobacter pylori (H. pylori) infection.
METHODS: A total of 63 patients with *H. pylori* positive patients were randomly assigned to either concomitant therapy group (pantoprazole 40mg b.i.d, amoxicillin 1000mg b.i.d, clarithromycin 500mg b.i.d, metronidazole 500mg b.i.d for 10 days, 33 patients, mean age 60±13 years, 19 men, 8 smokers) and sequential therapy group (5-day course with pantoprazole 40mg b.i.d and amoxicillin 1000 mg b.i.d., followed by 5-day course with pantoprazole 40mg b.i.d, clarithromycin 500 mg b.i.d. and metronidazole 500 mg b.i.d, 30 patients, mean age 58±9 years, 18 men, 8 smokers). *H. pylori* eradication was evaluated 4 weeks later by either histology whenever endoscopy was necessary or urea breath test. Stat:X2, t-test.
RESULTS: Intention to teat analysis: 29 (88%) patients successfully eradicated *H. pylori* with concomitant therapy, but only 19 (63%) with sequential therapy (p=0.02). Per protocol analysis: 29 (97%) patients successfully eradicated *H. pylori* with concomitant therapy and 19 (73%) with sequential therapy (p=0.01). 5 (45%) failures in sequential group were due to double antibiotic resistance (metronidazole and clarythromycin) but none in concominant treatment group (p=0.11).
20 (61%) patients in concomitant group and 22 (73%) in sequential group reported any side effect (p=0.28), while 3 (9%) in concomitant group and 2 (7%) in sequential group discontinued treatment due to side effects (p=0.72).
CONCLUSION: First-line pantoprazole-based concomitant therapy seems to be equally well-tolerated but significantly more effective than sequential therapy in terms of *H. pylori* eradication rate.
Disclosure of Interest: None Declared
Keywords: Concomitant therapy, Helicobacter pylori eradication, Sequential therapy

P1076 EFFECT OF THE SUPPLEMENTATION OF A HIGH-DOSE AMOXICILLIN BASED TRIPLE THERAPY WITH FRUCTOOLIGOSACCHARIDES LACOTFERRIN AND BACILLUS COAGULANS IN PATIENTS UNDERGOING H. PYLORI ERADICATION

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INTRODUCTION: We have previously demonstrated that increasing the dosage of amoxicillin results in an increased performance of a standard first-line *H. pylori* eradicating triple therapy. Whether the supplementation of a high-dose amoxicillin eradicating regimen with a mix of fructooligosaccharides, lactoferrin and Bacillus coagulans may increase the eradication rate or reduce antibiotic-related side effects has never been studies
AIMS&METHODS: AIM: To compare the efficacy and the occurrence of side effects of a standard first line triple therapy with a high-dose amoxicillin based therapy with or without a mix of fructooligosaccharides, lactoferrin and Bacillus coagulans. METHODS: 90 sex and age matched patients were randomized into 3 different therapeutic schemes (30 patients each): (1) standard LCA, lansoprazole 15 mg bid, clarithromycin 500 mg bid and amoxicillin 1000 mg bid for 7 days; (2) high dose LCA (HD-LCA), lansoprazole 15 mg bid, clarithromycin 500 mg bid and amoxicillin 1000 mg tid for 7 days; (3) high dose LCA plus a mix of fructooligosaccharides, lactoferrin and Bacillus coagulans for 7 days (HD-LCA-mix). Eradication was confirmed by ^{13}C-urea breath test. Occurrence of adverse effects was assessed by a validated questionnaire
RESULTS: Eradication rates were: LCA (53% PP, 50% ITT), HD-LCA (73% PP, 70% ITT), HD-LCA+mix (73% PP; 70% ITT). Eradication rates were significantly higher in HD-LCA and HD-LCA+mix group compared to LCA ($p<0.01$), while no significant differences were observed between HD-LCA and HD-LCA+mix group. Diarrhea, dysgeusia, headache and nausea were the most common side effects recorded by patients. Adding a mix of fructooligosaccharides, lactoferrin and Bacillus coagulans to a HD-LCA therapy resulted in a reduced occurrence of diarrhea (9 of 30 vs 2 of 30; $p<0.019$), and nausea (8 of 30 vs 2 of 30; $p<0.038$)
CONCLUSION: High dose amoxicillin based eradicating treatment is superior to standard triple therapy. The supplementation with a mix of fructooligosaccharides, lactoferrin and Bacillus coagulans does not increase the eradication rate but significantly improves some antibiotic-related side effects
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Disclosure of Interest: None Declared
Keywords: Bacillus coagulans, Helicobacter pylori

P1077 GELATINE TANNATE SUPPLEMENTATION REDUCES ANTIBIOTICS ASSOCIATED SIDE-EFFECTS OF ANTI-HELICOBACTER PYLORI FIRST-LINE THERAPY

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INTRODUCTION: Therapeutic schemes to eradicate Helicobacter pylori infection are based on the association of antibiotics and a proton pump inhibitor. Gastrointestinal side-effects during antibiotic therapy include diarrhea, nausea, taste distortion, stomatitis and bloating, and are major determinants for a lack of compliance, so to determine a failure to eradicate *H. pylori*. Gelatine tannate is a powder composed by a proteic portion, the gelatin, and a sequestrant, the tannic acid. It provides a mechanical protection to intestinal mucosa when becomes jelly-form in the small intestine, forming a protective film. It has been shown to be efficacious in treating acute diarrhea in infant. No information exists about its role in cure or prevent diarrhea in adults.
AIMS&METHODS: Aim: To explore whether Gelatine Tannate 500mg t.d supplementation is efficacious in preventing diarrhea and GI side effects related to anti-H. pylori standard first line eradication therapy with esomeprazole 20 mg b.d., clarithromycin 500 mg b.d. and amoxicillin 1 g b.d.
Methods: Forty (23F/17M, mean age 40±15) *H. pylori*-positive consecutive patients were enrolled to receive standard triple therapy with Gelatine Tannate for 14 days (Gelatine Tannate group, GTg). Each patient was required to complete a validated daily diary for 4 weeks, starting from the first day of the eradicating treatment. The diary was assessing onset, intensity and frequency of gastrointestinal side-effects. *H. pylori* status and side effects were assessed 6 weeks after treatment. We referred to our previous published study (Nista, 2004), as a control population (CT).
RESULTS: All patients completed Hp eradication therapy. Occurrence of nausea was 10 % in GTg at 1 week, way lower compared to 50 % of CT. At 2 weeks, incidence of nausea was respectively 5% in GTg and 30% in CT. Patients experienced diarrhea only in 5% at 1 week and 2,5% at 2 weeks in GTg compared to 30% and 10 % of CT. The incidence of epigastric pain, vomiting, constipation and skin rash were absent in GTg, as well as in CT. *H. pylori* eradication rate was similar (75 % eradication rate) between GTg and CP.
CONCLUSION: We report the efficacy of Gelatine Tannate in preventing *H. pylori* eradication therapy induced GI side effects. Although it is a non controlled and open label trial it can be argued that effects of gelatin tannate in preventing nausea and diarrhea are real. Data suggest that the efficacy of gelatin tannete is particularly visible in the first week of treatment while antibiotics are co-administered and the higher incidence of side-effects is usually registered.
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Disclosure of Interest: None Declared
Keywords: Gelatine tannate, Helicobacter pylori

P1078 EFFICACY OF SEQUENTIAL THERAPY IN NEVER BEEN TREATED HELICOBACTER PYLORI PATIENTS WITH MULTI-RESISTANT STRAINS.

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INTRODUCTION: Background: Sequential therapy was able to achieve remarkable results also in patients harbouring strains resistant to clarithromycin.
AIMS&METHODS: Objective: To assess the efficacy of Sequential therapy in eradicating never been treated *Helicobacter pylori* patients with multi-resistant strains, prospectively. **Methods:** Between 2010 and 2013, consecutive patients undergoing upper endoscopy were evaluated. Each patient had a ^{13}C-UBT, and during endoscopy 2 biopsies each from the antrum, angulus, and corpus were obtained to perform histology. Further biopsies from antrum were also taken for ultrafast urease test and to carry out culture and antimicrobial sensitivity performed by Epsilometer test (Etest). According to new EUCAST 2012 the following MIC breakpoints were used to evaluate resistance :> 0.5,>8 and 1 microgram/ml for clarithromycin, metronidazole and levofloxacin, respectively. Patients were considered infected if culture alone or histology and ultrafast urease test were positive. All received standard Sequential therapy. Four to 6 weeks after the end of the treatment, eradication was assessed by ^{13}C-UBT.
RESULTS: Results: Up to date, 717 naïve consecutive *Helicobacter pylori* infected patients were enrolled. Follow up are now available in 696 out of 717; eradication rate was achieved in 664 out of 696 (95.4%; 95% CI: 93.8-97). Eradication rates according to antibiotic resistance pattern were provided in the Table.

Resistance	Total cases	Cases controlled	Eradication rate (%)
Cla	196	189	89.5
Metro	207	199	93
Levo	149	145	94
Cla + Metro	109	105	86.6
Cla + Levo	79	75	89.3
Metro + Levo	93	90	93.3
Cla + Metro + Levo	60	57	89

CONCLUSION: Conclusions: Sequential therapy is able to overcome the problem of multi-resistant strains in a large proportion of patients. Sequential therapy may be the optimal treatment for patients suspected of having multi-drug resistant strains.
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Disclosure of Interest: G. Fiorini: None Declared, N. Vakil Consultancy for: Astra-Zeneca, Takeda, Axcan, Otsuka, V. Castelli: None Declared, I. Saracino: None Declared, C. Zaccaro: None Declared, C. Ricci: None Declared, L. Gatta: None Declared, A. Zullo: None Declared, D. Vaira: None Declared
Keywords: H Pylori, multiresistant strains, Sequential therapy

P1079 ERADICATION RATES OF HELICOBACTER PYLORI INFECTION FOR STOMACH CANCER PATIENTS WHO UNDERGO SUBTOTAL GASTRECTOMY

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INTRODUCTION: The eradication rate of *Helicobacter pylori* with standard triple treatment showed to decrease worldwide. So, many authors are introducing various regimens. We investigated the eradication rate and trend of it using standard triple regimen as first-line anti-*Helicobacter pylori* treatment on patients who were experienced subtotal gastrectomy for adenocarcinoma. Also, we looked into efficacy of bismuth containing quadruple regimen as rescue therapy.
AIMS&METHODS: From January 2004 to December 2010, a total of 430 patients with *H. pylori* infection after receiving subtotal gastrectomy for adenocarcinoma were treated with 7days-standard triple therapy (amoxicillin 1000mg b.i.d, clarithromycin 500mg b.i.d, esomeprazole 20mg b.i.d). We retrospectively analyzed overall eradication rate and trend of it using ITT(Intention To Treatment) and PP(Per-Protocol). As same way, we assayed efficacy of 10days-bismuth containing quadruple treatment(tripotassium dicitrato bismuth 300mg q.i.d, tetracyclin 500mg q.i.d, metronidazole 500mg t.i.d, esomeprazole 20mg b.i.d) as rescue therapy.
RESULTS: The overall eradication rates were 81.0%(95% CI, 77.2-84.3) and 88.3%(95% CI, 85.0-91.0) by ITT and PP. The annual eradication rate from year 2004 to 2010 were 89.4%, 95.4%, 85.2%, 89.7%, 85.5%, 86.5% and 87.3% by PP. There was no decreasing tendency and no statistical significant of the eradication rate(p=0.588). Twenty-eight patients treated with bismuth containing quadruple therapy as rescue regimen, only two of them were failed. PP was 92.8%(95% CI 77.3-98.0).
CONCLUSION: The postoperative eradication rate of *H.pylori* infection using standard triple therapy did not show satisfied result. But it had higher rate than it of other eradicated indications not having operation in Korea. And bismuth containing quadruple treatment after failure of first line therapy had high efficacy.
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Disclosure of Interest: None Declared
Keywords: eradication of h.pylori, Gastrectomy, quadruple, standard triple

P1080 COMPARISON WITH ERADICATION RATES OF MOXIFLOXACIN CONTAINING TRIPLE THERAPY AS SECOND LINE TREATMENT FOR HELICOBACTER PYLORI INFECTION ACCORDING TO FIRST LINE REGIMEN

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INTRODUCTION: There was a controversy the efficacy of eradication with moxifloxacin based triple therapy as second line treatment for *Helicobacter pylori* infection. And most of published papers focused on patients failed to treat with standard triple therapy. So, we investigated the efficacy of moxifloxacin as second line therapy and the eradication rates of that according to previous first-line regimen.
AIMS&METHODS: A total of 298 patients who were failed to eradicate with first line treatment received 14 days moxifloxacin containing triple therapy (moxifloxacin 400mg q.d, amoxicillin 1000mg b.i.d, rabeprazole 20mg b.i.d). As first line treatment, they were prescribed 7day-standard triple therapy (n=184), 7day-bisthmus containing quadruple therapy (n=29), 7day-concomitant therapy (n=39) and 14day-sequential therapy (n=46). Primary outcome was the eradication rate by intention-to treat (ITT) and per-protocol (PP) analysis
RESULTS: The eradication rate of moxifloxacin based triple therapy was 61.7%(95% CI 56.1-67.0) by ITT, and 73.6%(95% CI 67.8-78.6) by PP. ITT and PT according to first regimen were 63.5/77.0%(95% CI 56.4-70.2/69.6-82.9) in standard triple group, 62/69.2%(95% CI 44.0-77.3/50.0-83.5) in bisthmus containing quadruple group, 56.4/66.7%(95% CI 40.9-70.7/49.6-80.2) in concomitant group and 58.6/69.2%(95% CI 44.3-71.7/53.5-81.4) in sequential group. There was no significant difference between groups (p=0.504).
CONCLUSION: Two-week moxifloxacin based triple therapy as second line did not show expected level for the primary outcome. The group treated with moxifloxacin after failure of standard triple therapy had highest rate of eradication, but there was no statistical significance in the efficacy among the first line regimens.
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Disclosure of Interest: None Declared
Keywords: Eradication rate, *H. pylori*, moxifloxacin, second line therapy

P1081 THE TREND OF ERADICATION RATE OF FIRST-LINE THE TREND IN THE ERADICATION RATES OF FIRST-LINE THERAPY FOR HELICOBACTER PYLORI INFECTION AND RISK FACTORS OF ERADICATION THERAPY

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INTRODUCTION: The standard triple therapy which was combined with proton pump inhibitor (PPI), amoxicillin and clarithromycin was widely used for *Helicobacter pylori* (*H. pylori*) infection in Korea. However, the recent trend of the eradication rates in *H. pylori* using first-line triple therapy has been infrequently reported.
AIMS&METHODS: The aims of this study were to evaluate the trend of the *H. pylori* eradication rates in single center during recent six years and to identify the risk factors relating the failure of eradication therapy. From January 2007 to December 2012, *H. pylori* eradication rates in 1168 patients who diagnosed with *H. pylori* infection and received 7 days triple therapy were investigated according to years, demographic and clinical factors retrospectively. *H. pylori* eradication was confirmed by ^{13}C-urea breath test, rapid urease test or histopathological examination at least 4 weeks after the completion of triple therapy.
RESULTS: The overall *H. pylori* eradication rate was 84.5%. The annual eradication rates from the year 2007 to 2012 were 91.9%, 89.1%, 85.5%, 84.3%, 84.5% and 79.0% consecutively by per-protocol analysis. The eradication rate in first-line triple therapy was decreased during the recent six years ($p = 0.024$). Multivariate analysis showed that female (OR 1.55; 95% CI 1.02-2.36) and smoking (OR 1.60; 95% CI 1.03-2.48) were associated with the failure of *H. pylori* eradication therapy.
CONCLUSION: The effect of first-line triple therapy for *H. pylori* infection has decreased during recent six years, which suggests that the antibiotic resistant *H. pylori* has increased against the therapy based on the combination of PPI, amoxicillin and clarithromycin. Therefore, other variable first-line therapies might be considered for *H. pylori* eradication in the near future.
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Disclosure of Interest: None Declared
Keywords: First-line triple therapy, Helicobacter pylori

P1082 HIGH RATES OF MULTI-DRUG RESISTANT STRAINS IN PATIENTS WHO HAVE NEVER BEEN TREATED FOR H PYLORI

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INTRODUCTION: Antibiotic resistant strains of *H. pylori* have been increasing worldwide, and it has been speculated that this may account for progressive decrease in eradication rates reported in the literature.
AIMS&METHODS: Aim: to assess the prevalence of resistant strains to metronidazole, clarithromycin, and levofloxacin in a cohort of naïve patients performing an EGDS for dyspeptic symptoms in Italy.
Methods: 915 *H.pylori* infected patients who had never been treated for H pylori (Male: 39%; median age: 51 years; IQR: 40 and 62 years) underwent upper endoscopy and a biopsy sample was also obtained to perform culture and an *in vitro* antimicrobial susceptibility testing. According to new EUCAST 2012, susceptibility testing was performed by epsilometer test (Etest) and the following MIC breakpoints were used: resistance to clarithromycin (>0.5 microgram/ml); resistance to metronidazole (>8 microgram/ml), and resistance to levofloxacin (> 1 microgram/ml).
RESULTS: Data on resistance were available for 855 out of 915 (93%) patients. Resistance to metronidazole was found in 33%; to clarithromycin in 30%; and to levofloxacin in 21% of the strains. Double resistance to clarithromycin + metronidazole was found in 18%; to clarithromycin + levofloxacin in 11%; and to metronidazole + levofloxacin in 13% whilst 9% of the strains were resistant to metronidazole + clarithromycin + levofloxacin. Considering resistance to a single antibiotic, resistance to metronidazole was more likely to occur in women than men (OR: 2.8; 95% CI: 2.1 to 3.9); considering the double resistance, women were also more likely to have

resistance to both clarithromycin + metronidazole than men (OR: 2.6; 95% CI: 1.7 to 4.0).

Resistance	%
ClaR	30
MetroR	33
LevoR	21
ClaR + MetroR	18
ClaR + LevoR	11
MetroR + LevoR	13
ClaR + MetroR + LevoR	9

CONCLUSION: 1. Single and multiple-drug resistant strains are becoming widely prevalent in patients who have never been treated for H pylori. 2. Initial treatment for H pylori needs to account for these changes- failure rates for clarithromycin triple therapy will increase further 3. Levofloxacin based triple therapies are unlikely to represent an alternative front-line therapy as the resistance rates are already quite high.
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Disclosure of Interest: None Declared
Keywords: clarithromycin, *H. pylori*, levofloxacin, metronidazole, resistance

TUESDAY, OCTOBER 15, 2013 9:00–17:00
SMALL INTESTINAL II – Poster Area

P1083 RISK OF ADVERSE PREGNANCY OUTCOMES AMONG WOMEN WITH COELIAC DISEASE OR DERMATITIS HERPETIFORMIS COMPARED TO THE GENERAL POPULATION: A POPULATION BASED CASE-CONTROL STUDY

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INTRODUCTION: Knowledge about the adverse birth outcome and pregnancy related complications are crucial when counselling pregnant women with coeliac disease (CD) and dermatitis herpetiformis (DH). Limited population based data exist that have determined the association between CD, DH, pregnancy related complications and birth outcomes.
AIMS&METHODS: We calculated the proportion of pregnancies in women with and without CD or DH between 1997 and 2010 throughout England using linked primary care data from the Clinical Practice Research Datalink (CPRD) and secondary care Hospital Episode Statistics (HES) data. Risk of pregnancy related complications (postpartum haemorrhage, pre-eclampsia and emergency caesarean section) and adverse birth outcomes (pre-term birth, stillbirth and low birth weight) in pregnancies in women with CD or DH were compared to risks in pregnancies in women without either condition in terms of odds ratios (OR) using logistic regression model.
RESULTS: Of 245,969 singleton pregnancies resulting in live or stillbirths, 388 (0.16%) were among women with CD/DH. Overall all pregnant women with CD/DH were 31% (Table 1; OR=1.3 95%CI 1.03-1.67) more likely to develop pregnancy related complications (eclampsia/pre-eclampsia, postpartum haemorrhage or undergone emergency caesarean section). Finally women with CD/DH appeared to be at 14% higher risk of developing adverse birth outcome (stillbirth, low birth weight or preterm birth) however our result was not statistically significant (OR=1.14 95%CI 0.81-1.61) at the 5% level.
Table 1: Pregnancy related complication and adverse birth outcome in women with CD/DH

Variable	Controls (Total=246,581)		Cases (Total=388)		OR (95%CI) (Adjusted)*
	No.	%	No.	%	
Any one pregnancy related complication	55,087	22.5	106	27.5	1.31 (1.03-1.67)
Emergency Caesarean	35,108	14.2	67	17.3	1.38 (1.02-1.87)
Postpartum haemorrhage	22,858	9.3	48	12.4	1.36 (1.00-1.86)
Pre-eclampsia/eclampsia	5,735	2.3	12	3.1	1.43 (0.76-2.67)
Any one adverse birth outcome[1]	23,521	9.5	42	10.8	1.14 (0.81-1.61)

*Adjusted for age, body mass index and cigarette smoking
[1]Includes pregnancy of women resulting in low birth weight, stillbirth or pre-term birth

CONCLUSION: We have shown significantly increased relative risk of pregnancy related complications but not adverse birth outcome. The absolute differences are however small indicating that most women with CD/DH do not have a big excess risk. Though this association may well not be causal we believe that our study provides new evidence that will aid clinicians to better counsel pregnant women with CD/DH.
Disclosure of Interest: None Declared
Keywords: Coeliac disease, pregnancy outcome

P1084 CAN NARROW BAND IMAGING PREDICTDUODENAL HISTOLOGY IN CELIAC DISEASE? A PROSPECTIVE DOUBLE BLIND PILOT STUDY

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INTRODUCTION: Celiac disease(CD) is characterized by varying degrees of villous atrophy. Image enhancement with narrow band imaging(NBI) delineates villous patterns better than routine endoscopy. Role of NBI in delineating villous morphology ofCD is sparsely reported.
AIMS&METHODS: Aim: To compare the diagnostic accuracy of NBIwith histopathologyin predicting the duodenal villous morphology in CD.
Methods: Amongst the 50subjects(mean age-28.17±12.7 years, 29-females)included in the study, 34 were suspectedto have CD(serology positive), 4 were follow up patients ofCDon gluten free diet and 12had dyspepsia with no evidence of CDon complete evaluation. CD was diagnosed on the basis of modified ESPGHAN criteria. They underwentesophagogastroduodenoscopy(EGD) along with NBI using an Olympus GIF-180 gastroscope to evaluate the villous pattern of duodenal mucosa. These images were digitally recorded for further characterization. Four duodenal biopsies were taken from second part of duodenum for histopathology. Digitally recorded images were analyzed by twoexperienced endoscopists and biopsy specimen by an experienced pathologist all of whom were blinded to clinical details and serological investigations. Villous patterns on NBI were classified into Normal-villous pattern(NVP), Distorted&blunted-villous pattern(DVP)and Absent-villous pattern(AVP). NBI findings were correlated with histopathology.
RESULTS: NBI in total study population revealed AVP in 14, DVP in 13 and NVP in 23 patients. In CD, EGD revealed grooving pattern in 94.1% patients, scalloping in 82.3% and decreased fold height in 52.9%. In this study group(CD, n=34) 14 had AVP,13 had DVP and 7 had NVP on NBI, while on histopathology 11 had total villous atrophy, 11 had partial villous atrophy and 12 had no villous atrophy. CD patients on gluten free diet(n=4) and the 12 dyspepsia patients(control group) had normal villous pattern on both NBI and histopathology. Significant correlation was observed between NBI and histopathological examination($p<0.001$). The overall sensitivity and specificity of NBI for delineating villous pattern were 100% and 82.1% and the positive and negative predictive values were 81.4% &100% respectively.
CONCLUSION: NBI can predict villous atrophy with high sensitivity and negative predictive value in CD.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, narrow band imaging

P1085 SCREENING FOR COELIAC DISEASE IN WOMEN WITH PRETERM CHILDBIRTH.

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INTRODUCTION: Coeliac disease (CD) is a chronic, immuno-mediated entheropathy caused by ingestion of gluten in genetically predisposed individuals. It may present with a variety of symptoms (such as diarrhea, weight loss, iron deficient anemia, etc…) or completely silent. The association between CD and pregnancy outcome has been investigated, with contrasting results.
AIMS&METHODS: Our aim was to screen for CD women with preterm childbirth or low birth weight. In our prospective study, we performed a CD screening in a group of women with preterm childbirth (defined as <37 weeks of gestational age) or with low birth weight (< 2500 gr), using RIA IgA anti-transglutaminase antibodies (tTGAb). Positive patients were referred to our Operative Unit on Coeliac disease, where they were submitted to a further serological evaluation. Confirmed positive patients were submitted to upper gastrointestinal endoscopy with multiple duodenal biopsies, and if diagnosed to be celiac, started the gluten-free diet (GFD).
RESULTS: A total of 75 women (age range: 19-49 years) participated in the study. Four (5.3%) women resulted tTGAb positive (age range: 20-31 years, gestational age range: 31weeks+6 days- 35weeks+ 6 days, birth weight range: 1650-2720 gr). The four women were all primiparae but one, who already had a preterm child. All the patients were confirmed at the second serum sample. One of these women performed upper endoscopy with duodenal biopsies, showing subtotal villous atrophy (3b sec. Marsh modified by Oberhuber) and started the GFD. The other three women are still under evaluation, waiting to perform the upper endoscopy.
CONCLUSION: Our study demonstrates that CD prevalence is higher in women with preterm childbirth or low birth weight rather than in the Italian population. Screening for CD could be advisable as part of the diagnostic flow-chart in these patients. In fact, a timely diagnosis and the prompt GFD, in otherwise asymptomatic patients, could improve the pregnancy outcome.
Disclosure of Interest: None Declared
Keywords: Coeliac disease, preterm childbirth, Screening, women

P1086 INCREASED OSTEOPROTEGERIN AND DECREASED COOH-TERMINAL PROPEPTIDE OF TYPE I PROCOLLAGEN SELECT CELIAC DISEASE PATIENTS ON LONG-TERM GLUTEN-FREE DIET WITH PERSISTING LOW BONE MASS

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INTRODUCTION: Bone mass and mineral metabolism alterations are very frequent in untreated celiac disease (CD) but also the persistence of bone loss after long-term gluten-free. It was demonstrated that a high rate of osteosynthetic activity before treatment is predictive of the recovery of bone mass after two years of dietary treatment (1), but we have no information about the long-term predictivity of pretreatment bone metabolism indices. It was recently shown that mucosal immunity activation causes the production of circulating factors which stimulate osteoclastogenesis, through the RANKL/RANK/osteoprotegerin (OPG) pathway (2).
AIMS&METHODS: The aim of this study was to evaluate the role of inflammatory, hormonal and lifestyle factors in the pathogenesis of the persisting bone derangement in CD patients on long-term GFD.
Sixteen asymptomatic CD female patients (range 27-43 yrs) diagnosed in adult life, with a long period of GFD (> 8yrs) were enrolled. All patients showed a strict adherence to GFD and no-one was in menopausal or perimenopausal period. In all patients, lumbar and femoral BMD was measured by DEXXA and BMI was calculated. Circulating serum calcium, phosphate, PTH, OPG, RANKL, 1,25 OH vitamin D, 25 OH vitamin D, Il-1, IL-6, and TNF-alfa, COOH-terminal telopeptide of type I collagen (ICTP), COOH-terminal propeptide of type I procollagen (PICP) level were evaluated. Validated questionnaires for sunlight exposure and physical exercise were administered.
RESULTS: Eight out of 16 patients showed a pathological reduction in bone density. In comparison with the subgroup of patients with normal BMD, patients with low bone mass showed a lower BMI (19.9 ± 1.14vs22.8 ± 2.95 kg/m^2, $P<0.05$); no difference in age, age at diagnosis, duration of GFD, serum levels of cytokines and hormonal factors was found. On the contrary, femoral T score was significantly and indirectly correlated with OPG and significantly and directly correlated with PICP ($P<0.05$ for both). Finally, no difference was evident in physical activity or sunlight exposure score.
CONCLUSION: High levels of OPG and low levels of PICP select the subgroup of CD patients with a persistent reduction of bone mass, despite strict adherence to GFD and architectural villi reconstitution. These markers might be used to identify those patients who need a a mineralo-active treatment associated to gluten-free diet.
REFERENCES:
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Disclosure of Interest: None Declared
Keywords: celiac disease, gluten free diet, osteoporosis, osteoprotegerin, PROPEPTIDE OF TYPE I PROCOLLAGEN

P1087 FRAX SCORE CORRELATES WITH THE ACTIVATION OF LOCAL FACTORS IN ADULT PATIENTS WITH CELIAC DISEASE IN GLUTEN-FREE DIET

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INTRODUCTION: Celiac disease (CD) is frequently associated with bone mass and mineral metabolism alterations, often persisting besides a strict adherence to long term GFD. The incidence of fractures in CD is an incompletely clarified issue. FRAX score is a validated tool to estimate the risk of fracture in the general population.
AIMS&METHODS: Accordingly, in a group of celiac patients we calculated the FRAX score and correlated it to circulating levels of indices of bone and mineral metabolism.
28 asymptomatic CD female patients (range 18-43 yrs) with a long history of GFD (> 8yrs) were enrolled. Diagnosis was made in adult life, none of the patiens was in menopausal and perimenopausal period. All patients showed strict adherence to GFD. Lumbar and femoral BMD was measured by DEXXA. Circulating serum calcium, phosphate, PTH, OPG, RANKL, 1,25 OH vitamin D, 25 OH vitamin D, IL-1, IL-6, and TNF-alfa level were evaluated. The OPG/RANKL ratio was computed, as a marker of bone turnover. The FRAX score, a web-based clinical scale (http://www.shef.ac.uk/FRAX/) assessing the 10-year fracture risk, was evaluated.
RESULTS: All patients but one, showing a moderate risk, were classified by FRAX score as a low risk of fracture at 10 yrs. Nine out of 28 patients showed a pathological reduction in bone density. The FRAX score proved to be significantly correlated with OPG/RANKL ratio ($r=0.7$, $p<0.01$) and with serum TNFalfa levels ($r=0.6$, $p<0.05$).
CONCLUSION: OPG/RANKL ratio could be considered an accurate biomarker of fracture risk and could be used in the follow up of CD patient.
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Disclosure of Interest: None Declared
Keywords: celiac disease, FRAX SCORE, OPG/RANKL, osteoporosis, RISK OF FRACTURE, TNF-Alpha

P1088 HIGHER NUMBER OF ENTEROCHROMAFFIN CELLS IN REFRACTORY COELIAC DISEASE

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INTRODUCTION: In the gut serotonin-producing enterochromaffin (EC) cells are the prevalent neuroendocrine cell type, almost of all of which are characterised by the expression of the pan-neuroendocrine marker chromogranin A (CgA). Several immune-mediated gastrointestinal disorders, including coeliac disease (CD), are associated with EC cell hyperplasia. However, neither number nor function of EC cells have been ever explored in refractory CD type 1 (RCD1) and type 2 (RCD2).
AIMS&METHODS: Seriate duodenal sections from 17 refractory CD patients (6 RCD1, 11 RCD2), 16 uncomplicated CD patients before and after gluten-free diet (GFD), and 16 control subjects (CS) were processed for the immunohistochemical detection of neuroendocrine markers CgA, serotonin and somatostatin. Mucosal tryptophan hydroxylase (TpH)-1 and serotonin-selective reuptake transporter (SERT) transcripts were measured by quantitative RT-PCR. Serum CgA and 24-h urine 5-hydroxyindoleacetic acid (5-HIAA) were also measured. Uncomplicated treated CD biopsies were cultured with serotonin or peptic tryptic digest of gliadin (PT-gliadin), and interferon (IFN)-γ was detected by ELISA in culture supernatants.
RESULTS: Both CgA-positive cells and EC cells, counted per 100 crypt cells, were significantly increased in RCD1 and RCD2 patients compared to uncomplicated CD patients before and after GFD and CS, with no difference between RCD1 and RCD2, whereas no change was found for somatostatin-positive cells amongst all groups. Raised transcripts of mucosal TpH-1, but not SERT, were found in RCD1 and RCD2 patients. Serotonin up-regulated the *ex vivo* production of IFN-γ at levels comparable to those of PT-gliadin. Serum CgA, but not urine 5-HIAA, was increased in RCD1 and RCD2 patients.
CONCLUSION: EC cells are increased in refractory CD mucosa. The up-regulation of IFN-γ induced *ex vivo* by serotonin suggests that this monoamine may have a role in sustaining the local inflammatory response in CD.
Disclosure of Interest: None Declared
Keywords: chromogranin A, refractory coeliac disease, serotonin, somatostatin, tryptophan hydroxylase-1

P1089 PREDICTIVE VALUE OF "MARSH 1" TYPE HISTOLOGY IN SUBJECTS WITH SUSPECTED COEALIC DISEASE

R. Tortora[1,*], P. Capone[1], G. D. De Palma[1], N. Imperatore[1], G. De Stefano[1], S. Tafuto[1], N. Gerbino[1], M. Leo[1], N. Caporaso[1], A. Rispo[1]. [1]*Clinical Medicine and Surgery, University Federico II of Naples, Naples, Italy*

INTRODUCTION: The diagnosis of celiac disease (CD) is based on duodenal histology in combination with anti-tissue transglutaminase (aTG) and anti-endomysial antibodies (EMA). The sole increase of intraepithelial lymphocytes (IELs) defines the Marsh 1 type on histology. However, even if it is thought that Marsh 1 characterises the early phase of CD, it appears to be not specific for CD.
AIMS&METHODS: to explore the positive predictive value (PPV) and the clinical relevance of Marsh 1 type histology in subjects with suspected CD.
METHODS: From September 2011 to March 2013 we performed a prospective study evaluating the predictive value of Marsh 1 (IELs > 40) in diagnosing potential CD in all consecutive subjects referred to our third-level centre. All participants were tested for aTG, EMA and HLA DQ2/DQ8. Diagnosis of potential CD was defined in presence Marsh 1 histology associated with both aTG IgA > 7 U/ml and positive EMA. Furthermore, all patients were investigated for abdominal symptoms, CD familial aggregation, thyroid/intestinal/rheumatological diseases and drug assumption. Statistical analysis was performed by using X^2 and Mann-Whitney U test when indicated.
RESULTS: The study included 42 patients with Marsh 1. Final diagnosis of potential CD was made in 14 subjects (33%), so that Marsh 1 showed a PPV of 33%; all these patients were HLA DQ2/DQ8 positive. The remaining 28 patients (67%) were negative for celiac serology; 12 subjects (42,8%) were DQ2/DQ8 positive. About familial aggregation, patients with potential CD showed a higher frequency of familiarity (71,4% *vs* 14,8% ; $p< 0.01$). When comparing the CD patients to the other group, no significant difference was seen about symptoms (anaemia 14,2% *vs* 14,8% ; p=ns; abdominal pain 28,5% *vs* 25,9% ; p=ns; weight loss 14,3% *vs* 11,1% ; p=ns; bloating 21,42% *vs* 18,52% ; p=ns). Moreover, we defined the presence of diagnoses other than CD in the remaining population: 5 patients (17,86%) showed immune-mediated diseases including Hashimoto's thyroiditis (n=4 ; 14,28%) and ankylosing spondylitis (n=1 ; 3,6%); 4 patients (14,28%) were infected by Helicobacter pylori. About drug assumption, 2 patients (7,14%) were on NSAIDs while other 3 (10,71%) were treated with antihypertensive, anti-hyperglycemic and anti-arrhythmic drugs, respectively.
CONCLUSION: The Marsh 1 type at histology is not specific for CD, especially when not correlated with serologic panel and familial aggregation. Increased IELs can also be associated with the presence of autoimmune disorders, Helicobacter pylori infection and NSAIDs assumption.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, Marsh-Oberhuber classification

P1090 METABOLIC SYNDROME IN COELIAC DISEASE: EFFECT OF THE GLUTEN-FREE DIET

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INTRODUCTION: Several studies have shown that weight changes are common in coeliac patients after the adoption of a gluten-free diet (GFD). However data on the prevalence of metabolic syndrome (MS) in patients with coeliac disease (CD) on free diet and after GFD are still scarce.
AIMS&METHODS: Aim of our study was to evaluate the prevalence of MS in patients with CD at time of diagnosis and 1 year after starting GFD. Between January 2012 and April 2013, we enrolled all consecutive patients with newly diagnosed CD who were referred to our third-level CD Unit. All patients were investigated about waist circumference with BMI, blood pressure, lipid profile (HDL cholesterol, triglycerides) and levels of glucose. MS diagnosis was made according to International Diabetes Federation criteria for European countries. The prevalence of MS and the features of its sub-categories were revaluated after 12 months of GFD. Statistical analysis was performed by using X^2, Mann-Whitney U test and Wilcoxon signed-rank test for SPSS when indicated. The differences were considered significant with a $p < 0.05$.
RESULTS: Finally, 70 CD patients (22 men, 48 women; mean age: 36.5 years) were analysed at diagnosis and after 1 year of GFD. At diagnosis, only 1 CD patient (1.4%) fulfilled the criteria for MS while 22 patients (31.4%) met the diagnostic criteria of MS after 12 months of GFD ($p < 0.01$). According to MS criteria, 18 patients had an increase of BMI class (25.7%), 19 patients exceeded waist circumference cut-off (27.1%), 11 patients showed high values of blood pressure (15.7%), 13 patients had reduced levels of HDL cholesterol (18.6%), 15 patients exceeded glycemic threshold (21.4%), and 8 patients had high levels of triglycerides (11.4%); all these differences were statistically significant ($p < 0.01$) when compared to the pre-GFD status.
CONCLUSION: CD patients on gluten-free diet are at risk of metabolic syndrome. We suggest a deep nutritional assessment at diagnosis and during the follow-up of patients affect by coeliac disease.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, Metabolic syndrome

P1091 THERAPEUTIC RESPONSE IN BILE ACID DIARRHOEA – A TWO CENTRE EXPERIENCE IN THE UK

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INTRODUCTION: Bile acid diarrhoea (BAD) is a common cause of chronic diarrhoea, currently diagnosed using Se^{75}-homo-chloro-tauric-acid (Se^{75}HCAT) testing, the ''gold standard'' in the UK and available to centres which support a gamma camera. Although the test has been available for over two decades, uptake has been slow despite its diagnostic value and evidence that treatment with sequestrants can be effective. This stems from a lack of formal clinical trials, which encourages a belief the good results reported may reflect patient selection, resulting in therapeutic nihilism. Thus the aim of this study was to compare treatment results between two centres: experienced (α), using data reported earlier, and novice (β), with current data.
AIMS&METHODS: The patients recruited comprised those with structural disease (e.g. ileal resection, cholecystectomy), and non-structural, the majority with diarrhoea-predominant irritable bowel syndrome (D-IBS). Abnormal Se^{75}HCAT results were defined as $<10\%$ retention on Day-7. Response to treatment: 1st line (cholestyramine, colestid, colesitpol) or 2nd line (colesevelam) was recorded in three categories: good, partial or poor.
RESULTS: Centre α: 2001-2006; recruited n=162; treatment assessed n=129.
Centre β: 2008-2012; recruited n=126; treatment assessed n=99.
Response to treatment

Response	Centre α	Centre β
Good	60 (47%)	40 (40%)
Partial	30 (23%)	23 (23%)
Poor	15 (12%)	10 (10%)

D-IBS - Abnormal Se^{75}HCAT: centre α 33%, Centre β 31%.
CONCLUSION:
1. Both centres had similar proportions with abnormal Se^{75}HCAT values, suggesting gastroenterologists are able to select appropriate patients who are likely to benefit from the test.
2. Treatment response in both centres was similar, ~70% responding. This suggests treatment is genuinely effective and not limited only to centres with a special interest.
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Disclosure of Interest: None Declared
Keywords: Bile Acid Diarrhoea, Bile acid sequestrants, Se75HCAT testing

P1092 EXPRESSION OF FRUCTOSE TRANSPORTERS, GLUT5 AND GLUT2, MRNA IN PATIENTS WITH IRRITABLE BOWEL SYNDROME AND FRUCTOSE INTOLERANCE

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INTRODUCTION: Intolerances to food are a major complaint of patients with functional gastrointestinal disorders (FGID) and may underlie many of the symptoms. The prevalence of fructose intolerance in FGID is up to 70%, but in contrast to lactose intolerance, the causative mechanism is unknown[1]. The monosaccharide, fructose, is transported across the intestinal epithelia by glucose transporters 5 (GLUT5, Slc2a5) and 2 (GLUT2, Slc2a2) in the apical and basolateral membranes, respectively[2]. In mice, deletion of GLUT5 caused malabsorption of dietary fructose and typical signs of intolerance[3]. Several of the postulated underlying mechanisms in FGID, such as inflammation and stress, have been shown to reduce GLUT5 expression[2]. The aim of this study was to assess for the first time the hypothesis that reduced intestinal GLUT5 and/or GLUT2 expression is associated with fructose intolerance in humans with FGID.
AIMS&METHODS: Duodenal biopsies were obtained in 12 male or female Irritable Bowel Syndrome patients (IBS, Rome III criteria) with fructose intolerance diagnosed by breath testing (8 hours fasting, 35g fructose, symptom index, $H_2 > 20$ppm or $CH_4 > 10$ppm) and 15 matched healthy controls aged between 18 and 60 years. Coeliac's disease and IBD were excluded. mRNA for GLUT5 and GLUT2 was quantified by multiplex RT-qPCR, with β-actin as reference. Group comparisons were performed using the Mann-Whitney test.
RESULTS: The median (interquartile range) relative GLUT5 mRNA levels in the duodenal biopsies were 0.195 (0.132-0.251) in patients with fructose intolerance and 0.165 (0.123-0.194) in healthy controls (no significant difference). Relative GLUT2 mRNA expression was also not significantly different between the fructose intolerant, 0.262 (0.206-0.344), and the controls, 0.255 (0.186-0.312).
CONCLUSION: Duodenal GLUT5 and GLUT2 mRNA expression did not differ significantly between fructose-intolerant patients with FGID and healthy controls. Our results suggest that human fructose intolerance may not be associated with marked changes in GLUT5 and GLUT2 mRNA expression. However, efforts are underway to quantify GLUT5 and GLUT2 protein levels in these samples.
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Disclosure of Interest: None Declared
Keywords: FODMAP, Fructose intolerance, GLUT2, GLUT5, Irritable bowel syndrome, Malabsorpiton

P1093 CLINICAL VALUE OF SEHCAT SCAN IN PATIENTS WITH CHRONIC DIARRHOEA

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INTRODUCTION: Chronic diarrhoea accounts for vast majority of referrals to secondary care where patients are often given a diagnosis of irritable bowel syndrome with diarrhoea (IBS-D). Studies show that a significant proportion of these patients may have bile acid malabsorption (BAM). SeHCAT (75 Selenium HomotauroCholic Acid Taurine) is increasingly used to identify BAM which can be divided into 3 types depending on aetiology: Type 1 following ileal resection or inflammation of the terminal ileum; Type 2 idiopathic BAM and Type 3 associated with cholecystectomy, peptic ulcer surgery, chronic pancreatitis, coeliac disease or diabetes mellitus. The purpose of this study was to evaluate usefulness of SeHCAT scan at investigation patients with chronic diarrhoea.
AIMS&METHODS: Consecutive patients with chronic diarrhoea who underwent SeHCAT scan at our centre over a 3-year period (2009-2011) were identified retrospectively. BAM was defined as present at a 7 day SeHCAT retention of $<12\%$. Patients' medical records were reviewed to obtain information regarding demographics, previous medical and surgical history as well as investigations.
RESULTS: Of 147 who had SeHCAT scan during the study period, 91 patients (62%) were diagnosed with BAM. A diagnosis of Type 1 was established in 22 patients (24%), including 2 patients who received pelvic/abdominal radiation, whereas 18 patients (20%) had Type 3 and all of them underwent cholecystectomy. 51 patients (56%) were diagnosed with idiopathic BAM (Type 2) and half of these had previous diagnosis of IBS-D. In the group with normal SeHCAT retention only 2 underwent cholecystectomy and there were no patients with small bowel resections or terminal ileum inflammation. 21 out of 147 patients had borderline results, defined as bile acid retention between 12% and 19%, and 71% were diagnosed with IBS-D.
CONCLUSION: In the investigation of patients presenting with chronic diarrhoea, SeHCAT scan should be considered to assist in the diagnosis of idiopathic BAM. Patients with Type 1 and 3 BAM however should be easily detected by taking an adequate clinical history and SeHCAT testing in these groups should perhaps be restricted.
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Disclosure of Interest: None Declared
Keywords: Bile acid malabsorption, Chronic diarrhea, IBS-D, SeHCAT scan

P1094 CLINICAL ACCURACY AND USEFULNESS OF THE LACTOSE INTOLERANCE QUICK TEST FOR THE DIAGNOSIS OF LACTOSE MALABSORPTION

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INTRODUCTION: The lactose breath test (LBT) is considered the gold standard technique for diagnosing lactose malabsorption. The Lactose Intolerance Quick Test (LIQT) measures lactase activity and may offer an alternative to the LBT.
AIMS&METHODS: To assess the efficacy of LIQT to correctly diagnose lactose malabsorption.
The study group included 69 dyspeptic patients that were evaluated by upper gastrointestinal endoscopy. Duodenal biopsies were used to rule out celiac disease (CD) and for the assessment of the LIQT (Biohit, Helsinki, Finland). In addition, all participants were evaluated for lactose malabsorption by the LBT. The results of LIQT were compared to LBT in order to define sensitivity, specificity, and predictive values of LIQT.
RESULTS: Groups were matched by mean age 54.4 yrs; M/F ratio 1/3; mean BMI 25.2 and none had celiac disease. The LIQT indicated hypolactasia in 55 participants (80%) and of those: 14 (25%) had mild hypolactasia and 41(75%) severe hypolactasia. The LBT indicated lactose malabsorption in 32 participants (46%). Of those with a normal LBT: 13 (35%) had normal lactase activity, 11 (30%) mild hypolactasia, and 13 (35%) severe hypolactasia by the LIQT. The sensitivity, specificity, positive predictive value and negative predictive value of the LIQT were: 97%, 35%, 56%, and 93%, respectively.
CONCLUSION: A finding of normal lactase activity with the LIQT rules out lactose malabsorption in almost all participants. However, the LIQT is associated with a high rate of overdiagnosis, with low specificity and a low positive predictive value relative to the LBT.
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Disclosure of Interest: None Declared
Keywords: Lactose Intolerance, Lactose Malabsorption

P1095 SEHCAT TESTING IN A LONDON DGH - IS BILE ACID MALAPSORPTION OVERLOOKED?

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INTRODUCTION: Bile acid malabsorption (BAM) is a common cause of chronic diarrhoea and is an easily treatable condition. A therapeutic trial of bile acid sequestrants is commonly used to diagnose BAM but this approach lacks diagnostic accuracy. A recent systematic review confirmed that idiopathic BAM was diagnosed in one third of patients otherwise labelled as functional diarrhoea or diarrhoea predominant irritable bowel syndrome (D-IBS)[1]. British Society of Gastroenterology guidance for investigation of chronic diarrhoea places the use of 75Se-homocholyltaurine (SeHCAT) test at a late stage in the investigation algorithm[2]. SeHCAT test is a simple non-invasive method of diagnosing BAM, and perhaps not fully utilised. Our study reviewed the use of SeHCAT testing in a London District General Hospital (DGH).
AIMS&METHODS: A retrospective analysis of our local database was undertaken to identify all patients who have had SeHCAT testing performed between January 2010 and December 2011. Clinic letters, hospital notes, biochemical, endoscopic and radiological data were recorded. BAM was defined as SeHCAT retention of $<15\%$ (mild 10-15%; moderate 5-10%; and severe $<5\%$).
RESULTS: A total of 92 patients had SeHCAT testing during this period for chronic diarrhoea. Notes were not available in five cases, so 87 were included in the study. Mean age was 50 (range 26-85). BAM was found to be the cause of chronic diarrhoea in 44/87 (50.1%) patients. Of these, 28 (63.6%) had severe BAM, 10 (22.7%) had moderate and 6 (13.6%) had mild BAM. 24 (54.5%) had type 1 BAM (secondary to terminal ileal disease or resection), 15 (34.1%) had type 2 (idiopathic) and 5 (11.4%) had type 3 BAM (post cholecystectomy, celiac disease). Out of the 44 patients with an abnormal SeHCAT result, 34 (78%) were treated with bile acid sequestrants, either with colesevelam (n=23) or with cholestyramine (n=11) as 1st line therapy. 24/34 (70%) patients had either partial or good treatment response, 4 patients discontinued cholestyramine due to intolerance while no documentation of treatment response was available in 6 patients. Overall, colesevelam was found to be more effective and well tolerated. The remaining 10/44 patients had either no documented follow-up or their symptoms resolved spontaneously.
CONCLUSION: BAM appears to be common, easily treatable and probably an under-recognised cause of chronic diarrhoea. Despite the utility, safety and relatively low cost of the SeHCAT test, it is not commonly performed in patients with D-IBS type symptoms. Our study suggests that SeHCAT testing is useful in this group of patients and should be considered perhaps earlier in the investigation of unexplained chronic diarrhoea.
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Disclosure of Interest: None Declared
Keywords: Bile acid malabsorption, Se75HCAT testing

P1096 DETERMINANTS OF LONG-TERM OUTCOME IN PATIENTS WITH CHRONIC INTESTINAL FAILURE DUE TO SHORT BOWEL SYNDROME

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INTRODUCTION: Intestinal failure (IF) occurs in patients (pts) who are insufficiently nourished mostly due to post-surgical short bowel syndrome (SBS). IF leads to severe malnutrition due to decreased absorption of macro- and micronutrients as well as fluid imbalances. However, only limited data on complications and outcome of long-term parenteral nutrition (PN) are available. We therefore aimed to evaluate long-term outcome and prognostic factors in IF.
AIMS&METHODS: A retrospective analysis was performed in a single center cohort from a tertiary referral center. All pts were treated by a specialized interdisciplinary team between 2004-2012. Documented features of IF and complications were characterized and survival analysis for overall survival and specific risk factors was performed.
RESULTS: 144 pts with clinically diagnosed IF (143 due to SBS) were studied with a mean follow-up of 45.7 months. Overall survival was significantly shorter by log-rank-testing in pts with malignant vs. non-malignant cause of IF. The 5-year survival rate (YSR) byKaplan-Meier analysis was lower in pts with stoma (types I and II-SBS)vs. no stoma (type IIISBS; p=0.027), on PN vs. no PN (p=0.069) and remaining small bowel length of <100cm vs. >100cm (p=0.065). Longterm complications of PN with occurrence of catheter-related blood infections (CRBI, 28% of pts) vs. no CRBI (p=0.019) and with PN-associated liver disease as defined by pathological liver tests (PNALD, 50% of pts) vs. no PNALD (p=0.002) also indicated a poorer prognosis.
CONCLUSION: This analysis of a large cohort of IF/SBS-pts demonstrates the prognostic relevance of the underlying disease, post-surgical small bowel anatomy and remaining small bowel length as well as complications of long-term PN. Both, careful monitoring of these risk factors as well as meticulous management of complications are thus mandatory for improvement of long-term outcome in these challenging pts.
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Disclosure of Interest: None Declared
Keywords: catheter-related blood infection, chronic intestinal failure, hepatopathy, parenteral nutrition, prognosis, short bowel syndrome

P1097 PREVALENCE OF BILE ACID MALABSORPTION AS A CAUSE OF DIARRHOEA IN CONSECUTIVE NEW PATIENT REFERRALS TO A GASTROENTEROLOGY CLINIC

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INTRODUCTION: Diarrhoea is a common presenting complaint in the Gastroenterology outpatient department. The potential causes are numerous, but include irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), coeliac disease, and colorectal cancer. Interest in bile acid malabsorption (BAM) as a cause of diarrhoea has increased recently. However, guidelines from the British Society of Gastroenterology do not recommend routine exclusion of this condition using 23-seleno-25-homo-tauro-cholic acid (SeHCAT) scanning.
AIMS&METHODS: Review of consecutive unselected new patient referrals to a single Gastroenterologists' outpatient clinic during a 3-year period, from January 2010 to December 2012. All clinic letters were reviewed retrospectively, and symptoms reported by the patient at the initial consultation were recorded. Radiology, endoscopy, chemical pathology, and histopathology databases were then cross-examined in order to ascertain the final diagnosis following full investigation, to the level deemed appropriate by the consulting physician. We defined BAM using a SeHCAT retention value of $<15\%$ at 7 days.
RESULTS: Of 613 consecutive unselected new patient referrals to a single Gastroenterologist between January 2010 and December 2012, 151 (24.6%) reported diarrhoea. After investigation the final diagnoses are listed in Table 1. The second commonest cause of diarrhoea, after IBS, was BAM. Nine (45.0%) of 20 patients with BAM reported lower abdominal pain or discomfort. In 13 (65.0%) patients there was no obvious cause of BAM, and these were classified as idiopathic, or type II, BAM.

	Number (n = 151)	Percentage
IBS	32	21.2
BAM	20	13.2
IBD	16	10.6
Functional diarrhoea	7	4.6
Coeliac	7	4.6
Microscopic colitis	6	4.0
PPI-related	5	3.3
Pancreatic insufficiency	2	1.3
Colorectal cancer	1	0.7

CONCLUSION: BAM was the commonest underlying cause of diarrhoea after IBS. Idiopathic BAM was commoner than coeliac disease. Almost 50% of patients with BAM reported lower abdominal pain or discomfort, which may

lead to misdiagnosis as IBS unless further investigations are performed. BAM should be considered as a likely diagnosis in all patients with diarrhoea, and SeHCAT scanning should be moved up the hierarchy of diagnostic tests in such patients.
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Disclosure of Interest: None Declared
Keywords: Bile acid malabsorption, Coeliac disease, diarrhoea, prevalence, SeHCAT scan

P1098 CORRECTION OF THE MITOCHONDRIAL DYSFUNCTION IN THE EXPERIMENTAL MODEL OF PROTEIN-ENERGY INSUFFICIENCY IN THE GROWING RATS

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INTRODUCTION: The investigations of the activity of mitochondria in protein-energy insufficiency and medicamentous correction of the disorders revealed have been studied insufficiently.
AIMS&METHODS: The purpose of our investigation was to study in experiment the effect of phytoecdisteroid ecdisten on the correction of mitochondrial dysfunction in the growing rats with protein-energy insufficiency.
Material and methods. The protein-energy insufficiency was induced in the laboratory white rats (16) by method of chronic malnutrition (quantitative decrease of the diet of the vivarium by 50% from norm). On the 30^{th} day the animals were divided into 2 groups (n=8). One group was given phytoecdisteroid ecdisten in dose 2,5 mg/kg during 10 days (from the 30^{th} to 40^{th} day of life) (studied group), group 2 received physiological solution. Control group included healthy young rats (8). Mitochondria were isolated from the liver of the 40-day rats, measurement of the parameters of oxidative phosphorylation and respiration velocity of mitochondria were performed with use of polarogroaphy LP-7. The velocity of isolated mitochondria breathing in the metabolic state V4 and V3, as well as values of the respiratory control and ADP/O was determined by method of Chans (Leninger, 1986).
RESULTS: The velocity of oxygen consumption at the state V4 was also reduced and accounted for 13,27 ± 0,7 ng at M/min/mg of protein in group of the ill animals, while in the control group the velocity was 19,7± 0,9 ng at O/min/mg of protein ($P<0,02$). In addition of the disconnector of the oxidative phosphorylation 2,4-dinitrophenol (Vdnf) there was also obtained confirmation of the mitochondria uncoupling - in the control group this indicator was 123,9 ± 3,7, and in the group of ill animals – only 56,07 ± 1,7 ng at O/min/mg of protein ($P<0.001$). Respiratory control being indicator of the intact functionality of mitochondria in group of control animals accounted for 6,15 ± 0,38, at the same time in group of control animals this indicator was reduced by 20% and was 4,8 ± 0,36. The proportion ADP/O was also decreased and accounted for 2,5 ± 0,12 against 2,8 ± 0,15 in control group. In cases of the use of ecdisten as correcting agent there was found that the state V3 had value 93,72±1,9; V4 – 15,62 ± 0,8; V dnf – 109,34 ± 3,3 ng at O/min/mg of protein ($P<0.01$).
CONCLUSION: The data obtained indicated about obvious disconnection of the respiratory chain in the suspension of mitochondria in diet of animals poor with protein contents as well as about presence of significant correcting effect of preparation ecdisten.
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Disclosure of Interest: None Declared
Keywords: correction, mitochondrial dysfunction, protein-energy insufficiency

P1099 PREGNANT WOMEN INTRACERVICAL MICROFLORA INFLUENCE ON FORMATION OF INTESTINAL MICROFLORA AT NEWBORN CHILDREN IN EARLY NEONATAL THE PERIOD. A CONTROLLED, RANDOMISED STUDY

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INTRODUCTION: The role of mother's intracervical microflora in the microbe colonization of newborns intestines is unequivocal and determining.
AIMS&METHODS: The comparison of bacteriological researches results of the crop from vagina and newborns gastric allocation. Prospective research covered a group of 300 newborns with clinical signs of newborns prenatal infection (NPI) and their mothers. There were 145 newborn boys and 155 girls. Pursuant to newborn's development terms 168 children (56 %) were born in 30 - 36 weeks, 132 (44 %) - in terms of 37 - 40 weeks. The weight of children at a birth varied from 1000 to 4500 g. However among newborns prevailed 73 % babies with weight of a body from 1500±124 up to 2989±243 g. The newborn's majority 91 % were born with an estimation of vital parameters behind scale Apgar of 5-7 points.
RESULTS: In structure of pregnant women vaginal microflora were determined Staphylococcus epidermidis (31,9 %), Staphylococcus aureus (28,7 %), Escherichia coli (27,7 %), Klebsiella spp. (6,5 %), Enterobacter spp. (2,1 %), Proteus spp. (1,9 %), Citrobacter spp. (1,2 %). In the majority of researches (72 %) there were polymicrobic associations Staphylococcus epidermidis and Staphylococcus aureus with Candida, Escherichia coli, Chlamydia spp. According to the bacteriological researches in newborn's gastric allocation fluid prevailed Staphylococcus epidermidis (32,2 %), Staphylococcus aureus (23,3 %), Escherichia coli (87,1 %), Klebsiella spp (8,2 %). In 40 cases the anaerobic colonies growth was confirmed (Clostridium Pneumoniae (5,3 %) and Clostridium difficile (8 %)). With the aim of newborn's with NPI intestinal microflora renewal by used in the complex of medicamentous therapy the Saccharomyces boulardii during ten days according to the scheme - 1-3 day - 250 mg twice a day, 4-6 - 125 mg 3-times a day, next 4 days - 125 mg twice a day. Bacteriological per rectum researches of newborn's intestinal microflora structure, made on the 5-th day of neonatal period, confirmed in 267 (89 %) children authentically ($p<0,05$) the reduction of Escherichia coli, Staphylococcus epidermidis, Staphylococcus aureus and Candida krusei colonies and the growth of Bifidobacterium spp. colonies 10^{-9}-10^{-11} CFU/ml and Lactobacillus spp. 10^{-6}-10^{-8} CFU/ml.
CONCLUSION: In the newborn's majority microflora observation (87,7 %), as well as at their mothers, has been submitted polymicrobic associations Staphylococcus epidermidis, Staphylococcus aureus with Candida and Escherichia coli.
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Disclosure of Interest: None Declared
Keywords: INTRACERVICAL MICROFLORA, NEWBORN

P1100 STOOL SHORT CHAIN FATTY ACID CONCENTRATIONS IN A COHORT OF PRETERM VERY LOW BIRTH WEIGHT INFANTS WITH AND WITHOUT NECROTISING ENTEROCOLITIS

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INTRODUCTION: Diagnostic markers of necrotising enterocolitis (NEC) remain evasive. Stool short chain fatty acids (sSCFAs) are a product of bacterial fermentation of undigested carbohydrate and protein noted to alter in preterm infants with necrotising enterocolitis. According to the Lawrence Hypothesis, they may be implicated in the aetiology of NEC. We sought to correlate changes in sSCFAs over the first month of life in a cohort of preterm, very low birth weight infants with and without NEC.
AIMS&METHODS: 56 sequentially recruited infants <32 weeks and <1.5Kg birth weight within week 1 of life. Stool samples taken once weekly for the first 4 weeks, analysed by gas chromatography-mass spectrometry (mcg/g wet weight). 11 individual acids were measured: acetate, lactate, isobutyrate, butyrate, isocaproate, caproate, isovalerate, valerate, octanoate, heptanoate and lactate. NEC was diagnosed by consultant, external collaborator, radiologist, and classified by Bell's Criteria.
RESULTS: n=56. 32 developed NEC, 20 ≥Bell's 2a. 8 required surgery (5 ileostomy). NEC strongly correlated with low gestation and extremely low birth weight. There were no correlations between gestation, feed type, or NEC and sSCFA concentration. No significant differences were observed in weekly totals, and wide interquartile ranges were noted throughout. Acetate and lactate dominated each sample, regardless of gestation, feed type or NEC. Subgroup analysis revealed significant differences in stage 2a and 3b NEC. Stage 2a NEC showed higher concentrations of propionate in week 4 than week 3, and lower valerate in week 4 than 2. Stage 3b levels of isobutyrate and heptanoate were significantly lower in week 4 than 3. All analytes were non-normally distributed thus further multivariate regression analysis was deemed inappropriate. None of the analytes were significantly correlated according to Pearson's correlation.
CONCLUSION: Despite a wide variation in clinical status, the levels of sSCFAs remained remarkably consistent. Small yet significant differences in minor sSCFAs were seen in subgroup analysis in those with stage 2a and 3b NEC. Reasons for the high incidence of NEC require further investigation.
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Disclosure of Interest: None Declared
Keywords: necrotising enterocolitis, Preterm, short chain fatty acids

P1101 ADULT AUTOIMMUNE ENTEROPATHY : A RARE CAUSE OF NON CELIAC VILLOUS ATROPHY

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INTRODUCTION: Adult autoimmune enteropathy (AIE) is an uncommon intestinal disease. Clinical presentation, serological markers, phenotype and efficient treatments remain undefined.
AIMS&METHODS: Aim: to precise diagnostic criteria and outcome in a well defined series of patients with adult AIE.
Patients and Methods: medical files of 11 patients (8F/3M) with diagnosis of AIE or AIE-like were studied retrospectively. All the patients presented villous atrophy without diagnostic criteria of celiac disease (lacking serological markers, and/or celiac susceptibility HLA type II and no response to a gluten free diet (GFD)) or common variable immunodeficiency (normal dosage of IgA, IgG and IgM). The work included centralized histological review, molecular and phenotype analyses of intestinal specimens.
RESULTS: Results: Mean age at diagnosis was 47 years [21-79]. Mean body mass index was 19. The most frequent symptoms were chronic diarrhea (100%), abdominal pain (55%) and vomiting (45%). Personal and family histories of autoimmune diseases were noted in 45% and 36% of patients, respectively. Histological damages were intestinal villous atrophy, mainly of severe type, with glandular lesions. One third of patients presented associated lymphocytic colitis. More than half patients had positive serum anti-AIE 75KD antibodies at diagnosis and less frequently anti-enterocytes antibodies. Patients seronegative for AIE had no celiac antibodies and, except in one patient resisting to a GFD, no celiac susceptibility HLA. Phenotype of isolated lymphocytes showed increased expression of Natural Killer (NK) markers (CD57, NKG2C) in intestine and normal count of CD4+CD25+FoxP3+ peripheral blood lymphocytes, both in seropositive and seronegative (for AIE-75KD) patients. Majority of patients had clinical and histological response to immunosuppressive

drugs targeting T cell responses (Thiopurines, anti-TNF-alpha, cyclosporine, mTor inhibitors) but none with anti-B cells therapy. Regular endoscopic follow-up detected emergence of intestinal TCR gamma chain rearrangement in three patients treated by suppressive therapy. In one of them it raised in intestinal T cell lymphoma.
CONCLUSION: Adult AIE is characterized by severe villous atrophy, glandular destruction and intestinal infiltration by T lymphocytes expressing highly NK markers. AIE is commonly responsive to immunosuppressors but regular follow-up is necessary to screen emergence of clonal T cell proliferations.
Disclosure of Interest: None Declared
Keywords: Anti-AIE 75KD antibodies, Autoimmune enteropathy

P1102 DETECTION OF SMALL BOWEL TUMORS: GROWING TREND TOWARDS WELL-TIMED PREOPERATIVE RECOGNITION AND ENDOSCOPIC TREATMENT

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INTRODUCTION: For many years majority of small bowel tumors (SBT) have been diagnosed and treated untimely.
AIMS&METHODS: The aim of the study is to evaluate the detectability of SBT and changes in the management of patients after capsule (CE) and balloon-assisted enteroscopy (BAE) implementation. From I.2007 to IV.2013 we observed 61 pts. (m-27, f-34), ranged from 17 to 85 years, (mean age 50,8±17,6 years) with SBT. The main complaints in 26 (42,6%) pts. was recurrent obscure GI bleeding; a clinical picture of intestinal obstruction was in 7 (11,5%) pts.; nonspecific symptoms - in 22 (36,1%) pts.; the other 6 (9,8%) pts. were asymptomatic. Surgical interventions due to intestinal tumors underwent 10 (16,4%) pts in the past history. The duration of the disease lasted at least 6 months in 26 (42,6%) pts., up to 3 years - in 18 (29,5%) and more than 3 years in 17 (27,9%) pts. For the small bowel examination we have used CE in 22 (36,1%) pts. and BAE in 47 (77,0%) pts., including 20 cases after CE. In 10 (16,4%) pts. SBT were detected during urgent surgery, without prior endoscopy.
RESULTS: According to CE data SBT were revealed in 20 (39,2%) cases. BAE detected tumors in 43 (70,5%) cases. Endoscopic ultrasonography during BAE was performed in 9 (14,8%) pts. In 6 (9,8%) pts. SBT were revealed by laparoscopy. Histologically, in 29 (47,5%) cases that was malignant tumors: adenocarcinoma – 5, neuroendocrine tumors – 8 (incl. carcinoid - 5), GIST – 8, metastatic lesions – 2, undifferentiated carcinoma – 1, lymphoma – 5), and in 30 (49,2%) cases - benign tumors: Peutz-Jegher's hamartomas – 11, hyperplastic polyp - 8, tubular adenoma - 3, fibroid polyps – 2, lymphangioma – 2, angiofibrolipoma – 1, cavernous hemangioma – 1, leiomyoma -1, lipoma - 1. Two patients after CE with submucosal tumors abandoned the following treatment. There were 51 (83,6%) cases with intraluminal growth of the tumor, 2 (3,3%) cases with extraluminal growth and 8 (13,1%) cases had mixed variant. Conservative treatment have been applied in 11 (18,0%) pts. Endoscopic interventions were performed in 17 (27,9%) pts.: polypectomy - in 13 pts. (124 tumors were removed in course of 25 interventions), EMR - in 4 pts. A complication – bleeding after polypectomy in the ileum, was stopped endoscopically. Surgery was performed in 33 (54,1%) pts.
CONCLUSION: SBT can be estimated timely, before urgent surgery because of complications, in 83,6% of pts. BAE allows to perform endoscopic treatment in 27,9% and to avoid surgery in 45,9% of pts.
Disclosure of Interest: None Declared
Keywords: capsule endoscopy, enteroscopy, intestinal tumor, Small Bowel, surgery

P1103 CAPSULE ENDOSCOPY FINDINGS IN INTESTINAL FOLLICULAR LYMPHOMA

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INTRODUCTION: Cases of gastrointestinal follicular lymphoma (FL) has been increasingly reported in Japan. The duodenum, the jejunum and the ileum are the predominant sites involved by FL.[1] However, endoscopic characteristics of small bowel FL (SB-FL) have not been well documented.
AIMS&METHODS: We aimed to investigate endoscopic characteristics of SB-FL using capsule endoscopy (CE) and to assess a possible relevance between the findings of the duodenum and the small bowl. 26 patients with newly diagnosed gastrointestinal FL, who underwent CE and double-balloon endoscopy (DBE) together with biopsy were enrolled. Based on CE findings, SB-FL was divided into either whitish lesions (localized dense villi, multiple nodules, and flat protrusions) or non-whitish lesions (lymphoid hyperplasia like nodules and mass lesions). As for whitish lesions, the severity was graded according to the number of the segments involved by the lesions. Duodenal FL was classified into localized type (less than one-fourth circumferential spread) and circular type (greater than one-fourth) based on the findings in the descending duodenum under esophagogastroduodenoscopy (EGD). The prevalence of each type of SB-FL was analyzed in the jejunum and the ileum, and the severity of whitish lesions was compared with the severity of duodenal FL.
RESULTS: Under CE, jejunal involvement was found in 21 patients, and ileal involvement in 10 patients. CE identified whitish lesions in 21, and non-whitish lesions in 5, respectively. Among whitish lesions, multiple nodules and localized dense villi were frequently observed under CE (21patients and 19 patients, respectively), and such lesions were predominantly located in the jejunum (both in 19 patients). Whitish lesions were also found in the ileum in 7 of 21 patients, all of whom had jejunal involvement. When compared whitish lesions of SB- FL with the severity of duodenal FL, patients with circular type of duodenal involvement had more severe whitish lesions of SB-FL under CE than patients with localized duodenal involvement did ($p < 0.05$).
CONCLUSION: Multiple whitish nodules and localized dense villi in the jejunum are characteristic CE findings in SB- FL. There is a close association between the severity of SB-FL under CE and that of the descending duodenum under EGD.
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Disclosure of Interest: None Declared
Keywords: capsule endoscopy, follicular lymphoma

P1104 CD4 LYMPHOPROLIFERATIVE DISORDER OF THE INTESTINE: FEATURES AND OUTCOME

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INTRODUCTION: CD4 T cell lymphoproliferative disorder of the intestine is very rare, mainly diagnosed during investigations for suspicion of refractory celiac disease.
AIMS&METHODS: Aims: We aimed to better characterize pathological and molecular features and outcome was evaluated of intestinal CD4 T cell proliferation in a series of thoroughly characterized patients.
Patients and Methods: The medical files of 114 consecutive patients, investigated for suspicion of refractory celiac diseases in three Gastroenterology Departments in France, were studied retrospectively. The study focused on 9 of them who presented histological features of intestinal CD4 T cell lymphoproliferations and included centralized with histolopathological, phenotypical and molecular analysis.
RESULTS: The nine patients (4F/5M; mean age at diagnosis: 54 years) presented with chronic diarrhea and malnutrition. Aspect of intestinal villous atrophy was observed in six patients, mainly severe (total or subtotal) whereas the three other patients did not present architectural change. The common pathological feature was the dense infiltration of the lamina propria by a polymorphous population of monomorphic small lymphoid cells expressing CD3, CD4, betaF1 and specific Vbeta detected by immunohistochemistry or T Cell Receptor (TCR) beta chain sequencing. Clonal rearrangement of the TCR gamma was found in all patients with rearrangement of the beta chain in most cases. Phenotyping analysis of isolated intraepithelial and lamina propria lymphocytes confirmed histological aspect, showing huge infiltration of epithelium and lamina propria by CD4+ T cells. CGH array analysis showed a heterogeneous profile of chromosomal abnormalities. Gastric and colonic involvements were observed in one third of patients and extension outside the gut (liver, bone marrow) in 20% of patients. Regarding all the treatments tested (steroids, chemotherapy, purine analogs, anti-CD52), anti-CD52 antibodies appear the most efficient inducing clinical and histological responses with reversion of abnormal phenotype in the two treated patients. At latest news, all the patients were still alive.
CONCLUSION: CD4 T cell lymphoproliferative disorder of the intestine is an uncommon intestinal T cell lymphoma with various Vbeta repertoires. Except anti-CD52 antibodies efficient but responsible of strong immune depletion, there is no evident therapy for this indolent intestinal T cell lymphoma.
Disclosure of Interest: None Declared
Keywords: intestinal CD4 T cell lymphoproliferative disorder, intestinal T cell lymphoma

P1105 PREDICTION OF TUMOR RECURRENCE IN PATIENTS WITH GASTROINTESTINAL STROMAL TUMORS FOLLOWING RESECTION BY THE MODIFIED NIH CRITERIA

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INTRODUCTION: The modified National Institutes of Health (NIH) criteria is currently widely accepted to assess the risk of recurrence of gastrointestinal stromal tumors (GISTs). This criteria includes both tumor site and tumor rupture as additional prognostic factors. The aims of this study were to clarify the clinical usefulness of the modified NIH criteria for risk stratification in Korea and to determine the association of the prognostic factors for GIST recurrence.
AIMS&METHODS: From January 2000 through September 2012, 261 patients who underwent curative resection for primary GIST were included and those who received adjuvant chemotherapy after surgery were excluded. The enrolled patients were divided into two groups according to primary tumor site; each group was stratified to predict recurrence by the original NIH criteria and modified NIH criteria. Clinical and pathologic data were collected and analyzed retrospectively.
RESULTS: A total of 172 patients had gastric GISTs; 89 patients had non-gastric GISTs. The mean age was 58.9 years (range: 22-89 years) and the

median follow-up duration was 4.26 years (range: 0.04-12.75 years). In the gastric GIST group, both risk stratification systems yielded the identical classification. Only 1 patient (1.9%) in the intermediate category and 8 patients (19%) in the high risk category experienced tumor recurrence. In the non-gastric GIST group, all patients who were placed in the intermediate risk category by the original NIH criteria were reclassified into the high risk category according to the modified NIH criteria. Among the 22 reclassified patients, 6 patients suffered a recurrence during the observational period. The primary tumor site, tumor size, mitotic count, presence of microscopic tumor necrosis and presence of tumor hemorrhage were significantly associated with the risk of tumor recurrence with univariate analysis. With multivariate analysis, the primary tumor site, tumor size, mitotic count, and presence of tumor hemorrhage were statistically significant variables.

CONCLUSION: The high risk category by the modified NIH criteria was found to have a high recurrence rate of GIST; furthermore, the non-gastric GIST group had a worse prognosis than gastric GIST group. Therefore, the modified NIH criteria accurately predicted the recurrence of GISTs after curative resection. In addition, the presence of bleeding might be considered to be an additional prognostic factor for GIST.

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Disclosure of Interest: None Declared

Keywords: Consensus Development Conference, NIH, Gastrointestinal stromal tumors, recurrence

TUESDAY, OCTOBER 15, 2013 9:00–17:00

NUTRITION II – Poster Area

P1106 NATURAL DIETARY OLIVE OIL POLYPHENOLS, DOWNREGULATE MACROPHAGE LPS-INDUCED INFLAMMATORY RESPONSE THROUGH MAPKS AND NFKAPPAB SIGNAL PATHWAYS

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INTRODUCTION: Traditional Mediterranean diet is characterized by the usual high intake of extra virgin olive oil (EVOO), from olive tree, *Olea europaea*. Phenolic compounds present in EVOO (PE) are recognized as a group of highly bioactive components, with antioxidant and anti-inflammatory properties among others. Current epidemiological and experimental studies support a beneficial role of dietary polyphenols in several gastrointestinal diseases, including inflammatory bowel disease (IBD). Recent reports have demonstrated that dietary PE supplementation attenuated chronic ulcerative colitis in mice (Sánchez-*Fidalgo et al, 2013*). On the other hand, macrophages are dramatically involved in the pathogenesis of inmuno-inflammatory disorders. Regarding IBD, macrophages are pivotal mediators of innate immunity and appear to play a key role stimulating the subsequent adaptive immunity.

AIMS&METHODS: The present study was designed to evaluate potential anti-inflammatory effects of PE in lipopolysaccharide (LPS)-stimulated peritoneal murine macrophages and deep insight into the molecular action mechanisms. Nitric oxide (NO) production was analyzed by Griess method and intracellular reactive oxygen species (ROS) by fluorescence analysis. Moreover, changes in the protein expression of the proinflammatory enzymes cyclooxygenase (COX)-2, the inducible nitric oxide synthase (iNOS) and microsomal prostaglandin E synthase-1 (mPGES-1), as well as the role of mitogen-activated protein kinases (MAPKs) and the nuclear transcription factor kappa B (NFKappaB) signaling pathways were analyzed by western blot.

RESULTS: PE exerted significant anti-inflammatory and anti-oxidant effects inhibiting LPS-induced intracellular NO and ROS production. Additionally, PE induced a significant downregulation of iNOS, COX-2 and mPGES-1 proteins expression. Moreover, PE treatment reduced MAPKs activation and prevented the nuclear NFKappaB translocation in murine macrophages, which were increased in LPS-stimulated cells.

CONCLUSION: PE compounds could play an important role in the anti-inflammatory effect of virgin olive oils and probably might yield novel preventive or palliative nutritional treatments in the management of IBD.

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Disclosure of Interest: None Declared

Keywords: diet, Extra virgin olive oil, inflammation, macrophages

P1107 FOOD INTAKE IN HUMANS WAS NOT AFFECTED BY GLUCAGON-LIKE PEPTIDE-1 RECEPTOR BLOCKADE THROUGH EXENDIN9-39

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INTRODUCTION: Exogenous administration of glucagon-like peptide-1 (GLP-1), or of its potent, long-acting analogs, inhibits eating and improves postprandial glycemia in many species, including humans. In addition, chronic administrations of GLP-1 or its analogs effectively reduces body weight and improves glucose metabolism in overweight individuals and type 2 diabetics. In animals, GLP-1 receptor (GLP-1R) blockade by the specific GLP-1R antagonist exendin9-39NH2 (ex9-39) stimulates eating under some conditions indicating that satiation can be delayed when endogenous GLP-1 signalling is blocked. In other studies, however, ex9-39 administration fails to stimulate eating suggesting that endogenous GLP-1 is not involved in the control of eating.

The role of GLP-1 receptor antagonism in modulating eating in humans has not been investigated yet. The objectives were therefore to use the antagonist as a probe of the physiologic actions of glucose or fat stimulated endogenous GLP-1 by assessing the effects on a) food intake, b) plasma GLP-1 concentrations, and c) endocrine pancreatic functions.

AIMS&METHODS: Two double-blind, 4-way cross-over studies were performed, each with 10 healthy men. In part A, subjects received either an intravenous (iv) infusion of ex9-39 or saline (control) plus an glucose preload and an intraduodenal (ID) infusion of glucose or saline; in part B, iv infusions were identical, but an mixed liquid meal preload and an ID infusion of oleic acid or saline were administered. After 30 min, an ad libitum test meal was served and subjects were invited to eat and drink as much as they wished. The amount of food eaten and fluid drunk, the time to complete the meal as well as appetite sensations were quantified; Plasma GLP-1, insulin, glucose and glucagon were measured.

RESULTS: In both parts, iv exendin9-39 induced a significantly higher increase in plasma GLP-1 and glucagon levels compared to iv saline ($P \leq 0.001$). Insulin was lower with iv exendin9-39 in response to ID glucose ($P \leq 0.05$). Appetite sensations, energy intake, fluid intake, or eating duration were not affected by iv exendin9-39 in either parts.

CONCLUSION: We confirm the usefulness of the GLP-1R antagonist ex9-39 as a probe of the physiologic activity of endogenous GLP-1, revealing in healthy men 1) a central role of GLP-1 in postprandial control of insulin and glucagon secretion, and 2) a limited role of GLP-1 in controlling appetite and eating.

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Disclosure of Interest: None Declared

Keywords: food intake, glucagon, humans, insulin

P1108 PYRROLOQUINOLINE QUINONE SECRETING GENETICALLY MODIFIED ESCHERICHIA COLI NISSLE 1917 MINIMIZES OXIDATIVE STRESS AND REDUCES BLOOD LIPID LEVELS IN AGING RATS

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INTRODUCTION: Aging is a degrading mechanism accompanied by progressive increase in free radicals and decrease in antioxidant defense leading to functional decline of various cellular processes in the body. Mitochondrial dysfunction and decrease in mitochondrial content is observed with progressive age. Pyrroloquinoline quinine (PQQ) acts as potent antioxidant and helps in mitochondrial biogenesis through its interaction with cell signaling network.

AIMS&METHODS: This work aims to evaluate the effect of PQQ secreting genetically modified probiotic *Escherichia coli* Nissle 1917 (EcN-*pqq*) on colonic and hepatic antioxidant status, and blood lipid profile in aging rats. Since mitochondrial generation of reactive oxygen species in major cause of its damage, we analyzed protective efficacy of PQQ against rotenone (complex I inhibitor) induced oxidative damage *in vivo*. Adult male Charles Foster rats, 8 months of age were weekly treated with probiotics for 6 months. Rotenone (2mg/kg body weight) was given for 30 days with and without PQQ (10 μg/kg body weight) daily.

RESULTS: Native EcN treatment could minimize colonic lipid peroxidation as compared to untreated but did not have any effect on colonic antioxidant enzyme activities as well as hepatic parameters. However, EcN-*pqq* treatment reduced colonic lipid peroxidation more efficiently than native EcN, and elevated catalase and SOD activities. Additionally, it was able to reduce hepatic lipid peroxidation along with enhanced catalase, SOD, G6PDH activities and GSH levels. We also found elevated hepatic mitochondrial content in rats fed with EcN-*pqq* as compared to untreated or native EcN groups. Additionally, EcN-*pqq* treatment to aging rats lowered blood triglyceride and cholesterol levels when compared to untreated. Purified PQQ treatment given daily along with rotenone rescued oxidative colonic and hepatic damage along with increase in hepatic mitochondrial content.

CONCLUSION: Protective efficacy of *E. coli* Nissle 1917 on oxidative stress in aging rats is enhanced by incorporation of *pqq* gene cluster. Additionally, it also prevents hepatic oxidative stress along with reduction in blood lipid levels. Purified PQQ could also prevent oxidative stress induced by rotenone used to create model of accelerated aging. Thus PQQ secreting probiotic *E. coli* Nissle 1917 could be used as nutritional supplement for preventing oxidative stress and hyperlipidemia especially in aging.

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Disclosure of Interest: None Declared

Keywords: aging, E. coli Nissle 1917, nutritional supplement, oxidative stress, probiotics

P1109 A COMBINATION OF PRE- AND PROBIOTICS, VITAMINS, MINERALS, ANTIOXIDANTS AND ANTI-INFLAMMATORY AGENTS AS A NEW THERAPEUTIC APPROACH FOR INCREASED INTESTINAL PERMEABILITY IN PATIENTS WITH IRRITABLE BOWEL SYNDROME WITHOUT CONSTIPATION

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INTRODUCTION: Impairment of the intestinal barrier has been involved in the pathogenesis of several diseases. One of the most studied correlations is the one with irritable bowel syndrome (IBS). To date, there is no standard treatment for increased intestinal permeability.
AIMS&METHODS: Our aim was to assess the efficacy of a dietary complement containing pre- and probiotics, vitamins, minerals, antioxidants and anti-inflammatory agents in ameliorating the increased intestinal permeability and global state of health in subjects with IBS without constipation.
In this proof-of-concept study, a combination of pre- and probiotics (L. acidophilus NCFM, B lactis Bi-07), vitamins, minerals, antioxidants and anti-inflammatory agents (Nutrimonium®) was added to the common diet of 33 subjects (M/F:14/19, mean age 42 yo, range 19-72) with IBS-D or IBS-M and increased intestinal permeability (measured with ^{51}CrEDTA Test) at the dosage of 1 sachet per day for 60 days. After the treatment, each patient repeated the intestinal permeability test with ^{51}CrEDTA. Global health state with a slightly modified version of EQ-5D VAS (0-100 mm) was evaluated at baseline and after the treatment.
RESULTS: All the patients completed the treatment. Five patients were unable to repeat the ^{51}CrEDTA Test and were withdrawn from the study. In the remaining 28 patients, the mean ^{51}CrEDTA score was respectively 7,43 (SD: ±2,75) at baseline and 5,93 (SD: ± 2,7333) after the treatment (P=0.089). Mean EQ-5D VAS was respectively 40 (SD: ±14,86) at baseline and 64.61 (SD: ± 9) after the treatment (P<0.0001).
CONCLUSION: Restoring the impaired gut barrier may be challenging, especially since there are several therapeutic targets to hit, as gut microbiota, intestinal mucus, intestinal immune cells, tight-junction function, et cetera. A multimodal approach, with a combination of different healing agents, seems to be effective both in improving intestinal permeability and in ameliorating symptoms. Since this study has many limitations, further, randomized controlled trials, with an adequate sample size, are needed to confirm these results.
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Disclosure of Interest: G. Ianiro : No Conflict of Interest to declare", V. Ojetti : No Conflict of Interest to declare", E. Gaetani : No Conflict of Interest to declare", L. Laterza : No Conflict of Interest to declare", F. Scaldaferri : No Conflict of Interest to declare", F. Beghella Bartoli : No Conflict of Interest to declare", S. De Martino : No Conflict of Interest to declare", G. Dinoi : No Conflict of Interest to declare", G. Gigante : No Conflict of Interest to declare", G. Cammarota : No Conflict of Interest to declare", G. Gasbarrini : No Conflict of Interest to declare", A. Gasbarrini : No Conflict of Interest to declare"
Keywords: antioxidants, gut barrier, intestinal permeability, Irritable bowel syndrome, probiotics

P1110 LACTIC ACID BACTERIA (LAB) MODULATE ANGIOPOIETIN-LIKE 4 (ANGPTL4) EXPRESSION IN HUMAN INTESTINAL EPITHELIAL CELLS

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INTRODUCTION: Over the last decades, an increase of metabolic diseases (obesity, type-2 diabetes) has been reported with dramatic consequences on human health. Scientific interest has extended for a better understanding of LAB regulation of host energy balance. ANGPTL4, also known as Fiaf (fasting-induced adipose factor), is an adipokine expressed in several tissues including liver, intestine and heart. ANGPTL4 (overexpressed in fasting and in hypoxia) displays a role in angiogenesis, lipid metabolism and glucose tolerance. ANGPTL4 inhibits lipoprotein lipase (LPL), an enzyme that converts triglycerides in monoglycerides and fatty acids (FA) and promotes lipolysis resulting in increased triglyceride serum level and decreased FA and cholesterol uptake into tissues. *In vivo* and *in vitro* studies have shown the regulation of ANGPTL4 by bacteria. As an example an ANGPTL4-dependent decrease of fat storage under high fat diet supplemented with *L.paracasei* bacteria in a gnotobiotic mice model has been described (Aronsson et al, PLoS one, 2010).
AIMS&METHODS: These data underline the pivotal role of the bacterial regulation of ANGPTL4 in energy balance and lipid storage. However, molecular mechanism and microbial factors regulating its expression are still poorly understood.
The aim of this study was to assess the mechanisms by which LAB are able to modulate ANGPTL4 expression in intestinal epithelial cells.We selected the intestinal epithelial cells HT-29 as a relevant *in vitro* model, being in direct contact with luminal content including bacteria. Twenty LAB strains have been selected belonging to *Lactobacillus rhamnosus* and *Lactobacillus paracasei* species and tested.
RESULTS: We identified strains modulating ANGPTL4 expression in intestinal epithelial cells. The molecular mechanisms involved in the modulation of ANGPTL4 expression by LAB strains have been studied, and it seemed to be independent of PPARγ activity..
CONCLUSION: In conclusion, these strains may be useful tools to modulate lipid metabolism *in vivo*.

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Disclosure of Interest: None Declared
Keywords: epithelial function, metabolic parameters, Metabolic syndrome, Microbiota, probiotics

P1111 GAMMA CAMERA IMAGING FOR STUDYING INTESTINAL ABSORPTION AND WHOLE-BODY DISTRIBUTION OF SELENOMETHIONINE

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INTRODUCTION: Selenium (Se) is recognised as a nutrient that is essential to human health. Se metabolism in humans is not well characterised. Currently, estimates of Se absorption, whole-body retention, and excretion have been obtained from balance and tracer studies. We used gamma camera imaging to evaluate whole-body retention and distribution of radio-labelled selenomethionine (SeMet), the predominant form of Se present in food.
AIMS&METHODS: Eight healthy young men participated in the study. After a meal that contained 4 MBq ^{75}Se-L- selenomethionine (^{75}Se-SeMet), whole-body gamma camera scanning was performed for 45 min every hour over a 6-hr period, every second hour for the next 18 hr, and once on each of the subsequent 6 days. Blood, urine, and faeces samples were taken to determine the plasma content of ^{75}Se-SeMet as well as its excretion in urine and faeces.
RESULTS: Imaging showed that 87.9 ± 3.3% (mean ± standard deviation) of the administered activity of ^{75}Se-SeMet was retained within the body after 7 days. For comparison, the measured excretion in urine and faeces for the 7-day period was 8.2 ± 1.1% of the activity. Time-activity curves were generated for whole-body, stomach, liver, abdomen (other than the stomach and the liver), brain, and thigh muscle.
CONCLUSION: Gamma camera imaging allows for the assessment of postprandial absorption of SeMet. This technique may also permit concurrent studies of organ turnover of SeMet.
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Disclosure of Interest: None Declared
Keywords: Absorption, Gamma camera imaging, Organ turnover, Selenomethionine

P1112 THE ROLE OF LACTOSE AS AN IMMUNOMODULATOR:IMPLICATIONS FOR HUMAN HEALTH

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INTRODUCTION: Our interest in lactose as a new immunomodulatory molecule results from studies showing that TIM-3/Gal-9 pathway is crucial in the regulation of T cell responses both *in vitro* and *in vivo* [1-6]. In animal models, *in vivo* administration of lactose has been shown to mediate similar effects on T cell immunity and disease state as specific silencing of the interaction between TIM-3 and Gal-9 [4]. *In vitro,* lactose can block the anti-allergic effects of IgE-binding Gal-9 [5], and is capable of disrupting Gal-9 mediated regulatory T cell (Treg) control over cytotoxic CD8+ T cells [6].
AIMS&METHODS: We wanted to study the role of lactose as a possible inhibitor of human Treg-mediated immune regulation. We enriched from peripheral blood of healthy donors (n=20) $CD4^+CD25^{high}$ Tregs and $CD4^+CD25^{low}$ effector T cells by magnetic column separation. We tested the effect of lactose in co-cultured Treg and effector T cells stimulated with anti-CD3+anti-CD28. Sucrose was used as a control sugar. We used RT-qPCR and ELISA to measure effector T cell cytokine production.
RESULTS: In the presence of Tregs, the levels of secreted IFNγ and IL-17 in T effector cells were decreased from median of 8.8 to 3.9 units for IFNγ (p=0.003) and from 0.7 to 0.64 units for IL-17 (p=0.04). When lactose was added, Treg-mediated suppression was inhibited, which led to elevated levels of secreted IFNγ and IL-17 (median 16.4 vs 3.9 units and 0.74 vs 0.64 units; p<0.0001 and p=0.005, respectively).
CONCLUSION: The inhibition of Treg function with lactose enhanced Th1 and Th17 immunity. Since lactose is the main carbohydrate in breast milk it could promote the induction of mucosal immune protection, i.e Th1 and Th17 immunity, and be beneficial as an immunostimulator during infancy. However, later in life dietary lactose could induce harmful pro-inflammatory mechanisms by disrupting Treg-mediated tolerance in the gut. The uncontrolled Th1 and Th17 responses and the inability of Treg cells to down-regulate immune responses have been implicated in the pathogenesis of many human immune mediated diseases [7,8]. In the light of current knowledge and our recent findings further studies are needed to reveal the possible beneficial and/or harmful effects of dietary lactose.
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P1113 WHEAT BRAN IMPROVES REGULARITY AND SYMPTOMS OF DIGESTIVE DISCOMFORT WITHIN 3-5 DAYS

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INTRODUCTION: Average intakes of fibre in Europe are lower than the recommended 25g/day and in countries like the UK, 29% suffer from constipation and 43% from digestive discomfort as a result of fibre deficiency. Although not life threatening, sub optimal gut function affects physical and emotional quality of life and are common place amongst clinical referrals. Dietary fibre intervention can improve gut function and motility by reducing transit time and increasing faecal bulk but amongst non-constipated individuals with poor fibre intakes can also improve well being and quality of life. Wheat bran compared to other fibre sources is considered the gold standard for promoting laxation and regularity. Indeed the EUropean Food Standard Agency recently approved 2 health claims for wheat bran and faecal bulking and transit time.
AIMS&METHODS: Amongst healthy adults, the objective was to assess the length of time required to demonstrate the benefits of consuming wheat bran fibre as a serving of Kellogg's All-Bran breakfast cereals on transit time, faecal bulking and symptoms of digestive discomfort. A systematic review of the scientific literature was conducted to evaluate dose and time response of wheat bran on physiological and psychological function. MEDLINE and bibliographic searches identified 20 relevant human intervention trials, many using Kellogg'All-Bran as the wheat bran source dating back to 1942.
RESULTS: Wheat bran intervention in the form of a serving of Kellogg's All-Bran cereals reduces transit time and increases faecal bulk within as little as 3-5 days in healthy adults. It also reduces symptoms of digestive discomfort such as bloating and feelings of sluggishness as well as improves psychological well being with levels as low as 3.5g of wheat bran.
CONCLUSION: The Kellogg's All-Bran range of breakfast cereals provide 4-10g of wheat bran fibre (up to a third of daily fibre requirements). This additional fibre can reverse the consequences of fibre deficiency by increasing stool weight and reducing transit time. In addition symptoms of digestive discomfort and feelings of wellness can be improved within as little as 3-5 days. This could be expected to be translated into increased feelings of well being of an estimated 43% of the UK population who report symptoms of digestive discomfort

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P1114 ASSOCIATIONS WITH WATER-SOLUBLE VITAMINS DEFICIENCIES AND PATIENTS WITH COMPLICATED PEPTIC ULCERS IN THE EARLY PHASE AFTER THE ONSET, EVEN IN PRESENT-DAY JAPAN: TIME COURSE OF THESE CHANGES

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INTRODUCTION: To investigate whether patients with complicated peptic ulcers (PUs) have deficiencies of water-soluble vitamins (WSVs) in the early phase after the onset, even in present-day Japan.
AIMS&METHODS: This prospective cohort study included the inpatients who had confirmed PUs. Concentrations of fasting serum WSVs (vitamins B1, B2, B6, B12, C, and folic acid) and homocysteine were measured at 3 time points (at admission, hospital discharge, and 3 months after hospital discharge).
RESULTS: Ten consecutive patients (58.4 ± 15.1 years, 3 gastric/7 duodenal ulcers, fasting period after hospitalization 4.0 ± 1.6 days, and duration of hospitalization 12.2 ± 4.6 days,. 8 *H. pylori* / 2 NSAID users) who met the inclusion criteria and completed measurements of blood samples at all 3 time points were enrolled in the study.
The mean levels of vitamins B1, B2, B6 and C, but not those of vitamin B12 and folic acid, were low normal at the time of admission. Time-dependent effects during the time course of changes in serum levels of the WSVs were statistically confirmed for vitamin B1 ($P < 0.01$) and vitamin B6 ($P < 0.05$), but not vitamins B2, B12, C and folic acid.
Vitamin B1 and B6 levels were significantly higher at 3 months after discharge that at admission (vitamin B1: 45.4 ± 12.2 vs. 33.7 ± 10.7 ng/ml, $P < 0.01$, vitamin B6: 11.2 ± 5.4 vs. 6.6 ± 2.9 ng/ml, $P < 0.05$). Furthermore, vitamin B1 and B6 levels were significantly higher at 3 months after discharge than at discharge (vitamin B1: 45.4 ± 12.2 vs. 31.5 ± 11.0 ng/ml, $P < 0.01$, vitamin B6: 11.2 ± 5.4 vs. 6.3 ± 3.7 ng/ml, $P < 0.05$).
The proportion of patients with a deficiency of serum WSVs were as high as 50% for vitamin B6 and vitamin C (5 patients each) at admission and 60% (6 patients) for vitamin B6 and 40% (4 patients) for vitamin C at discharge. Time-dependent changes in the proportion of patients with a deficiency of serum WSVs were statistically confirmed by the Friedman test for vitamin B6 ($P < 0.05$), but not for vitamins B1, B2, B12, vitamin C and folic acid. Therefore, the proportion of patients with vitamin B6 deficiency were compared between the measurement time points and were found to be significantly higher at admission and discharge (50% and 60%, respectively, $P < 0.05$) than at 3 months after discharge (10%).
CONCLUSION: Till date, most Japanese patients with complicated PUs have deficiencies in some WSVs in the early phase after the onset of PUs. Supplementation with WSVs should be considered for complicated PUs requiring dietary restrictions.

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P1115 EFFECT OF YOGURT CONTAINING POLYDEXTROSE, LACTOBACILLUS ACIDOPHILUS NCFM AND BIFIDOBACTERIUM LACTIS HN019: A RANDOMIZED, DOUBLE-BLIND, CONTROLLED STUDY IN CHRONIC CONSTIPATION

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INTRODUCTION: Constipation is a frequent complaint and the combination of a prebiotic and probiotics would have a potentially synergic effect on the intestinal transit. The present study therefore aims to investigate the combination of polydextrose (Litesse®), *L. acidophilus* NCFM® and *B. lactis* HN019 in a yogurt on intestinal transit in subjects who suffer from constipation
AIMS&METHODS: Patients with constipation were randomly divided into two groups, Control Group (CG) and Treatment Group (TG), and had to eat 180 ml of unflavored yogurt every morning for 14 days. Those in the CG received only yogurt, while the TG received yogurt containing polydextrose, *L. acidophilus* NCFM® (ATCC 700396) and *B. lactis* HN019 (AGAL NM97/09513)
RESULTS: There was a decrease in the colonic transit time (CTT) when comparing initial and final transit time. However, this reached only statistical significance for the treatment group (TG) (t-test, p=0.001). The subjects in the treatment group also had a shorter transit time at the end of the intervention compared to the control group (p=0.01).
CONCLUSION: The product containing yogurt with polydextrose, *B.* lactis HN019 and *L. acidophilus* NCFM® significantly shortened colonic transit time after two weeks. This was also a significant reduction colonic transit time compared to the placebo group.

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Keywords: Bifidobacterium lactis HN019, chronic constipation, Lactobacillus acidophilus NCFM

P1116 BOWEL FUNCTION AND DIGESTIVE SYMPTOMS DURING THE MENSTRUAL CYCLE

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INTRODUCTION: There is limited research which suggests that women experience variations in digestive discomfort and bowel function during the menstrual cycle. Harder stools are more likely during the luteal (premenstrual) phase with looser, more frequent stools during menstruation.
AIMS&METHODS: This series of studies examines bowel function and digestive discomfort during the menstrual cycle using data from an online UK survey of 1012 premenopausal women, representative of the female population for age and socio-economic status. It is corroborated by results from a prospective diary study of 57 women selected from the original survey, who completed online questionnaires for one whole menstrual cycle. 24 women using oral contraceptives were included in the prospective study to examine the effect of oral contraceptive use on bowel function. The Bristol Stool Form Scale was used in both studies to describe form and frequency of bowel movements during each phase of the menstrual cycle and other symptoms and behaviours including fibre intake were recorded in the online questionnaires.
RESULTS: Graphical data analysis was used to analyse the patterns of stool form across menstrual cycle phases. Only a third of women showed the typical pattern of bowel function during the menstrual cycle. More than 160 different patterns of stool form changes were observed during the cycle presenting a confusing and complex experience for many women. Use of hormonal contraceptive methods is associated with more stable stool form suggesting that female hormonal fluctuations do affect bowel function.
CONCLUSION: Greater awareness of cycle related fluctuations in stool form and bowel habits would help women to identify changes and alert them to possible underlying problems. Dietary strategies could be helpful in some cycle phases to aid stool form and reduce digestive symptoms.
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Keywords: Digestive discomfort, Menstrual Cycle, Oral Contraceptives

P1117 WHAT ABOUT THE COMBINED CONSUMPTION OF ETHANOL AND FRUCTOSE ON LIVER STEATOSIS AND HEPATIC METABOLIC PROFILE? 1H HRMAS SPECTROSCOPIC STUDY IN THE RAT LIVER.

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INTRODUCTION: Liver steatosis (LS) can precede steatohepatitis. Diets induce LS in rat: ethanol (EtOH) and high-fructose (HF) with insulinoresistance (IR). Non-alcoholic fatty liver disease patients often have high fructose supply (soft drinks) [1]. Little is known about the large consumption of beverages with fructose+ethanol, mainly in the young population. Inversely resveratrol (RSV) suppresses LS in fat-diet mice [2]. Liver metabolic profile was studied by ^{1}H HRMAS in rat eating combinations of HF, moderate EtOH and RSV.
AIMS&METHODS: 7wks-old male Wistar rats (n=60) were pair-fed (10wks, 10g/d$_*$100g body weight). Control: standard chow; HF: 60% fructose (instead of starch); EtOH: 11mmol/d$_*$kg body weight in drinking water; HF+EtOH; HF+EtOH+RSV: +30mg/l RSV force-feeding. At the 3rd, 6th and 10th wks, blood was withdrawal. A piece for histology was removed before livers freeze-clamping (N_2). NMR (Brucker AVANCE500 11.7T; 6min acquisition) was performed on 20mg liver.
RESULTS: HF or EtOH alone induced IR (normoglycaemia+hyperinsulinemia) from 3wks, partly counteracted by RSV. At 10wks, all HF groups had (i) macro- and micro- LS and inflammation, (ii) oxidative stress with plasmatic αtocopherol 2-fold higher (26.38±0.67µmol/l, $p<0.05$) than control (transaminases were normal). EtOH alone induced no histological or αtoco change. HF+EtOH increased interleukins ($p<0.001$ *vs* control). Histology was improved with RSV added to HF+EtOH. By HRMAS, the number of fatty acids (FA) were similar in EtOH (+5±2.7%) *vs* control, but increased in HF+EtOH (+23±4.7%), in HF (+42±5.3%) and HF+EtOH+RSV (+47±10%). In all HF groups, choline/Pcholine ratio increased (2.50±0.23 *vs* 1.35±0.06 in control and EtOH), correlated to αtoco (R^2=0.96).
CONCLUSION: NMR was in agreement with histology: HF led to steatosis and inflammation, moderate EtOH induced no change, except increase in IR and TNFα. In HF+EtOH, fructose effects were the largest. Chol/Pchol was increased by fructose supply (in contrast to EtOH alone) and underlined early membranes changes which could explain later functional impairments, perhaps linked to inflammation. Chol/Pchol changes could converge with the steatohepatitis seen in methionine/chol deficient diet [3] but also with change in protein expression involved in LS observed in Lieber-de-Carli diet [4]. IREB Grants.
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Keywords: Choline, Ethanol, Fructose, NMR, Steatosis

P1118 GASTROPARESIS RECOGNIZED BY THE GASTROPARESIS CARDINAL SYMPTOM INDEX (GCSI) ASSESSMENT, DOMINATING SYMPTOM AND METABOLIC CONTROL IN DIABETES AND IDIOPATHIC GASTROPARESIS

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INTRODUCTION: Gastroparesis predominantly occurs in diabetics as a result of long-standing disease, but also in otherwise healthy subjects in an idiopathic form believed to be due to a passing viral infection. Gastroparesis is cumbersome as the disease entails severe symptoms of nausea and vomiting in its idiopathic form and in diabetics an even worse situation with metabolic derangement.
AIMS&METHODS: The aim of the study was to identify clinical characteristics in order to predict gastroparesis in diabetes types 1 and 2, as well as in its idiopathic form.
Patients with diabetic and idiopathic gastroparesis were evaluated using the gastroparesis cardinal symptom index (GCSI) and dominating symptoms of gastroparesis. In diabetics, symptom scoring was evaluated against glycaemic control (A1c) as well as scintigraphic gastric emptying test. Patients were studied at a tertiary referral centre with symptoms suggestive of gastroparesis. Totally 120 patients (87 females, 33 males) were evaluated by scintigraphic measurement of gastric emptying and symptoms scored using the standardized GCSI as well as HbA1c for glycaemic control.
RESULTS: Of a total of 72 diabetic patients (type 1 58, type 2 14) with symptoms from the upper gastrointestinal tract, 63 were found to have a derangement of gastric emptying profile. Of these, 44 had gastroparesis with gastric retention $>60\%$ at 120 min or $>10\%$ retention at 240 min. Among these, there was relationship between gastric retention and GCSI >2.50 $r=0.43$, $p<0.01$). The dominating symptoms were stomach fullness (84%), followed by loss of appetite (60%) and nausea (55%). Only about one tenth had overt vomiting (9%). A severe finding among the gastroparesis diabetics was a greatly deranged A1c (>80 mmol/mol in 53%, and >10 mmol/mol in 11%). Only 5 diabetics displayed a rapid gastric emptying, displayed GCSI <2.66 and A1c $<6\%$, thus presenting a separate issue. The symptom profile of idiopathic gastroparesis did not differ from that in diabetics in terms of GCSI.
CONCLUSION: High global GCSI scores as well as stomach fullness and loss of appetite and nausea scores correlated with gastroparesis. In addition, high A1c supports the presence of gastroparesis, most likely due to a long-lasting postprandial hyperglycemia. The GCSI symptom score can be used along with dominant symptoms such as an indicator of gastroparesis.
Disclosure of Interest: None Declared
Keywords: diabetes mellitus, gastroparesis, gastroparesis cardinal symptom index, HbA1c

P1119 EVIDENCE OF BENEFICIAL EFFECTS OF MULTICOMPONENT PROBIOTICS CONSUMPTION ON PANCREATITIS-LIKE SYMPTOMS UPON LONG-TERM HYPOCHLORHYDRIA

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INTRODUCTION: Hypochlorhydria is a frequent pluricausal disorder of gastrointestinal tract (GIT), which is caused, in most cases, by chronic proton-pump inhibitors (PPI) or antacids consumption, *H. pylori* infection or atrophic gastritis [1]. Low stomach acidity is associated with a range of negative consequences, such as colonization of GIT by opportunistic microbiota favouring inflammatory processes both in GIT and associated organs, such as pancreas [2]. Oxidative stress is a non-specific mechanism leading to pancreatitis-like symptoms in these conditions. Cure of dysbiosis by probiotic nutrient additives can be an effective way for pancreatic protection upon long-term hypochlorhydria.
AIMS&METHODS: The **aim** of work was to establish the effects of multistrain probiotics preparation "Symbiter" on the state of rat pancreas upon long-term gastric hypochlorhydria.
All experiments were performed with non-strain white male rats. 28-day long abdominal injection of PPI omeprazole (14 mg/kg once a day) was used for gastric hypochlorhydria induction (second group). "Symbiter" was administrated daily *per os* (third group). Control animals were treated with water. Indices of lipid functional groups were selected as markers of oxidative stress development. Total lipids were extracted from the pancreas by standard procedure. In the obtained fraction the spectrums of lipid functional groups, such as hydroxyl (HG), carbonyl (CG), aldehyde (AG), methyne (MG), methylene (MLG) and phosphate (PG) groups, were studied with infrared Fourier-spectroscopy. It was also measured the amount of fatty acid cis- and trans-isomers (FACI and FATI, respectively). The rate of superoxide (SO) and hydrogen peroxide (HP) generation, as well as xanthine oxidase activity were determined in pancreatic cells by established assays.
RESULTS: It was established the escalation of SO, HP, FATI, HG and AG content, as well as XO activity after prolonged injection of omeprazole – on 53%, 35%, 85%, in 3 times and on 25%, respectively. At the same time, FACI, CG, MG, MLG, and PG levels were lower than control on 58%, 31%, 20%, 64% and 50%, correspondingly.
The quantity of SO, HP, HG, FATI, AG and XO activity in animals of third group were lower on 17%, 43%, 39%, 25%, 99% and 28%, while level of FACI, CG, MG, MLG and PG was higher on 60%, 22%, 15%, 71% and 50% in relation with the second group animals.
CONCLUSION: So, there is clear evidence of beneficial action of multicomponent probiotic "Symbiter" on the state of rat pancreas upon conditions of experimental long-term hypochlorhydria suggesting the capability of probiotics to restore impaired functions of not only gut, but also associated organs.

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Disclosure of Interest: None Declared
Keywords: Hypochlorhydria, oxidative stress, pancreas, probiotics

P1120 EFFECT OF THE BITTER AGONIST DENATONIUM BENZOATE ON GASTRIC ACCOMMODATION IN RATS

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INTRODUCTION: Intragastric administration of bitter receptor agonists decreased food intake in mice (Janssen *et al.*, PNAS 108(5): p2094). In man, the bitter agonist denatonium benzoate (DB) decreased nutrient tolerance and impaired gastric accommodation (Verschueren *et al.*, Gastroenterol 2012 142(5) S294).
AIMS&METHODS: Our aim was to study the effect of DB on gastric accommodation in conscious rats.
Nine Wistar rats were surgically equipped with a gastric fistula and given 1 week for recovery and adjustment to restraint. After an overnight fast, the rats were treated with a subcutaneous injection of the NO-donor molsidomine (M, 20 mg/kg) or vehicle (0.9% NaCl). After 1 hour, animals received DB (70 mg/kg) or placebo (PLA, water) via intragastric gavage. The fistula was then opened and connected with a manometry probe to measure intragastric pressure (IGP, a surrogate marker of gastric accommodation) as well as an infusion system to directly administer a liquid meal into the stomach, and rats were positioned in a restraint device. Fifteen min after gavage, meal infusion (Nutridrink®, 150 kcal/100ml) was initiated at a constant rate of 0.5 mL/min for 20 min. IGP was recorded before and during nutrient infusion. Comparisons of 1) DB vs PLA, and 2) M vs M+DB, were made separately using a linear mixed model analysis with time and treatment as factors. Results were compared in 5-minute blocks between groups (0-5 min, 6-10 min, 11-15 min, 16-20 min), with Bonferroni correction for multiple testing.
RESULTS: In all groups, IGP initially increased in response to nutrient infusion. For comparison 1, DB and PLA had similar IGP increases initially, then diverged after 15 minutes, with increasing IGP in the DB compared to a plateau effect in the PLA group ($p=0.011$). This suggests that the accommodation response is attenuated in response to DB. IGP values between molsidomine and molsidomine + DB did not differ ($p>0.1$ for all 5-min blocks).
CONCLUSION: Bitter treatment increases IGP during nutrient infusion, suggesting an attenuation of the gastric accommodation response in rats. DB did not affect IGP in the presence of a NO-donor, suggesting either a modest effect or a mechanism that does not involve NO pathways.
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Disclosure of Interest: None Declared
Keywords: bitter, gastric accommodation, rats

P1121 EFFECT OF SOY MILK ON GASTRIC ACCOMMODATION, GASTRIC EMPTYING, SATIATION AND SATIETY IN SUBJECTS WITH DYSPEPTIC SYMPTOMS

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INTRODUCTION: Gastric accommodation (GA) is impaired in 40 % of patients suffering from functional dyspepsia, and is associated with early satiety and weight loss. Consumer research suggests that the public perceives soy milk as easier to digest and gives a lighter feeling in the stomach compared to cow's milk. Previously we showed that gastric emptying (GE) of soy milk was faster than cow's milk in healthy subjects, but this was not accompanied by a change in GA or differences in sensation during and after the milk meal.
AIMS&METHODS: We aimed to investigate the effect of soy milk on GA, GE and abdominal symptoms compared to cow's milk in subjects with dyspeptic symptoms.
16 patients (6 male, age 33 ± 3 yrs, BMI 23.8 ± 1.1 kg/m^2) with uninvestigated dyspeptic symptoms (postprandial fullness, early satiation, epigastric pain or burning, for at least 3 months) were recruited. After an overnight fast, a manometry probe to measure intragastric pressure (IGP) and an infusion catheter were positioned through the nose into the proximal stomach. After a stabilization period, cow's milk (45 kcal/100 ml) or soy milk (38 kcal/100 ml) was infused into the stomach at a constant speed (60 ml/min). At 1-minute intervals, subjects scored their satiation on a scale graded from 0–5. At 5-minute intervals subjects scored epigastric symptoms (hunger, expected amount to eat, satiation, bloating, fullness, nausea, belching, abdominal cramps and pain) using a visual analogue scale (VAS). Milk infusion was stopped at maximal satiation. We analyzed volume intake, maximal IGP decrease (nadir IGP) and time to nadir using paired t-test. GE was tested using the ^{13}C-octanoic acid breath test. Breath samples were collected before and every 15 minutes after the milk infusion started until 6 hours thereafter. Samples were measured by isotope ratio mass spectrometry and GE half-time was analyzed using paired t-test. Symptoms were scored using a VAS.
RESULTS: Subjects tolerated similar volumes of both milks (997 ± 73 ml cow milk vs. 1064 ± 92 ml soy milk; $p=0.36$). During infusion, nadir IGP ($p=0.9$) and time to nadir ($p=0.6$) were not different between milk types. Satiation scores during milk infusion were not different. GE of soy milk was significantly faster

than GE of cow's milk (GE half-time 82.4±5.9 min vs. 139.9±13.3 min, respectively; p=0.026). No differences were seen in symptom scores during and after milk infusion.
CONCLUSION: Soy milk empties faster compared to cow's milk, but does not affect GA or abdominal sensation in uninvestigated dyspepsia.
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Disclosure of Interest: S. Verschueren: None Declared, C. Andrews: None Declared, A. Maes: None Declared, K. Verbeke: None Declared, J. Tack Financial support for research from: Unrestricted scientific grant from Alpro
Keywords: gastric accommodation, hunger, satiety, soy

P1122 DIETARY INTERVENTION WITH A DIET RICH IN ARABINOXYLANS AND RESISTANT STARCH MODULATES T-CELL ACTIVATION ESTIMATED BY CD25 EXPRESSION IN METABOLIC SYNDROME

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INTRODUCTION: Arabinoxylans and resistant starch are substrates known to stimulate colonic short chain fatty acids production of which especially butyrate is suggested to exert an anti-inflammatory function in the colon. Metabolic syndrome is characterized by abdominal obesity, dyslipidaemia, elevated blood pressure and hyperglycaemia and is associated with a chronic low-grade colonic inflammation.
AIMS&METHODS: To investigate a four-week dietary intervention with arabinoxylans and resistant starch on mucosal T-cell activation estimated by their CD25 and CD69 expression in subjects with metabolic syndrome.
Methods: Nineteen subjects with metabolic syndrome were included in the study and followed the dietary intervention. Sigmoideoscopy with tissue samples was performed before and at the end of the four-week dietary intervention. Lamina propriae cells were isolated using enzymatic digestion of mucosal specimens. Isolated cells were stained for CD3 (T-cell marker), CD4, CD25 and CD69 expression.
RESULTS: T-cells showed decreased CD25 expression following a four-weeks intervention (p=0.01) but had unchanged CD69 expression. Also CD4+ T-cells and non-CD4+ T-cells showed decreased CD25 expression but unchanged CD69 expression (p=0.05 and p=0.009, respectively).
CONCLUSION: Dietary intervention with arabinoxylans and resistant starch in subjects with metabolic syndrome seems to be associated with reduced activation in intestinal mucosal T-cells.
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Disclosure of Interest: None Declared
Keywords: colon, Metabolic syndrome, Nutrition

P1123 THE EFFECT OF ADJUVANT SYNBIOTIC COMBINATION ON INDUCTION OF REMISSION IN PATIENTS WITH MILD-MODERATE ULCERATIVE COLITIS

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INTRODUCTION: Ulcerative colitis (UC) is a chronic disease that characteristically has a relapsing and remitting course. Probiotics might possibly induce remission in the treatment of active UC. Aims of our study were to assess the efficacy of Probiotic Gold NBL® (*Lactobacillus acidophilus, Lactobacillus rhamnosus, Bfidobacterium bifidum, Enterococcus faecium, Bfidobacterium longum,* fructooligosaccharide, lactulose) on clinical response in patients with active UC.
AIMS&METHODS: Twenty-two patients (mean age 42±13 (17-67), M/F: 13/9) were enrolled. These patients had clinical and endoscopy score 4 and above levels. All patients received mesalazin 4 grams/day plus Probiotic Gold NBL® one sachet per day. After 8 weeks of treatment, patients were re-assesed for clinical and disease activity. We have compared these data with a historical cohort of 16 UC patients.
RESULTS: Among 22 patients, 2 patients did not have endoscopy control, and the remaining 20 patients were re-assesed after 8 weeks. Two patients had flare-up under probiotic plus mesalazin treatment in the first week and these patients were switched to steroid treatment. Intention-to-treat analysis (ITT) showed that, complete remission was achieved in 81.1% (18/22) vs 62.5% (10/16) (p<0.01) in study and control groups, respectively. Partial remission was achieved in 9% (2/22) vs 31.2%(5/16) (p<0.01) and non-response was seen in 9% (2/22) vs 6.25%(1/16) (NS) in study and control groups, respectivey. The mean decrease in the clinical activity score was 5.89±1.22 vs 4.35±1.56 (p=0.044), respectively.
CONCLUSION: Our study demonstrated that Probiotic Gold NBL® is effective in achieving clinical responses and remissions in patients with mild-to moderately active UC, further supporting the potential role in UC therapy.
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Disclosure of Interest: None Declared
Keywords: probiotics, ulcerative colitis

P1124 EARLY PEAK OF HYDROGEN DURING LACTOSE BREATH TEST PREDICT INTESTINAL MOTILITY

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INTRODUCTION: Lactose breath test (LBT) is considered the gold standard for the diagnosis of lactose malabsorption. The test is considered positive for a peak over 20 ppm above the baseline. Some patients (pts) showed a rapid peak between 30 and 90 after lactose ingestion. Aim of the these study was to evaluated the predictive value of an early peak during a LBT and an accelerated orocecal transit time (OCTT).
AIMS&METHODS: From January to September 2012 we retrospectively analyzed all pts who referred to our Gastroenterology unit for IBS who were submitted to a LBT with an early peak (between 60-90 min) and to a lactulose BT. We considered a normal OCCT a peak of hydrogen ≥10 ppm between 40- 170 min after lactulose load. The breath test were performed according to the guidelines. Correlation between LBT and OCTT was evaluated by Pearson score.
RESULTS: 93 pts (65F/28M mean age 47+/-6 yrs) with a positive LBT who performed also a lactulose breath test were analyzed: 46 pts (32F/14M; mean age 48+/-6 yrs) with early peak of H2 (≥ 20 ppm) were used as case, and 47 pts matched for sex and age with peak of H2 (≥ 20 ppm) after 90 min were used as controls. 71% (33/46) of the group with an early peak showed an accelerated, 17% (8/46) a normal and 10% (5/46) a delayed OCTT. Meanwhile, in control group 40.4% (19/47) showed a normal, 57.5% (27/47) a delayed and just 1 pts (2.1%) an accelerated OCTT. The specificity and sensibility of LBT for an accelerated OCTT was 97.9 and 71.7% respectively. The positive predictive value of LBT for an accelerated OCCT is 97.1%; the negative predictive value is 78 %. There is a significant correlation between LBT and OCTT (p<0.05)
CONCLUSION: The presence of an early peak of H2 between 30 and 90 min after the ingestion of 25 gr of lactose could predict the presence of an accelerated OCTT in 97% of pts. If confirmed by further study, in this subset of pts lactulose breath test for evaluating OCTT could be avoided.
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Disclosure of Interest: None Declared
Keywords: breath test, lactose intolerance, orocecal transit time

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00
POSTER PLUS VIDEO III – Poster Area

P1125 COMBINATION OF ENDOSCOPIC LITHOTOMY AND EXTRACORPOREAL SHOCK-WAVE LITHOTRIPSY OR ELECTROHYDRAULIC LITHOTRIPSY FOR CHRONIC PANCREATITIS

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INTRODUCTION: The efficacy of extracorporeal shock wave lithotripsy (ESWL) electrohydraulic lithotripsy (EHL) is well documented for the treatments of chronic pancreatitis lithiasis when endoscopic lithotripsy failed. To evaluate the efficacy of the combination of endoscopic lithotomy and ESWL or EHL for the treatment of pancreatic duct stones, we retrospectively evaluated the patients with symptomatic pancreatic duct stones that was treated at our institution.
AIMS&METHODS: Standard ERCP was performed for the treatment of pancreatic duct stones, and ESWL was considered in cases with endoscopically unremovable stones. If the ESWL and endoscopic lithotomy combination failed, EHL and ESWL on an outpatient basis was performed and was considered a second attempt. The Spyglass peroral pancreatoscopy system has been used for EHL since 2010 in our hospital. X-Ray guided EHL (using a 7Fr. outer sheath) was performed when a Spy glass system delivery catheter (10Fr) was difficult to insert.
RESULTS: A total of 98 patients with symptomatic chronic pancreatitis underwent endoscopic lithotomy for chronic calcific pancreatitis at our center between May 2005 and December 2012 (24 cases in single lithiasis group, 74 cases in diffuse lithiasis group). Fragmentation was successful in 80 (81.6%) patients (single 17 vs diffuse 63; p = 0.87). The successful results were obtained in 67 of 98 patients (74.5%) by combination treatment, 7 of 14 patients (7.1%) by EHL (Spyglass system 3, X-Ray guided EHL 4), and 6 of 6 patients (6.1%) by ESWL on an outpatient basis, respectively. Sixteen patients were out of indication, 12 cases had radiolucent stones, and 4 cases failed in selective pancreatic duct cannulation with radiolucent stones. Seventy-four of 92 patients (90.2%) with painful lithiasis reported complete pain relief and no analgesic use (single 17 vs diffuse 57; p = 0.89). On multivariate analysis, negotiating the guidewire through a severe MPD stricture was significantly associated with a higher rate of stone fragmentation (p = 0.0003).
CONCLUSION: EHL using the Spy glass system was effective in cases with MPD stricture when an ENPD or Endoscopic pancreatic stenting (EPS) could be placed and visualised directly. Combination EL and ESWL is safe and effective for the treatment of pancreatic duct stones. However further prospective randomized studies are needed to perform.
Disclosure of Interest: None Declared
Keywords: Chronic Pancreatitis, Electrohydraulic lithotripsy, Extracorporeal shock wave lithotripsy

P1127 ENDOCOPIC APPLICATION OF THE OTSC MACROCLIP: INDICATIONS AND OUTCOMES - A 3 YEAR EXPERIENCE

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INTRODUCTION: The OTSC (OVESCO, Germany) is a novel endoscopic device successfully applied for severeGI bleeding, perforations, fistulas and experimental NOTES procedures.
AIMS&METHODS: We performed a retrospective analysis of all OTSC applications from February 2009 to October 2012 using our endoscopy database, hospital PIS and individual patient records. IRB was obtained for unpersonalised evaluation of patient's data and outcome.

RESULTS: Eighty-four patients [median 71 y (2-98) 34 women, 50 men, ASA 2-4] were treated with 101 OTSC clips (12/6 T-type: n=75; 14/6 T-type: n=26). In 59 patients (69 %), OTSC was placed to treat digestive bleeding: 41 severe upper GI bleeding (48.8 %), 3 lower GI bleeding (3.6 %), 12 patients after successful primary haemostasis (14.3 %) for prevention of re-bleeding in high risk situations after EMR/ESD. In 38/41 patients, upperGI bleeding was related to peptic ulcer disease, in 2 cases to a malignant gastric ulcer (1 adenocarcinoma, 1 lymphoma). One patient bled from a muscle laceration after balloon dilation for achalasia. Among the 44 patients with bleeding, 13 (29.5%) received an OTSC after failure of standard haemostasis (haemoclip or injection). OTSC placement allowed permanent haemostasis in 38/44 (86.3%). Despite OTSC application, 5 patients (11.4 %) died because of persistent or recurrent severe bleeding.
In 25 cases (29.7 %) the OTSC was used for closure of a wall defect: In 7 patients (8.3 %) OTSC was placed to treat a perforation, with successful closure in 4 (57.1%). In 18 patients OTSC was used for prevention of a secondary defect after EMR/ESD (21.4 %) with closure of the defect in all cases. In 3 patients with fistula, closure was achieved in all cases. Complications related to OTSC placement occured in 3 patients: In 1 case, the grasper was caught within the teeth of the OTSC due to an insufficient retrieval of the grasper before firing the OTSC. In 1 case, the clip was prematurely released in the stomach due to adhesion of the traction string to the grasper and uneventfully retrieved. One patient with right colon perforation after EMR underwent successful local treatment using two 14/6 t OTSC devices. However, a secondary perforation occurred due to a narrow diverticulosis of the sigmoid colon and patient underwent uneventful sigmoid resection.
CONCLUSION: The OTSC system is a promising new tool for the management of GI emergencies and complications. Further clinical experience will help to identify optimal indications.
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Disclosure of Interest: None Declared
Keywords: closure of perforation, haemostasis, OTSC (over-the-scope clip)

P1128 THE NEW TECHNIQUE OF HYBRID APC FOR THE ABLATION OF BARRETT'S ESOPHAGUS: INTERMEDIATE RESULTS OF A PILOT SERIES

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INTRODUCTION: Thermal ablation techniques such as radiofrequency ablation (RFA) or argon plasma coagulation (APC) have been shown to be effective in Barrett's esophagus. However, stricture formation is reported to occur in 5-15% of patients treated. Therefore, new ablation techniques are under evaluation.
AIMS&METHODS: The aim of the present trial was to evaluate efficacy and safety of the new technique of Hybrid APC which is a combination of APC with submucosal injection of sodium chloride pior to ablation.
Patients who had undergone endoscopic resection of early Barrett's neoplasia (adenocarcinoma or high-grade dysplasia) and in whom a Barrett's remainder of at least 1 cm in length was present were included into the present pilot series. After submucosal injection of sodium chloride in a dilution of 0.9% using a water-jet system (ERBE JET 2, Erbe Elektromedizin, Tuebingen, Germany), the remaining non-neoplastic Barrett's mucosa was ablated dynamically using APC with a wattage of 50 to 60 (pulsed effect 2). Three months after completion of Barrett's ablation, upper GI endoscopy was carried out (1) for evaluation of treatment-related strictures and (2) for taking 4-quadrant biopsies from the whole area of the former Barrett's segment including the Neo-Z-line.
RESULTS: A total of 60 patients were included into the study (male 55 (92%), female 5 (8%)). The mean age of patients was 62.2 years (range 42-78). 5/60 patients were excluded from analysis (insufficient wound healing during ablation / wrong inclusion). 19 of the 55 remaining patients were still under ablation treatment at the date of analysis. In 36 of the 55 patients complete macroscopic Barrett's ablation was achieved after a mean of 3.4 treatment sessions (range 1-10). In 17 patients, 3-month follow-up was obtained, and the rate of histologically complete Barrett's ablation was 88% (15/17). In none of the patients stricture formation was observed after hybrid APC.
CONCLUSION: According to the intermediate results of this pilot series on Hybrid APC for Barrett's ablation, this new ablation technique appears to be effective and safe, with a stricture rate that may be lower than rates known from conventional ablation techniques. Randomized trials comparing the various ablation techniques available would be helpful to clarify the value of Hybrid APC.
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Keywords: Argon plasma coagulation, Barrett's esophagus, Thermal Coagulation

P1129 PER ORAL ENDOSCOPIC MYOTOMY: THE FIRST EXPERIENCE IN THE CZECH REPUBLIC

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INTRODUCTION: Peroral endoscopic myotomy (POEM) is an endoscopic alternative to laparoscopic myotomy. This promising procedure is still considered experimental. Herein, we report the short-term results of the prospective study of POEM in the Czech Republic.
AIMS&METHODS: A single center study. POEM procedure was conducted under general anesthesia. For mucosotomy, dissection and myotomy, a triangle knife was used. We analyzed short term results of 13 consecutive patients (8 female, 5 male, mean age 46 years, range 22-71). A 3-months follow-up was completed for all patients. The primary outcome was symptom relief at 3 months defined as an Eckhard score ≤ 3. All patients had a diagnosis of achalasia based on endoscopic, manometric (high resolution or standard manometry) and radiologic examinations. Seven patients (53%) had undergone treatment previously with limited success (4x balloon dilatations (BD), 3x BD with botulinum toxin (BT) injection).
RESULTS: *A. PROCEDURE*: POEM was completed in all patients. The mean length of procedure (LOP) was 96 ± 12 minutes. The mean myotomy length was $9{,}6 \pm 1{,}3$ cm (range 8-12). In two patients (1x after previous BD and 1x after previous BD+BT), an inadvertent mucosotomy occurred in the gastric cardia. These minor complications were repaired intraoperatively with clips. In 5 patients (38%), capnoperitoneum was decompressed by using a standard venous cannula. One patient had radiologic evidence of minor leakage at the mucosotomy site which resolved spontaneously. No serious intraoperative or postoperative complications occurred and all patients were dismissed 2nd or 3rd postoperative day.
B. TREATMENT RESULS: Three months after POEM, treatment success (Eckhard score ≤ 3) was achieved in 12 patients (92%; mean score pre- vs. post-treatment $6.6 \pm 1{,}6$ vs. $0{,}8 \pm 0{,}7$; $p < 0{,}001$). The mean percentage of overall improvement was $88\% \pm 9$. Manometric parameters (IRP for HRP or LES pressure for standard manometry) improved in 12 patients. One patients (8%) developed minor reflux symptoms (heartburn). This patients has been treated with a proton pump inhibitor on demand. A pathological gastro-esophageal reflux (DeMeester score >14) was detected in 6 (46%) patients.
CONCLUSION: POEM is a safe and effective treatment modality in patients with achalasia with excellent short term results. There is a significant (though almost) asymptomatic reflux postoperatively in 46% of patients in 3-months pH metry studies.
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Disclosure of Interest: None Declared
Keywords: achalasia, POEM

P1130 CLINICAL AND PROCEDURAL FACTORS PREDICTIVE OF COMPLETE SYMPTOMS RELIEF AFTER PERORAL ENDOSCOPIC MYOTOMY (POEM). RESULTS OF A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Peroral Endoscopic Myotomy (POEM) is gaining international consensus in the treatment of achalasia. The severity of achalasia is summarized by Eckardt score (ECK), that includes data on dysphagia, regurgitation, pain and weight loss. Clinical success is usually defined by ECK < 3. The reasons why some patients have residual symptoms after treatment (ECK >1) and other do not is unknown.
AIMS&METHODS: Aim of this study is to identify clinical, manometric and procedural factors associated with complete symptoms relief (CSR) after POEM. Sixty-three patients underwent POEM in our tertiary referral center between 2011 and April 2013. Fifty-three patients (18 men, mean age 46 years) completed a 3-month follow-up (mean 8 months) and were included in the study. Patients underwent scheduled follow-up 3, 6, 12, 18 and 24 months after POEM. Demographics (sex and age), data on the clinical history (symptoms duration, preoperative ECK and previous treatments), the esophageal manometry (preoperative and postoperative basal LES pressure, achalasia type and absolute variation of basal LES pressure after POEM) and the procedure (length of myotomy) were prospectively collected and analyzed. ECK was used to evaluate response to therapy. Chi-square and ANOVA test were used to identify factors related with CSR after POEM.
RESULTS: Forty-six patients had classic- type achalasia, 7 vigorous-type. Mean symptoms duration before POEM was 29 months (3-120 months). Nine patients had received previous endoscopic treatments. Mean preoperative basal LES pressure and ECK were 40.2 mmHg (11-97.4 mmHg) and 7.7 (4-11), respectively. Mean length of myotomy was 11.6cm (7-17cm). POEM was clinically successful in 98% patients (ECK < 3). No major complications occurred. After POEM, mean basal LES pressure decreased by 23.4mmHg; 29 patients had CSR (ECK=0), 24 had some residual symptoms (ECK > 1).
At univariate analysis CSR was positively associated only with the duration of symptoms before POEM (35 months (ECK 0) vs 21 months (ECK >1), p=0.05). Variation of the basal LES pressure was substantially higher in the CSR group (30.2 mmHg vs 19.0 mmHg, p=0.07). CSR was not associated with sex, age, preoperative ECK, preoperative and postoperative basal LES pressure, previous treatments, vigorous-type achalasia
CONCLUSION: POEM procedure is associated with very good mid-term outcomes. Treatment failure occurred in 1 patient (2%) only, but mild residual dysphagia remained in up to 43% of patients (ECK $>1<3$). CSR may be associated with the duration of symptoms before treatment
Disclosure of Interest: None Declared
Keywords: Achalasia, dysphagia, manometry, Peroral Endoscopic Myotomy (POEM), POEM

P1131 FLEXIBLE ENDOSCOPIC TREATMENT OF ZENKEŔS DIVERTICULUM: A SAFE AND EFFICIENT METHOD

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INTRODUCTION: Zenkeŕs diverticumlum (ZD) is a cause of dysphagia and can cause serious complications such as aspiration pneumonia and malnutrition. Treatment is usually surgical or by rigid endoscopic diverticulotomy.
AIMS&METHODS: We present the results of a serie of patients treated with ZD flexible endoscopic mucomyotomy using an electric generator, as a forceps, which allows vessel sealing, autologous and permanent, before the section of the septum between the diverticulum and the esophagus, which prevents bleeding and tissue dissection. (Ligasure, Valleylab, Boulder, CO).
RESULTS: Prospective study. 27 ZDs mucomyotomies from may 2010 to april 2013 in 24 patients: 17 males and 7 females, median age 74.8 years (54-92). All with dysphagia (71% solids, 25% mixed and 4.2% for liquids) and other symptoms as regurgitation 42%, chronic cough 21%, aspiration pneumonia 12.5% or weight loss 12.5%. Mean length of ZD was 23 mm. Under propofol sedation a wire is housed in the esophagus to facilitate isolation of the diverticular septum with placement of a rubber bivalve diverticuloscope (Cook Medical) previously to his section with Ligasure device inserted through the diverticuloscope. Each patient received an average of 1.3 cuts/ session (1-3). After the procedure, one or more clips (Boston Scientific®) was placed in 70% of cases with profhylactic sense but two: to sealling a small perforation or to hemostasis in the other. Immediate complications: two mild (moderate cervical pain and minimun bleeding easily controlled with a clip) and a major complication (pneumomediastinum secondary to small perforation without require surgery) and no subsequent complications. The procedure was entire ambulatory except in the two patients who suffered severe neck pain or pneumomediastinum. A month after the procedure 23 of 24 patients reported no dysphagia. During the follow-up (18.8 months, 1-36) there were two recurrences: one month early, after a slight initial improvement, and another in the form of regurgitationat 8 months. In both cases there was a new session mucomiotomía getting a poor result in the first case, she was a woman of 92 years in which neither third session later got the resolution of her dysphagia because it was associated a severe dysmotility, and in a male with a diverticulum larger than 3 cm were treated effectively in a second session.
CONCLUSION: The flexible endoscopic mucomyotomt of ZD with Ligasure device provides a safe and effective treatment of Zenker's diverticulum. The use of this technique, usually ambulatory, it is probably most cost-effective than conventional surgical treatment.
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Disclosure of Interest: None Declared
Keywords: flexible endoscopic mucomyotomy, vascular sealing device, ZENKER DIVERTICULUM

P1132 A NEW DEVICE TO EXPEDITE ENDOSCOPIC SUBMUCOSAL DISSECTION PROCEDURES: A RANDOMIZED ANIMAL STUDY OF EFFICACY AND SAFETY

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INTRODUCTION: Endoscopic Submucosal Dissection (ESD) is a recognized method for the curative treatment of superficial neoplasia, but its use is limited by lengthy procedures and the lack of versatility of existing knives. We developed a prototype ESD device with the ability to work as a needle, as a hook or as a "scythe". This new device was compared to regular ESD knives in a randomized animal study.
AIMS&METHODS: Eight pigs (4 pigs in the serie 1 and 4 pigs in the serie 2) underwent 2 gastric ESD procedures each, similar in size and difficulty, one with a standard ESD device (Dual Knife, Olympus in serie 1, and FlushKnife 1.5mm, Fujifilm Corporation in serie 2) and the other with the new device (prototype 1 in serie 1, and prototype 2 in serie 2, with additionnal features as a flushing port and a modified tip). The order and location of each ESD, as well as the performing operator, were randomized. Primary judgment criterion was safety of procedures. Overall and submucosal dissection procedure times were measured. Time to surface ratios were measured and estimated for ESDs larger than those performed. Histopathology of the resected tissue and remaining stomach was done after each experiment.
RESULTS: No complication was observed throughout the study and all resections were completed en-bloc and uneventfully. The submucosal extension of resections was similar with both the standard and the new devices. Table A shows characteristics of gastrics ESDs in the serie 2. A comparison of time-consumption between groups did not show statistically significant differences, but a dramatic reduction of procedure duration was observed in some procedures with the new device; based on observed data, a potential time-saving of up to 66% was anticipated, with a relatively short learning curve.
CONCLUSION: This new versatile device proved to be as safe as regular ESD knives, and seems likely to help reducing procedure durations.
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Disclosure of Interest: S. Leblanc: None Declared, A. Brehm Consultancy for: Medwork Medical Products, A. Rouquette: None Declared, F. Prat: None Declared
Keywords: animal study, Endoscopic submucosal dissection (ESD)

Table: P1132

N° animal		Type of ESD device*	Circular Incision Time (min)	Submucosal Dissection Time (min)	Overall Dissection Time (min)	Lesion Diameter (Max x min, mm)	Lesion Area** (mm^2)	Time to Surface Ratio (min/cm^2)
Series 2	**5**	Prototype 2	3	25	28	30x20	490.62	5.70
		Regular	5	23	28	30x20	490.62	5.70
	6	Regular	6	31	37	36x25	730.24	5.07
	Prototype 2	4	15	19	43x35	1193.98	1.60	
	7	Prototype 2	5	11	16	38x34	1017.36	1.57
	Regular	10	31	31	35x30	829.15	3.74	
	8	Regular	7	18	25	28x28	615.44	4.07
	Prototype 2	4	18	22	28x26	572.26	3.84	

P1133 BLUE LASER IMAGING (BLI) FOR DETERMINING EARLY GASTRIC CANCERS

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INTRODUCTION: Blue LASER Imaging (BLI) is a new endoscope system with two semiconductor lasers as a light source instead of xenon lamp. BLI might enhance images of the irregular mucosal structures and micro-vessels of neoplasia. BLI could be considered as a more clinically useful endoscopy system in detection and diagnosis for gastrointestinal neoplasia including gastric cancer.
AIMS&METHODS: This study aimed to evaluate the usefulness of BLI observation for early gastric cancer. The first 7 cases of BLI observation for early gastric cancers in our institution were enrolled and analyzed retrospectively in this study. The procedures were performed using BLI system (LL-4450, Fujifilm Co., Tokyo, Japan) and an endoscope (EG-L590WR). Written informed consents for chromo-endoscopy examination and endscopic submucosal dissection (ESD) were received from all patients. All ESD were attempted under deep sedation using propofol. Three different type of endoscopic images using BLI, white light mode (WL) and white light mode after indigo-carmine dye-spray(IC) were obtained at just prior to ESD. Afterwards ESDs were performed. The images obtained by each method were ranked on the basis of the ease of recognition of demarcation using a 4-point system (1: unclear, 2: visible, 3: good, 4: excellent).
RESULTS: Mean tumor size and resection size were 19mm and 33mm, respectively. All lesions were able to be recognized and removed en bloc. All tumors were diagnosed as differentiated-type of early gastric cancer and as curative histopathologically. Further, the lateral and vertical margins of all specimens were free of neoplasia. The mean score of BLI images was significantly higher than that obtained from WL images (3.7 and 2.4, respectively, $p<0.05$). There was no significant different between the mean score of BLI images and IC Images. However, the scores of BLI images were higher than IC images in tumors located anterior wall of lower third where is difficulty in viewing because of retained indigo-carmine.
CONCLUSION: BLI appears to be a feasible endoscopy system to determine differentiated-type of gastric cancerous lesions.
Disclosure of Interest: None Declared
Keywords: Gastric cancer, image enhanced endoscopy, laser

P1134 THE "SPEEDBOAT": A NEW MULTI-MODALITY INSTRUMENT FOR ENDOSCOPIC RESECTION IN THE GASTROINTESTINAL TRACT.

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INTRODUCTION: Large sessile or flat intestinal lesions >2cm are optimally removed en-bloc for accurate histology and complete resection. Current

submucosal dissection devices are technically challenging to use, resulting in long and sometimes incomplete procedures with a relatively high risk of major complication. We describe, a simple to use, multi-modality endoscopic device (''Speedboat'') for wide-field, en-bloc mucosal resection.
AIMS&METHODS: The 'Speedboat' cuts in forward, lateral and oblique planes using bipolar radio frequency (RF) cutting, provides haemostasis with microwave coagulation and incorporates a retractable needle for submucosal injection and tissue irrigation. The instrument blade has an insulated 'hull' to prevent thermal injury and the device catheter is partially torque stable allowing rotation and orientation of the hull to protect the underlying muscularis propria. The electrosurgical generator is comprised of 2 power sources, one operating at 400KHz (RF) and the other at 5.8GHz (microwave).
Speedboat submucosal dissection technique (SSD) was performed and video recorded on 4 consecutive 60kg pigs. Mucosal areas to be resected were marked prior to submucosal injection. The mucosa was then circumferentially incised and resected by SSD. The time taken to complete resection, complications encountered and power settings used were recorded. Immediately after the procedure, the animals were euthanized, and the resection defects measured and assessed histologically.
RESULTS: Eight consecutive resections were performed (2 per animal), 7 in the colorectum and 1 in the antrum of the stomach. The median time to complete a resection was 37 minutes range (30-60 minutes) using RF cutting 24W, voltage circa 300Vrms. Median defect size (longest diameter) was 53.5mm, range 40-80mm. Microwave coagulation was applied for either minor bleeding or visible vessels on 32 occasions (mean energy 7.5W). An endoclip was used once to control arteriolar bleeding but no other haemostatic device was required. There were no perforations and histology showed an intact and viable muscle layer with some remaining submucosa in all cases.
CONCLUSION: This initial evaluation of the ''Speedboat'' suggests that it facilitates rapid and safe en-bloc mucosal resection in the large bowel and gastric antrum.
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Disclosure of Interest: B. Saunders Consultancy for: Creo MedicalLtd, Other: Intellectual Property Agreement, Z. Tsiamoulos Consultancy for: Creo Medical Ltd, L. Bourikas: None Declared, P. Sibbons Financial support for research from: Creo Medical Ltd, Consultancy for: Creo Medical Ltd, C. Hancock Shareholder of: Creo Medical Ltd, Directorship(s) for: Creo Medical Ltd
Keywords: polypectomy, submucosal, new technique, submucosal dissection, en bloc dissection

P1135 FOLLOW UP AFTER COMPLETE ENDOSCOPIC RESECTION OF SUBMUCOSAL INVASIVE COLORECTAL CARCINOMAS

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INTRODUCTION: The aim of this study was to evaluate the efficacy and outcomes of treatment by endoscopic resection (ER) of patients with colorectal carcinoma with submucosal involvement.
AIMS&METHODS: Datas of patients with endoscopically resected colorectal carcinoma with submucosal invasion from 2006 to 2012 were retrospectively reviewed. Submucosal invasion was classified according as the Paris classification[1]. Patients staged SM1 with poor prognostic factors (budding, poorly differenciated, embols) or SM2/SM3 were referred to surgery while SM1 patients were purposed for follow up.
RESULTS: 41 patients (16 female, median age = 30 yr [35-88]) were treated by ER for 43 colorectal adenocarcinoma with submucosal invasion (rectum=17, colon=26).
Median tumor size was 30mm (range 10-50mm). Endoscopically complete resection rate was 100%, En bloc in 51%. Complications occurred in 14% (hemorrhages=4, perforations=2) and all were managed conservatively.
Histological examination showed adenocarcinoma in all cases, poorly differenciated in 0%. Budding, vascular or lymphatic embols was found respectively in 5%, 11% and 2%. Clear deep resection margins were found in only 58%. Lateral resection margins was free in 77% of evaluable specimen (only after en bloc resection). Submucosal invasion was classified SM1, SM2 or SM3 respectively in 32%, 28% and 5%. In 15 cases (35%), it was not possible to precise the level of submucosal invasion (SMx).
Surgical resection (27%) were performed for 11 patients (27%; 4 SM2, 6 SMx, 1 SM1 (budding+). No residual parietal tissue was found in all cases then postoperative staging was pT0N0 in 9 cases, pT0N+ in 2.
18 patients were followed during median follow up period of 27 months (range 4-73): SM1=9, SM2=3, SM3=1, SMx=5. Local recurrence was found in only 1 case (5%) treated endoscopically. No distant metastasis was observed.
12 patients were lost during follow up.
CONCLUSION: Endoscopic resection is a safe and efficient treatment for colorectal adenocarcinoma with submucosal invasion. Endoscopic examination of resection margins seems to be superior to the histopathological examination to predict R0 resection. A better knowledge of prognostic factors would improve identification of patients with risk of lymph node metastasis and thus to avoid unnecessary surgeries.
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Disclosure of Interest: None Declared
Keywords: colorecal cancer, en bloc resection, polypectomy,, submucosal invasive adenocarcinoma

P1136 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) UP TO 19 CM FOR 116 LARGE LATERALLY SPREADING TUMORS OR LOCAL RECURRENCES IN THE RECTO-SIGMOID, A SINGLE CENTER PROSPECTIVE TRIAL

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INTRODUCTION: After piecemeal-EMR of lateral spreading tumors (LST) larger than 2cm in the colo-rectum, recurrence rate is about 15%. Moreover, adenomas have a size-dependent progressive risk of malignant transformation. ESD provides an 'en bloc' specimen allowing a precise vertical and lateral pathological evaluation of resection margins. We report in the present study the indications, technical data and outcomes of 116 consecutive recto-sigmoid ESD.
AIMS&METHODS: PATIENTS & METHOD: From 03/2006 to 09/2012, all patients referred for treatment of LST in the rectosigmoid were included in a prospective cohort. Data were obtained for patient demographics, technical conditions of the procedure, follow-up and outcome.
RESULTS: 116 ESDs were performed in 113 patients (Median age 68 years (47-90 y) - 41 women, 72 men). In one patient, 3 lesions were resected in 2 sessions. 22 patients (19.4%) had previous treatment by EMR (n=15) or surgical full-thickness resection (n=7). 61 (52.6%) lesions were located in the rectum, 36 (31%) at the rectosigmoid junction and 19 (16.4%) in the sigmoid colon. En bloc resection was possible for 107 lesions (92.2%) with tumour-free margins confirmed in 80 (71.5%). In 5 (4,3%), pathological assessment was not possible due to thermal artefacts. The size of the formalin-fixed specimen ranged from 2.5x1.5 to 19x13.9 cm. Pathology revealed 11 adenocarcinomas (9.5%), 6 pTis (5.2%), 1 neuroendocrine tumor and 1 lymphoma. 40 lesions (34.5%) were low grade dysplasia adenomas and 56 (48,3%) high grade ones. Median follow-up was 550 days (17-2362 days). Two patients died from unrelated causes and 7 pT1 cancers underwent surgery. All other cases were followed conservatively, no recurrence being observed at control endoscopies. In one case (1.8%) a secondary 6 mm LGD adenoma was resected at month 12 close to resection scar. Four perforations during or following ESD (3.4 %) were managed conservatively. In one case, ESD was accompanied by a rare colonic methan gas explosion and the patient operated on for safety reasons (prior ESD specimen R0). 5 minor bleedings (4.3%) occurred, no patient requiring blood transfusion.
CONCLUSION: ESD appears to be an effective treatment for LST in the rectosigmoid, even in patients having previously undergone other therapeutic attempts. The high rate of lesions with high grade dysplasia or malignancy on the resected specimen (66%) highlights the importance of an 'en bloc' resection for lesions >3 cm. The low local recurrence rate of 0-3% underlines the potential value of the technique.
Disclosure of Interest: None Declared
Keywords: Colorectal cancer, en bloc resection, Endoscopic submucosal dissection (ESD), polypectomy, submucosal, new technique

P1137 THE LEARNING CURVE FOR IN-VIVO CHARACTERISATION OF SMALL COLONIC POLYPS: COMPARISON BETWEEN EXPERT AND TRAINEE ENDOSCOPIST

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INTRODUCTION: The learning curve for a new technology for real-time characterisation of small colonic polyps has not been determined. The ASGE has set performance criteria for 'resect and discard' and 'do not resect' policies for diminutive colonic polyps.
AIMS&METHODS: We aimed to assess the learning curve of a novel electronic in-vivo characterisation technology (Pentax i-Scan). Patients presenting for colonoscopy were prospectively recruited. Colonoscopies were either performed by an expert endoscopist or a trainee endoscopist. Both had no prior experience of i-Scan. Polyps <10mm in size were assessed using high definition white light (HDWL) followed by i-Scan.
Predicted histology with each modality was compared to the final histopathological diagnosis. Results were unblinded and fed back to the endoscopist after each 50 polyps. To assess any learning effect, results were analysed in sets of 100 consecutive polyps for overall accuracy and PIVI criteria performance.
RESULTS: 598 polyps found in 233 patients were eligible for inclusion in the study. 400 polyps were examined by the expert endoscopist and 198 by the trainee. Mean polyp diameter was 4.1mm, median 3mm. 249 polyps were non-neoplastic, 347 were adenomatous and 1 cancer.
For the expert endoscopist a $>90\%$ accuracy was achieved with both modalities once 200 polyps had been examined. Expert accuracy was significantly higher for polyps 201-300 compared to polyps 1-200 on both HDWL (92% vs 79% respectively, p=0.005) and iScan (93% vs 82% respectively, p=0.014). The ASGE threshold of $>90\%$ negative predictive value for adenomatous histology for a 'do not resect' policy in diminutive rectosigmoid polyps (DRSP) was achieved consistently by the expert endoscopist after 200 polyps and by the trainee from the first 100 poylps. However the ASGE threshold of $>90\%$ correct surveillance interval prediction for a 'resect and discard' policy of all diminutive polyps was not achieved by either endoscopist in the first 200 polyps, but was achieved after 200 polyp assessments by the expert endoscopist.

Table 1 - Accuracy rates with HDWL & iScan. E = Expert, T=Trainee

Polyp number		1-100	101-200	201-300	301-400
WL Accuracy %	E	75	83	92	95
	T	83	81		
i-Scan Accuracy %	E	82	82	93	97
	T	86	82		
WL NPV DRSP%	E	96	94	100	100
	T	88	90		
i-Scan NPV DRSP %	E	96	85	100	100
	T	92	93		
WL Surveillance interval accuracy %	E	77	89	95	93
	T	86	82		
i-Scan Surveillance interval accuracy %	E	81	87	95	98
	T	81	80		

CONCLUSION: 1) In expert or trainee hands there is a significant learning curve when using a new technology for the in-vivo characterisation of small colonic polyps.
2) The PIVI threshold for a 'resect and discard' policy may require a longer training period than for a 'do not resect' policy
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Disclosure of Interest: None Declared
Keywords: COLONIC POLYPS, in-vivo characterisation, i-scan, learning curve

P1138 COMPLICATIONS AFTER ERCP USING A SHORT DOUBLE BALLOON ENTEROSCOPE (DB-ERCP) IN PATIENTS WITH ALTERED GASTROINTESTINAL ANATOMY: A RETOROSPECTIVE EVALUATION OF 473 PROCEDURES

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INTRODUCTION: ERCP is technically challenging for patients with altered gastrointestinal anatomy. With a conventional endoscope, ERCP was very difficult for the patients with altered gastrointestinal anatomy. A recently introduced double balloon enteroscope (DBE) has made ERCP possible for these patients. Although ERCP using DBE (DB-ERCP) has been established as an effective tool, little has been known about the complications after DB-ERCP.
AIMS&METHODS: The aim of this study was to evaluate the result of DB-ERCP and to highlight complications after DB-ERCP. Between February 2006 and February 2013, we performed ERCP with the use of a short type DBE in 269 patients with various anatomic variations (473 procedures; 248 procedures for Roux-en-Y reconstruction (R&Y), 95 procedures for Billroth II gastorectomy (BII), 65 procedures for pancreatoduoderectomy (PD), 40 procedures for pylorus preserving pancreaticoduodenectomy (PpPD), and 25 procedures for others), evaluated the technique and revealed complications after DB-ERCP.
RESULTS: Deep insertion of the DBE to the blind end was successful in 463 of the 473 procedures (97.9%). The success rate was 97.2% (241/248) for R&Y, 100% (95/95) for BII, 98.5% (64/65) for PD, 95.0% (38/40) for PpPD, and 100% (25/25) for others. Deep biliary cannulation was successful in 440 of the 463 procedures (95.0%). The success rate was 97.1% (234/241) for R&Y, 93.7% (89/95) for BII, 98.4% (63/64) for PD, 97.4% (37/38) for PpPD, and 96.0% (24/25) for others. Therapeutic intervention was achieved in all of the 440 procedures of successful deep cannulation (100%). Complications occurred in 20 of the 473 procedures (4.2%) (20 procedures; 11 procedures for R&Y, 7 procedures for BII and 2 procedures for PD), including perforation (12 procedures; retroperitoneal perforation (n=3), post ES perforation (n=3), intestinal perforation (n=5), and subcutanus emphysema with pneumothrax (n=1)), laceration (n=4), acute pancreatitis (n=3), and carbon dioxide narcosis (n=1). Although two patients (one with intestinal perforation and the other with juxtrapapillary duodenal diverticula perforation) required urgent surgery, the other 18 patients were managed successfully with conservative treatments, including nothing per mouth, placement of nasojejunal tube, endoclip closure and placement of chest tube. Although severe pancreatitis occurred in one patient, the patient recovered with conservative treatments.
CONCLUSION: Complications after DB-ERCP were revealed and showed in the details. DB-ERCP is highly effective and relatively safe for patients with altered gastrointestinal anatomy.
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Disclosure of Interest: None Declared
Keywords: double balloon endoscopy, ERCP, ERCP complications, Roux-en-Y reconstruction

P1139 PERORAL PANCREATOSCOPY WITH SPYGLASS INFLUENCES CLINICAL DECISION MAKING IN SUSPECTED INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMN)

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INTRODUCTION: The prompt diagnosis and evaluation of intraductal papillary mucinous neoplasms (IPMN) remain an important clinical challenge to pancreatologists, in spite of advanced imaging modalities employed. There are only few studies about peroral (SpyGlass) pancreatoscopy in the evaluation of IPMN or cystic tumours of pancreas
AIMS&METHODS: To assess the usefulness and impact on clinical decision-making of peroral pancreatoscopy in suspected IPMN.
The study included all consecutive cases with suspected IPMN in which ERCP and peroral pancreatoscopy were performed between July 2007 and March 2013 in a single tertiary centre (Karolinska University Hospital, Huddinge). Three cases with unsuccessful pancreatic cannulation were excluded.
RESULTS: SpyGlass investigation was performed to 41 patients (median age 65 years, 41% female) with suspected IPMN (44% incidental findings). The desired part of the pancreatic duct was reached in all cases. Brush cytology was taken in 88% and directed biopsies in 39% (4% and 10% of which showed malignancy, respectively). Of 21 cases consequently operated, the most common diagnoses were IPMNs with moderate (42%) and high-grade dysplasia (29%). During follow-up (median 1.8 years), 3 more cases were referred to operation due to radiologic progression after 1-3 years from pancreatoscopy. Endoscopy gave additional information in up to 95% and strongly affected the clinical decision-making in 76% of all cases. The incidence of post-ERCP pancreatitis was 17%.
CONCLUSION: Peroral pancreatoscopy with directed biopsies is an expert technique complementing the diagnostic imaging in this group of patients. It allows for the evaluation of IPMNs extent and main duct involvement. It is also guiding the clinical decision-making between follow-up and surgery. The post-ERCP pancreatitis rate, even in the hand of experts, needs careful consideration in the selection of patients.
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Disclosure of Interest: None Declared
Keywords: diagnostic approach, ERCP, IPMN

P1140 EMERGENT EUS GUIDED DRAINAGE OF SYMPTOMATIC PANCREATIC PSEUDOCYST UTILIZING NASOCYSTIC CATHETER WITH CONTINUOUS NEGATIVE PRESSURE

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INTRODUCTION: Endoscopic ultrasound-guided transmural drainage (EUS-GTD) has become the first line therapy for symptomatic pancreatic pseudocysts.
AIMS&METHODS: The aim of this pilot study was to evaluate the efficacy and safety of emergent nasocystic catheter drainage with a continuous negative pressure for early stage pseudocysts. From Feb 2009 to Oct 2012, 27 patients (23 M; median age 46) with symptomatic pancreatic pseudocysts found during the previous 6 weeks were treated with EUS-guided insertion of a 7 Fr nasocystic catheter between the gastric wall and the pseudocyst after making a fistula by electrocautery. The nasocystic catheter was connected to an aspirator to produce negative pressure, and the negative pressure was kept constant before the catheter was pulled out.
RESULTS: With this method, we obtained a 100% cure rate. After a median drainage time of 24 days, 11 patients showed complete pseudocyst resolution, while the other 16 patients showed a reduction in the pseudocyst size (to less than 3 cm in diameter) and complete resolution of symptoms. For infected pseudocysts (11/27), the nasocystic catheter remained longer (median 36 days) than those (16/27) without infection (median 21 days) (P=0.032). Intermediate bleeding occurred in one case and was stopped by clips. Three patients had fevers after the procedure, which were alleviated with short- term antibiotics. Only one pseudocyst was recurred 12 months after treatment, but it was asymptomatic.
CONCLUSION: Emergent nasocystic catheter drainage with a continuous negative pressure was an effective and safe treatment for early stage pancreatic pseudocysts.
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Disclosure of Interest: None Declared
Keywords: EUS guided cyst drainage, Pancreatic Pseudocyst

P1141 TEMPORARY ENDOSCOPIC HEPATICO-GASTROSTOMY (EHG) WITH COVERED SELF-EXPANDABLE METAL STENTS (SEMS) AS A THERAPEUTIC ACCESS FISTULA (TAF) IN BENIGN BILIARY OBSTRUCTION NOT AMENABLE TO ERCP.

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INTRODUCTION: There is a growing experience with EUS-guided biliary drainage for palliation of malignancy after failed ERCP. Preliminary experience with EHG as an alterantive to the percutaneous approach in patients with altered anatomy and anastomotic strictures or refractory bile-duct stones is limited.
AIMS&METHODS: To assess the feasibility and efficacy of EHG using temporary transmural covered SEMS to provide interval biliary drainage and to act

as a transhepatic entry port (or therapeutic access fistula, TAF) for biliary endotherapy under cholangioscopic or fluoroscopic guidance in patients with complex anatomy. Two time periods (early and late) were compared to assess trends in clinical use.
18 patients were reviewed (9male; 66.5[47-91] years old) in whom EHG was performed with covered-SEMS to provide therapeutic access route and interval drainage. Indications, technique, complications, interventions and final therapeutic success were compared between early (2006-2011) and late periods (2011-2012).
RESULTS: Temporary EHG was considered in 12 patietns in the early (E) and 10 in the late (L) periods. 4 Patients were excluded from analysis, 3 E (no puncture in 2 because of insufficient dilation, no follow-up data in 1) and 1 L (pending SEMS removal), leaving 9 for comparison in each group. Indications grouped by stones (hepatholithiasis) and strictures (transections) in E Vs L was 3 (0) and 6(4) Vs 3(1) Vs 6(3) was similar for both groups, as was the number of cases with EHG just for interval drainage (1 each). SEMS could be removed uneventfully in 7/9 in E (one inward migration) Vs 9/9 in L. The therapeutic burden (number of failed sessions), incidence of complications, and time to remove EHG appeared greater in group E (8 Vs 4, 66% Vs 33%, 129[51-277] Vs 40[11/130] days) but no statistical difference was found. Final clinical success (stone removal, stricture-transection remodelling) appeared greater in group L Vs E (88% Vs 33%), but again no significance was found.
CONCLUSION: A select group of patients with bile-duct transections and refractory stones not amenable to ERCP can be treated using temporary SEMS hepaticogastrostomy as TAF for serial endotherapy without external drains. This shift from percutaneous to EUS-guided anastomoses for benign disease replicates prior experience in malignancy. Our data show increased use of EUS-guided HG as TAF and trend to improved effectiveness. Hepatectomy or surgical diversion can be avoided in select instances, although this novel approach carries morbidity and is labour-intensive.
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Disclosure of Interest: None Declared
Keywords: benign biliary strictures, EUS-biliary drainage (EUS-BD), SEMS

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00
GENETICS OF GI AND LIVER DISEASES III – Poster Area

P1142 THE EARLY GROWTH RESPONSE GENES (EGR) CAUSE CELL CYCLE ARREST AND INDUCE APOPTOSIS IN COLON CANCER

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INTRODUCTION: The Egr familly (Early Growth Respone Genes) of zinc finger transcription factors, which consists of four members; Egr-1, -2, -3 and -4, have been proved to have dynamic functions in the regulation of cell growth and the immune responses. Moreover, in a number of malignancies-which is a cell growth and immune related process- it seems that Egr1 and 2 are able to induce cell cycle arrest and apoptosis. The importance of such an observation relies on the fact that -by definition- a cell becomes malignant when the cell cycle arrest mechanism is not functional.
AIMS&METHODS: The present study was designed to answer the question whether the colon cancer cells stop dividing and undergo apoptosis when the EGR genes are exogenously introduced and if the presence of a mutant p53-a common tumor suppressor gene- can affect this apoptotic pathway.
Two cell lines deriving from human colon cancer; one p53 negative (DLD1) and another p53 positive (HCT116) were transfected with Egr-1, -2 and -3 and a fluorescent protein which was used as marker of the transfection. The transfected cells were incubated for 48 hours. Flow cytometry was used to create a pure population of transfected cells and 24hours later these cells were examined in the fluoroscopic microscope and compared with the controls. The transfected cells were also tested one week later to identify if they are viable.
RESULTS: We found that all the transfected cell stop undergoing divisions. In addition, their morphology was changed to round shape indicating of senescence. Interestingly, in one week time there were no viable transfected cells in our wells. It was also noticeable that both cell lines (P53-positive and P53-negative) used to undergo cell cycle arrest and apoptosis in the same rate, suggesting that the process was p53-independent or that other tumor suppressor genes could be involved.
CONCLUSION: This suggests that Egr molecules are important to control the unwanted growth in response to malignant transformation. Our results not only demonstrated an important function of Egr molecules but also indicate the therapeutic potential for the treatment of tumour.
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Disclosure of Interest: None Declared
Keywords: apoptosis, colon cancer, cell cycle arrest, early growth response genes

P1143 LOW DETECTION RATES OF GENETIC TESTING FOR HEREDITARY COLORECTAL POLYPOSES: SEARCH FOR NEW GENES A PRIORITY FOR PROPER CANCER SURVEILLANCE IN PATIENTS AND THEIR RELATIVES

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INTRODUCTION: Hereditary colonic polyposes are all characterized by increased risk for cancer development, but display variable phenotypes, genetic heterogeneity, and assorted inheritance patterns. The most well-known of these conditions include familial adenomatous polyposis (FAP), attenuated adenomatous polyposis (AFAP), MutYH-associated polyposis (MAP), Peutz-Jeghers syndrome (PJS), Juvenile Polyposis Syndrome (JPS) and Cowden Syndrome (CS). An optimal patient management is ensured by the combination of the genetic evaluation and the endoscopic diagnosis, resulting in an accurate classification of these syndromes and early detection in other family members.
AIMS&METHODS: To clarify the genetic basis and to evaluate the detection-rate of available genetic tests in a series of 90 patients with clinical and endoscopical diagnosis/suspicion of hereditary colonic polyposes, studied between March 2004 and September 2012. Sixty-three patients were eligible for genetic testing and were divided in two groups based on polyps' histological pattern. One group consisted of 56 patients with adenomatous polyps: mutational analysis of APC was performed in 25 patients with clinical/familial diagnosis of FAP, analysis of both APC and MutYH in 18 patients with suspicion of FAP/AFAP/MAP, search for MutYH mutations in 13 patients with clinical suspicion of MAP. The other group consisted of 7 patients with hamartomatous polyps: two patients with clinical suspicion of PJS were screened for germ-line STK11 mutations, while two patients with clinical suspicion of JPS were screened for germ-line SMAD4, BMPR1A and PTEN mutations, and 3 with suspicion of CS for germ-line PTEN mutations.
RESULTS: The causative germline mutation was identified in 30 out of 63 tested patients (48%). When considering each group, the detection-rate was 72% for patient with clinical diagnosis of FAP, 28% for patients where the differential diagnosis of FAP/AFAP/MAP was uncertain, 31% for MAP, 50% for PJS, 50% for JPS, 33,3% for CS. Thirty-one at risk relatives underwent genetic testing of the familial mutation, which was detected in 58% of them, thus leading to early or pre-symptomatic diagnosis.
CONCLUSION: The detection rates of genetic testing for hereditary polyposes vary significantly, showing highest concordance with clinical suspicion for classic FAP and lowest for AFAP/MAP. The failure to identify a genetic mutation might be due to the presence of mutations in unknown genes, or to unusual genetic alterations that cannot be detected by current techniques.
Disclosure of Interest: None Declared
Keywords: colon cancer, Familial adenomatous polyposis, Genetic susceptibility, genetic testing, hamartomatous polyposis

P1144 INTRATUMORAL VARIATIONS IN PIT PATTERNS REFLECT GENETIC HETEROGENEITY REVEALED BY HIGH-THROUGHPUT SEQUENCING OF COLORECTAL TUMOR

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INTRODUCTION: The detection of high-risk precursor lesions is essential for preventing colorectal cancers (CRCs), and pit pattern observation using magnifying endoscopy enables us to detect neoplastic lesions with malignant potential. Colorectal tumors are composed of genetically diverse cells with branched evolutionary growth; however, little is known about the association between intratumoral genetic heterogeneity and endoscopic findings.
AIMS&METHODS: Our aim in this study is to analyze the intratumoral variability of the endoscopic and genetic alterations in colorectal tumors. All colorectal lesions were analyzed by high-resolution magnifying endoscopy. Colorectal tumors (n=160), which consisted of at least two subcomponents with different pit patterns, were analyzed. Based on the differences, more than 2 biopsy specimens were obtained from respective portions. *KRAS, BRAF* and *TP53* mutations were analyzed by pyrosequencing and direct sequencing. Whole exome sequencing and array-based comparative genomic hybridization (array CGH) have been carried out.
RESULTS: Intratumoral heterogeneities in *KRAS* mutation (e.g., portion 1, G12D; portion 2, G13D) and *TP53* were frequently observed (early tumor; *KRAS* 60%, *TP53* 59%: advanced tumor; *KRAS* 23%, *TP53* 14%) in colorectal tumors, while such heterogeneities were rarely observed for *BRAF* mutations (8%). Particularly, we observed unexpectedly frequent intratumoral variations in *KRAS* and *TP53* mutations in early colorectal tumors. Our exome sequencing identified a large number of somatic mutations and revealed that most somatic mutations were not commonly observed among the two or more subcomponents with different endoscopic features. Array CGH analysis revealed that copy number alterations were exclusively observed in the malignant potions.
CONCLUSION: Our results may provide a model that morphological and molecular alterations are directly linked each other and intratumoral variation in pit patterns could be predictive of the extent of the molecular abnormalities in a given tumor.
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Disclosure of Interest: None Declared
Keywords: Carcinogenesis, Colorectal Cancer, exome sequencing, genetic alteration, Magnifying endoscopy

P1145 THE CHARACTERISTICS OF GENETIC AND EPIGENETIC ALTERATIONS IN LATERALLY SPREADING COLORECTAL TUMORS.

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INTRODUCTION: Laterally spreading tumors (LST) characterized by lateral extensions along the luminal wall with a low vertical axis, are categorized into 2 subtypes based on their morphological appearance: granular type (LST-G) and non-granular type (LST-NG). The relationship between their macroscopic appearance and the genetic or epigenetic alterations has been rarely reported.
AIMS&METHODS: Previously, we identified two groups of methylation markers through genome-wide analyses of DNA promoter methylation, and classified colorectal adenoma and cancer into three distinct methylation epigenotypes (HME, IME and LME, respectively). Group 1 markers including most of the previously established CIMP markers were characterized to be methylated only in HME colorectal adenomas/cancers. In contrast, group 2 markers were characterized to be methylated in both HME and IME, but not in LME colorectal adenomas/cancers. In this study, we evaluated mathylation rates of 7 group1 and 14 group2 markers in 108 LST (51 LST-G and 57 LST-NG) samples using pyrosequencing method, and epigenotyped according to the result of unsupervised two-way hierarchical clustering. In addition, mutation of *BRAF*, *KRAS*, *p53* and *PIK3CA* were evaluated to confirm whether LST could be classified into distinctive clusters.
RESULTS: LST could be classified into two distinct epigenotypes; IME with higher frequency of *KRAS* mutation and associated with LST-G morphology, and LME with less frequency of *KRAS* mutation and associated with LST-NG morphology. *BRAF* mutation was hardly observed in both in LST-G and LST-NG, suggesting that LST do not show HME as well as conventional adenomas. Although there was no significant difference of the frequency of *p53* mutation between LST-G and LST-NG, *p53* mutation positive LST showed advanced pathology compared with *p53* mutation negative LST. As the results of logistic regression analysis, LST-NG with central depression was revealed to be significantly associated with the frequency of submucosal invasion (OR 18.7; 95% CI 4.15 – 83.9, $P = 0.0001$).
CONCLUSION: Although the macroscopic appearance of LST-G and LST-NG are similar, their genetic and epigenetic background was widely different, suggesting that they probably develop through distinct carcinogenic process. The sizes of LST-NG were relatively smaller than those of LST-G, however, they were associated with advanced pathology, especially they showed central depression. Therefore early detection and subsequent endoscopic resection of these lesions may be clinically meaningful to reduce colorectal cancer mortality.
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Disclosure of Interest: None Declared
Keywords: colorectal carcinogenesis, genetic alteration, laterally spreading tumor, methylation

P1146 A NON-INVASIVE CITOGENETIC BIOMARKER FOR COLORECTAL NEOPLASTIA PREDICTION

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INTRODUCTION: The aim of our study was to identify a feasible, non-invasive method to predict the presence of significant colorectal neoplastic lesions in patients undergoing colonoscopy.
AIMS&METHODS: We included patients about to have colonoscopy in our departments between January 2011 and March 2012. Patients with known neoplastic disease, inflammatory bowel disease or prior radiation exposure were excluded. Blood samples for cytogenetic analysis using Cytogenetic-Bloked Micronucleus Assay (CBMN) technique were taken from patients. An expression of lymphocytic proliferation in specific stimulated cultures - the Nuclear Division Index (NDI) – was calculated trough this method. NDI represents a measure of general cytotoxicity. For statistics we used SPSS 11.0 software.
RESULTS: 94 patients were included. Their mean age was 55.1 years, men and women were equally represented, 47 each (50%). There were: 37 patients with normal colonoscopy, 4 patients with hyperplastic polyps, 30 patients with adenomas (from these 9 were advanced: size over 10mm, with high grade dysplasia or with a villous component larger than 25%), 23 patients with colorectal cancer. NDI was significantly lower in patients with adenomas and cancer than in patients with normal colonoscopy or hyperplastic polyps (AUC ROC = 0.637, p = 0.036). Secondly, NDI was also significantly lower in patients with advanced adenomas or cancer than in patients with normal colonoscopy, hyperplastic polyps or non-advanced adenomas (AUC ROC = 0.0677, p = 0.005). Finally, patients with colorectal cancer had a significantly lower NDI than patients with no colorectal cancer (AUC ROC = 0.655, p= 0.026).
CONCLUSION: A lower Nuclear Division Index calculate by CBMN technique may predict the presence of significant colonic lesions in a population undergoing colonoscopy.
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Disclosure of Interest: None Declared
Keywords: biomarkers, colorectal cancer

P1147 EFFECTS AND MECHANISMS OF THALIDOMIDE ON THE GROWTH AND MIGRATION OF HUMAN COLORECTAL CANCER CELL HCT116

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INTRODUCTION: Colorectal cancer recurrence or metastasis is the major cause of clinical treatment failure and mortality. Thalidomide was formerly used as a non-barbiturate sedative drug against vomiting of early pregnancy in the 1950s, since Singhal reported its curative effects on treatment of multiple myeloma in 1999 [3], following studies have shown its therapeutic effects on hematological malignancies and some solid tumors [4-6]. To date, there were only few studies on colorectal cancer.
Cell cycle is closely related to the proliferation of tumor cells. The p53-p21-CDK-cyclin pathway is a typical pathway of DNA repair. The p21 protein, as the most important downstream protein of p53, is also involved in the regulation of cell cycles at G1 and G2 phases[8-10]. VEGF plays important role and CXCR4 was found to be involved in colorectal cancer liver metastases homing[13-16].
This study was to examine the effects of thalidomide on the growth and migration of human colorectal cancer cell HCT116, and analyze its relationships with expression of p53, p21, VEGF and CXCR4.
AIMS&METHODS: To investigate the effects of thalidomide on proliferation and migration of human colorectal cancer cell HCT116 and reveal the underlying molecular mechanisms.
MTT assay, colony formation assay were performed to examine the effects of thalidomide on HCT116 growth and proliferation. Flow cytometry was used to analyze the cell cycle of the treated cell. Transwell chamber assay was done to detect the influence on cell migration. Expression of p53, p21 and CXCR4 proteins were detected by Western blot. The levels of secretory VEGF protein were assessed by ELISA.
RESULTS: MTT assay showed thalidomide had no effect on growth of HCT116 cells. Thalidomide inhibited the plate colony formation of HCT116 cells. Flow cytometry (FCM) showed that cells treated with thalidomide were arrested in G2/M phase. The migration capability was decreased significantly after thalidomide treatment. Western blot showed that there were no changes in the p53, p21 and CXCR4 proteins levels. ELISA showed that VEGF was significantly reduced by thalidomide.
CONCLUSION: The inhibition of colorectal cancer cell colony formation line by thalidomide is likely to be associated with cell cycle arrest, independent on p53 and p21 proteins. Inhibition of migration by thalidomide was significantly correlated to VEGF, but not CXCR4 protein expression.
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Disclosure of Interest: None Declared
Keywords: cell cycle arrest, colony formation, colorectal cancer cell, migration, thalidomide, VEGF

P1148 CLINICAL PATHOLOGY AND RECENT FOLLOW-UP STUDY ON GASTRIC INTRAEPITHELIAL NEOPLASIA AND GASTRIC MUCOSAL LESIONS

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INTRODUCTION: Our aim was to explore the correlations between endoscopic gastric mucosal lesions and pathological gastric intraepithelial neoplasia, and to investigate outcomes of gastric intraepithelial neoplasia after various treatments.
AIMS&METHODS: A total of 18566 Chinese patients undergoing diagnostic gastroscopy, and biopsies were taken from every patients. Typing and grading of endoscopic and pathological diagnosis were performed. Among them, 130 cases of patients were given various treatments, including medication, endoscopic treatment and surgery. Three months later, re-gastroscopy was carried out, and biopsies were taken to evaluation the efficiency.
RESULTS: There were 433 patients with GIN by initial pathological diagnosis. Among them, there were 367 LGIN and 66 HGIN, 348 cases accompanied with chronic gastritis, and 85 cases accompanied with localized foci. Eighty cases of Hp-positive patients with LGIN were given anti-Hp therapy. Three months later, re-gastroscopy was carried out and biopsies were taken. Our results showed that 45 cases of intraepithelial neoplasia disappeared with only chronic inflammation left. and also, 33 cases were given the original diagnoses and two cases developed into intraepithelial neoplasia of higher grade. Surgery was then performed, after that, one case of them was confirmed to have early gastric carcinoma, and the other case was diagnosed as advanced gastric carcinoma. Pathological examinations were carried out undergoing EMR or ESD treatment for 18 cases of patients with localized foci accompanied with LGIN. Results showed four cases of only chronic inflammation, 11 cases with original diagnoses maintained, and three cases of HGIN. Three months later, re-gastroscopy was carried out and biopsies were taken, the results revealed no intraepithelial neoplasia. Surgery and pathological examinations were performed for 32 cases of patients with HGIN. Our result showed that 15 cases maintained the original diagnoses, 12 cases of early gastric carcinoma and five cases of advanced gastric carcinoma. Three months later, re-gastroscopy was carried out and no relapse of foci was observed.
CONCLUSION: There were various endoscopic findings of gastric intraepithelial neoplasia, which occurred frequently in localized foci and atrophic gastritis. NBI magnifying endoscopy had a value of targeted biopsy. Meanwhile, GIN occurred frequently in patients with more severe pathological inflammations under endoscope, which also had certain correlations with intestinal metaplasia.
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Disclosure of Interest: None Declared
Keywords: gastric intraepithelial neoplasia, gastric mucosal lesions

P1149 IDENTIFICATION OF A GEN RESPONSIBLE OF THE FAMILIAL GASTRIC CARCINOID TYPE 1 BY EXOME ULTRASEQUENCIATION

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INTRODUCTION: Carcinoids belong to neuroendocrine tumors family. Its incidence is rare (0,1%). Gastric carcinoids represents 7%. Multifocal gastric carcinoid type I (MFGC-I) present hypergastrinemia, chronic gastritis and achloridia. In some cases, MFGC-I develops mucosa invasion that can progress into tumor. The majority are sporadic and their genetic basis is unknown.
AIMS&METHODS: We present a study of a family with consanguineous healthy parents of ten sons, five with MFGC-I (ages between 24 and 37), three of them with nodal infiltration. We performed an exome sequencing of both parents and three affected sons.
Pipeline: Exome deep sequencing was permormed with SoliD Technology. Reads obtained were mapped with Bioscope v1.3 against the human reference genome GRhg37/hg19. PCR duplicates and redundant reads were removed using Picard tools. Variant calling was performed using a combination of three different algorithms: VarScan [1], GATK [2] and Bioscope. 'In- house' scripts were developed to combine, filter and variant annotation (using Ensembl release 64 database). In order to identify new potential candidate genes assuming a recessive model (parents being heterozygous and their progeny homozygous for the variant) the following allele frequency thresholds were set up: <0.2 for homozygous for the reference, 0.2-0.85 heterozygous variants and >0.85 homozygous for the alternative allele.
RESULTS: Candidate gene. A variant (C > T) was founded segregating as (T/T) in affected patients and C/T in non-affected parents. The other non affected members of the family segregate as C/C or C/T. The variant is a NON_SYNONIMOUS missense and produces an Arginina > Valina change and is putative patological (CONDEL tools). The missense was located in the 14th exon of a 22-exon gene which was annotated as conseved cytoplasmatic Dehalogenase-Domain. The variant could be inactivating this Domain.
The gene codifies a protein which is related with the metabolic pathway of gastrin and stomach acidification. Gastrin up- regulates enterochromaffin cells which up-regulate parietal cells throw histamine.
CONCLUSION: The described mutation is within a gene which acidificates stomach. The achloridia found in patients could be explained with this mutation in parietal cells. This achloridia would explain hypergastrinemia.
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• A recessive heredity mutation could explain MFGC type I
• To relate this missense with the disease and to identify potential diagnostic markers, we are: a) analyzing the gene in other patients with carcinoid type I, b) performing immunohistochemistry with our gene and gastrin in tumor samples from patients.
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Disclosure of Interest: None Declared
Keywords: exome ultrasequenciation, gastric carcinoid

P1150 DOES A PROSPECTIVE INTENSIVE SURVEILLANCE PROGRAMME REDUCES INTERVAL COLORECTAL CANCER RATE AMONG PATIENTS WITH LYNCH SYNDROME?

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INTRODUCTION: Patients with Lynch Syndrome have a lifetime cumulative colorectal cancer incidence of 40%. Interval colorectal cancer is still high despite recommanded colonoscopic surveillance. An optimized surveillance programme is needed in order to reduce interval cancer rate.
AIMS&METHODS: All patients with a genetically confirmed Lynch Syndrome subscribed at our center were prospectively included and offered an optimized colorectal surveillance programme as follow: Colonoscopy with indigo carmin chromoendoscopy was proposed to all patients with a 2-year interval. If adenoma was detected, the interval surveillance colonoscopy was reduced to one year. If the bowel preparation was poor or insuffisant, or if chromoendoscopy was not performed, a 6-month colonoscopy interval was then required. We also retrospectively analysed prior colonoscopy data for each patient and compared them with the actual ones. Data were analysed separately for each patient and for each colonoscopy. When criteria for the optimized surveillance program were all present, colonoscopy was considered to be observant. In the other case, il would be considered as non-observant. Interval cancer detection rate (ICDR), adenoma detection rate (ADR) and polyp detection rate (PDR) were calculated using Fisher's Exact test.
RESULTS: Between january 2010 and april 2013, 108 patients (M/F=37/71, mean age = 44 years [21-74]) with genetically confirmed Lynch Syndrome (MLH1=42.6%, MSH2=37.9%, MSH6=17.6%, PMS2=1.9%) were prospectively included. A total of 134 prospective and 196 prior colonoscopies were analysed. Five were excluded because of colorectal cancer diagnosed at first colonoscopy. Mean Follow-up was 43.6 [12-74] months. We identified 168 observant colonoscopies and 157 non-observant ones. PDR was 58.9% (99/168) in the observant group (OG) vs 35.0% (55/157) in the non-observant group (NOG)

($p<0.0001$, OR=2.6 [1.6-4.2]). ADR was 32.7% (55/168) in the OG vs 21.0% (33/157) in the NOG ($p=0.018$, OR=1.8 [1.1-3.1]). ICDR was 0.6% (1/168) in the OG vs 4.5% (7/157) in the NOG ($p=0.03$, OR=0.12 [0.003-1.02]. All interval cancers were stage 1 or 2. The only interval cancer in the OG was a local recurrence after colectomy for a T4N1 tumor. The cancer was probably missed because of extrinsic colonic invasion 22 months after a normal colonoscopy.

CONCLUSION: Optimized colonic surveillance program in Lynch patients members of a specialized network, increases polyp and adenoma detection rates and decreases significantly interval cancer occurrence. This strategy should be validated in a larger prospective population.

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Disclosure of Interest: None Declared

Keywords: Colonoscopy surveillance, Colorectal adenoma, Colorectal cancer, interval cancer, LYNCH SYNDROME AND VARIANTS

P1151 FAMILIAL COLORECTAL CANCER TYPE X MULTICNETER COHORT PRESENTS A SEVERE PHENOTYPE

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INTRODUCTION: Familial Colorectal Cancer type X (FCCTX) defines families who fulfill Amsterdam-1 criteria(AC1), but are not mismatch repair (MMR) deficient (Lynch syndrome families-LS), according to either tumor testing (microsatellite instability and/or MMR proteins immunohistochemistry) or gene sequencing. Few studies suggested that these families demonstrate lower CRC and extra-colonic cancer incidence, with less affected family members then MMR deficient families. Age of onset for CRC is older in FCCTX families then for LS families.

AIMS&METHODS: Our aim was to compare cancer phenotype between FCCTX and LS families in Israel. Families which fulfill the AC, and in which LS was ruled out by tumor testing for microsatellite instability(MSI) and MMR-immunohistochemistry(IHC) were collected from 3 major referral centers in Israel. Pedigree was studied for detailed cancer history.

RESULTS: 46 FCCTX families (612 family members) were studied and compared with 42 LS families (537 family members). Data is shown in Table 1. CRC laterality and age of CRC onset in the family were the only significantly different parameters between the groups. There was no difference in regard to extra-colonic cancer occurrence and number of cancer affected family members between the groups, as well as cancer onset age.

Table 1

	LS	FCCTX	P
Number	42	46	
Right sided CRC	33(78.6%)	15(32.6%)	<0.001
Extra Intestinal Tumor in proband	8(19%)	7(15.2%)	0.7
Earliest age of CRC in family	45.7± 17.1	53±16.6	0.047
Earliest age of any cancer in family	40.7±13.84	41.3±13.33	0.83
Number family members with cancer	179(32.3%)	204(32.5%)	0.89 0.77
Mean N	4.2±2.1	4.43±2.1	
Number family members CRC	94(20%)	117(21.7%)	0.91 0.27
Mean N	2.2±1.26	2.5±1.3	
Number family members with cancer before age 50	1.66±1.525	1.36±1.11	0.28

CONCLUSION: The clinical phenotype of FCCTX families in Israel is very similar to LS families. Colonic and extracolonic cancer surveillance recommendations for these FCCTX families may be more vigorous then previously recommended.

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Disclosure of Interest: None Declared

Keywords: Cancer risk, colon cancer, Hereditary nonpoliposys colorectal cancer, LYNCH SYNDROME AND VARIANTS, surveillance colonoscopy

P1152 PREVALENCE OF MLH1 CONSTITUTIONAL EPIMUTATIONS AS A CAUSE OF LYNCH SYNDROME IN UNSELECTED CONSECUTIVE CASES OF COLORECTAL CANCER

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INTRODUCTION: The epigenetic inactivation of MLH1 has been reported in a small number of cases of CRC with a phenotype similar to Lynch Syndrome. However, the prevalence of MLH1 constitutional epimutations in patients with CRC is unknown.

AIMS&METHODS: To assess the prevalence of MLH1 constitutional epimutations as a cause of Lynch Syndrome in unselected consecutive cases of CRC. Patients from a prospective, population-based, observational cohort including 871 CRC patients from the Epicolon II cohort and 1,513 cases from Hospital General Universitario de Alicante were included. From them, 121 patients showed loss of expression of MLH1. For comparisons, a group of 973 selected CRC patients fulfilling revised Bethesda guidelines was also included, 122 showed loss of MLH1 expression. Somatic *MLH1* methylation and germline *MLH1* mutations were assessed. Constitutional *MLH1* methylation was studied with Methylation Specific-MLPA of MLH1 in patients with somatic *MLH1* methylation.

RESULTS: A total of 110 (45.2%) patients with loss of expression of MLH1 showed somatic MLH1 methylation, 43 (39%) from selected population and 67 (61%) from unselected population. The frequency of fulfilment of the revised Bethesda guidelines in the group of unselected consecutive patients was 26%. In the group of unselected consecutive CRC cases none constitutional epimutation was found. Whereas, in the group of selected patients we found 4 out of 43 (9.3%) cases with *MLH1* epimutation (p=0,002).

CONCLUSION: We did not find any case of MLH1 constitutional epimutation in an unselected population of 2,384 CRC cases. However, there are a considerable number of cases of constitutional MLH1 epimutations between selected patients fulfilling revised Bethesda guidelines. These results could suggest that the analysis of MLH1 constitutional epimutation should be included in the screening for Lynch Syndrome only in selected cases with high risk of this syndrome.

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Disclosure of Interest: None Declared

Keywords: genetic testing, Hereditary nonpoliposys colorectal cancer, immunohistochemistry

P1153 A DEDICATED FAMILY HISTORY OF COLORECTAL CANCER CLINIC IMPROVES ADHERENCE TO COLONOSCOPIC SCREENING GUIDELINES

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INTRODUCTION: In 2010, the British Society of Gastroenterology (BSG) published guidelines for colonoscopic screening of people with family history (FH) of colorectal cancer (CRC). In the UK, most patients anxious about their FH of CRC are referred by primary care doctors to non-specialist hospitals. Previous studies indicate guideline adherence is poor. This could be due to a lack of dedicated genetic services to triage and counsel patients for appropriate screening. We compare guideline adherence before and after introducing a CRC FH clinic in a non-specialist hospital.

AIMS&METHODS: Guideline adherence was assessed in a hospital with catchment population of ~300,000. Data was collected from all colonoscopies in which FH was the primary indication over a 32-month period from guideline publication up to August 2012. The FH clinic was started in April 2011. Data from the 16 months periods before and after its initiation were compared.

RESULTS: In total 146 screening colonoscopies were performed. Following the establishment of the dedicated FH Clinic there was a reduction in inappropriate colonoscopies (40% vs 11%, $p=0.0004$, X^2) ; screening took place at a more appropriate age (11.80 vs 6.47 years early, $p=0.013$, t-test); and neoplasia detection rate was also significantly enhanced (18% vs 35%, $p=0.03$, X^2).

Risk	Life time risk of CRC death	*n* (%)		Number screened early (Mean years screened early)			Polyp/ CRC cases found	
Before/After FH clinic		**Before**	**After**	**Before**	**After**	***p***	**Before**	**After**
Appropriate for screening								
High (i.e. known familial syndrome)	1 in 2-5	11 (12%)	14 (20%)	-	-	-	2	5
Moderate	~1 in 6-12	44 (48%)	35 (63%)	18 (4.57)	18 (6.13)	0.806	8	11
Inappropriate for screening								
Low	>1:12	36 (40%)	6 (11%)	36 (23.73)	6 (23.60)	0.982	6	3
Total		**91**	**55**	**54 (11.80)**	**24 (6.47)**	**0.013**	**16 (18%)**	**19 (35%)**

CONCLUSION: The BSG guidelines are based on robust evidence. Despite this, in the first 16 months after its publication, 40% of patients undergoing screening in our centre did not meet guideline criteria and were on average screened 11.8 years too early. These patients were exposed to the risk of colonoscopy earlier than recommended without justifiable benefits. Non adherence to guideline occurred at multiple levels from referral onwards. Clinicians often lacked awareness of the BSG guidelines and felt compelled to offer unnecessary screening to reassure anxious patients. After the introduction of FH clinics in our non-specialist centre, there was better evaluation of patients' risks of CRC, resulting in a significant reduction in inappropriate colonoscopic screening. It also allowed counselling of anxious patients about their risks of CRC.

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Disclosure of Interest: None Declared

Keywords: colorectal cancer screening, Family history, genetics

P1154 N-MYC DOWNSTREAM-REGULATED GENE 2 (NDRG2): A CANDIDATE TUMOR SUPPRESSOR FOR COLORECTAL CANCER

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INTRODUCTION: Identification of hyper-methylated tumor suppressor genes is an appealing strategy for the noninvasive detection of colorectal cancer (CRC). In the previous genome-wide expression array, we identified that the promoter hypermethylation of N-Myc downstream-regulated gene 2 (NDRG2) and its down-regulation in CRC. Because the expression of NDRG is repressed by the proto-oncogenes Myc, NDRG2 considers as a new class of Myc-repressed genes. Here we examined the role of NDRG2 as a novel tumor suppressor in CRC.

AIMS&METHODS: NDRG2 promoter methylation was confirmed by using methylation-specific PCR. mRNA and protein expression were identified using RT-PCR, western blot and immunohistochemistry. After the cloning of NDRG2 gene, human CRC cell lines were stably transfected with an NDRG2 expression construct. To investigate the exact function of NDRG2, colony formation, cell viability, proliferation, invasion assays, and xenograft was performed using stable transfectants.

RESULTS: The promoter of NDRD2 was methylated and reversed by demethylation in human CRC cell lines DLD-1 and RKO. The NDRG2 promoter was methylated in 80% of CRC (24/27), whereas that in 7% of non-cancerous colonic mucosa (2/27, $p<.001$). In RT-PCR, western blot, and immunohistochemistry, NDRG2 expression were decreased in CRC significantly compared to those in noncancerous colonic mucosa. Over-expression of NDRG2 in stable tansfectants inhibited colony formation ($p=.012$), cell viability ($p<.001$), proliferation ($p<.001$), and invasion ($p=.045$). Tumor volume in NDRG2 xenograft mice was smaller than that in control mice.

CONCLUSION: NDRG2 may act as tumor suppressor in CRC carcinogenesis and might serve as novel prognostic marker and therapeutic target in CRC.

Disclosure of Interest: None Declared

Keywords: colorectal cancer, Methylation, NDRG2, tumor suppressor gene

P1155 DIFFERENCES OF METHYLATION, HISTOLOGY AND ENDOSCOPIC MORPHOLOGY BETWEEN PROXIMAL AND DISTAL COLORECTAL LESIONS WITH BRAF MUTATIONS

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INTRODUCTION: Sessile serrated adenomas (SSAs), which are characterized by their preferential locations in the proximal colon and frequent *BRAF* mutation, are thought to be precursor lesions of colorectal cancer with microsatellite instability and CpG island methylator phenotype (CIMP), while other serrated lesions such as traditional serrated adenomas (TSAs) and mixed polyps (MPs) also exhibit frequent *BRAF* mutation.

AIMS&METHODS: In the current study, we carried out quantitative methylation analysis of cancer-associated genes in a cohort of *BRAF*-mutant precancerous lesions (n=124) using bisulfite pyrosequencing and compared with clinicopathological variables including locations, histologies and magnifying endoscopic findings.

RESULTS: Although majority of the *BRAF*-mutant precursors were found in the proximal colon, a considerable number of lesions were observed in the distal colon and rectum. In concordance with the proximal predominance of CIMP and *MLH1* methylation, a number of cancer-associated genes showed greater methylation levels in the proximal lesions than those in the distal colon. Histologically, SSAs and MPs were enriched in the proximal colon, while TSAs were prevalent in the distal colorectum. With magnifying endoscopy, flat lesions with type II-open (type II-O) pit pattern were frequently seen in the proximal colon, while protruded lesions with type IV plus serration pit pattern were predominantly observed in the distal colorectum.

CONCLUSION: Our data suggest that, among *BRAF*-mutant precursors, DNA methylation patterns are significantly associated with their locations and histologies as well as their endoscopic findings.

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Disclosure of Interest: None Declared

Keywords: Colorectal cancer, DNA methylation, magnifying endoscopy, precursor lesions, serrated lesion

P1156 DOWN-REGULATION OF CLAUDIN-18 IS ASSOCIATED WITH PROLIFERATIVE AND INVASIVE POTENTIAL OF GASTRIC CANCER AT THE INVASIVE FRONT

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INTRODUCTION: Claudins are tight junction proteins and claudin-18 expression is relatively restricted to gastric epithelial cells. Causal relationship between expression patterns of claudin-18 and gastric cancer is still far from clear.

AIMS&METHODS: The aims of this study were to investigate expression pattern of claudin-18 and Ki-67 in early gastric cancer at the invasive front and surrounding normal gastric mucosa and to investigate the biological function of claudin-18 on the proliferation and migration of cancer cells. Fifty three early gastric cancer lesions removed via endoscopic mucosal resection or endoscopic submucosal resection were evaluated. All of the gastric cancer is diagnosed with well to moderate differentiated adenocarcinoma in the Japanese Classification of Gastric Carcinoma. To assess epithelial proliferation, immunostaining of Ki-67 was performed and the labeling index was calculated. To assess the expression of epithelial tight junction proteins, immunofluorescent staining of claudin-18 was performed. The immunoreactivity of claudin-18 was graded according to the number of stained cells (grade 0 to 4). Correlation analysis was performed by Spearman's rank correlation coefficient (rs). The subject gave informed consent and patient anonymity was preserved. Small interfering RNA (siRNA) mediated knockdown of claudin-18 was transfected to MKN74, a claudin-18 positive gastric cancer cell line, to examine the influence of claudin-18 on proliferation and invasion of cancer cells.

RESULTS: Claudin-18 in gastric cancer was significantly down-regulated compared to surrounding gastric normal mucosa or intestinal metaplasia. Ki-67 labeling index of gastric cancer at invasive front was inversely correlated with claudin-18 expression ($rs = -0.596$, $p < 0.01$) but that at mucosal lesion was not correlated ($rs = 0.104$). The expression level of claudin-18 was inversely correlated with claudin-4 expression ($rs = -0.369$, $p < 0.05$). Claudin-18 siRNA transfection significantly down-regulated the level of claudin-18 on MKN74. Claudin-18 knockdown significantly promoted the proliferation of MKN74 compared with control siRNA transfected cells. The invasion of MKN74 significantly increased by claudin-18 siRNA transfection compared with control siRNA transfection.

CONCLUSION: Down-regulation of claudin-18 is associated with proliferative potential at the invasive front of gastric cancer, suggesting a pivotal role in the progression of gastric cancer.

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Disclosure of Interest: None Declared

Keywords: Gastric cancer, immunohistochemistry, invading the subepithelial layer, siRNA

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00

LIVER & BILIARY III – Poster Area

P1157 SPONTANEOUS BACTERIAL PERITONITIS AND BACTERASCITES IN CIRRHOTIC PATIENTS – CHARACTERIZATION OF 100 EPISODES

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INTRODUCTION: Spontaneous Bacterial Peritonitis (SBP) and bacterascites are serious complications of cirrhosis with high mortality. Traditionally, the major pathogens involved are Gram negative enteric bacteria.

AIMS&METHODS: To determine the clinical, analytical and microbiological characteristics in a cohort of cirrhotic patients with SBP/Bacterascites admitted to a gastroenterology department. We evaluated, retrospectively, 100 inpatient episodes diagnosed with SBP/bacterascite with positive microbiological study. The characteristics of the ascitic fluid concerning differential cell count and culture results were registered.

RESULTS: We included 100 hospital admissions/ascitic fluid samples from 88 patients (male sex – 78%; Mean Age – 58 ± 11 years). All patients had hepatic cirrhosis mainly of alcoholic etiology (88%) with previous episodes of SBP/bacterascites in 19 cases. The median value of leukocytes in the ascitic fluid was 3150/mm3 (100-22300) with 75% of neutrophils (1-99). The infection was monomicrobial in 92% of cases and polymicrobial in the others. The major etiologic agents were: *Escherichia coli* – 25%; *Staphylococcus aureus* – 17%; *Streptococcus* spp – 13%; *Enterococcus faecium* – 8%; *Klebsiella pneumoniae* – 6%; *Enterococcus faecalis* – 5%; *Pseudomonas aeruginosa* – 5%; *Candida* spp – 4%, *Staphylococcus epidermidis* – 4%. The bacteria had resistance to at least one of the tested antibiotics in 78% of isolates (71/91). Mortality rate was 45% considering all 100 admissions.

CONCLUSION: In this series of cirrhotic patients with SBP/bacterascites there was a similar distribution between Gram-positive and Gram-negative agents. The observed resistance rates are significant and could jeopardize the efficacy of current recommended empirical antibiotic therapy that must be redefined to consider more effective coverage of Gram-positive microorganisms.

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Disclosure of Interest: None Declared

Keywords: antibiotic resistance, bacterascites, CIRRHOSIS, spontaneous bacterial peritonitis

P1158 MULTISTRAIN PROBIOTICS AND LACTULOSE IN THE TREATMENT OF MINIMAL HEPATIC ENCEPHALOPATHY: A CONTROLLED TRIAL

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INTRODUCTION: Some evidence has shown benefits of probiotics in the management of minimal hepatic encephalopathy (MHE).
AIMS&METHODS: We evaluated the efficacy of a multistrain probiotic compound, alone and in combination with lactulose, in the treatment of MHE. Consecutive adult patients with MHE were randomized to receive lactulose (30-60 ml/day) + probiotic (200 million colony forming units of seven bacteria species/day) (Gp-LPr) or lactulose + placebo (Gp-L). Another non-randomized group of patients received probiotic alone (Gp-Pr). Medication duration was for two weeks and patients were followed-up for another eight weeks. Improvement in MHE status was assessed by psychometric hepatic encephalopathy score (PHES). Development of overt encephalopathy, hospitalization, and death were considered as secondary outcomes.
RESULTS: Sixty patients (80% male, mean age 38.4±9.6 years) completed the intervention. PHES significantly improved after medication in all the three groups (Gp-LPr: -3.8±3.9 to -1.6±3.0; Gp-L: -4.8±4.1 to -1.6±2.9; and Gp-Pr: -4.9±3.7 to -2.1±2.5, $P<0.001$). After 8 weeks follow-up, improvement maintained in Gp-LPr and Gp-Pr, but there was deterioration in those who did not receive probiotic (Gp-L: reverse to -4.8±4.2). Two patients (one in each of the Gp-L and Gp-Pr) experienced overt encephalopathy. One patient was hospitalized due to worsening of ascites (Gp-LPr) and one due to spontaneous bacterial peritonitis (Gp-L). Side effects were mild and the same among the groups.
CONCLUSION: Lactulose and probiotics are effective for the treatment of MHE; however, probiotics, but not lactulose, has long-term effects. More studies are required before suggesting probiotics for the standard treatment of MHE.
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Disclosure of Interest: None Declared
Keywords: hepatic encephalopathy, lactulose, probiotics

P1159 IN-HOSPITAL MORTALITY IN SPONTANEOUS BACTERIAL PERITONITIS: PREDICTIVE VALUE OF THE MODEL OF END-STAGE LIVER DISEASE

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INTRODUCTION: Spontaneous bacterial peritonitis (SBP) is a frequent complication among patients with cirrhosis. Because of the significant morbidity and mortality related to SBP, it is of great interest to identify predisposing factors. The model for end-stage liver disease (MELD) relies on few data, easily available and may predict the short-term survival**.**
AIMS&METHODS: In order to improve stratification of patient care in Albania, we assessed the predictive value (determined by in-hospital mortality) of MELD score in SBP patients.
We included 111 consecutive patients (82 men and 29 women) hospitalized at the University Hospital Center ''Mother Theresa'' in Tirana diagnosed with SBP from January 2009 to December 2012. SBP was defined upon admission as a neutrophil count of $\geq$250 cells/mm^3 in the ascitic fluid, and then cefotaxime was immediately started. MELD score was based on laboratory parameters [bilirubin, International Normalized Ratio (INR) and creatinine levels] and determined by using the UNOS Internet site MELD calculator. General Linear Model was used to compare mean values and their respective 95% confidence intervals (95%CI) of MELD scores by case - fatality status.
RESULTS: In-hospital mortality rate was 30.6% (*n=34*). MELD score was significantly higher in fatal patients than non-fatal patients: age-adjusted mean score: 27.7 (95%CI=25.1-30.3) vs. 18.1 (95%CI=16.4-19.8), $P<0.001$. The association of MELD score with case-fatality was stronger in men (28.0 in fatal cases vs. 17.0 in non-fatal cases; $P<0.001$) than in women (26.3 vs. 20.7, respectively, P=0.12) [P-value for sex - case - fatality interaction: 0.158].
CONCLUSION: Our findings confirm the good predictive value of MELD score in patients with SBP, as assessed by in-hospital mortality. Therefore, this new model can be effectively employed to stratify patients upon hospital admission.
Disclosure of Interest: None Declared
Keywords: MELD, mortality, spontaneous bacterial peritonitis

P1160 ASCITIC DRAINS, ADVERSE EVENTS AND ABDOMINAL ULTRASOUND

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INTRODUCTION: Ascites is the most common cause of hospital admission in patients with cirrhosis.1 Ascites refractory to diuretics is often managed by therapeutic paracentesis. Although, considered a relatively safe procedure, 2 serious life threatening complications can occur.3 Paracentesis practice often differ between centres. Moreover, in many European countries gastroenterologists are trained in the use of abdominal ultrasound and utilize this when inserting paracentesis catheters.
AIMS&METHODS: To obtain a snapshot of current UK trainee practice and experience of paracentis including serious complications and their views on abdominal ultrasound training. A cross sectional survey was conducted of current UK trainees in gastroenterology over a 3 week period(Dec2012-Jan2013).
RESULTS: 92 trainees completed the survey. 76%(70/92) of respondents have more than 3 yrs' experience in gastroenterology at registrar level. 41% (38/92) report having performed or supervised >100 procedures and a further 42% (39/92) have performed >50 procedures. 32% (29/92) reported to have witnessed serious complications; 14% (13/92) report significant haemorrhage requiring blood transfusion, 15% (14/92) have encountered bowel perforation and 7% (6/92) attribute a patient's death to a paracentesis. Only 11%(10/91) of trainees routinely take informed written consent. 62% (49/92) of trainees exclusively use a suprapubic 'Bonnano' catheters despite the fact that this product is unlicensed for use as a paracentesis catheter. The majority of trainees 77% (71/92) estimate a failure rate requiring ultrasound guided catheter placement is <10%. 73% (67/92) report that radiology colleagues are unwilling to insert catheters in patients with INR >1.5 without administration of fresh frozen plasma. 87%(80/92) of trainees expressed desire to learn basic abdominal ultrasound if provided as part of gastroenterology training and 50%(49/92) feel that this would also improve the safety and efficiency of paracentesis.
CONCLUSION: The number of UK trainees reporting serious adverse events due to paracentesis is higher than expected, perhaps due to the fact that this survey reflect their cummlative experince of complicatons. It is therefore of concern that very few trainees are taking written consent for this procedure. Abdominal paracentesis has been recently added to list of potentially life threatening procedure in medical training curriculum in the UK. The majority of trainees are still using the unlicensed 'Bonnano' catheter. The majority of UK gastroenterology trainees express a desire to be trained in abdominal ultrasonography and believe this would improve the safety of paracentesis.
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Disclosure of Interest: None Declared
Keywords: ascites, Complications, Drainage, paracentesis, Ultrasound

P1161 SHORT TREATMENT WITH RIFAXIMIN IMPROVES BLOOD CEREBRAL FLOW AT TRANSCRANIAL DOPPLER AND PSYCHOMETRIC TESTS IN CIRRHOTIC PATIENTS WITH MINIMAL HEPATIC ENCEPHALOPATHY

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INTRODUCTION: Minimal hepatic encephalopathy (MHE) includes a number of cognitive deficits such as alterations of psychomotor speed and executive functions, detectable in patients with liver cirrhosis only by psychometric or electrophysiological techniques. It has been shown that a long term treatment with rifaximin improves psychometric tests, quality of life and driving ability in these patients.
Cerebral blood flow seems to be decreased in patients with chronic liver disease and cerebral vascular resistance indices (resistive index, RI and pulsatility index, PI) are closely correlated with the severity of cirrhosis, hepatic encephalopathy and ascites.
AIMS&METHODS: The aim of this study was to evaluate the effect of a short treatment with rifaximin on psychometric tests, cerebral hemodynamic parameters and blood ammonia levels in cirrhotic patients with MHE.
Sixteen cirrhotic patients (10 male and 6 female) that resulted positive to at least one of the three psychometric tests performed in our Unit (TMT A, TMT B and DST) were enrolled in this study. All the patients enrolled were treated with rifaximin 1200 mg/die per os for 15 days. Transcranial Doppler (TCD) with measurement of RI and PI of both mean and posterior right cerebral arteries (MCA, PCA respectively), psichometric tests and blood ammonia levels measurement were performed at baseline and after 15 days of treatment. Data were analyzed with ANOVA test.
RESULTS: All patients completed the treatment with no side effects.
The short treatment with rifaximin was associated with a significant improvement of psychometric tests and in particular of TMT-B (mean±SD, 111±74 *vs* 123±77 seconds; $p<0,05$) and DST (mean±SD, 31±12 *vs* 27±9 seconds; $p<0,05$)
Among TCD parameters, we found a significant reduction of PCA-RI (mean±SD, 0,57±0,08 *vs* 0,61±0,07; $p<0,05$) and a trend toward reduction of PCA-PI (p=0,06). Blood ammonia levels after treatment were lower than before but the differences were no statistically significant.
CONCLUSION: A short term treatment with rifaximin could be effective in improving psychometric tests and cerebral hemodynamic parameters in patients with MHE.
These results indicate that the cerebral vascular resistance may reflect functional reversible changes rather than anatomical irreversible damage. We can hypothesize that rifaximin treatment and in particular the effects on intestinal microflora could be associated with a reduced production of toxins with consequent improvement of cerebral metabolism.
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Disclosure of Interest: None Declared
Keywords: minimal hepatic encephalopathy, Rifaximin, transcranial doppler

P1162 ROLE OF TRANSCRANIAL DOPPLER (TCD) IN THE EVALUATION OF CEREBRAL HEMODYNAMIC IN CIRRHOTIC PATIENTS: CORRELATION WITH SEVERITY OF THE DISEASE AND MINIMAL HEPATIC ENCEPHALOPATHY (MHE) DEVELOPMENT

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INTRODUCTION: Several studies showed that cerebral blood flow is decreased in patients with chronic liver disease, especially in the presence of hepatic encephalopathy.
Recently, it has been suggested that, in cirrhotic patients, cerebral vascular resistance indices (resistivity index, RI and pulsatility index, PI) are good indicators of cerebral hemodynamic abnormalities and are closely correlated with the severity of cirrhosis, hepatic encephalopathy and ascites. However there are still poor data about cerebral vascular indices and MHE.
AIMS&METHODS: The aim of this study was to correlate cerebral arteries resistance indices with the seerity of liver disease and the development of MHE. 19 consecutive cirrhotic patients (13 male and 6 female) were enrolled in this study. Exclusion criteria were overt hepatic encephalopathy (West Haven >0), age <18 years, active alcohol consumption, sepsis, cerebrovascular diseases, cerebral neoplasms, cardiac diseases, peripheral vascular diseases, treatment with rifaximin and lactulose in the previous 30 days.
All patients underwent TCD with the detection of right mean and posterior cerebral artery (MCA and PCA) and measurement of RI and PI. Blood samples were collectd for detection of ammonia, bilirubin, creatinine, INR and albumin levels and the Child-Pugh score was calculated. Psychometric tests (TMT-A, TMT-B and DST) were performed in order to assess the presence of MHE.
RESULTS: Among the patients enrolled 12 had MHE (63%). When we compared patients with and without MHE we found a statistically significant difference in MCA-RI (mean±SD: 0,58±0,05 vs 0,65±0,08; $p<0,05$), MCA-PI (mean±SD: 0,96±0,1 vs 1,18±0,2; $p<0,05$) and blood ammonia levels (mean±SD: 107±54 vs 58±16; $p<0,05$). Differences in PCA-RI and PCA-PI between the two groups showed a trend toward significancy ($p=0,06$).
MCA-RI and MCA-PI were also correlated with Child-Pugh score (MCA-RI: 0.58±0.05, 0.68±0.07, 0.68±0.8 in Child A, B and C respectively; $p<0,05$) (MCA-PI: 0.96±0.13, 1.3±0.28, 1,27±0.19 in Child A, B and C respectively; $p<0,05$).
CONCLUSION: Cerebral vascular resistance indices assessed by TCD seem to be related with the severity of liver disease and could be useful for the diagnosis of MHE in cirrhotic patients.
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Disclosure of Interest: None Declared
Keywords: minimal hepatic encephalopathy, transcranial doppler

P1163 VALIDATION OF LIVER STIFFNES MEASUREMENT BY FIBROSCAN VALUES IN PORTAL HYPERTENSION

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INTRODUCTION: Among patients with cirrhosis, those with advanced disease, with complications such as significant (at least grade II) esophageal varices (EV) have a shorter survival and a high risk to develop variceal bleeding. Thus it seems reasonable to screen this patients for EV. In an anterior study we establish some cut-off values obtained by transient elastography measurement (FibroScan, Echosense, Paris) for significant portal hypertension
AIMS&METHODS: Our aim is to validate the anterior established Fibroscan values in another batch of patients.
We have a group of 773 patients admitted in ourclinic, 302 females and 471 males with liver cirrhosis, mean age 59.3+/- 11 years in which we performed liver stiffness measurement by transient elasography.
RESULTS: Dividing the batch in patients without significant portal hypertension (EV grade 0 and 1) and with significant portal hypertension (EV grade 2 and 3) we obtained the following mean values:
27.35 ± 0.7471 (305 patients without significant portal hypertension) versus 48.79 $\pm$ 0.9989 (468 patients with EV grade 2 and 3), $P< 0.0001$ ES
In a study from our group that included 1000 cirrhotic patients, we found out that for a cut-off value of >40 kPa can predict significant portal hypertension with a positive predictive value of more than 85%. In patients with TE values <40 kPa, 5/10 cases had significant esophageal varices (NPV 54.9%) A cut-off value of 17.1 kPa excluded patients with EV grade 2 and 3 with a negative predictive values close to 90%.
Starting with these cut-off values previously established we analyzed the batch of 773 patients obtaining the following results:
>40 kPa criterion we had 332 pacients, 288 with significant portal hypertension 86.7%, PPV 86,7%
<17 kPa criterion 100 cases, of which 75 patients without significant portal hypertension - 75%, NPV 72.12. We analized those 25 patients with significant portal hypertension from this group and we observe that the majority, 80% (20 patients), had decompensated liver cirrhosis (Child-Pugh class B or C)
CONCLUSION: According to our data, in patients with TE values >40 kPa almost 9/10 cases will have significant portal hypertension. Therefore it is reasonable to recommend prophylactic beta-blocker therapy without endoscopy. Below the cut-off value of 17 kPa the chance of those patients having significant EV is only 1 in 10 (NPV 89.3%) in the previous study but, in this batch of patients, the 17 KPa criteria misclassify 3 of 10 patients. However, from those misclassified patients, 80% had decompensated liver disease, thus we recommend endoscopy for screening for portal hypertension in all patients with B and C Child Pugh class regardless of Fibroscan values
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Disclosure of Interest: None Declared
Keywords: fibroscan, portal hypertension

P1164 CIRRHOTIC CARDIOMYOPATHY IS A FREQUENT COMPLICATION OF CHRONIC LIVER DISEASE AND IS ASSOCIATED WITH A WORSE PROGNOSIS.

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INTRODUCTION: Cirrhotic patients present features of cardiac dysfunction, a clinical term that is already known as "cirrhotic cardiomyopathy" (CC). However, the frequency of the disease as well as its relevance to the clinical course of the cirrhosis has not adequately investigated.
AIMS&METHODS: We assessed the frequency and the characteristics of CC in our cohort of cirrhotic patients and we prospectively evaluated its impact on the clinical outcome of cirrhosis. In a period of 6 months, we enrolled 45 cirrhotics (73.3% males; mean age 57.2±12.4 years; 46.6% alcohol-related; 48.9% decompensated cirrhosis) after excluding those with known heart or pulmonary diseases, hypertension, recent gastrointestinal bleeding, clinical or laboratory signs of active infection and hepatocellular carcinoma. A Pulsed-wave Doppler echocardiography with Tissue Doppler imaging was used to assess the cardiac function of these patients. The diagnosis of left ventricular diastolic dysfunction (LVDD) was made according to the latest guidelines of the American Association of echocardiography. All patients were followed-up for a period of 2 years. The end-points of the study were death, liver transplantation and decompensation of cirrhosis.
RESULTS: LVDD was diagnosed in 17 (37.7%) patients (20% grade I, 17.7% grade II), while 28 (62.3%) patients had no evidence of diastolic dysfunction. LVDD was diagnosed in 8/23 patients (34.78%) with compensated cirrhosis and in 9/22 patients (40.90%) with decompensated liver disease. Patients with decompensated cirrhosis and LVDD had more severe cardiac dysfunction (grade II) as compared to patients with compensated cirrhosis and LVDD (7/9, 77.77% vs. 1/8, 12.5%, $p=0.015$). At the end of follow-up, 13 patients reached the composite end-point; 8 patients with LVDD (8/17, 47%) and 5 patients without LVDD (5/28, 17.8%). On Kaplan-Meier analysis, the actuarial probability of reaching the composite end-point was significantly increased in patients with LVDD ($p=0.032$, log rank: 4.607). On multivariate analysis, albumin levels ($p=0.003$) and the development of LVDD ($p=0.034$) were independently associated with the deterioration of liver disease during follow up.
CONCLUSION: Cirrhotic cardiomyopathy is a common complication of liver cirrhosis independently of the stage and the etiology of the disease. The development of cardiomyopathy seems to be associated with more rapid deterioration of liver disease and a worse prognosis.
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Disclosure of Interest: None Declared
Keywords: cardiomyopathy, cirrhosis, diastolic dysfunction, prognosis

P1165 SPLENIC ARTERIAL RESISTIVE INDEX IS USEFUL FOR THE DIAGNOSIS OF SIGNIFICANT PORTAL HYPERTENSION IN CIRRHOTIC PATIENTS WITHOUT SPLENOMEGALY

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INTRODUCTION: Most but not all cirrhotic patients with significant portal hypertension have splenomegaly. It is clinically important to determine, if possible noninvasively, whether a cirrhotic patient especially without splenomegaly has significant portal hypertension.
AIMS&METHODS: Aims: To investigate if the splenic arterial resistive index (SARI) correlates with hepatic venous pressure gradient (HVPG; a surrogate marker of portal hypertension) measured in cirrhotic patients, and to determine the role of SARI in diagnosing significant portal hypertension in patients who have same or less than 12 cm of spleen size measured by ultrasonography.
Total of 51 patients (mean age, 52 years; M:F=39:12), who underwent HVPG measurement for risk stratification of portal hypertension, also underwent splenic US and Doppler to measure the spleen maximum diameter and SARI at the same day. First we calculated the correlation coefficients of spleen size and SARI with HVPG by Pearson correlation respectively, and then tested their difference statistically by z-test. And to investigate the diagnostic performance of spleen size and SARI in diagnosing significant portal hypertension (HVPH$\geq$10mmHg), we did the receiver operating characteristic (ROC) curve analyses and compared the areas under the ROC curves (AUC). Finally, after dividing patients into two groups by spleen size in length as 'same or less than 12 cm', and 'more than 12 cm', and then we calculated the correlation coefficient of SARI with HVPG value. And we also calculated the diagnostic performances of SARI in diagnosing significant portal hypertension in patients who have spleen size same or less than 12 cm.
RESULTS: The correlation coefficient of spleen size and SARI with HVPG were 0.17 ($p=0.23$) and 0.44 ($p<0.01$) respectively, and there was no significant difference between them ($p=0.14$). And the AUC values of spleen size and SARI in diagnosing significant portal hypertension were 0.627 and 0.779 respectively, and also there was no significant difference ($p=0.27$). And in patients who have spleen size same or less than 12 cm (n=23), the correlation coefficient with HVPG value was 0.62 ($p<0.01$), and the AUC value was 0.794.

CONCLUSION: SARI had significant correlation with HVPG value. It also showed a good diagnostic performance in diagnosing significant portal hypertension in the patients without splenomegaly (same or less than 12 cm of spleen size).
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Disclosure of Interest: None Declared
Keywords: splenomegaly, Cirrhosis, HVPG, portal hypertension

P1166 USEFULNESS OF SUPERSONIC SHEAR WAVE ELASTOGRAPHY TO MONITOR THE IMPROVEMENT OR AGGRAVATION OF PORTAL HYPERTENSION IN CIRRHOTIC PATIENTS

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INTRODUCTION: It is clinically important to monitor, if possible noninvasively, the improvement or aggravation of portal hypertension in cirrhotic patients. Supersonic shear wave elastography (SWE) is a new tool to measure the liver stiffness.
AIMS&METHODS: To investigate whether it is feasible to estimate the change of hepatic venous pressure gradient (HVPG) using SWE as a non-invasive tool in the cirrhotic patients with portal hypertension.
Twenty-three consecutive patients who were diagnosed with portal hypertension on initial HVPG measurement and who underwent follow-up measurement to evaluate response to treatment were enrolled in this retrospective study. Liver stiffness measurement was performed in all of the subjects, followed by HVPG measurement. The relationship between the HVPG and liver stiffness on initial measurement and on follow-up was investigated. Furthermore, we evaluated whether a change in the HVPG (ΔHVPG) was correlated with a change in the liver stiffness (ΔLS). The subjects were subdivided into the group with clinical improvement, no change or aggravation. The performance to determine the change of portal hypertension was investigated.
RESULTS: Liver stiffness was significantly correlated with HVPG at initial and follow-up measurements (r=0.501 and 0.527, respectively). The mean rate and difference of ΔLS were strongly correlated with ΔHVPG (r=0.863 and 0.707, respectively). To determine the change of portal hypertension, the area under the ROC curve was 0.79 of rate of ΔLS, and 0.78 of difference of ΔLS.
CONCLUSION: Supersonic SWE is a feasible non-invasive method to determine the improvement or aggravation of portal hypertension in cirrhotic patients.
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Disclosure of Interest: None Declared
Keywords: Cirrhosis, HVPG, liver stiffness, portal hypertension, shear wave elastography

P1167 EARLY PHASE OF THE 13C-AMINOPYRINE BREATH TEST RELIABLY PREDICT THOSE OBTAINED WITH THE CONVENTIONAL 2-HOUR STUDY. RESULTS OF ANALYSIS OF LARGE COHORT (292 SUBJECTS) FROM SINGLE CENTRE.

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INTRODUCTION: In clinical settings, use of ^{13}C-aminopyrine breath testing (^{13}C-ABT) for noninvasive assessment of liver function is limited, largely because it is time-consuming for staff and tedious for patients.
AIMS&METHODS: To assess the feasibility of developing a simpler, less time-consuming ^{13}C-ABT, we administered the standard 2-h ^{13}C-ABT to a large cohort of patients with chronic liver disease.
METHODS: Isotope ratio mass spectrometry (IRMS) was used to measure the ratio of $^{13}CO_2$ to $^{12}CO_2$ in each breath sample. Cumulative ^{13}C recovery, expressed as a percentage of the administered dose (cPDR), was calculated for the entire 120-min test period (cPDR-120) and for the initial 15 and 30 minutes of the test (c-PDR-15 and c-PDR-30). Receiver operating curve analysis was used to assess the ability of the cPDR-15 and cPDR-30 to predict a c-PDR-120 in the 25th percentile (indicative of severely impaired liver function).
RESULTS: A cPDR-120 of 3.57% or less (indicative of severe impairment of liver function) was predicted with good sensitivity (81.27%) and specificity (86.11%) by a cPDR-15 of 0.245% or less. A cPDR-30 cut-off of 0.735% displayed even higher predictive accuracy (sensitivity 88.58%, specificity 90.28%). Data collected during the first 30 minutes of ^{13}C-ABT performed with IRMS seems to reliably predict results normally obtained on the basis of 120 minutes of testing. This experience indicates that a shorter, more tolerable version of this test might one day be developed as a reliable tool for measuring the functional hepatic reserve in patients with chronic liver disease.
CONCLUSION: Data collected during the first 30 minutes of ^{13}C-ABT performed with IRMS seems to reliably predict results normally obtained on the basis of 120 minutes of testing. This experience indicates that a shorter, more tolerable version of this test might one day be developed as a reliable tool for measuring the functional hepatic reserve in patients with chronic liver disease.
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Disclosure of Interest: None Declared
Keywords: Aminopyrine breath test, breath test, Liver function tests

P1168 ENDOTHELIAL DYSFUNCTION IN CIRRHOSIS AND ITS RELATIONSHIP WITH PORTAL HYPERTENSION AND LIVER FAILURE

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INTRODUCTION: Brachial artery flow-mediated vasodilation (FMD) by ultrasound is the gold-standard for assessing systemic endothelial dysfunction (SED). It has been suggested that SED might play a role in the pathophysiology of the complications of cirrhosis but data are lacking in this field. In this study we assessed the relationship of SED with liver failure, portal hypertension and Doppler indices in cirrhotic patients undergoing measurement of portal venous pressure.
AIMS&METHODS: The examinations included a standard abdominal B-mode scan, Doppler ultrasound (US) examinations, presence of carotid plaques and FMD. Portal flow velocity, damping index of the hepatic vein, congestion and resistivity index of hepatic and splanchnic vessels were measured with Doppler US. According to literature systemic endothelial dysfunction was defined as FMD by BAUS $<$10%.
RESULTS: In 38 patients (25 men, 55$\pm$16 yrs) with cirrhosis (Child-Pugh score 7.2$\pm$2.3; MELD 12$\pm$5) we assessed on the same day the presence of portal hypertension (mean HVPG 17.6$\pm$4.5mmHg) and FMD by BAUS (mean value 8.0$\pm$3.0%). FMD increased in parallel with worsening of liver function as measured by Child-Pugh and MELD score (r=0.39). The proportion of patients with systemic endothelial dysfunction decreased with deterioration of Child class, being higher in patients belonging to Child A class (83%) and the lowest in Child C decompensated cirrhosis (25%). Moreover, SED decreased progressively with the severity of portal hypertension and a significant difference was found between patients with HVPG $<$10 mmHg and those with HVPG $>$10 mmHg (6.4$\pm$3.8% vs 8.6$\pm$3.3). Carotid plaques were more prevalent in patients with SED (25% vs 3%). No significant correlation was found between SED and intra- and extra-hepatic Doppler flow parameters.
CONCLUSION: Endothelial dysfunction measured with FMD correlates inversely with the severity of portal hypertension and liver failure. In patients with cirrhosis FMD increases as liver function deteriorates, and it decreases according to cardiovascular risk. Further studies to elucidate role of FMD in cirrhotic patients are warranted as hyperdynamic syndrome of advanced cirrhosis may alter vascular reactivity.
Disclosure of Interest: None Declared
Keywords: CIRRHOSIS, endothelial dysfunction

P1169 HYALURONIC ACID (HA) LEVEL IN ASCITIC FLUID OF CIRRHOTIC PATIENTS WITH SPONTANEOUS BACTERIAL PERITONITIS (SBP)

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INTRODUCTION: Spontaneous bacterial peritonitis (SBP) is a common problem that affects liver cirrhotic patients. It is also, a major contributor to the deterioration and aggrevation of liver failure complications. Complement deficiency considered as a major complication of liver cirrhosis and bacterial overgrowth in the intestine is the major source of bacterial peritonitis. Hyaluronan or hyaluronic acid (HA) is a connective tissue polysaccharide, synthesized by many cell types, although mesenchymal cells are believed to be predominant. The serum level of HA is regulated by the influx from the tissues via lymphatic system and its receptor-mediated clearance by liver endothelial cells. So, marked increase in serum levels are noted in liver diseases, especially in patients with cirrhosis, when the clearance is impaired. The hyaluronic acids (HA) have an important role in controlling tissue permeation, bacterial invasiveness and macromolecular transport between cells. HA was observed to enhance cellular infiltration and migration by facilitating cell detachment. It also, increase the proinflammatory cytokines TNF-α and IL-8 production. It is interesting to note that HA not only can promote the inflammation, but also can moderate the inflammatory response, which may contribute to the stabilization of granulation tissue matrix. The innate immune system uses TLRs to recognize microbes and initiate host defense. The repeating disaccharide structure of HA has features of pathogen-associated molecular patterns. Many pathogen-associated molecular patterns on pathogens utilize Toll-like receptors to initiate innate immune responses.
AIMS&METHODS: To measure the level of complement-3 (C3) and hyaluronic acid in ascetic fluid of liver cirrhosis patients with and without spontaneous bacterial peritonitis
RESULTS: In our study we found that there was a significant decrease in C3 level in ascetic fluid of cirrhotic patients in comparison to ascetic fluid of patients with other causes (i.e. Nephrotic syndrome, and cardiac failure) ($P<0.05$). Also, HA level shows significant decreased in ascetic fluid of cirrhotic patients in comparison to ascetic fluid of patient with other causes (i.e. Nephrotic syndrome, and cardiac failure) ($P<0.05$). HA level in serum of liver cirrhosis patients have a highly significant increase ($p<0.001$) in comparison to control group.
There was a highly significant decrease in HA level in ascetic fluid of cirrhotic patients with SBP in comparison to HA level in ascetic fluid of cirrhotic patients without SBP ($p<0.001$).
CONCLUSION: C3 and HA are significantly decreased in ascetic fluid of cirrhotic patients. HA significantly decreased in ascetic fluid of cirrhotic patients with SBP in comparison to patients without SBP.
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Disclosure of Interest: None Declared
Keywords: Asdites, Hyaluronic acid, spontaneous bacterial peritonitis

P1170 NOVEL PROGNOSTIC MODEL FOR PRIMARY SCLEROSING CHOLANGITIS

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INTRODUCTION: Primary Sclerosing Cholangitis (PSC) is a disease with no effective drug treatment options, eventually leading to biliary fibrosis, cirrhosis and liver failure. The MAYO risk score (MRS) is often used to estimate survival of PSC patients. However, MRS is based on a patient group derived from tertiary referral centres. Other limitations of MRS are the use of parameters that can be highly variable over the course of the disease, and a relatively short follow-up period with a median of 36 months. Aim of this study was to develop a prognostic model for survival of PSC patients based on intrinsic parameters.
AIMS&METHODS: 690 PSC patients were identified in a large geographically defined area of the Netherlands, comprising 50% of the Dutch population. Four independent hospital databases were searched in 44 hospitals. A range of variables, including date of PSC diagnosis, date and type of IBD, and follow up time were retrieved from patient records. All variables were assayed as potential predictors of survival by univariate analysis. To develop the survival model, time dependant Cox regression proportional hazard analysis was performed.
RESULTS: The median follow up time was 85 months (range 0-468 months). The variables PSC type, age at diagnosis PSC, co-existing inflammatory bowel disease (IBD), IBD-type, sex, auto-immune hepatitis overlap, cholelithiasis, cholecystectomy and appendectomy before diagnosis PSC and variceal bleeding were considered for the model. Using manual backward elimination in the multivariate analysis, the following formula was created: Prognostic Index (PI) =– 0.916*PSC Type$(0/1)^1$–0.480*Age at DiagnosisPSC^2-0.570*Ulcerative Colitis(UC)/IBD Unspecified (IBDU)$(0/1)^3$ –1.212*Crohn's Disease (CD)$(0/1)^3$ +1.082*Follow up time $(0/1)^4$ *UC/IBD U $(0/1)^3$+1.317*Follow up time$(0/1)^4$ * CD $(0/1)^3$. With this PI, estimations of survival up to 25 years can be made.
1: PSC type: Large duct PSC=0; Small duct PSC=1
2: Age at diagnosis PSC: >30 years=0; <30 years=1
3: IBD: No IBD =0; UC/IBDU/CD=1
4: Follow up time: <36 months=0; >=36 months=1
CONCLUSION: We have created a unique prognostic model based on an unselected group of 690 patients. This model consists of intrinsic variables and is thus applicable in all PSC patients and independent from disease stage. To confirm the accuracy of this prognostic model, validation in an independent patient cohort is warranted.
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Disclosure of Interest: None Declared
Keywords: Primary sclerosing cholangitis, Prognostic model

P1171 RISK FACTORS FOR THE ONSET OF PRIMARY SCLEROSING CHOLANGITIS

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INTRODUCTION: Primary sclerosing cholangitis (PSC) is a cholestatic liver disease, affecting intra-and extrahepatic bile ducts. PSC is strongly associated with inflammatory bowel disease (IBD). Pathogenesis of both diseases is unknown. PSC and IBD are considered complex genetic diseases, meaning that environmental risk factors trigger disease in a genetic susceptible host. The aim of this study was to assess possible risk factors for PSC.
AIMS&METHODS: For this case control study, PSC patients and IBD controls from the population-based Epi-PSC-PBC database were asked to fill-out a questionnaire. Only patients that filled out the questionnaire were included. The following data could be obtained: smoking behaviour, history of appendectomy before diagnosis PSC and medical family history. Possible risk factors were analysed by Chi square analysis. Relative frequencies of risk factors were expressed as Odds Ratio (OR).
RESULTS: 342 PSC patients (46% Ulcerative colitis (UC), 15% Crohn's disease (CD), 3% IBD-Unspecified (IBD-U)) and 372 IBD patients (42% UC, 54% CD, 4% IBD-U) were included. In the PSC cohort there were significantly less current and former smokers compared to the control group, with 8,2 % vs. 22,6 %, OR 0,31 (95% CI 0,13-0,73) current smokers and 15,8% vs. 32,0%, OR 0,38 (95% CI 0,19–0,76) former smokers. Comparing PSC-UC patients with UC patients there were also significantly less current and former smokers in the PSC-UC group compared to the UC control group with 5.7% vs. 18.6 %, OR 0.24 (95% CI 0.09-0.67) current smokers and 17.1 % vs. 33.3 %, OR 0.42 (95% CI 0.21-0.81) former smokers. Comparing PSC-CD patients with CD patients this finding was again confirmed with 10.0% vs. 29.9%, OR 0,27 (95% CI 0.12-0.59) current smokers and 8,0% vs 25,9%, OR 0.26 (OR 0.11-0.60) former smokers. There were significantly more appendectomies in de PSC cohort compared to the IBD control group, 12,9 % vs. 4,0 %, OR 3,31 (95%CI 1,03–10,65). PSC patients had significantly more often a first degree relative with an autoimmune liver disease compared to IBD controls, 2,0% vs. 0,3%, OR 2,05 (95% CI 0,24-106,26), but significantly less often a first degree relative with IBD 10,2 % vs. 17,5%, OR 0,54 (95% CI 0,24-1,25).
CONCLUSION: Current and former smoking was associated with a decreased risk of PSC independent of IBD, as well as it was associated with a decreased risk of PSC-UC independent of UC and a decreased risk of PSC-CD independent of CD. PSC patients more often have a first degree family member with autoimmune liver disease then IBD control patients. For the first time appendectomy before diagnosis PSC was shown to be associated with an increased risk of PSC.
Disclosure of Interest: None Declared
Keywords: Primary sclerosing cholangitis, risk factors

P1172 TARGETING STRATEGIES TO IMPROVE URSODEOXYCHOLIC ACID ACTION IN PRIMARY BILIARY CIRRHOSIS

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INTRODUCTION: Ursodeoxycholic acid (UDCA) has been shown to stabilize or significantly improve the grades of both ductular proliferation and lymphocytic piecemeal necrosis. Because of the multiple players, it may be anticipated that anti-inflammatory drugs with broad specificity are efficient in a subset of patients not responding to UDCA alone.
AIMS&METHODS: The aim of the study was to determine if the addition of budesonide or methotrexate to UDCA would improve liver histology. Secondary endpoints included comparison of treatment arms with respect to overall survival and time to clinical decompensation.
PBC stage I to III patients (n=58) were randomized into two treatment arms: UDCA 15 mg/kg/day and budesonide 6 mg/day (n=28, group A) or UDCA 15 mg/kg/day plus methotrexate 15 mg/week (n=30, group B). Patients were excluded if they had end-stage liver disease: serum bilirubin level greater than 10 mg/dl or serum albumin less than 3 g/dl; hepatic encephalopathy; hemorrhage from esophageal varices and/or portal gastropathy. Patients were followed-up for a median period of 5.5 years (range 4.2-7.6 years) or until treatment failure. Treatment failure was defined as: histological progression by at least two stages or to cirrhosis; death without liver transplantation; transplantation; variceal bleeding; development of ascites, hepatic encephalopathy or varices; a doubling of serum bilirubin levels.
RESULTS: Values for serum ALP, ALT and GGT improved in both groups. Bilirubin levels remained stable in group A and increased in group B (p=0.01). Analysis of liver histology after 36 months of therapy revealed a significant histological improvement in both groups when baseline was compared with the final biopsy. No patients in either group progressed to cirrhosis or extensive fibrosis. Overall, mean necro-inflammatory scores fell from 12.5 to 4.6 in group A and from 12.8 to 6.2 in group B. Fibrosis decreased 28.5% in group A (p=0.05) and 13.3% in group B (p=0.08).
CONCLUSION: 1. Combination therapy might be beneficial for all PBC patients with pre-cirrhosis liver disease. 2. Inflammation decreased in both groups, but the histological stage was significantly decreased in the group with budesonide and UDCA.
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Disclosure of Interest: None Declared
Keywords: primary biliary cirrhosis, ursodeoxycholic acid

P1173 MALE GENDER IS ASSOCIATED WITH MORE RAPID PROGRESSION AND INCREASED RISK OF BILIARY DYSPLASIA IN PRIMARY SCLEROSING CHOLANGITIS

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INTRODUCTION: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterized by inflammation and fibrosis of bile ducts with unknown patogenesis. Association with other autoimmune disease, and at a genetic level the predominant HLA association suggest autoimmune etiology (1). Unlike in other autoimmune disorders, ~70% of patients with PSC are men. In Nordic countries 80 % of PSC patients have a concomitant IBD. In PSC patients without IBD, the M:F ratio is lower, 0.72:1 (2). Progression of the disease is varying and unpredictable with association of markedly increased risk of cholangiocancer with life time risk of 10-15 % (3). Factors associated with disease progression and development of biliary dysplasia are poorly known.
AIMS&METHODS: To evaluate the role of gender in the PSC progression and the risk of biliary dysplasia and transplantation. The study population consists of patients referred for ERCP for the first time to confirm the diagnosis of PSC during years 2006-3/2011 at Helsinki University Central Hospital due to the suspicion of PSC (S-ALP > UNL in conjunction with IBD or MRI/liver biopsy suggestive for PSC) irrespective of symptoms. ERCP findings were scored according to modified version of Ponsioen (4). Brush cytology (BC) from intra- and extrahepatic bile ducts was collected in every patient and a sample for DNA-flow cytometry was obtained in patients with advanced disease (ERC-score≥3). Moreover, also the sex distribution of the patients transplanted for PSC in Finland were analyzed.
RESULTS: Altogether 262 patients with confirmed PSC were included, of whom 129 were males (49.2%). Of the all patients, 81 % were asymptomatic. Concomitant IBD was diagnosed in 68 % of patients, in 79,1 % in males and in 57.1% in females. M:F ratio in patients(n=83) with more advanced disease (PSC-score≥3) was 51/32 (61.4%). Cytological dysplasia was detected in BC in 17 patients out of 262 (6.5%), of whom 12 were males (71%), and 2 (0,76%) were diagnosed with malignant cytology consistent with cholangiocancer, both males. Our patients transplanted for PSC (n=127) 80 (63%) are males.
CONCLUSION: In this large series of mostly asymptomatic patients with newly diagnosed PSC, no sex difference could be found (M:F=49.2/50.8%), in contrast to previous studies, but males had more commonly advanced disease (61.4%), cytological dysplasia or malignant cytology (74%) and male gender predominated in transplanted PSC-population (63%). Male gender seems to be associated with more rapid progression of PSC, increased risk of biliary dysplasia and for liver transplantation.
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Disclosure of Interest: None Declared
Keywords: disease progression, Male gender, Primary sclerosing cholangitis

P1174 ESTABLISHMENT OF A SERUM IGG4 CUT-OFF VALUE FOR THE DIFFERENTIAL DIAGNOSIS OF IGG4-RELATED SCLEROSING CHOLANGITIS

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INTRODUCTION: IgG4-related sclerosing cholangitis (IgG4-SC) must be precisely distinguished from primary sclerosing cholangitis (PSC) and cholangiocarcinoma (CC)because the treatments are completely different. However, the pathological diagnosis of IgG4-SC is difficult. Therefore, highly specific non-invasive criteria such as serum IgG4 should be established. This study established a cut-off for serum IgG4 to differentiate IgG4-SC from respective controls using serum IgG4 levels measured in Japanese centers.
AIMS&METHODS: A total of 344 IgG4-SC patients were enrolled in this study. As controls, 245, 110, and 149 patients with pancreatic cancer, PSC, and CC, respectively, were enrolled. IgG4-SC patients were classified into 3 groups: type 1 (stenosis only in the lower part of the common bile duct), type 2 (stenosis diffusely distributed throughout the intrahepatic and extrahepatic bile ducts), and types 3 and 4 (stenosis in the hilar hepatic region) with 246, 56, and 42 patients, respectively. Serum IgG4 levels were compared, and the cut-offs were established.
RESULTS: The cut-off obtained from receiver operator characteristic curves showed similar sensitivity and specificity to that of 135 mg/dL when all IgG4-SC and controls were compared. However, a new cut-off value was established when subgroups of IgG4-SC and controls were compared. A cut-off of 182 mg/dL can increase the specificity to 96.6% (4.7% increase) for distinguishing type 3 and 4 IgG4-SC from CC. A cut-off of 207 mg/dL might be useful for completely distinguishing type 3 and 4 IgG4-SC from all CC.
CONCLUSION: Serum IgG4 is useful for the differential diagnosis of IgG4-SC and controls.
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Disclosure of Interest: None Declared
Keywords: IgG4 related sclerosing cholangitis, IgG4-SC

P1175 CORRECTION OF LOW-GRADE CHRONIC INFLAMMATION BY MULTIPROBIOTIC "SYMBITER" IN PATIENTS WITH TYPE 2 DIABETES AND NON-ALCOHOLIC FATTY LIVER DISEASE

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INTRODUCTION: Obesity and diabetes are both characterised by low-grade inflammation of unclear origin. Bacterial lipopolysaccharide (LPS) is a gut microbiota-related factor that triggers secretion of proinflammatory cytokines. Continuous subcutaneous low-rate infusion of LPS led to excessive weight gain and insulin resistance in mice.
AIMS&METHODS: Evaluate the effect of multiprobiotic "Symbiter" on low-grade chronic inflammatory state in patients with type 2 diabetes (T2D) and non-alcoholic fatty liver disease (NAFLD).
Materials and methods: We examined 86 patients with T2D and NAFLD. All patients divided by us on the way of therapy into 2 groups. The main group (56 subjects) received oral antidiabetic therapy and multiprobiotic "Symbiter" within 30 days. Patients of comparison group (30 subjects) received only hypoglycemic drugs. Also in each group we identified patients with normal and elevated level of transaminases. The concentration of proinflammatory cytokines in the serum - IL-6, IL-8, IL-1β, TNF-α and IFN-γ - determined by ELISA using commercial kits "Cytokine Ltd." (Russia).
RESULTS: We observed 4-5 times increasing of cytokines in patients with NAFLD and elevated transaminase levels, compared to a 2-3-time increase in patients with normal transaminase levels. Our data shows that positive hepatoprotective effect of multiprobiotic "Symbiter" in patients of main group accompanied by decrease manifestations of low-grade systemic inflammatory response. We noted statistically significant reduction of proinflammatory cytokines in plasma, after 30 days of therapy, in patients with elevated levels of transaminases. In particular, the level of IL-6 decreased on 40% (p=0.041), IL-8 - 26.54% (p $<$0.001), TNF-α - 20.83% (p $<$0.001), IL-1β - 17.7% (p$<$0.001) and IFN-γ on 21.84% (p $<$0.001) respectively. In patients with normal levels transaminases and NAFLD were significantly decreased only IL-6 on 17.1% (p = 0.041), IL-8 - 21.4% (p $<$0.001) and TNF-α on 13.8% (p = 0.008). Significant changes in cytokines levels in patients of comparative group we don't observed.
CONCLUSION: Multiprobiotic "Symbiter" shows hepatoprotective effect which accompanied by decrease manifestations of low-grade systemic inflammatory response. That's why can be recommended for use in patients with different stages of NAFLD and T2D as an adjunct to standard treatment regimens.
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Disclosure of Interest: None Declared
Keywords: Multiprobiotic, non-alcoholic fatty liver disease, type 2 diabetes

P1176 SAFETY AND EFFICACY OF SUBCUTANEOUS HEPATITIS B IMMUNOPROPHYLAXIS USING"ON DEMAND"APPROACH:A SINGLE CENTER EXPERIENCE

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INTRODUCTION: HB immunoglobulin(HBIG)administration is the backbone for prophylaxis of HBV re-infection after liver transplantation (LT). Long term effects and efficacy of HBIG are well known only for intravenous(IV)and intramuscular(IM)formulations. Aim:to investigate efficacy, safety and feasibility of "on demand" subcutaneous (SC) administration of the new formulation of HBIG BT088 (Zutectra®)LT patients
AIMS&METHODS: a total of 37 LT patients(9F,28M, mean age60±7years)were switched from IV or IM to SC HBIG administration during a period of 2 years from
January 2011. The conversion to SC administration occurred at a mean time of 44 months from the LT. They were prospectively enrolled and followed up for at least 48 weeks. The dose of HBIG was initially standardized to 1000IU/week. After a period of stabilization, patients were offered a"on demand"approach, with a targeted level of serum antiHBs of minimum100UI/L
RESULTS: all patients were HBV-DNA negative at the time of transplantation(5spontaneously-14%,32 under NUCs -86%). All patients were on a combination prophylaxis with HBIG and NUCs. All patients became rapidly independent for the weekly SC self-injection. The treatment was effective in maintaining trough anti-HBs levels greater than 100 UI/l in all patients. 90%of patients showed a mean HBsAb titer greater than 155 UI/l. Overall, mean values of HBsAb were 262 UI/l(±118). The mean HBsAb titre prior to switching to SC formulation was 318±124, with a mean monthly injection of 5000U/L. No drug related side effects or injection site problems were observed.
CONCLUSION: SC HBIG for long term prophylaxis of post LT HBV re-infection has proven to be safe, well-accepted and effective in maintaining the targeted protective anti-HBs levels. Moreover individualization of immuneprophylaxis according to the lowest protective anti-HBs titers is easily applicable with the SC formulation, allowing the exploration of new schedules in order to improve costs while maintaining efficacy.
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Disclosure of Interest: None Declared
Keywords: HB immunoglobulin (HBIG), liver transplantation (LT)

P1177 LIVER STIFFNESS MEASUREMENTS BY MEANS OF SUPERSONIC SHEAR IMAGING (SSI) SHOULD BE PERFORMED IN FASTING CONDITION OR NOT?

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INTRODUCTION: SSI is a new method for non-invasive evaluation of liver fibrosis.
AIMS&METHODS: Aim: to assess the influence of food intake on liver stiffness (LS) measurements by means of SSI, knowing that food intake increase LS values assessed by means of other two elastographic methods (Transient Elastography and Acoustic Radiation Force Impulse elastography).
Patients and methods: Our study included 75 healthy volunteers, with a median age of 25 years (19-58 years), 58 women (77.3%) and 17 male (22.7%). SSI measurements were performed in fasting condition, then 1h and 3h after a standard meal. All subjects included in the study received the same meal: one sandwich and 500ml water. SSI measurements were performed in supine position. In each patient 5 valid SSI measurements were performed by intercostals approach, a median value was calculated and expressed in kilopascals (kPa).
RESULTS: In 3 patients we could not obtain 5 valid LS measurements assessed by means of SSI in at least one condition (fasting, 1h and 3 h after food intake), so in the final analysis were included 72 subjects (96% of all healthy volunteers). The mean LS values were similar in fasting condition, 1h and 3 h after food intake were: 6.1±1.3 kPa, 5.8±1.1 kPa and 5.7±1.1 kPa, respectively. No significant differences were observed between mean SSI values in the different food conditions: fasting vs. 1h after food intake: p=0.28, fasting vs. 3h after food intake: p=0.17 and 1h. vs. 3h after food intake: p=0.80 respectively.
CONCLUSION: LS values assessed by means of SSI had similar values in fasting condition and after food intake, so probably food condition is not an issue for SSI measurements, but further studies are still necessary.
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Disclosure of Interest: None Declared
Keywords: Aixplorer, elastography, liver fibrosis, liver stiffness, Supersonic Shear Imaging

P1178 ACCURACY OF INVALID FIBROSCANS IN DIAGNOSE SIGNIFICANT LIVER FIBROSIS

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INTRODUCTION: Transient liver elastography (Fibroscan ® - FS) is an instrumental method for noninvasive assessment of liver fibrosis. One limitation of this procedure is the need to get at least 10 valid measurements with IQR/liver stiffness ratio < 30% and success rate > 60%, which limits the interpretation of the exam.
AIMS&METHODS: The presente study proposes to evaluate the diagnostic accuracy for significant liver fibrosis of the invalid fibroscans.
Retrospective analysis of patients with invalid FS who underwent liver biopsy (LB) between 2008 and 2013. Significant fibrosis was defined as Metavir F ≥ 2. It was determinated the capacity (sensitivity, specificity, positive and negative predictive values and AUROC) of invalid FS for the diagnosis of F ≥ 2, using the cut-off of liver stiffness for significant fibrosis according to the underlying pathology. Statistical analysis was performed with SPSS 20.0 for Mac®.
RESULTS: Included 56 patients (mean age 47±11 years, 62.5% males) with invalid FS, 18 due to IQR/liver stiffness ratio > 30% (median 40.5%, min 34%, max 136.8%), 29 with success rate <60% (median 43%, min 5%, max 56%) and 9 due to both. The indication for FS was chronic hepatitis B in 21 patients, chronic hepatitis C in 15, non-alcoholic fatty liver desease in 8 and other reasons in 12. Liver biopsy revealed F0, F1, F2, F3 and F4 in 19, 20, 11, 3 and 3 cases, respectively. The sensitivity, specificity, positive and negative predictive values and AUROC for the diagnosis of F ≥ 2 was 76% (95% CI: 50-93%), 92% (95% CI: 79-98%), 81.2% (95% CI: 54.3 to 95.7%), 90% (95% CI: 76.3 to 97.1%), 0.84 (95% CI: 0.71 to 0.97, p <0:01). The reason for invalid FS was not associated with significant change in the negative predictive value, which remained > 88%.
CONCLUSION: In our series, the results show a good accuracy of invalid FS for exclusion of significant liver fibrosis.
Disclosure of Interest: None Declared
Keywords: fibroscan, Fibrosis

P1179 THE USEFULNES OF ACOUSTIC RADIATION FORCE IMPULSE (ARFI) ELASTOGRAPHY (ARFI) FOR EVALUATION OF LIVER FIBROSIS – LARGE MONOCENTRIC EXPERIENCE

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INTRODUCTION: ARFI is an ultrasound elastographic method for non-invasive evaluation of liver fibrosis.
AIMS&METHODS: Aim: To assess the value of liver stiffness (LS) measurements by means of ARFI as a predictive factor for the severity of fibrosis.
Methods: Our study included 1150 subjects with an median age of 55 years (18-87): 652 patients (56.7%) diagnosed with liver cirrhosis by clinical, ultrasound, endoscopy criteria; 244 subjects (21.2%) without known liver disease, 133 patients (11.6%) with chronic hepatitis C in whom liver biopsy (LB) was performed, 72 chronic hepatitis B patients (6.3%) with LB and 49 patients (4.2%) with non-cirrhotic ascites. Ten LS valid ARFI measurements were performed in each subject and a median value was calculated, expressed in meters/second (m/s). Reliable LS measurements were considered the median of 10 valid measurements with a success rate≥60% and an interquartile range interval<30%.
RESULTS: Reliable LS values by means of ARFI measurements were obtained in 1076/1150 (93.5%) subjects.
In . . .normal subjects" the mean LS value assessed by ARFI was 1.22 ± 0.31 m/s (median 1.19 m/s)
In patients with LB, the best LS ARFI cut-offs values for predicting different stages of liver fibrosis were: F≥2 – 1.48 m/s (AUROC=0.671), F≥3 – 1.61 m/s (AUROC=0.709) and F=4 – 1.75 m/s (AUROC=0.824).
The mean LS values were significantly higher in cirrhotic patients with significant esophageal varices (al least grade 2) as compared with those without or with grade 1 varices: 2.96±0.71 m/s vs. 2.81±0.71 m/s, p=0,01; also in cirrhotic with ascites as compared with those without ascites: 3.01±0.70 m/s vs. 2.78±0.68 m/s, p=0.0001.
The mean LS values assessed by ARFI were significantly higher in cirrhotic patients with ascites as compared with patients with non-cirrhotic etiology of ascites: 3.01±0.70 m/s vs. 1.43 ±0.49 m/s, p<0.0001.
CONCLUSION: ARFI is a good method for noninvasive liver fibrosis assessment.
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Disclosure of Interest: None Declared
Keywords: ARFI elastography, liver fibrosis, liver stiffness

P1180 WHICH ARE THE CUT-OFF VALUES OF LIVER STIFFNESS MEASUREMENTS ASSESSED BY SUPERSONIC SHEAR IMAGING (SSI) FOR PREDICTING SIGNIFICANT FIBROSIS AND LIVER CIRRHOSIS?

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INTRODUCTION: SSI is a new ultrasound elastographic method used for non-invasive assessment of liver fibrosis.
AIMS&METHODS: Aim: to identify the cut-off values of liver stiffness (LS) assessed by SSI for predicting significant fibrosis (F≥2) and liver cirrhosis (F=4), considering Transient Elastography (TE) as the reference method.
Methods: 383 consecutive subjects were evaluated by means of TE and SSI. Reliable TE measurements were defined as: median value of 10LS measurements with a success rate≥60% and an interquartile range interval<30%, values expressed in kPa. Reliable LS measurements by means of SSI was definied as the median value of 5 LS measurements expressed in kPa. To discriminate between various stages of fibrosis by TE we used the liver stiffness (LS) cut-offs (kPa) proposed in the most recently published meta-analysis (1): F1-6, F2-7.2, F3-9.6 and F4-14.5.
RESULTS: Our subjects were: healthy volunteers-14.6%; patients with chronic hepatitis B -17.6%; with chronic hepatitis C – 25.8%; with coinfection (B+C or B+D) – 1.6%; with non-viral chronic hepatopathies (most of them with non-alcholic fatty liver disease)-29.2%; and with liver cirrhosis diagnosed by means of clinical, biological, ultrasound and/or endoscopic criteria-11.2%. The rate of reliable LS measurements was statistically similar for TE and SSI: 73.9% vs. 79.9%, p=0.06. Reliable LS measurements by both elastographic methods were obtained in 65.2% of patients. The distribution of liver fibrosis in this cohort of patients, using TE prespecified cut-off values were: F0-40.8%, F1-14.8%, F2-19.2%, F3-12.8%, F4-12.4%. The best SSI cut-off value for predicting significant fibrosis was 7.8 kPa (AUROC=0.859 with 76.8% Se and 82.6% Sp), while the best SSI cut-off value for predicting liver cirrhosis was 11.5 kPa (AUROC=0.914 with 80.6% Se and 92.7% Sp).
CONCLUSION: The best SSI cut-off values for predicting significant fibrosis (F≥2) and cirrhosis were 7.8 kPa and 11.5 kPa, respectively.
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Disclosure of Interest: None Declared
Keywords: Aixplorer system, liver fibrosis, liver stiffness, Supersonic Shear Imaging

P1181 THE FEASIBILITY OF SHEAR-WAVE ELASTOGRAPHIC METHODS FOR NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS IN CHRONIC VIRAL HEPATITIS PATIENTS

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INTRODUCTION: Ultrasound elastographic methods are more and more used for non-invsive evaluation of liver fibrosis
AIMS&METHODS: Aim : to assess the feasibility ("intend to diagnose") of the 3 shear waves elastographic methods (Transient Elastography-TE, Acoustic Radiation Force Impulse-ARFI and SuperSonic Shear Imaging-SSI) in chronic viral hepatitis patients.
Methods: Our study included 172 patients with chronic viral hepatitis, in which liver stiffness (LS) was evaluated by means of TE (using the standard M-probe), ARFI and SSI. Reliable measurements were defined as: median value of 10 (TE, ARFI) LS measurements with a success rate≥60% and an interquartile range interval<30%, values expressed in kPa (TE) or m/s (ARFI). Reliable LS measurements by means of SSI were definied as the median value of 5 LS measurements expressed in kPa.
RESULTS: The etiology of liver disease was: chronic hepatitis C – 99 patients (57.6%), chronic hepatitis B – 67 patients (38.9%), coinfection (B+C virus or B+D virus) – 6 patients (3.5%). Reliable LS measurements were obtained in a significantly higher percentage of patients by means of ARFI elastography as compared with TE and SSI: 92.5% vs. 79.1%, (p=0.0007) and 92.5% vs.81.9%, (p<0.0001), respectively. The rate of reliable LS measurements was similar for TE and SSI: 79.1% vs. 81.9%, (p=0.60).
CONCLUSION: The most feasible shear-waves ultrasound elastographic method for non-invasive assessment of liver fibrosis in chronic viral hepatitis patients was ARFI.
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Disclosure of Interest: None Declared
Keywords: elastography, liver fibrosis, liver stiffness

P1182 EARLY PREDICTION OF RESPONSE TO SORAFENIB IN PATIENTS WITH ADVANCED HEPATOCELLULAR CARCINOMA: THE ROLE OF DYNAMIC CONTRAST ENHANCED ULTRASOUND

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INTRODUCTION: Sorafenib has become the standard first-line treatment for patients with advanced hepatocellular carcinoma (HCC). This molecularly targeted therapy acts not only by inhibiting proliferation but also by inducing alterations in tumor vascularity that cannot be evaluated by traditional morphological criteria to assess tumor response. Contrast enhanced ultrasound (CEUS) is now recognized as a functional imaging technique able to evaluate tumor vascularization. In particular, recently developed quantitative approaches able to measure the amount and the time course of contrast uptake have shown great promise in revealing effective tumour response to anti-angiogenic drugs before tumour changes occur.
AIMS&METHODS: We wanted to evaluate the feasibility of dynamic CEUS (D-CEUS) as a predictor of early tumor response to Sorafenib and to correlate these functional parameters with clinical efficacy endpoints.

Twenty-eight HCC patients treated with Sorafenib 400 mg bid were prospectively enrolled. CEUS was performed at baseline (T0) and after 15 (T1) and 30 (T2) days of treatment. Tumor vasculature was assessed in a specific harmonic mode associated with a perfusion and quantification software (Q-Lab, Philips). Variations between T1/T2 and T0 were calculated for five D-CEUS functional parameters (peak intensity, PI; time to PI, T_P; area under the curve, AUC; slope of wash in, P_w; mean transit time, MTT) and were compared for responders and non responders. The correlation between D-CEUS parameters, overall survival (OS) and progression free survival (PFS) was also assessed. A p value < 0.05 was considered statistically significant.

RESULTS: The percentage variation at T1 significantly correlated with response in three D-CEUS parameters (AUC, PI and P_{wi}; $p = 0.002$, <0.001 and 0.003 respectively). A decrease of AUC ($p= 0.045$) and an increased/unchanged value of T_P ($p=0.029$) and MTT ($p=0.010$) were associated with longer survival. Three D-CEUS parameters (AUC, T_P, P_w) were significantly associated with PFS.

CONCLUSION: Dynamic US provides a more reliable and early measure of efficacy for antiangiogenic therapies and could be an excellent tool for selecting patients who will benefit from treatment. Further studies with a greater number of patients are required to confirm these results.

Disclosure of Interest: None Declared

Keywords: contrast-enhanced ultrasound, sorafenib

P1183 META-ANALYSIS OF CONTRAST-ENHANCED ULTRASOUND FOR DIFFERENTIATION OF BENIGN AND MALIGNANT FOCAL LIVER LESIONS

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INTRODUCTION: International guidelines of Ultrasonography (EFSUMB) recommend the performance of contrast-enhanced ultrasound (CEUS) as the first method of choice for the diagnostic work up of focal liver lesions, which are unclear on conventional ultrasound. However, these recommendations are based on the results of multiple single studies and only few large multicenter studies.

AIMS&METHODS: The aim of the present meta-analysis was to assess the overall sensitivity and specificity of CEUS for the diagnosis of malignant liver lesions.

Literature databases were searched up to March 2012. Inclusion criteria were: evaluation of CEUS, assessment of sensitivity and specificity of CEUS for the diagnosis of malignant liver lesions. The meta-analysis was performed using the random-effects model based on the DerSimonian Laird method. In addition, quality analyses were carried out to assess sources of heterogeneity.

RESULTS: 45 studies with 8147 focal liver lesions were included in the analysis. Overall sensitivity and specificity of CEUS for the diagnosis of malignant liver lesions was 93% (95%>CI: 91%, 95%) and 90% (95%>CI: 88%, 92%), respectively. A significant heterogeneity was found between the single studies. However, funnel plot evaluating publication bias showed symmetric distribution of studies. Subanalysis revealed no significant difference when evaluating studies using histology for all liver lesions, when comparing high quality and low quality studies, and blinded versus non-blinded studies. Comparison of CEUS and CT/MRI was possible using data of seven studies with overall 838 focal liver lesions. No significant difference of specificity (88% vs. 83%, p= 0.11) was found between CEUS and CT/MRI for the diagnosis of malignant liver lesions.

CONCLUSION:

The results of this meta-analysis support the EFSUMB recommendations to use CEUS as first method of choice in the diagnostic work-up of liver lesions following conventional ultrasound selecting patients who need further diagnostics (MRI, fine-needle biopsy).

The results of this meta-analysis support the EFSUMB recommendations to use CEUS as first method of choice in the diagnostic work-up of liver lesions following conventional ultrasound selecting patients who need further diagnostics (MRI, fine-needle biopsy).

Disclosure of Interest: None Declared

Keywords: contrast-enhanced ultrasound, focal liver lesions, metaanalysis

P1184 IS ACOUSTIC RESONANCE FORCE IMPULSE (ARFI) A GOOD TECHNIQUE FOR IMAGING LIVER CIRRHOSIS AND FIBROSIS? AN OBSERVATIONAL STUDY IN AN AUSTRALIAN TERTIARY HOSPITAL LIVER CLINIC SERVICE.

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INTRODUCTION: Current investigations of hepatic fibrosis include liver biopsy and the AST Platelet Ratio Index (APRI). However, liver biopsies can be plagued by sampling error, are invasive and associated with some serious complications (1, 2). APRI has been widely accepted as a noninvasive tool for clinical use (3). A newer technique, ARFI imaging is a modality of transient elastography which has been validated for the assessment of hepatic fibrosis (4, 5)

AIMS&METHODS: In this study we evaluated the use of ARFI as a tool for assessing hepatic fibrosis in a heterogenous population of 87 patients presenting to a tertiary hospital liver clinic.

An observational study was performed through The Geelong Hospital Liver Clinic. 87 subjects were recruited over a 12 month period. The subject population consisted of 50 males and 37 females, with a mean age of 51 years. 45/87 (51%) had chronic hepatitis C virus (HCV) alone, 26 (37%) had concurrent alcohol abuse. Other diagnoses included HBV in 6 (7%) cases, NASH in 7 (9%) and autoimmune chronic active hepatitis (1 case).

The ARFI score was compared against predictors of liver fibrosis such as the APRI and liver biopsy measurements where available. The ARFI scores correlated with increasing grades of fibrosis.

RESULTS: 17/87 patients were found to be cirrhotic based on their ARFI score. When correlated with their APRI score, 12 of these 17 patients were confirmed cirrhotic. The average APRI score in the ARFI-deemed cirrhotic group was 2.16, which was well above the APRI cut off score of >1.0 for cirrhosis. 7/87 patients had severe fibrosis based on the ARFI score, and the average APRI score was 1.28, just above the APRI cut off score for cirrhosis. 56/87 patients had mild or moderate fibrosis based on the ARFI score, and the average APRI score in this group was 0.62, well below the APRI cut off score for cirrhosis.

CONCLUSION: In this group tested, patients with a higher ARFI score suggesting cirrhosis or severe fibrosis also had a higher APRI score. This and other early studies suggest that ARFI may be a useful non-invasive modality to help clinicians assess hepatic fibrosis.

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Disclosure of Interest: None Declared

Keywords: ARFI elastography, CIRRHOSIS, Imaging

P1185 E2F-1 IMMUNOPHENOTYPE IS AN INDEPENDENT MARKER OF POOR PROGNOSIS IN HUMAN HEPATOCELLULAR CARCINOMA

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INTRODUCTION: E2F-1 transcription factor induces expression of genes controlling G1/S phase transition, DNA synthesis/repair, and apoptosis. E2F-1 activation depends on pRb phosphorylation. We have shown that E2F-1 is overexpressed and pro-apoptotic in hepatocellular carcinoma (HCC)*, while others have suggested that increased apoptosis in HCC could be indirectly oncogenic. The prognostic significance of E2F-1 immunoexpression in human HCC has not as yet been clarified.

AIMS&METHODS: Aim of the present study was to evaluate the prognostic significance of E2F-1 immunoexpression in human HCC.

Immunohistochemistry for E2F-1 and phospho(Ser795)pRB was employed on 57 surgically resected HCCs (grade I:8,II:24,III 16,IV:9). Patients were followed for 39.7±27.2 months.

RESULTS: Nuclear E2F-1 (nE2F-1) immunoexpression was observed in 32/57(54.3%) HCCs and correlated with phospho(Ser795)pRB immunoexpression ($p=0.045$), indirectly suggesting E2F-1 transcriptional activity. E2F-1 cytoplasmic immunoexpression (cE2F-1) was observed in 46/57(80.7%) HCCs. There was no significant correlation of nE2F-1 or cE2F-1 with clinico-pathological parameters. Portal vein thrombosis and nE2F-1 immunophenotype were correlated with poor overall survival ($p=0.05$ and $p=0.0001$, respectively), but not with recurrence-free survival. Stepwise Cox regression analysis highlighted nE2F-1 as an independent marker of poor prognosis in HCC (95% CI=2.55-52.43, $p=0.002$).

CONCLUSION: E2F-1 is expressed and transcriptionally active in the majority of human HCCs. E2F-1 immunophenotype is an independent marker of poor overall patient survival in a cohort of Greek HCC.

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Disclosure of Interest: None Declared

Keywords: E2F-1, Hepatocelluar carcinoma, prognosis

P1186 LIVER CANCER MORBIDITY IN RELATION TO CHANGES IN THE DIET IN POLAND IN THE YEARS 1980-2010

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INTRODUCTION: Liver cancer occurs in approximately 1% of Poles affected by all cancers. In 2010 its standardised incidence rate amounted to 2.9/100 thousand for males and 1.4/100 thousand for females.
AIMS&METHODS: The aim of the study was to identify the dietary factors, which could contribute to trends in liver cancer morbidity in Poland.
Standardised liver cancer incidence rates according to gender were derived from the National Cancer Registry. The information source on the dietary trends was data derived from the national food balance sheets showing food quantities available for consumption per capita/year. The Spearman rank correlation coefficient was used as a measure of the relationship between examined variables. Dietary variables included the consumption of fruit, cereals (as potential source of aflatoxins) and alcohol.
RESULTS: High adverse correlations were found for liver cancer incidence rates and fruit consumption, (-0.69 for males and -0.64 for females). Fruit consumption significantly increased in studied period – from 37.7 to 55.5 kg. Positive correlations (0.45 for men and 0.57 for women) were noted with respect to cereals consumption, which decreased from 130.2 to 110.0 kg.
Obtained results do not indicate positive correlations between liver cancer incidence rates and alcohol consumption. However in the in the early 80's an important decline in alcohol consumption was noted and could contribute to later decrease in liver cancer morbidity.
CONCLUSION: It seems that the trends in liver cancer incidence rates in 1980-2010 in Poland were affected by the growing fruit consumption. The decline in cereals consumption could play a protective role also. Improvement of cereal grains storage and implementation of food quality systems into cereal production could lead to decline in aflatoxins content in grains and thus strengthen this protective effect.
It is difficult to determine the influence of alcohol consumption on liver cancer morbidity. It is not unlikely that downward trends observed since beginning of the 90's were affected among others by earlier decline in alcohol consumption, but statistical analysis did not confirm it.
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Disclosure of Interest: None Declared
Keywords: cancer, diet, liver

P1187 SERUM ENDOCAN AS A NOVEL PROGNOSTIC BIOMARKER IN HEPATOCELLULAR CARCINOMA PATIENTS

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INTRODUCTION: Endocan is a vascular endothelium-derived factor regulated by angiogenic factors. Recent studies have shown that endocan is overexpressed at the mRNA and/or protein levels in various types of tumours.
AIMS&METHODS: We examined whether serum endocan can be a prognostic biomarker for survival in hepatocellular carcinoma (HCC) patients. Serum endocan levels were measured for 64 naïve HCC patients (median age 71 years, male 41; female 23) and 15 non-HCC subjects. Prognostic factors for survival were investigated by univariate and multivariate analyses using the Cox proportional hazard model. The following variables recoded into binary categories were assessed as potential prognostic factors: age (<70 years vs. ≥ 70 years), gender (female vs. male), etiology of liver disease (non-viral vs. viral), tumour stage (stage I/II vs. III/IV), Child-Pugh grade (A vs. B/C), treatment option (curative vs. non-curative), serum endocan (<2.20 ng/mL vs. ≥ 2.20 ng/mL), serumα-fetoprotein (AFP) (<100 ng/mL vs. ≥ 100 ng/mL) and serum des-γ-carboxy prothrombin (DCP) (<26 mAU/mL vs. ≥ 26 mAU/mL). The overall survival rates were calculated using Kaplan–Meier analysis, and the differences were evaluated by the log-rank test.
RESULTS: Serum endocan levels were 3.73 (0.74–10.95) ng/mL in HCC patients and 1.25 (0.93–3.54) ng/mL in non-HCC subjects, respectively ($P = 0.0002$). Elevated serum endocan levels were significantly associated with poor hepatic function ($P = 0.015$), a higher number of tumours ($P = 0.034$) and presence of vascular invasion of HCC ($P = 0.043$). During a median follow-up period of 23.0 months, 33 patients died due to the following causes: HCC in 23 patients, hepatic failure in 7 patients, other diseases in 2 patients and unknown cause in 1 patient. The cumulative overall survival rates were 78.8%, 56.5% and 37.9% at 1, 3 and 5 years, respectively. On multivariate analysis, elevated serum endocan levels, as well as elevated serum AFP and DCP levels, were significantly associated with poor survival (hazard ratio 2.36, 95% confidence interval 1.22–5.36, $P = 0.008$). When combining serum endocan and tumour markers, increase in number of elevated markers provided a worse survival ($P < 0.0001$).
CONCLUSION: Serum endocan may be a promising prognostic biomarker for survival in HCC patients. The combined use of serum endocan with serum AFP and DCP can allow a better prognostic stratification for such patients.
Disclosure of Interest: None Declared
Keywords: Endocan, Hepatocelluar carcinoma, Prognostic Value

P1188 CANCER-STEM CELL-LIKE SPHERE CELLS INDUCED FROM A CELL LINE DERIVED FROM POORLY-DIFFERENTIATED HEPATOCELLULAR CARCINOMA EXERTS LIVER METASTATIC POTENTIAL AND CHEMORESISTANCE

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INTRODUCTION: It is thought that cancer-stem cell (CSC) plays important roles in carcinogenesis, recurrence, metastasis, and chemoresistance. Recently, it was suggested that the possible existence of plasticity between CSCs and their more differentiated derivative cancer cells. We hypothesized that poorly-differentiated hepatocellular carcinoma (HCC) has potential that convert to CSC, which would responsible for metastasis and recurrence.
AIMS&METHODS: Human HCC cell lines, SK-HEP-1, HLE, HuH-7, and Hep 3B, were used for sphere induction. Sphere induction was accomplished by using specified medium based on the medium for neural stem cells. Liver metastatic potential was examined by injection of the cells to immune-deficient mice spleen. Cell viability was measured by MTS assay. 9 anti-cancer agents (5-Fluorouracil, Cisplatin, Carboplatin, Docetaxel, Doxorubicin, SAHA, Irinotecan, Sorafenib, Sunitinib) were used. The mRNA and protein levels were examined by real-time PCR and flow cytometry analyses. ALDH activity was measured by ALDEFLUOR assay. Reactive oxygen species (ROS) activity was measured with the cell-permeable fluorogenic probe, 2', 7'-Dichlorodihydrofluorescin diacetate.
RESULTS: A cell line derived from poorly-differentiated HCC, SK-HEP-1, formed Sphere, although cell lines derived from well-differentiated HCCs, HuH-7 and Hep 3B, could not form sphere. Sphere cells induced from SK-HEP-1 cells (SK-sphere) showed higher mRNA levels of NANOG, LIN28A, and ABC transporters and ALDH activity compared to SK-HEP-1 cells. SK-sphere cells also showed increased liver metastatic potential compared to parental cells. SK-sphere cells represented obvious decreased-sensitivity to 5-Fluorouracil, Docetaxel, Doxorubicin, and SAHA. Sorafenib was effective in both SK-HEP-1 and SK-sphere cells. SK-sphere cells showed induced P21 mRNA and cell cycle arrest in G0/G1 phase. The ROS activity in SK-sphere cells was lower than those in SK-HEP-1 cells. On the other hand, the HIF1-alpha expression in SK-sphere cells was higher than those in SK-HEP-1 cells. Increased expression of Vimentine and decreased expression of EpCAM were observed in SK-sphere cells compared to parental cells. Higher SNAI1 mRNA level of SK-sphere cells was also observed.
CONCLUSION: Our induced sphere cells, SK-sphere, showed increased metastatic potential, chemoresistace, and epithelial-mesenchymal transition.
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Disclosure of Interest: None Declared
Keywords: cancer stem cell, chemoresistance, hepatocellular carcinoma, recurrence

P1189 MOLECULAR INVESTIGATIONS BY RAMAN IMAGING FOR A RELIABLE DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

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INTRODUCTION: Patients with hepatocellular carcinoma (HCC) can only be treated curatively at early stages thus providing a favorable prognosis of this often fatal disease. However, histopathological examinations of different liver lesions remain a challenge for pathologists. Because of its high information content Raman spectroscopy is particularly suitable for investigating cellular and subcellular constituents. By using recognition and classification algorithms tissue-specific patterns can be discovered in order to develop an independent model for secure HCC prediction.
AIMS&METHODS: The aim of the present study is to investigate molecular information about HCC and non-malignant liver tissue by Raman imaging in order to use the obtained spectral patterns for diagnosis.
Human hepatic tissue sections were measured with the confocal Raman microscope. A parallel section of each sample was stained with HE to assign tissue regions to HCC (n=12), fibrotic tissue (n=14) and regenerative nodules (n=4). Raman spectra were acquired and the average and difference spectra of each region were calculated. A training data set including the spectral data from regions of HCC (n=6) and fibrosis (n=7) were used to generate a classification model based on a support vector machine algorithm. The obtained classifier was applied to independent validation data sets of HCC regions (n=6) together with regions of fibrosis (n=7) and the same HCC regions (n=6) together with regenerative nodules (n=4).
RESULTS: Analyzing the difference spectra of malignant and non-malignant tissue, distinct spectral differences in the negative bands at 1676, 1387, 1345, 1241, and 936 cm^{-1} and in the positive bands at 1739, 1653, 1436, 1300, 1076, 890, and 721 cm^{-1} were identified. The classification model based on the training data set calculated a prediction accuracy of the classification model of 81%. The developed classifier was able to predict previously unknown HCC and fibrotic tissue with an accuracy of 90% (sensitivity 78%, specificity 100%). The performance of the same classification model to predict regions of HCC and regenerative nodules resulted in an accuracy of 82% (sensitivity 72%, specificity 83%).
CONCLUSION: In this study Raman imaging spectroscopy was for the first time applied successfully to tissue of the cirrhotic liver with the aim to differentiate, classify and predict with high accuracy malignant and non-malignant tissue regions. The demonstrated results highlight the enormous potential which light scattering techniques have for future diagnostics of cancer.
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Disclosure of Interest: None Declared
Keywords: Classification model, Fibrosis, Hepatocellular cancinoma, Prediction, Raman imaging, Regenerative nodules

P1190 CAPSAICIN IMPAIRS CARCINOGENESIS OF HUMAN CHOLANGIOCARCINOMA CELLS

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INTRODUCTION: Capsaicin, the most abundant pungent molecule produced by pepper plants, represents an important ingredient in spicy foods consumed throughout the world. Previous studies have shown that capsaicin has anti-proliferative effects on various human malignancies like leukemia, esophageal carcinoma, gastric and pancreatic cancer, as well as colon carcinoma and breast cancer. In contrast, capsaicin has also been considered to promote the growth of cancer cells. It is also known that capsaicin application can relieve inflammation and pain.
AIMS&METHODS: The aim of the present study is to explore the anti-tumor activity of capsaicin in human cholangiocellular carcinoma (CC) cell lines (TFK1, SZ1). We analyzed the effect of capsaicin by testing different dosages on CCs growth and epithelial plasticity by using WST-1 assay, wound healing assay and invasion assay respectively.
RESULTS: The effect of capsaicin by using different dosages on CCs growth, migration and metastasis was analyzed using WST-1 assay, wound healing assay and invasion assay respectively.
CONCLUSION: Our data demonstrate that treatment with capsaicin can successfully decrease the carcinogenesis of CC cells *in vitro* and suggest an appealing potential therapeutic strategy for human CCs *in vivo*. Further studies are needed to confirm our preliminary results.
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Keywords: Capsaicin, Carcinogenesis, Cholangiocarcinoma

P1191 VARIATION IN PRACTICE OF HEPATOCELLULAR CARCINOMA (HCC) SURVEILLANCE

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INTRODUCTION: The annual risk for development of HCC in cirrhotics range between 1% and 6%. EASL guidance (2012) recommends implementation of surveillance program for all cirrhotics[1]
AIMS&METHODS: We wanted to determine if there is difference in practice of HCC surveillance in cirrhotics among hospitals in Wales, UK. Invitation to participate in an online survey was sent via email link to all WAGE members (Welsh Association for Gastroenterologists and Endoscopists). 42 members responded and results analysed. There were total of 10 questions with focus on belief in surveillance, selection of target group and methodology used. Among the respondents, there were 1 hepatologist, 2 hepatology specialist nurses and 2 radiologists; rest all gastroenterologists with interest in hepatology.
RESULTS: Three gastroenterologists did not believe in the policy and would not routinely offer surveillance to any cirrhotics (no comments given). Rest 39 believe in surveillance, but 9 not for all cirrhotics. 71% offer 6 monthly Ultrasound (US) and alphafetoprotein (AFP) measurements as method for surveillance, 5% 6 monthly US only; 5% 6 monthly AFP only; 10% yearly US only and 9% skipped this question. Only 78.5% believed surveillance for all cirrhotics; 13% would offer to cirrhotics who are abstinent from alcohol and 4.3% to viral hepatitis cirrhotics only. 4 members admitted age cut-off for surveillance. 66.6% do surveillance depending on patients co-morbidities and 57.1% practice based on patients wishes. 73.8% arrange surveillance from review during follow-up clinic, 9.5% through recall system from database and 16.6% arrange during hospital admissions. The Consultant organises surveillance according to 51.9%, while the hepatology nurse contribute 21.6% and other doctors in 9.5%. Any radiographer performs surveillance imaging as per 40.4%, any radiologist in 47.6% and a dedicated liver radiographer / radiologist only in 11.9%. 43.5% believe that the surveillance program in their hospital is not funded and rest are not aware of any funding.
CONCLUSION: There is wide variation in belief and practice of HCC surveillance in Wales. There is need to standardise surveillance method as there is risk of missing interval cancers. Whether the difference in opinions apply universally and whether mortality / morbidity of patients is affected by early HCC detection need to be explored further.
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Disclosure of Interest: None Declared
Keywords: Hepatocelluar carcinoma, surveillance

P1192 HEPATOCELLULAR CARCINOMA (HCC) DEVELOPED ON NON-FIBROUS LIVER (F0-F1): EPIDEMIOLOGIC, CLINICAL, HISTOLOGICAL AND PROGNOSTIC PARTICULARITIES. A MONOCENTRIC STUDY OF 142 CASES. COMPARISON TO HCC DEVELOPED ON FIBROUS LIVER (F2-F3) AND CIRRHOTIC LIVER.

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INTRODUCTION: HCC on non fibrotic liver (nfHCC) is uncommon and risks factors, clinical feature as well as prognosis remain poorly known. The aim of this study was to analyse a cohort of 141 cases of nfHCC compared to HCC on fibrotic or cirrhotic liver.
AIMS&METHODS: From a prospective database of 1009 consecutive patients diagnosed with HCC since 2005, 141 cases of nfHCC (histologically proved F0-F1) were identified and compared to 93 patients F2-F3, and 470 cirrhotic patients CHILD A. Epidemiological, clinical, biological, pathological data were recorded. Follow-up included CT-Scan or RMI every 3 to 6 months.
RESULTS: Usual risk factors of HCC (alcohol, hepatitis B/C, metabolic syndrome (MS)) were found in 2/3 of nfHCC. MS was present in 37% of F0/F1 vs 50% (F2/F3) and 33.5% (F4). Pathological features of NASH were observed in F2/F3 patients but not in F0/F1 patients. Diagnosis is delayed in nfHCC due to the lack of screening (7,8%). Tumors were larger at diagnosis (74 mm F0/F1 vs 50 F2/F3 vs 35 F4 $p < 0.05$). The rate of patients eligible to curative treatment is higher in nfHCC (68% vs 43%) leading to a better overall survival (OS) (4.01 years F0/F1 vs 2.14 F4 $p = 0.02$). After curative treatment, time to recurrence (TTR) and OS are similar in both groups (1.31 years vs 1.06 $p = 0.88$ and 60 months vs 54 respectively). Patients F0-F1 without known risk factors (34%), were younger (62.4 vs 65.7 year old F4) with a different sex ratio (female 44% vs 14.9% F4) and tumors massively expressed the glutamine synthase (86.4% of patients). This group exhibited a better prognosis in OS (6.35 years vs 2.13 F4 Child A) and TTR (2.03 years vs 1.06 F4).
CONCLUSION: Usual risk factors of HCC are observed in 2/3 of nfHCC including MS in 1/3 of cases. Prognosis is better in nf-CHC frequently eligible to curative treatment. However, after curative treatment, OS and TTR are similar to those observed in patients with cirrhosis. In the subgroup of nfHCC without identified risk factor, tumors occur in a younger and female population, and the prognosis is better.
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Disclosure of Interest: None Declared
Keywords: epidemiology, Hepatocelluar carcinoma, Metabolic syndrome, Non cirrhotic liver, Prognosis

P1193 COMPARISON OF DIFFERENT MACHINE LEARNING SYSTEMS IN CLASSIFYING FOCAL LIVER LESIONS BASED ON CLINICAL AND DYNAMIC IMAGING DATA

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INTRODUCTION: Early diagnosis of hepatocellular carcinoma (HCC) is of upmost importance for ensuring best chances of survival for the patient. A suspicion can be raised from routine clinical investigation; however, only experienced clinicians may suspect an underlying HCC in some cases. Machine learning (ML) and especially artificial neural networks (ANNs) and support vector machines (SVMs) are currently employed in various medical settings.
AIMS&METHODS: Our aim was to test two ML approaches in a typical clinical setting for the diagnosis and possible prognosis of HCC. Based on our extensive experience with ANNs in HCC diagnosis [1,2], we extended our study on a lot of 486 patients with focal liver lesions who underwent diagnostic work-up in a large main referral center (University County Hospital of Craiova, Romania) between January 2009 – September 2012. Final diagnosis was obtained through pathology, post-treatment evaluation or six months follow-up. Relevant demographic and clinical data (sex, age, alcohol consumption, viral hepatitis infections, cirrhosis/Child-Pugh parameters, laboratory data) and imaging data from dynamic investigations, CE-CT/MRI or CEUS – time-intensity curve (TIC) parameters (time to peak, rise time, fall time, mean transit time, area under the curve), calculated as previously described [1,2], were imputed. We thus constructed two distinct models, one with only clinical data (ML1) and one with combined clinical and dynamic imaging data (ML2).
RESULTS: We included 178 cases of HCC, 26 intrahepatic cholangiocarcinomas, 243 liver metastases (102 hypovascular), 16 liver hemangiomas and 23 focal fatty changes. We employed a SVM and an ANN for ML1 and attempted classification into malignant and benign lesions. The SVM correctly classified 401/486 (82.5%) and the ANN 447 (91.9%) cases. For ML2 we used an ANN system to classify lesions into six distinct categories, obtaining an overall accuracy of 92.7%. Their specificity/sensitivity 95.5/89.7%, while the training and testing accuracy were 92.5/87.2% respectively. Both TIC data and clinic parameters proved to be good classifiers, significantly improving the diagnostic accuracy of the ANN system.
CONCLUSION: ANNs seem more appropriate than other approaches when employed in medical classification problems. More parameters improve the accuracy of diagnosis. ANNs can provide data on which are the most suitable prognostic factors for HCC.
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Disclosure of Interest: None Declared
Keywords: artificial neural networks, contrast-enhanced ultrasound, hepatocellular carcinoma, support vector machine, time intensity curves

P1194 HEPATOCELLULAR CARCINOMA (HCC) AND METABOLIC SYNDROME: CLINICAL, BIOLOGICAL, PATHOLOGICAL FEATURES AND PROGNOSIS. ANALYSIS OF A PROSPECTIVE COHORT OF 925 HCC

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INTRODUCTION: Metabolic syndrome (MS) is a risk factor of HCC usually via underlying NASH/NAFLD. The aim of this study was to compare clinical, biological, pathological features as well as prognosis of HCC in patients with or without MS.
AIMS&METHODS: 941 consecutive patients with HCC were included between 01/2005 and 03/2012. Clinical, biological, pathological, radiological data were recorded and compared between patients with and without MS (NCEP ATP III). Follow-up included CT-Scan or RMI every 3/6 months (median follow-up 16.5 months)
RESULTS: MS was present in 29% of patients who were older (68.3 vs 64.48 years $p < 0.001$) and often male (90% vs 82% p=0.02). Underlying liver disease was less advanced and HCC was developed more often on non-cirrhotic livers (28.8 vs 21.5% $p = 0.01$). Diagnosis is delayed in the MS group, with a low screening rate (28 vs 40% in non-MS ($p < 0.01$)).
Overall survival (OS) was similar in the 2 groups (2,68 years (MS) vs 3,23 p=0,44). Recurrence free survival (RFS) after curative treatment was similar in the 2 groups (2,18 years (MS) vs 2,49 p=0,509) but late recurrences (> 2 years) were more frequent in the MS group.
A subgroup analysis was performed, comparing patients with MS only ($n = 80$), with those with alcoholic disease ($n = 271$) or hepatitis C ($n = 106$). HCC occurred more often on non-cirrhotic livers in the MS group (49 %) vs 15% (HCV) and 13% (OH) ($p = 0.01$). Overall survival was similar for MS group and HCV group (36 months) but inferior for alcoholic disease group exhibiting a more severe underlying liver disease (22 months). No difference was observed between the 3 groups for the RFS after curative treatments.
CONCLUSION: One third of patients diagnosed with HCC had MS, frequently associated with an excessive alcohol intake. In 9% of cases, MS was the only risk factor found. HCC with MS occurred more often on non-cirrhotic livers. In spite of a less severe hepatic disease in the MS group, OS was not better and the rate of recurrence, especially late recurrences (> 2years) are high.
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Disclosure of Interest: None Declared
Keywords: Hepatocelluar carcinoma, Metabolic syndrome, NASH, hepatoma, familial risk

P1195 PROGNOSIS OF PATIENTS WITH HEPATOCELLULAR CARCINOMA (HCC) IN THE NONCIRRHOTIC LIVER (NCL)

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INTRODUCTION: In 15-20% of patients with HCC the malignancy arises in the absence of liver cirrhosis (LC). In patients with LC, liver function strongly influences patient survival.
AIMS&METHODS: Aim: To analyse clinical characteristics and course of disease in patients with HCC in the noncirrhotic liver and to compare their outcome to patients with HCC and LC.
Methods: A retrospective analysis of medical records of 664 patients with HCC with respect to epidemiological data, tumor characteristics, tumor stage at diagnosis according to BCLC classification and survival was performed, comparing 93 patients (14.01%) without LC to 571 pts (85.99%) with LC.
RESULTS: Results: The median age of patients with LC was 66 years (y) compared to 69 y in patients with NCL ($p = 0.004$). In patients with LC 18 % were female compared to 27% in patients with NCL (p=0.045). Statistically significant differences were depicted concerning tumor stage at diagnosis (LC: BCLC-A 17.5%, -B 29.6%, -C 42.4%, -D 10.5%; NCL: BCLC-A 14%, -B 34.4%, -C 51.6, -D 0%, p=0.006) with more patients diagnosed in intermediate and advanced stage in NCL. Overall survival according to BCLC-stage (median values in days of survival: BCLC-A 951 (LC) vs 945 (NCL) days (d); BCLC-B 501 (LC) vs 925 (NCL) d; BCLC-C 209 (LC) vs 229 (NCL) d) did not show statistically significant differences between patients with HCC in LC and patients with HCC in NCL (p=0.061). Both, the tumor stage according to BCLC ($p = 0.011$) and the Clip score ($p = 0.010$) correlated with survival in patients with HCC in NCL. While statistically significant differences were found concerning concentrations of bilirubin, albumin, quick and platelets, no statistically significant differences were found concerning concentrations of creatinine, alcalic phosphatase, alpha-fetoprotein, alanin-aminotransferase and ferritin.
CONCLUSION: Patients with HCC in NCL are diagnosed at higher age and with a larger proportion of female patients. Absence of LC leads to diagnosis in more advanced tumor stages. Patients with HCC in NCL show a trend towards longer survival in intermediate tumor stage.
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Disclosure of Interest: None Declared
Keywords: BCLC, hepatocellular carcinoma, liver cirrhosis, survival

P1196 REAL-LIFE MANAGEMENT OF HCC WITH SORAFENIB AND TACE IN EUROPE FROM GIDEON (GLOBAL INVESTIGATION OF THERAPEUTIC DECISIONS IN HCC AND OF ITS TREATMENT WITH SORAFENIB)

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INTRODUCTION: The global, prospective, non-interventional GIDEON study of >3200 patients (pts) with unresectable (u) HCC treated with sorafenib (SOR) in real-life practice conditions evaluated the safety/efficacy of SOR in a diverse range of settings and pt groups where data are currently limited. We describe the safety/efficacy in uHCC pts, treated with SOR in Europe, according to prior transarterial chemoembolization (TACE) and concomitant (ct) TACE.
AIMS&METHODS: Patient demographics, disease characteristics and treatment history, were recorded at enrolment; SOR dose, liver function, adverse events (AEs) and efficacy were recorded at follow-up.
RESULTS: In Europe, 1113 pts were enrolled and valid for safety. A third of pts (33%) received prior TACE, and 5% received ctTACE. The proportion of ECOG PS 0 was slightly higher in patients who had prior TACE or ctTACE than others (52.7%, 41.6%, 55.8%, 44.9% in patients with prior TACE, no prior TACE, ctTACE and no ctTACE respectively). Median daily SOR dose was 780 mg (n=1026) and similar across all the groups. Duration of treatment was longer in patients who had prior TACE or ctTACE than others (20.1 weeks [wks], 16.0 wks, 31.8 wks and 16.4 wks in patients with prior TACE, no prior TACE, ctTACE and no ctTACE, respectively). AEs and serious AEs (SAEs) were similar across these groups. There is no new unexpected AE. Median OS was 66.3 wks, 44.1 wks, 70.6 wks and 48.0 wks in patients with prior TACE, no prior TACE, ctTACE and no ctTACE respectively.
CONCLUSION: The data suggest AE profiles of sorafenib in patients treated with TACE prior to sorafenib or concurrently are consistent with the safety profiles observed in previous clinical trials with monotherapy as well as combination therapy with TACE. Sorafenib treatment in combination with TACE appears to be tolerable and feasible.
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Keywords: hepatocellular carcinoma, sorafenib

P1197 RESIDUAL VIABLE TUMOR VOLUME MEASUREMENT FOR EARLY PROGNOSTIC ASSESSMENT OF HEPATOCELLULAR CARCINOMA PATIENTS TREATED WITH SORAFENIB

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INTRODUCTION: The introduction of the targeted agent Sorafenib with anti-angiogenic activity has not only changed the way advanced hepatocellular carcinoma (HCC) is treated, but also how it is monitored.
AIMS&METHODS: To evaluate the prognostic value of early radiological tumor response to sorafenib treatment according to Response Evaluation Criteria in Solid Tumors (RECIST), modified RECIST (mRECIST), European Association of Liver Disease (EASL) criteria and arterial enhancing tumor volume ratio (Rvol: 2 months/baseline) in patients with HCC.
Twenty-two patients (18 male, mean age 68 years) with HCC treated with sorafenib were enrolled in this retrospective study. The 2-months response to treatment was evaluated by RECIST, mRECIST, EASL, Rvol and alfa-fetoprotein ratio (2 months AFP / baseline AFP) and compared to survival. Two independent blinded readers evaluated radiological tumor response twice to assess measurements' reproducibility.
RESULTS: At 2-months follow-up, rates of objective response (complete and partial response), stable disease and progressive disease were 18.2%, 22.7% and 72.7% for RECIST, 18.2%, 22.7% and 59.1% for mRECIST and 9.1%, 31.8% and 59.1% for EASL. A good intra- and inter-observer agreement was observed in the assessment of tumor response (k=0.83-0.86) and in maximum (k=0.95-0.96) and total diameter calculation (k=0.93-0.94). Mean post-processing time for volume calculation was 1.8 ± 1.2 minutes (range, 0.5-5.5), with high reproducibility of volume measurements (k=0.99). Mean Rvol was 1.76 ± 2.17, and it was >1 in 12/21 patients (57.1%). Mean AFP ratio was 14 ± 37, and it was >1 in 15 patients (68.2%). The 1-year cumulative survival rate was 65.9%. Overall

survival was significantly associated only to Rvol, with an identified Rvol cut-off value of 1.17 (AUC 0.71); the 12-month cumulative survival rate was 90% in patients with Rvol £1,17 and 40% in Rvol >1.17 (p=0.04).
CONCLUSION: Assessment of arterial enhancing tumor volume variation should be considered as an alternative to RECIST, mRECIST and/or EASL for early assessment of tumor response and prognosis of patients with HCC treated with sorafenib.
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Disclosure of Interest: None Declared
Keywords: alfa-fetoprotein, HCC, mRECIST, sorafenib

P1198 PROGNOSTIC FACTORS FOR SURVIVAL IN PATIENTS WITH HEPATOCELLUAR CARCINOMA AFTER CURATIVE SURGERY INCLUDING THE INFLAMMATION-BASED PROGNOSTIC SCORES

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INTRODUCTION: Several studies have shown that inflammation-based prognostic scores, including Glasgow Prognostic Score (GPS), neutrophil to lymphocyte ratio (NLR), and Prognostic Nutritional Index (PNI) are correlated with survival in patients with hepatocellular carcinoma (HCC).
AIMS&METHODS: The aims of this study are to validate the power of prognostic scores, which are based on preoperative inflammation status and widely used score systems, of patients who underwent curative and initial hepatectomy for HCC. Inflammation-based prognostic scores and established clinical scores were retrospectively analyzed in 242 patients.
RESULTS: In multivariate analysis elevated AFP (Hazard Ratio [HR] 1.89, 95% Confidence interval [CI] 1.19-3.00, $P = 0.007$), NLR > 5 (HR 2.41, 95% CI 1.07-5.39, $P = 0.033$), and PNI < 45 (HR 2.26, 95% CI 1.34-3.81, $P = 0.002$) remained as significant independent predictors of overall survival in HCC. On the contrary, elevated AFP (HR 1.89, CI 1.34-2.69, $P < 0.001$), high Barcelona Clinic Liver Cancer score (HR 5.48, 95% CI 1.19-25.4, $P = 0.029$), larger tumour (HR 1.50, 95% CI 1.04-2.16, $P = 0.031$), multiple tumour (HR 2.37, 95% CI 1.19-4.71,$P = 0.014$), and presence of microsatellite lesions (HR 2.74, 95% CI 1.81-4.15, $P < 0.001$) remained as significant independent predictors of recurrence-free survival in HCC.
CONCLUSION: The present study reveals that the prognostic scores based on preoperative inflammation status (NLR and PNI) but not tumour factors are validated for predictor of overall survival in the patients who underwent curative and initial hepatectomy for HCC.
Disclosure of Interest: None Declared
Keywords: curative hepatectomy, hepatocellular carcinoma, inflammation-based prognostic score, recurrence, survival

P1199 TREATMENT STRATEGY FOR COLORECTAL LIVER METASTASIS BASED ON GENETIC PROFILES

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INTRODUCTION: Discovery of practical biomarkers is important to realize personalized medicine for patients with malignant neoplasia, including colorectal cancer (CRC). Liver is the most frequent metastatic sight in CRC. The treatment strategy for colorectal liver metastases (CRLM) based on genetic profiles is essential for further improvement of CRC prognosis.
AIMS&METHODS: Genomic DNA was obtained from a cohort of 240 CRC patients with distant metastasis. *KRAS*/*BRAF*-mutation (Mt) spectrum and microsatellite instability (MSI) status were analyzed by direct sequence and multiplex PCR. And these genetic profiles were compared with their clinical outcomes.
RESULTS: The cohort of 240 CRC patients with distant metastasis consisted of 148 synchronous and 92 metachronous metastasis. And 149 patients had liver metastasis alone and 91patients had extra-liver spreading with/without liver metastasis. In MSI analysis, only 3 cases (1.2%) revealed evidence of MSI. As regard to genetic profiles about *KRAS*/*BRAF*, the proportions of *KRAS*-Mt/*BRAF*-Mt/ wild type were 28/4/63 (%) in the group of liver metastasis alone and 17/11/72 (%) in the group of extra-liver spreading, respectively. Liver resection was performed for 106 patients with CRLM, the resectabilities of which were 67.5% in wild type, 38.5% in *KRAS*-Mt, and 20% in *BRAF*- Mt, respectively. Recurrence rate after liver resection was 59% in *KRAS*-Mt, which was comparable to that in wild type. However *KRAS*-Mt showed the higher risk of extra-hepatic sight recurrence. Furthermore, all CRLM with *BRAF*-Mt showed intractable extra-hepatic sight recurrence after liver resection. In survival analysis, the overall 1-, 3-, and 5- year survival rates were 94.1%, 77.1%, and 65.1% in wild-type, 84.9%, 54.3%, and 43.4% in *KRAS*-Mt, and 33.3%, 0%, and 0% in *BRAF*-Mt, respectively.
CONCLUSION: The cohort of CRLM patients were mainly occupied by non-MSI tumors. These supported that MSI cancer in primary CRC would rarely have metastatic potential. *BRAF* mutations are suggested to be extremely poor prognostic factor in CRLM. Genetic information could play a key role as a prognostic marker and could contribute to the decision of treatment strategy for CRLM.
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Disclosure of Interest: None Declared
Keywords: BRAF, Colorectal cancer, KRAS, liver metastasis, Microsatellite Instability

P1200 COMPARISON OF SELF EXPANDING METAL STENTING WITH RADIOFREQUENCY ABLATION VERSUS STENTING ALONE IN THE TREATMENT OF MALIGNANT BILIARY STRICTURES: IS THERE AN ADDED BENEFIT?

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INTRODUCTION: Radiofrequency ablation (RFA) has been reported to be a beneficial treatment option for palliation of malignant biliary strictures. Both pancreatic and cholangiocarcinoma carry a poor prognosis with a median survival of less than a year even with palliative therapy.
Biliary obstruction is a common complication and many require stenting for definitive decompression. The added benefit of RFA to stenting is unknown.
AIMS&METHODS: The objective of this study was to compare the safety, efficacy and survival of patients with RFA and metal stent versus stent alone.
Methods: A prospectively collected database was reviewed identifying 64 patients with malignant biliary strictures from July 2010 to March 2013. Cases were patients who underwent RFA with metal stenting. Controls were patients who were treated conventionally with metal stenting. The groups were matched on age, diagnosis and palliative chemotherapy. The Habib TM EndoHPB catheter (Emcision Ltd., Hitchin Herts, UK) was used for ablation. All patients received covered or uncovered self expanding metal stents (SEMS). Immediate and 30-day complications were recorded. Patient status and last known date was collected for survival and cox proportional hazard analysis.
RESULTS: RFA and control groups were closely matched- age 65.5±13.4 vs. 66.8±12.16yrs, p=0.0.69; and diagnosis (36 patients with cholangiocarcinoma and 28 patients with pancreatic cancer), (29 in stent group vs 13 in RFA group, p=0.3). Technical success rate for the both groups was 100%. Multivariable cox proportional regression analysis showed RFA to be independently predictive of survival (HR 0.29 (0.11-0.76) p=0.012) as well as age, and chemotherapy (1.04 (1.01-1.07)p=0.011, 0.26 (0.10-0.70)p=0.007). Overall SEMS patency rates were the same across both groups. Complications of RFA were few (1 pancreatitis, 1 cholangitis) vs 3 cholangitis in the non RFA group, p=NS.

	Univariate HR ratio (95% CI)	P value	Multivariable HR ratio (95% CI)	P value
rfa	0.77(0.41-1.45)	0.424	0.29 (0.11-0.76)	0.012
age	1.04 (1.01-1.07)	0.002	1.04 (1.01-1.07)	0.011
chemotherapy	0.37 (0.0.97-0.71)	0.002	0.26 (0.10-0.70)	0.007
Stricture improvement	0.81 (0.64-1.02)	0.067	0.84 (0.65-1.09)	0.208

CONCLUSION: The use of RFA appears to improve survival in patients with endstage cholangiocarcinoma and pancreatic cancer. In a disease with limited treatment options, this modality may prove to be beneficial as compared to stenting alone. Randomized controlled trials and evaluation of quality of life measures should be performed to confirm these findings.
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Keywords: biliary obstruction, metal stent, radio frequency ablation

P1201 COMPARISON OF ACCURACY AMONG ENDOSCOPIC ULTRASONOGRAPHY, MULTIDETECTOR COMPUTED TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING FOR PREOPERATIVE STAGING OF CHOLANGIOCARCINOMA

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INTRODUCTION: Preoperative imaging modalities including multidetector computed tomography (MDCT), magnetic resonance imaging (MRI) and endoscopic ultrasonography (EUS) can visualize the bile duct tumor and predict unresectability with variable degree of accuracy. The role of EUS as a preoperative staging work-up compare to MDCT and MRI for bile duct tumor remains less clear. The aim of the present study was to evaluate the utility of EUS for preoperative staging of cholangiocarcinoma compared to MDCT and MRI.
AIMS&METHODS: Twenty nine patients with cholangiocarcinoma who underwent curative surgical resection between February 2007 and May 2012 at our institution were enrolled in the current study. The medical records, laboratory data, radiologic imagings and endosopic results were retrospectively reviewed.
RESULTS: Mean (standard deviation, years) age of enrolled patients was 68.3 (9.3) and 20 (69.0%) were male. The final diagnoses according to surgical pathology were cholangiocarcinoma (n=28, 96.6%) and gallbladder adenocarcinoma (n=1, 3.4%). The locations of the bile duct stricture were distal (n=19, 65.5%), mid (n=5, 17.5%) common bile duct (CBD) and common hepatic duct (hilar, n=5, 17.5%). The primary mass lesion was only detected by EUS and not by MDCT in Six (20.7%) patients. Compared to finally reported AJCC staging results of surgically resected specimens, the accuracy of tumor (T) staging of EUS, MDCT and MRI were 89.7%, 31.0% and 75.0%, respectively. The accuracy of node (N) staging of EUS, MDCT and MRI were 93.1%, 79.3% and 75.0%, respectively. The accuracy of AJCC stage grouping of EUS, MDCT and MRI were 79.3%, 41.4% and 58.3%, respectively.
CONCLUSION: EUS is more sensitive in the detection of bile duct tumor than MDCT. The accuracy of EUS for the preoperative AJCC tumor staging of cholangiocarcinoma is higher than MDCT and MRI.
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Disclosure of Interest: None Declared
Keywords: accuracy, cholangiocarcinoma, endoscopic ultrasonography, magnetic resonance imaging, multidetector computed tomography, stage

P1202 A TRIAL OF NON-SELECTIVE BETA-BLOCKER: IS A VIABLE OPTION FOR MAKING THE PERCUTANEOUS LIVER BIOPSY POSSIBLE IN CHILDREN WITH THROMBOCYTOPENIA DUE TO HYPERSPLENISM

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INTRODUCTION: Thrombocytopenia due to hypersplenism precludes liver biopsy in many cases of chronic liver disease. So far there is no study on using non-selective beta-blockers to ameloriate hypersplenism to make percutaneous liver biopsy possible.
AIMS&METHODS: The aim of this study was to assess whether normalization of platelet count ($\geq$100,000/mm^3) and subsequent liver biopsy was possible with the use of non-selective beta-blocker in children with intrahepatic portal hypertension or not.
Methods: From January 2005 to December 2012, 51 children with intrahepatic portal hypertension with hypersplenism were recruited. Hypersplenism was defined as decrease in platelet counts $<$100,000/mm^3 and total leucocyte counts $<$ 4000/mm^3. These children were started on long-acting beta-blocker (propranolol), at a dose of 1.5 to 2 mg/kg/day (maximum 80mg) and 4 weeks later repeat platelet counts and whenever possible percutaneous liver biopsy was done. Resting heart rate, blood pressure and spleen size were measured before and 4 weeks after starting propranolol therapy.
RESULTS: The mean age was 11.5 $\pm$ 3.0 years, with 34 boys. Etiology was chronic liver disease 38 (autoimmune hepatitis 13, hepatitis B 9, Wilson disease 3, hepatitis C 1, cryptogenic 12), non-cirrhotic portal fibrosis (NCPF) 10 and congenital hepatic fibrosis (CHF) 3. Thirty two (62.7%) children responded to propranolol therapy (platelet counts $>$ 100,000/mm^3) and their mean platelet counts increased from 57.5 $\pm$ 13.0 x 10^3 /mm^3 to 140.7 $\pm$ 43.3 x 10^3/mm^3, p= 0.0001. Liver biopsy was done in 29 and associated coagulopathy precluded biopsy in 3. Comparing the responders with non responders, spleen size (7.4 $\pm$ 3.3 *vs* 12.7 $\pm$ 4.5 cm, p=0.0001) and baseline platelet counts (57.5 $\pm$ 13.0 x 10^3 *vs* 39.5 $\pm$ 14.5 x 10^3, p=0.0001) were the two factors which determined the effectiveness of therapy. With beta-blocker therapy, mean arterial pressure (MAP) reduced significantly (p=0.01) and also spleen size (7.40 $\pm$ 3.36 *vs* 5.68 $\pm$ 3.25 cm, p=0.0001) in responders but not in non-responders.
CONCLUSION: Beta-blocker therapy corrected thrombocytopenia (hypersplenism) and made liver biopsy possible in two-third of cases by reducing MAP and splenic size. The baseline spleen size and platelet counts determine the effectiveness of therapy. A trial of beta-blocker is worth in cases where percutaneous liver biopsy is contraindicated due to hypersplenism related thrombocytopenia.
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Disclosure of Interest: None Declared
Keywords: liver biopsy, Propanolol, thrombocytopenia

P1203 A DETAILED PATHOLOGICAL INVESTIGATION OF THE MURINE BILIARY ATRESIA MODEL: PROOF OF CONCEPT?

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INTRODUCTION: The murine biliary atresia (BA) model is widely used for examining BA pathogenesis, but morphological characteristics of the model have not yet been described in detail, and the development of fibrosis in this model is debated. This ongoing fibrosis in BA is important to examine, because it leads to liver transplantation in 70% of children with BA. Aims of the study were to describe the model using the Biliary Atresia Research Consortium (BARC) histological assessment system and to investigate the development of fibrosis.
AIMS&METHODS: In newborn mice Rhesus Rotavirus (RRV) was injected intra-peritoneally within 15 hours after birth. Animals were sacrificed at 7 or 14 days after birth (N=17) and compared with healthy mice of the same age (N=29). Two experienced pathologists without knowledge of the state of disease scored the most important morphological features using the BARC items. Development of fibrosis was further investigated using immunohistochemistry for CK19, collagen type I, and aSMA (e.g. negative/weak/moderate/strong). Scores were analysed with Chi-square test for trend or Fisher's test when applicable. All experimental procedures were approved by the Ethical Committee for Animal Experiments of the Hannover Medical School and the University Medical Center Groningen.
RESULTS: In the RRV group, a strong portal lymphoplasmacytic cellular infiltrate was found at 7 days, which decreased to moderate at 14 days (p=0.058). In the healthy group there was minimal cellular infiltrate. The morphological differences between RRV and control animals were significant at 7 and 14 days ($p<0.001$). Bile plugs or necrosis were not observed. CK19 bile duct staining was mainly absent/weak in the RRV group but moderate in the control group ($p<0.001$). Only in the RRV group fibrous expansion of most portal areas with focal bile duct proliferation was found, in 2/17 animals (12%) there was focal portal-to-portal bridging. Although expression of aSMA was present in the portal tracts of control mice, there was more expansion of aSMA staining in the RRV group ($p<0.001$). Portal staining of collagen type I was more pronounced in the RRV group (p=0.020).
CONCLUSION: Morphological features of the murine BA model are mostly in accordance with the features found in (early) BA. In addition, we have demonstrated the presence of (portal) fibrosis. Therefore, this model is considered applicable for investigating early pathogenesis of BA, including the development of BA related fibrosis.
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Disclosure of Interest: None Declared
Keywords: biliary atresia, Fibrosis, immunohistochemistry, murine BA model, rhesus rotavirus

P1204 INFANT STOOL COLOR CARD: THE INTEROBSERVER VARIABILITY BETWEEN PARENTS AND MEDICAL CAREGIVERS.

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INTRODUCTION: Because early recognition of biliary atresia remains a challenge, the Infant Stool Color Card (ISCC) has been implemented in several countries. This non-invasive screening tool leads to higher surgical success rates and improved long-term outcomes. However, the validity and optimal administration method of the ISCC are unknown. Therefore, we examined the interobserver variability of the ISCC.
AIMS&METHODS: A prospective longitudinal study on the ISCC assessment of stool samples was conducted. In total 83 children aged 2 weeks to 2 years admitted at the Beatrix Children's Hospital Groningen were included. The stool color in the nappy was independently scored by one parent, one nurse and two doctors using the ISCC. Kappa coefficients (κ–value) were calculated as indicators of the interobserver variability of the ISCC and values were compared between parents, nurses and doctors (scores 1-3: abnormal; 4-7: normal). Sensitivity and specificity of the ISCC were determined. The eight children with clinically and biochemically proven cholestatic disease were considered as the group *with* disease.
RESULTS: The κ -values between doctors and between doctors and nurses were 1.00 and 0.93 respectively. The κ –values between doctors and parents, and between parents and nurses were 0.72 and 0.67 respectively. The sensitivity and specificity of the ISCC for doctors were 100%, for nurses 100% and 99% respectively, with one false-positive score. The sensitivity and specificity for the parents were 75% and 97% respectively, with two false-positive scores and two false-negative scores.
CONCLUSION: The ISCC seems a reliable tool for screening for BA. Because of the lower sensitivity and specificity for parents, in combination with the average interobserver variability between parents and caregivers, we recommend the ISCC used by parents should be confirmed by caregivers.
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Disclosure of Interest: None Declared
Keywords: biliary atresia, infant stool color card, interobserver variability, sensitivity, specificity

P1205 DEOXYCHOLIC ACID INDUCES APOPTOSIS IN PRIMARY RAT HEPATOCYTES VIA JNK1/P53/MIR-34A/SIRT1

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INTRODUCTION: microRNAs (miRNAs or miRs) are being increasingly implicated in the pathogenesis of human liver diseases. In fact, we have recently shown that the miR-34a/Sirtuin1(SIRT1)/p53 pathway correlates with non-alchoholic fatty liver disease severity and apoptosis, and that ursodeoxycholic acid, an endogenous hydrophilic bile acid, counteracts this pro-apoptotic pathway. In turn, hydrophobic bile acids, such as deoxycholic acid (DCA), are know to modulate the expression of several apoptosis-related proteins, including c-Jun N-terminal kinase (JNK), leading to cell death.
AIMS&METHODS: The purpose of this study was to evaluate whether DCA-induced apoptosis of primary rat hepatocytes occurs *via* miR-34a-dependent pathways and whether they connect with JNK induction. Primary rat hepatocytes were incubated with 100 microM DCA, and transfected with a specific miRNA-34a inhibitor or with a p53 overexpression plasmid. p53 transcriptional activity was assessed in nuclear extracts and by using target reporter constructs. JNK function was evaluated by immunoblotting and silencing experiments. Viability, caspase-3 activity and apoptosis were determined using the ApoTox-Glo^T Triplex Assay and Hoechst staining.
RESULTS: Our results show that DCA enhances miR-34a/SIRT1/p53 pro-apoptotic signalling in cultured primary rat hepatocytes, in a dose- and time-dependent manner. In turn, miR-34a inhibition and SIRT1 overexpression significantly rescued cells from targeting of the miR-34a pathway and apoptosis by DCA. In addition, p53 overexpression activated the miR-34a/SIRT1/p53 pathway, further induced by DCA. DCA increased p53 expression, as well as p53 transcriptional activation of PUMA and miR-34a itself, providing a functional mechanism for miR-34a activation. Finally, JNK1, but not JNK2, was shown to be a major target of DCA, upstream of p53, in engaging the miR-34a pathway and apoptosis.
CONCLUSION: In conclusion, our results support a link between liver cell apoptosis, miR-34a/SIRT1/p53, and JNK signalling. JNK1-mediated activation of p53 is the key mechanism behind induction of miR-34a by DCA. The JNK/miR-34a/SIRT1/p53 pro-apoptotic pathway may represent an attractive pharmacological target for the development of new drugs to arrest metabolic and apoptosis-related liver pathologies.
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Disclosure of Interest: None Declared
Keywords: Cell Death, Deoxycholic acid (DCA), JNK, microRNA-34a, p53, Sirtuin 1

P1206 NON-CONJUGATED BILE ACIDS INHIBIT THE ION TRANSPORTER ACTIVITIES IN HUMAN COLONIC CRYPTS

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INTRODUCTION: Under pathophysiological conditions, such as short bowel syndrome, bile acids can reach the colon in high concentrations and can induce diarrhea.
AIMS&METHODS: Our **aim** was to investigate whether impaired ion transport activities are involved in the pathomechanism of bile acid-induced diarrhea.
Methods: Colonic biopsies were obtained from control patients (with negative colonoscopic findings) and from cholecystectomised/ileum-resected patients with/without diarrhea. Colonic crypts were isolated by collagenase digestion, and intracellular pH (pH_i), Ca^{2+} concentration ($[Ca^{2+}]_i$) and ATP levels (ATP_i) were measured by microspectrofluorometry. Na^+/H^+ exchangers (NHEs), Na^+/HCO_3^- cotransporter, Cl^-/HCO_3^- exchanger (AE) activities were determined. Changes of the mitochondrial transmembrane potential (MTP) was measured by confocal microscopy. Intracellular mophological changes were analysed with transmission electron microscopy (TEM).
RESULTS: The non-conjugated chenodeoxycholate (CDC) and the conjugated glycochenodeoxycholate (GCDC) caused dose-dependent acidosis in colonic crypts. The pH_i decrease was significantly greater in case of CDC vs. GCDC. 0.3 mM CDC strongly inhibited the activities of acid/base transporters. TEM showed mitochondrial damage after 1 mM CDC-treatment, but no such alteration was detected in case of lower concentrations of CDC or 1 mM GCDC. 0.3 mM CDC significantly but reversibly reduced ATP_i and MTP. CDC caused dose-dependent increase of the $[Ca^{2+}]_i$. Inhibition of Ca^{2+} release from the endoplasmic reticulum or plasma membrane Ca^{2+} channels decreased the CDC-induced increase of $[Ca^{2+}]_i$. Chelation of intracellular Ca^{2+} did not prevent, but ATP_i depletion mimicked the inhibitory effect of CDC on ion transporter activities. Impaired NHE and AE activities were observed in cholecystectomised/ileum-resected patients suffering from diarrhea compared to control patients.
CONCLUSION: Non-conjugated bile acids inhibit the function of ion transporters, disturb the energy level and Ca^{2+} homeostasis of colonic epithelial cells. These processes may reduce fluid and electrolyte absorption in the colon and promote the development of diarrhea.
This work was supported by OTKA, MTA and NFÜ (TÁMOP).
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Disclosure of Interest: None Declared
Keywords: Colonic epithelial cells, ion transporters

PANCREAS III – Poster Area

P1207 ENDOTHERAPY OF CHRONIC CALCIFIED PANCREATITIS BY ESWL+ERCP: PRELIMINARY LONG-TERM RESULTS

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INTRODUCTION: Most studies on pancreatic extracorporeal shock wave lithotripsy (ESWL) and ERCP for the treatment of chronic calcifying pancreatitis (CCP) report on a medium-term follow-up (6 months-6 years).
AIMS&METHODS: Aim of this study is to evaluate the long-term clinical outcome after combined treatment of CCP with ESWL and ERCP, focusing on ductal clearance and pain relief. 348 patients with painful CCP treated by ESWL + ERCP were identified from a prospectively collected database. Before ERCP, patients underwent ESWL of the pancreatic stones using an electro-hydraulic lithotripter with radiological focusing. ESWL was repeated until signs of stone fragmentation were evident on X-ray pictures. ERCP with pancreatic sphincterotomy was performed with a sphincterotome over the wire. Stone fragments were extracted with small Dormia baskets and by flushing with sterile saline. After stone clearance a pancreatic stent was inserted in case of a main pancreatic duct (MPD) stricture associated with stones. Primary objective was evaluation of the success rate in pancreatic stone clearance and MPD drainage. Secondary objectives were evaluation of pain after treatment, need for surgery, occurrence of endocrine insufficiency and mortality.
RESULTS: Preliminary results of 172 patients (76.4% male, mean age 50.3 years) that completed the follow-up (mean 8.36 years, SD 4.1 years) are reported. Follow-up of the remaining patients is ongoing. Alcohol abuse was present in 38.3% of the cases and 65% were smokers. According to Cremer's classification 83.7% had type IV CP; 87.2% had the pancreatic stones located in the head of the pancreas. MPD drainage and stone fragmentation was obtained in all patients with a mean of 3.8 (SD ± 2.9) ERCPs and 2 (SD ± 1.4) ESWL for patient. ESWL related complication were mild and resolved by interruption of the procedure or medical therapy. No cases of ERCP related pancreatitis were recorded. Procedures related mortality was absent. Follow-up results in 172 patients are reported in **table 1**.

Table 1. Follow-up results (172 patients treated by ESWL+ERCP for calcified chronic pancreatitis)

Mean follow-up (years)	8,36 ± DS 4,1	
Complete pain relief	99	57.6%
Partial pain relief (yearly/monthly pain)	52	30.2%
No pain relief (weeklt, daily pain)	12	12.2
Need for surgery	19	11%
Deaths	**36**	**20.9%**
Pancreatic cancer	10	5.8%

CONCLUSION: The combined therapy of CCP with ESWL + ERCP provides long-term complete pain relief in two thirds of the patients in our experience. Endotherapy of CCP can be considered the first line approach for painful CCP since it is repeatable and do not preclude future surgical approach.
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Disclosure of Interest: None Declared
Keywords: CHRONIC CALCIFIED PANCREATITIS, ENDOTHERAPY, ERCP, ESWL

P1208 IS THE ASSOCIATION OF THE P.N34S SPINK1 VARIANT EXPLICABLE BY A HIGH RISK HAPLOTYPE RATHER THAN THE POLYMORPHISM?

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INTRODUCTION: The p.N34S polymorphism of the SPINK1 gene (PSTI) is associated with idiopathic chronic pancreatitis however there is no clear functional effect of the sequence variant. It has been suggested that the polymorphism is associated with a high risk haplotype but this is widely disputed.
AIMS&METHODS: Aim: To identify whether a haplotype exists that distinguishes pancreatitis cases from controls where both cohorts have the p.N34S variant.
Methods: DNA from patients with chronic pancreatitis of no known aetiology (idiopathic) and controls were analysed by PCR Restriction Fragment Length Polymorphism analysis and or direct sequencing to test for the p.N34S variant. 20 control patients and 38 cases all heterozygous for the p.N34S variant were then used for long range PCR followed by sequencing between 146Mb and 148Mb of chromosome 5 (build 37). Haplotypes based on 7 single nucleotide polymorphisms within this region were constructed. These were analysed using the "haplo.stats" package.
RESULTS: 29 haplotypes were identified; only haplotype 13 was significantly associated with pancreatitis (p=0.0009, hapscore: -3.31).
CONCLUSION: It is possible that a high-risk haplotype rather than a simple base variant is responsible for SPINK1 associated pancreatitis.

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Disclosure of Interest: None Declared
Keywords: idiopathic pancreatitis, pancreatitis, SPINK-1 polymorphism

P1209 THE DIFFERENT FACETS OF PANCREATIC PAIN: A SYSTEMATIC COMPARATIVE STUDY OF 1032 PATIENTS WITH PANCREATIC DISORDERS

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INTRODUCTION: Abdominal pain is a major clinical feature in chronic pancreatitis/CP and pancreatic cancer/PCa. Little is known about pain sensations in pancreatic tumors other than PCa and CP.
AIMS&METHODS: With this study, we aimed to systematically characterize the specific pain pattern in the most frequent pancreatic diseases. Pain pattern of patients with CP (n=314), PCa (n=469), and other pancreatic tumors (n=249) including mucinous/MC (n=20) and serous cystadenoma/SC (n=31), invasive / IPMNi (n=37) and non-invasive intraductal papillary mucinous neoplasia/ IPMN (n=48), benign/NTb (n=18) and malignant/NTm neuroendocrine tumors (n=44), and ampullary cancer/AmpC (n=51) was registered and correlated with clinicopathological data.
RESULTS: 49.1% of all PCa patients revealed no pain, whereas in CP only 18.3% were pain free. In contrary, moderate to severe pain was registered in 15.1% in PCa patients that was noticeable increased in CP with up to 34.2%. SC was asymptomatic in the majority of cases (58.1%), whereas 78.9% of all MC patients suffered pain. In NT abdominal pain seems not to be a key clinical symptom since 64% of NTb and 59% of NTm patients did not reveal any pain. Tumor localization in the pancreatic body led to more frequent and more severe pain. Patients with malignant pancreatic neoplasms suffered from more severe pain than patients with benign disease. Tumor grading and stage did not show any impact on pain. Only in PCa, pain was directly associated with impaired survival.
CONCLUSION: Pancreatic pain depicts different patterns of abdominal pain sensation according to the respective pancreatic disorder and does not allow a unification of the term *pancreatic pain*. Since pancreatic pain is not uniform it may be used as an additional diagnostic tool.
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Disclosure of Interest: None Declared
Keywords: chronic pancreatitis, cystadenoma, IPMN, neuroendocrine tumor, pain, pancreatic cancer

P1210 IGG4-RELATED DISEASE IN THE PROSTATE: A CASE-CONTROL STUDY

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INTRODUCTION: IgG4-related disease (IgG4-RD) is characterized by elevated serum levels of IgG4, increased numbers of tissue IgG4-positive plasma cells and excellent response to prednisone. The most frequent manifestation is autoimmune pancreatitis (AIP), but the disease can affect multiple organs including the prostate. The histopathology of prostatic IgG4-RD has not been well established.
AIMS&METHODS: The aim of this study was to evaluate the occurrence and histopathological characteristics of IgG4-related prostatic involvement in patients diagnosed with AIP. We performed a cross search for AIP patients with prostatitis symptoms in our AIP database. Histology was examined by two blinded pathologists. As a control group patients with prostatitis without a history of IgG4-RD were assessed. All tissue samples were immunostained for IgG4 and evaluated for the following characteristic pathologic features of IgG4-RD: maximum number of IgG4+ cells/high power field (HPF); dense lymphoplasmacytic infiltrate; fibrosis, arranged at least focally in a storiform pattern; phlebitis with or without obliteration of the lumen; and increased number of eosinophils.
RESULTS: We identified 9 cases of prostatitis (median age 67, IQR 64-73) among 116 men with established AIP. All cases had a history of lower urinary tract symptoms (LUTS). In 5/9 (56%) these symptoms preceded a diagnosis of AIP; the interval between the diagnoses did not exceed 3 years. Median serum IgG4 was 7.3 g/L (IQR 3.3-13.6). The histological findings were compared with those obtained in 18 control patients (median age 68, IQR 62-74). Specimens evaluated had been obtained by biopsy (n=8) and prostatectomy (n=17). In IgG4-RD patients, the median number of IgG4+ cells in prostatic tissue was 150 (IQR 20-150), compared with 3 (IQR 1-11) in control patients (p=0.008). Furthermore, eosinophil numbers were more often elevated (>10/HPF) in IgG4-RD patients compared to control patients ($p<0.001$). Dense lymphoplasmacytic infiltrate was not discriminating and storiform fibrosis, a characteristic histological finding in AIP, was only sporadically found. Two patients were treated with corticosteroids and responded well.
CONCLUSION: We report on 9 patients with IgG4-related prostatitis. The histological hallmark is an elevated number of IgG4+ cells. Our results suggest that this is a relatively frequent entity among men diagnosed with AIP. A proportion of AIP patients presenting with symptoms of prostatitis or prostate enlargement may suffer from IgG4-related prostatitis and benefit from corticosteroid treatment.
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Disclosure of Interest: None Declared
Keywords: autoimmune pancreatitis, IgG4-related prostatitis

P1211 THE THERAPEUTIC EFFECT OF PNP THERAPY IN CHRONIC PANCREATITIS CLINICAL COURSE IMPROVEMENT. CLINICAL PANCREATIC INDEX.

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INTRODUCTION: Recently developed PNP-therapy for chronic pancreatitis (CP) involves a combination of enteric-coated pancreatic enzymes (ECPE), proton pump inhibitor (PPI) and non-steroidal anti-inflammatory drug (NSAID). CP PNP-therapy is rational because it is basically justified, effective and easy to apply in clinical practice and has few side effects.
Integral CP severity index – clinical pancreatic index (CPI) has been developed. CPI formulizes the next criteria: the number of surgeries due to CP complications, out-patient treatment efficiency, hospitalizations due to CP, weight loss, pain severity (evaluated by the doctor), steatorrhea intensity, defecations per day, other complaints (postprandial discomfort, bloating, nausea, etc.), glucose tolerance. Maximal CPI accounts 25 points. CP severity evaluation by CPI: mild - 6-8 points, moderate - 9-15 points, severe - 16-25 points.
AIMS&METHODS: The aim of this study was to determine PNP therapy efficiency in CP clinical course improvement, using CPI.
The study included 105 patients with confirmed small duct CP, who had no indications for endoscopic and surgical treatment. Patients were divided into three groups according to the treatment applied: P group received ECPE at a dose of 25 000 V (lipase) three times daily (n = 20); PP group received ECPE in a dose of 25 000 V (lipase) three times a day and PPI at a dose of 20 mg twice daily (n = 46); PNP group received ECPE in a dose of 25 000 V (lipase) three times a day, PPI at a dose of 20 mg twice a day, and Aceclofenac 100 mg twice daily (n = 39). Before and after 1-month therapy CPI was calculated and abdominal pain (VAS, evaluated by the patient) was determined in all the patients. Before treatment, patients were similar according to CPI as well as considering indicator of abdominal pain (VAS, evaluated by the patient). Statistical analysis was performed using the Mann-Whitney, Kruskal-Wallis test, Pearson's correlation and Cronbach's alpha.
RESULTS: After the treatment CPI difference was revealed between the groups (p=0.000), CPI decreased in all the groups: in P group - by 2 points (p=0.068), in PP group - by 7 points (p=0.000), in PNP group - by 9 points (p=0.000). CPI correlation with abdominal pain severity (VAS, evaluated by the patient) ($r=0.394$; $p<0.01$) before and after the treatment ($r=0.701$; $p<0.001$) was revealed. The value of Cronbach's alpha in this study was 0.68, after removing hospitalizations due to CP it was 0.711.
CONCLUSION: PNP-therapy is more effective in improving CP clinical course, compared with monotherapy by ECPE and ECPE/PPI combination. CPI reflects severity of the clinical course of CP and medical treatment efficiency.
Disclosure of Interest: None Declared
Keywords: Clinical course of chronic pancreatitis, Clinical pancreatic index, PNP therapy

P1212 AUTOIMMUNE PANCREATITIS AND THE ROLES OF IGE: A RETROSPECTIVE STUDY WITH 19 PATIENTS

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INTRODUCTION: Autoimmune pancreatitis (AIP) is a special type of chronic pancreatitis, which is characterized by diffuse or focal enlargement of pancreas, hyperglobulinemia, specific pathological features, and responded to corticosteroid therapy, but the pathogenesis is still unknown.
AIMS&METHODS: In this retrospective study, we evaluate the clinical manifestations, radiological characteristics and histologic presentations of AIP in adult patients in Chnia. Nineteen patients diagnosed as AIP were admitted to our hospital from May, 2007 to Jun, 2012. All patients with autoimmune pancreatitis fulfilled the 2006 revised clinical diagnostic criteria proposed by Japan's Pancreas Society. These patients' clinical records were reviewed and analyzed.
RESULTS: the ratio of male: female was 16:3, and the age of the patients from 41 to 82, the mean age was 63.3 years. The duration of symptoms prior to diagnosis ranged from one week to three years, Epigastric pain (13/19, 68.4%), Jaundice (11/19, 57.9%) and weight loss (14/19, 73.7%) were the most common symptoms. Two patients were misdiagnosed as pancreatitic cancer and receive partly pancreatectomy. 11(57.9%) patients had elevated level of CA19-9. IgG was elevated in 42.1% (8/19) of patients, and IgG4 was in 72.7% (8/11) of patients. Interesting, the level of serum LgG4 was in normal limit when the patients diagnosed as AIP, but was elevated after corticosteroid therapy in two patients. IgE was elevated in 18(94.7%) of the 19 patient. Imaging studies showed diffuse enlargement of pancreas in 42.1% (8/19) of patients, and tumor like local swelling can occur. The patients with diffuse enlargement seemly had a higher level of serum lgE than the patients with local enlargement had. Pancreatic duct is diffusely or segmentally narrowed. All patients showed narrowed common bile duct, and among them, 9(47.4%) patients were found with thicken of wall of bile duct. Thirteen patients were treated with prednisone, while 15 underwent stents in bile duct or pancreatic duce. The symptom remission and imaging improving were found in all patients. The level of IgE got decreased after therapy. Two patients suffered relapse during the follow up, and the IgE elevated in the meantime
CONCLUSION: IgE maybe play an important role in the pathogenesis of AIP, and the level of serum IgE is a useful marker for monitoring therapeutic response and recurrence of the disease.

Disclosure of Interest: None Declared
Keywords: autoimmune pancreatitis, IgE, IgG4

P1213 THE FREY PROCEDURE FOR THE TREATMENT OF CHRONIC PANCREATITIS ASSOCIATED WITH COMMON BILE DUCT STRICTURE: BE AWARE OF DUCT REINSERTION INTO THE RESECTION CAVITY OR CHOLEDOCHODUODENOSTOMY.

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INTRODUCTION: The Frey procedure (FP) is the treatment of choice for symptomatic, chronic pancreatitis (CP). In cases of biliary stricture, biliary derivation can be performed by choledochoduodenostomy, Roux-en Y choledochojejunostomy or, more recently, reinsertion of the common bile duct (CBD) into the resection cavity. The objective of the present study was to evaluate the outcomes associated with each of these three types of biliary derivation.
AIMS&METHODS: We retrospectively analyzed demographic, CP-related, surgical and follow-up data for patients having undergone FP for CP with biliary derivation between 2004 and 2012 in our university medical center. The primary efficacy endpoint was the rate of CBD stricture recurrence. The secondary endpoints were surgical parameters, postoperative complications, postoperative follow-up and the presence of risk factors for secondary CBD stricture.
RESULTS: Eighty patients underwent surgery for CP during the study period. Of these, 15 (males: 12 (80%); median age: 51; median BMI: 19.8 kg/m^2; mean time (range) to onset of CP: 6 years (1-20)) received biliary derivation with the FP. Eight of the FPs (53.3%) were combined with choledochoduodenostomy, 4 (26.7%) were combined with choledochojejunostomy and 3 (20%) were combined with reinsertion of the CBD into the resection cavity. The mean operating time was 390 min. Eleven complications (73.3%) were recorded, including one major complication (6.6%) that necessitated radiologically-guided drainage of an abdominal collection. The mean (range) length of stay was 17 days (8-28) and the median (range) follow-up time was 35.2 months (7.2-95.4). Two patients presented stricture after CBD reinsertion into the resection cavity; one was treated with radiologically-guided dilatation and the other underwent revisional Roux-en-Y choledochojejunostomy. Three patients presented alkaline reflux gastritis (37.5%), one (12.5%) presented cholangitis and one presented CBD stricture after FP with choledochoduodenostomy. No risk factors for secondary CBD stricture were identified.
CONCLUSION: As part of a biliary derivation, the FP gave good results. We did not observe any complications specifically related to surgical treatment of the biliary tract. However, CBD reinsertion into the resection cavity appeared to be associated with a higher stricture recurrence rate. In our experience, choledochojejunostomy remains the "gold standard" treatment for CBD strictures.
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Disclosure of Interest: None Declared
Keywords: Chronic Pancreatitis, Common bile duct stricture, duodenum preserving pancreatic head resection, Frey's procedure

P1214 PROPOSAL OF THERAPEUTIC STRATEGY FOR PATIENTS WITH TYPE 1 AIP DEVELOPED CYSTIC FORMATION

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INTRODUCTION: AIP with cyst formation (ACF) is rare complication and often shows refractory course to corticosteroid treatment (CST), however, the therapeutic strategy and risk factor for these AIP patients has not been fully elucidated.
AIMS&METHODS: We conducted a cohort study to determine if the predictive factors might be related to the ACF and propose the therapeutic strategy. The diagnosis of AIP was made according to the international consensus diagnostic criteria for AIP (*Pancreas* 2011;40:352-358). We conducted a study on 115 consecutive patients with type 1 AIP followed up at average 60 months, to determine whether the factors might be related to cyst formation of the pancreas, such as the presence of diabetes mellitus, abdominal pain, elevation of pancreatic enzymes, IgG4 seropositivity, diffuse pancreatic swelling, presence of extra-pancreatic involvement, splenic vein/artery involvement, presence of varix, and history of relapse.
RESULTS: There were 10 ACF (8.7%;10/115); pseudocyst were 7, retention cyst was one, wall-off like cyst formation in one and one was mucinous cancer. Regarding the location, body and tail of the pancreas were 9 patients, the one in the head was mucinous cancer. Male and female ratio was 9:1. Serum IgG4 was positive in 70% of the ACF (422mg/dl in average). Diffuse pancreas swelling noted in 70%. CST was administered to 70% (7/10) of the patients, however, relapse was noted in 40% (4/10) of these patients. The results of univariate analysis revealed significant association of ACF with presence of abdominal pain, elevation of pancreatic enzyme, splenic vein and/or artery involvement and varix formation ($p<0.05$), and multivariate analysis revealed the presence of abdominal pain (OR4.389, $p=0.0377$), elevation of pancreatic enzyme (OR4.677, $p=0.0345$), abdominal pain (OR4.389, $p=0.0377$), splenic vein and/or artery involvement (OR105, $p=0.001$) and varix formation (OR34.5, $p=0.043$) as the significant independent are factors predictive of ACF.
CONCLUSION: AIP presented with abdominal pain and pancreatic enzyme elevation, strong inflammation at the background of splenic vein and/or artery involvement accompanied with varix has independent risk for cyst formation. AIP with large cystic lesions over 60mm in diameter, may be irreversible stage, involving splenic vessels tended to show refractory course even if CST was administered. Those AIP patients should be treated by surgical operation rather than CST. However, cystic neoplasm could encounter in those AIP patients.
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Disclosure of Interest: None Declared
Keywords: autoimmune pancreatitis, corticosteroids

P1215 ALTERED BONE METABOLISM AND BONE DENSITY IN PATIENTS WITH CHRONIC PANCREATITIS AND PANCREATIC EXOCRINE INSUFFICIENCY

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INTRODUCTION: Chronic pancreatitis is characterized by a progressive inflammatory destruction of pancreatic parenchyma with concurrent increasing fibrosis. Established chronic pancreatitis harbors the risk of pancreatic exocrine insufficiency (PEI) due to diminished production of pancreatic enzymes. PEI can potentially lead to malnutrition. Maldigestion of fat and malabsorption of fat-soluble vitamines are key features of PEI.
AIMS&METHODS: To prospectively study a cohort of male patients with chronic pancreatitis and pancreatic exocrine insufficiency regarding parameters of maldigestion, bone metabolism, and bone mineral density. Female patients were excluded to rule out a bias as a consequence of hormonal effects. A standardised questionnaire for osteoporosis was applied. Parameters of bone metabolism and vitamin D were measured. Bone mineral density was measured by conventional X-rays of the vertrebrate column. Statistical analysis was done with the SPSS package (version 10.0).
RESULTS: A total of 50 male patients with proven chronic pancreatitis (36/50 alcohol; 42/50 smokers) and PEI (28/50; fecal elastase-1 < 200 ug/g) were studied. Fifty percent (25/50) had pain radiating from the bones, 21/50 a history of fractures. Calcium in the urine, 25-OH cholecalciferol, and desoxy-pyridinoline were significantly decreased whereas serum calcium, phosphate, alkalic phosphatase, PTH were normal. Conventional X-ray of the vertebra ($N = 42$) demonstrated normal in three, discrete reduction in 32, significant reduction in 6, and maximal reduction of bone mineral density (BMD) with fracture in one patient. Reduced BMD upon conventional X-ray correlated with low fecal elastase-1 ($p < 0.05$).
CONCLUSION: Bone mineral density was reduced in the majority of patients with chronic pancreatitis and correlated with pancreatic exocrine function. This patient group should be closely monitored for malnutrition and and an optimal pancreatic enzyme replacement therapy should be a mainstay of treatment to prevent complications such as osteopathy.
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Disclosure of Interest: None Declared
Keywords: Chronic Pancreatitis, osteoporosis, ostepenia, pancreatic exocrine insufficiency

P1216 A SHORT ENDOSCOPIC SECRETINTEST GIVES USEFUL ADDITIONAL INFORMATION IN CYSTIC FIBROSIS PATIENTS

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INTRODUCTION: Faecal elastase (FE) is a simple and widespread test for determining exocrine pancreatic function in Cystic fibrosis (CF) patients. New short endoscopic secretin tests are not validated in CF.
AIMS&METHODS: We aimed to evaluate the diagnostic quality and possible additional diagnostic information using a concentration-based EST in a small CF population. Consecutive patients attending regular control at the CF clinic, and healthy controls underwent EST. Endoscopic collection of duodenal juice was performed between 30 and 45 minutes after secretin stimulation. Duodenal juice was analysed for bicarbonate concentration and lipase-, amylase-, chymotrypsin- and elastase-activities. Stool was analysed for FE. Information of CF genotype was collected from patient journal.
RESULTS: Thirty seven consecutive CF patients were included in a protocol for extended pancreas function testing. 30 patients fulfilled EST and are presented here. 25 healthy controls (HC) were also tested. Using FE cut-off of 200µg/g, patients were classified as exocrine pancreatic sufficient (CFS, n=17) or insufficient (CFI n=13). Both bicarbonate-concentrations and enzyme activities in duodenal juice differentiated CFI patients from CFS patients and HC ($p<0.001$). Calculating ROC curves, we get a sensitivity of 100% and a specificity of 88% for EST using the usual cut-off of 80meq/L for duodenal bicarbonate. The population displays strong correlation between severe CF genotype in both alleles and pancreatic insufficient phenotype ($p<0.001$).
CONCLUSION: Pancreatic exocrine insufficient CF patients could be differentiated from exocrine sufficient patients and healthy controls using this new test. EST supplied detailed information on duodenal peak concentration of HCO_3- and pancreatic enzymes. We observe the phenomenon of decreased bicarbonate and hyper-concentrated duodenal pancreatic enzymes in 2 patients, indicating that EST is capable of demonstrating early ductal failure in patients where acinar function is still intact.
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Keywords: cystic fibrosis, exocrine pancreatic function, genotype

P1217 PANCREAS-PRESERVING SURGERY FOR PARADUODENAL PANCREATITIS. WHEN AND HOW? EXPERIENCE OF 61 CASES OF DUODENAL DYSTROPHY TREATMENT .

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INTRODUCTION: Paraduodenal pancreatitis or duodenal dystrophy (DD) is infrequent disease, characterized by chronic inflammation of the aberrant pancreatic tissue in the duodenal wall which may be isolated or accompanied by chronic pancreatitis in the orthotopic pancreas. Different treatment options of DD treatment are debated.
Objective: To assess the efficacy of pancreas-preserving surgery for treatment of duodenal dystrophy different approaches to judge the advisability of amalgamating the above-mentioned pathologies
AIMS&METHODS: To assess the efficacy of pancreas-preserving surgery for treatment of duodenal dystrophy different approaches to judge the advisability of amalgamating the above-mentioned pathologies
1. Prospective analysis of 61 cases of DD (2004-2012), comparing preoperative assessment and histopathological findings in 37 surgical specimens; 2. Assessment of clinical presentation and the results of DD treatment.
RESULTS: No case of groove pancreatitis was revealed throughout the observation. Correct diagnosis was made in all the cases except one suspected cystic tumor of the pancreatic head (1,9%). Patients presented with abdominal pain(100%), weight loss(76%), vomiting(30%) and jaundice(18). CT,MRI and endoUS were the most useful diagnostic modalities. Patients underwent 25 pancreatoduodenectomies (PD), pancreatico- and cystoenterostomies(7), Nakao procedures(4), duodenum-preserving pancreatic head(DPPH) resections(5) and 9 pancreas-preserving duodenal resections(PPDR). No mortality. Full pain control was achieved after PPRDs in 83%, PDs in 85%, and after PPPH resections and draining procedures in 18% of cases. Diabetes mellitus developed thrice after PD.
CONCLUSION: 1. PPDR is effective procedure for treatment of DD with mild changes in orthotopic gland; 2. The diagnosis of DD can be confidently determined with the aid of modern-day techniques prior to surgery; 3. The effectiveness of PPDR provides compelling proof that DD is a duodenal entity distinct from groove and orthotopic pancreatitis.
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Disclosure of Interest: None Declared
Keywords: duodenal dystrophy, groove pancreatitis, pancreas-preserving surgery, paraduodenal pancreatitis

P1218 EXPRESSION OF BCL-2, P53 PROTEINS AND CD31 IN HUMAN CHRONIC PANCREATITIS

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INTRODUCTION: Objective. To study bcl-2, p53 and CD31 expression in pancreas at chronic pancreatitis (CP).
AIMS&METHODS: Materials and methods. Using morphological, immunohistochemical, morphometric methods, we investigated the pancreas specimens of 45 patients with CP who underwent duodenum saving resection of the pancreas head. Control group included 7 pancreas head specimens without any pancreas pathology from people died by accidents. Statistic analysis included Mann-Whitney's, Kruskal-Wallis 's, and Spearman's tests. All p value ≤ 0.05 was considered statistically significant.
RESULTS: Results. Histological examination of the pancreas specimens with CP revealed interlobular and perilobular fibrosis, degenerative changes of pancreatic parenchyma, foci of lymphocytic infiltrates. The nerves have been found to be damaged by the inflammatory process.
Depending on fibrosis area all patients were subdivided into 3 groups: I group – <25%, II group – 25-50%, III group – >50%. Fibrosis area of control specimens was <10%
The evaluation of lymphocytic inflammatory infiltration of the pancreas specimens with CP has distinguished 4 degrees of the inflammation as follows: absent (0), mild (1+), moderate (2+) or severe (3+).
Degree of bcl-2 expression varied from 1.12 up to 38.77 points. Our research has shown more than 5-fold increasing the bcl-2 expression degree in pancreatic tissue of patient with CP in comparison with control group. The p53 expression was very low in investigated and control groups. The degree of CD31 expression changed in limits from 0.2 up to 8.9 points and was more low in samples of pancreas at CP. The results of the markers expression are displayed in Table 1.
Table 1. The marks of the expression of markers *(Me (LQ-UQ))*

Groups	Bcl-2 expression, points	P53 expression, points	CD31 expression, points
Chronic pancreatitis	10.55 (7.99 – 14.67)	0.0015 (0.00005 – 0.19)	2.86 (2.21 – 3.49)
Control group	1.81 (0.6 – 4.57)	0.00013 (0 – 0.0004)	7.16 (4.95 – 8.85)
p value (Mann-Whitney)	**0.003052**	0.085528	**0.003115**

There was no correlation between expression of markers and fibrosis and inflammation. However, we found negative correlation of CD31 expression with pancreas nerve tissue total area ($r = -0.3$).
CONCLUSION: Conclusions. The CP is characterized by increasing of the bcl-2 expression, thus degree of the expression is not connected with fibrosis and inflammation degree. Low p53 expression degree at CP shows about low risk of malignisation.
The revealed changes of the apoptosis markers (bcl-2, p53) expression and angiogenesis marker CD31 at CP underlie in morphogenesis of diseases and define progressive degenerative changes and structural reorganization in the pancreas with disturbance of regeneration processes.
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Disclosure of Interest: None Declared
Keywords: angiogenesis, apoptosis, Chronic Pancreatitis, immunohistochemistry

P1219 DO THE DIFFERENT IMMUNOGLOBULIN G SUBCLASSES HAVE SIGNIFICANCE IN AUTOIMMUNE PANCREATITIS?

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INTRODUCTION: We observed that not only immunoglobulin (Ig) G4 subclass but also the other IgG subclasses could be elevated in autoimmune pancreatitis (AIP).
AIMS&METHODS: The aim of our study is to further investigate the importance of the elevation of different IgG subclasses in AIP. Patients treated at Karolinska University Hospital with different types of pancreatitis were involved in the study. Group of cases with AIP (both type 1 and type 2) were compared to a control group of patients with chronic pancreatitis caused by other reasons and/or with recurrent acute pancreatitis. Serum samples were taken all of them and IgG and its subclasses (IgG1, IgG2, IgG3 and IgG4) were measured. Other organ involvement (OOI), jaundice, response to steroid therapy and relapse after the therapy were observed.
RESULTS: Twenty-seven patients were enrolled in our study (16 male, 11 female, mean age: 54.5±15.2 year), 19 into the AIP and 8 into the control group. There was no significant difference between the two groups according to the age and gender ($p=0.605$ and $p=0.824$, respectively). We found significantly elevated IgG2-level in case of jaundice among all the patients (3.9±1.7 g/L vs. 6.4±3.8 g/L, $p<0.04$), and significantly more cases were accompanied by elevated IgG2 in the icteric AIP group ($p<0.04$), but not in the control group. In the group of AIP patients in case of jaundice only the IgG3-level was significantly elevated (0.5±0.2 g/l vs. 1.0±0.5 g/L, $p<0.03$), while there was no significant difference in the control group. In point of the other three observed clinical signs we did not find any significant difference either in the total group of patients or between the AIP and the control group.
CONCLUSION: Serum IgG2 and IgG3 seem to be in relation to jaundice in chronic or recurrent acute pancreatic patients; however more cases are needed for further investigations and for confirmation of our results.
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Disclosure of Interest: None Declared
Keywords: autoimmune pancreatitis, immunoglobulin G subclasses, jaundice

P1220 FATTY PANCREAS IS A RISK FACTOR FOR PANCREATIC PRECANCEROUS LESIONS (PANIN)

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INTRODUCTION: Obesity was recently described as a risk factor of pancreatic cancer with a specific link with significant metabolic abnormalities including insulin resistance, glucose intolerance and diabetes.
AIMS&METHODS: Aims: To characterize the frequency of pancreatic intraepithelial neoplasia (PanIN) in case of fatty pancreas, to correlate pathological findings with dysmetabolic characteristics and tobacco intake.
Methods: Consecutive pancreatic specimens of patients operated on for neuroendocrine tumors (NETs) (ductal tumors, ie adenocarcinomas and IPMN were excluded)) from 2009 to 2011 were analyzed. The pancreatic parenchyma was analyzed at least 2 cm apart from the tumor. Fatty infiltration and fibrosis of the parenchyma in intra and extra lobular locations were assessed by two investigators according to specific scores. Dysplastic lesions were described according to the WHO 2010 PanIN classification. General characteristics of the patients were collected, especially the body mass index (BMI), diabetes and tobacco intake.
RESULTS: Results: 110 pancreatic specimens of patients (males: 42%) were analyzed (median surface per specimen: 7.5 cm^2). Median age at surgery was 53.8 [17-85] years. Arterial hypertension, diabetes, tobacco consumption were found in 19%, 10% and 26%, respectively. Median BMI was 24 [16-37]. PanIN lesions type 1, 2 and 3 were observed in 62, 38 and 1% of cases, respectively. Fatty pancreas was found in 56% of cases (extralobular 30%, intralobular 51%). Intralobular fibrosis was noticed in 24% of cases. PanIN lesions were correlated to fatty pancreas (either extra- (0.005) or intra lobular (0.0001)), intralobular fibrosis (0.002), tobacco intake (0.05) and age at surgery (0.05). Fatty pancreas was associated with age (0.0001), higher BMI (0.05), intralobular fibrosis (0.009), hypertension (<0.001), hyperlipidemia (0.01) and diabetes

(0.09). We found no correlation between PanIN lesions and dysmetabolic disorders.
CONCLUSION: Conclusion: Fatty pancreas is an independent risk factor of PanIN lesions, especially in case of intralobular location. These results suggest that fatty infiltration itself plays a specific role in pancreatic oncogenesis.
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Disclosure of Interest: None Declared
Keywords: Fatty pancreas, Obesity, PanIN, precancerous lesions

P1221 RELATIONSHIPS AMONG PLASMA AMINO ACID LEVELS, PANCREATIC PAIN AND THE EFFECT OF A LOW-FAT ELEMENTAL DIET IN ALCOHOLIC CHRONIC PANCREATITIS

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INTRODUCTION: We reported that patients with chronic pancreatitis (CP), especially those with exocrine insufficiency, exhibit alterations in levels of several amino acids, such as histidine, methionine and glutamate. These amino acid deficiencies seem to correlate with exocrine insufficiency and be improved by elemental diet. Relationship between amino acids and pancreatic pain had not been known yet.
AIMS&METHODS: Our aim was to examine their relationships among plasma amino acid levels, pancreatic pain, and the effect of a low-fat elemental diet in alcoholic chronic pancreatitis. We selected a total of 39 patients with a history of alcoholic CP, based on our criteria. CP patients were divided into an exocrine normal group (n=28) and exocrine insufficiency group (n=11) based on PFD (pancreatic functioning diagnostic) test results (normal range: more than 70%). And a low-fat elemental diet "elental®" was ingested for eleven consented patients with pancreatic exocrine insufficiency to observe the effect of the diet. This elemental diet was performed for two months. Before and after diet, selected clinical and laboratory values were examined and compared. We used Visual Analogue Scale (VAS) as assessment of pancreatic pain.
RESULTS: There was no significant difference in BMI between pre- and post-elemental diet. Serum albumin level of post-elemental diet was significantly higher than that of pre-elemental diet (P=0.041). There was no significant difference in HbA1c between pre- and post-elemental diet. Total amino acid concentration was significantly higher in post-elemental diet than in pre-elemental diet (P=0.032). The concentrations of serum histidine and methionine in post-elemental diet was significantly higher than that of pre-elemental diet (histidine: P=0.014, methionine: P=0.016). The concentration of serum glutamate in post-elemental diet was significantly lower than that of pre-elemental diet (P=0.024). The imbalance of amino acids was revised. And VAS was significantly lower in post-elemental diet than in pre-elemental diet (P=0.014), Correlation between amino acids and pancreatic pain was recognized (P=0.0096).
CONCLUSION: CONCLUSION: These amino acid deficiencies, such as histidine, methionine and glutamate, seem to correlate with pancreatic pain and be improved by elemental diet. Supplementation of these amino acids in patients with exocrine insufficiency may minimize the pancreatic pain.
Disclosure of Interest: None Declared
Keywords: Alcoholic chronic pancreatitis, Amino acid, Pancreatic pain

P1222 MICRORNA BIOMARKERS FOR EARLY DETECTION OF PANCREATIC CANCER FROM SAMPLES OBTAINED BY ENDOSCOPIC ULTRASONOGRAPHY-GUIDED FINE NEEDLE ASPIRATION (EUS FNA)

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INTRODUCTION: Pancreatic ductal adenocarcinoma (PDAC) is the 4th cancer-related death cause in occidental countries. Effective early detection methods are needed in order to improve its prognosis. Many expectations in this sense have arisen since the discovery of microRNAs (miRNA), which are small non-coding RNAs that regulate gene expression. On the other hand, samples from pancreatic lesions may be easily obtained by EUS FNA.
AIMS&METHODS: 1- To investigate if EUS FNA samples are suitable for miRNome analysis and 2- To analyze the miRNome of PDAC and the preneoplastic lesion IPMN, in order to find new miRNA-based biomarkers for early detection of pancreatic cancer. **Methods:** EUS FNA was performed using a linear echoendoscope together with an Aloka Alpha-5 system. FNA was performed using a standard 22G needle. After sampling the lesion for diagnosis, an extra-sample was intended to determine genome-wide miRNA profiling. Biomarker discovery was done using genome-wide miRNA profiling by next-generation sequencing in a set of 18 tissue samples (11 PDAC; 4 IPMN; 3 Healthy, H). Biomarker validation was done in a different set of 53 samples (24 PDAC; 8 IPMN; 15 H) by qRT-PCR.
RESULTS: Genome-wide miRNA profiling by next-generation sequencing technology could be determined in all samples, as well as biomarker validation by qRT-PCR. A total of 592 and 387 miRNAs were found significantly deregulated (FDR <0.05) in NGS data in PDAC and IPMN samples vs H, respectively. 41 miRNAs were selected for further validation according to the following criteria: FC >2 and FDR <0.05 in PDAC and IPMN samples; mean counts >400 and IQRmax(intra-group) <1.4. Among them, upregulation of 31 miRNA was confirmed (22 with $p<0.05$, and 9 $p<0.1$) in PDAC samples from the validation set by qRT-PCR. Most of these miRNAs (27) were also significantly upregulated in the IPMN group.
CONCLUSION: 1- EUS FNA samples are suitable for miRNome analysis. 2- Genome-wide miRNome analysis shows that PDAC, IPMN and healthy pancreatic tissue have differential miRNA profiles. Moreover, PDAC and IPMN lesions share a large number of deregulated miRNAs, making them good biomarker candidates for early detection of pancreatic cancer.
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Disclosure of Interest: None Declared
Keywords: biomarkers, endosonography, IPMN, pancreas

P1223 CLINICAL UTILITY OF SERUM DUPAN-2 IN DIAGNOSIS OF PANCREATICO-BILIARY MALIGNANCY

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INTRODUCTION: Serum carbohydrate antigen (CA 19-9) is the most common tumor marker assessed in pancreatico-biliary disease and health examination. However, its clinical limitation were poor sensitivity, false negative results and increased false positivity. The objective of this study was to identify usefulness of Duke pancreatic monoclonal antigen type 2 (DUPAN-2) such as tumor marker that might compensate for the drawback of the CA 19-9 assay.
AIMS&METHODS: From October 2010 to April 2013, DUPAN-2 levels of one hundred thirty patients (53 men and 77 women) were measured due to elevated CA 19-9 levels in health examination (54 cases) or pancreatico-biliary malignancy (76 cases). The normal levels for each marker are as follows and were measured in each patient: CA 19-9, 37 U/mL or lower and DUPAN-2, 150 U/mL or lower. The mean age of the patients was 64 years (range 26-95). Measurement of DUPAN-2 was assayed with an enzyme immunoassay kit.
RESULTS: The sensitivity and specificity of DUPAN-2 to malignant disease in total 130 patients, were 52/78 (66.7%) and 49/52 (94.2%), respectively. The patients with malignant diseases were 78/130 (60%), including 34 pancreatic cancer, 25 bile duct cancer, 11 GB cancer, 6 ampulla cancer, 1 prostate cancer, and 1 Warthin's tumor. There was a positive correlation between CA 19-9 and DUPAN-2 in malignant disease (r=0.358, P=0.000). In 114 patients excluding sixteen patients with normal CA 19-9 levels, the sensitivity and specificity of DUPAN-2 were 44/62 (70.9%) and 49/52 (94.2%), respectively. Eight of 16 (50%) patients with negative CA 19-9 level and pancreatico-biliary malignancy, including 3 pancreatic cancer, 3 CBD cancer, and 2 GB cancer, were measured positive for DUPAN-2. In 54/130 (41.5%) healthy patients with asymptomatic elevated CA 19-9 levels, the sensitivity and specificity of DUPAN-2 were 2/6 (33.3%) and 47/48 (97.9%), respectively. The benign cause of asymptomatic elevated CA 19-9 levels, excluding six malignant patients, were 14 lung problems (DILD, Bronchiectasis, emphysema, COPD, tuberculosis), 12 gynecologic problems (ovarian cyst, endometrial hyperplasia, uterine myoma), 18 unknown origin, and 4 other problems (congestive heart failure, chronic B viral hepatitis, back sprain, chronic cholecystitis).
CONCLUSION: DUPAN-2 is useful method for differential diagnosis of asymptomatic elevated CA 19-9 levels. Also, the combined assay of CA 19-9 and DUPAN-2 are sufficiently independent to complement each other in diagnosing the malignant disease. But, each tumor marker cannot be used as substitutes one for the other.
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Disclosure of Interest: None Declared
Keywords: CA 19-9, DUPAN-2

P1224 LONG-TERM SURVIVAL AFTER PALLIATIVE RESECTION AND BYPASS PROCEDURE IN PATIENTS WITH PERIAMPULLARY ADENOCARCINOMA

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INTRODUCTION: Non-radical resections (R1/R2) for cancer in the pancreatic head area may limit long-term survival. Aggressive surgery can lead to non-radical resections and discrepancy exists on the presumed survival benefit for these patients after R1/R2 resection compared to patients undergoing palliative bypass procedure due to locally advanced disease. Survival and postoperative outcomes for these patients were analyzed in this study
AIMS&METHODS: The study population consisted of all patients who underwent surgical exploration with intent to perform a resection between 1992 and 2012, with a histopathologically proven cancer in the pancreatic head area: pancreatic head, distal common bile duct, duodenum or ampulla. Patient characteristics, postoperative outcomes and median overall survival between patients with an R1/R2 resection and patients with locally advanced disease without metastasis undergoing a palliative bypass (PBP) were compared. R1 was defined as microscopically non-radical, tumor cells within 1.0 mm of the resection margin; R2 was defined as macroscopically non-radical.
RESULTS: 1195 patients underwent surgical exploration for a malignancy; 716 resections and 479 PBPs were performed. In 33% of the resected patients (n=234) an R1/R2 resections was performed, 222 patients underwent PBP due to locally advanced disease. Age and gender did not differ between R1/R2 group and PBP group. Morbidity rates (ISGPS grade B/C, Clavien-Dindo $\geq$II) were 53% in R1/R2 group and 35% in PBP group (p=0.001), mortality was 1.3% vs. 3.2% respectively (p=0.1). Median survival for patients after R1 resection was 17.2 months vs. 9.3 months after PBP (log rank $p<0.001$). Median survival after R2 resection (n=10) was 8.5 months.

CONCLUSION: Although morbidity after non-radical resection is higher than after PBP, survival of patients after R1 resection is significantly better than after PBP in case of locally advanced disease. Therefore R1 resection can be accepted as adequate palliative treatment. However R2 resections, probably confirmed by positive frozen sections performed perioperatively, should be discouraged.
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Disclosure of Interest: None Declared
Keywords: pancreatic surgery, Resection margins, survival

P1225 OPTIMAL EMERGENCY INTERVENTION IN PATIENTS WITH LATE HAEMORRHAGE AFTER SURGICAL EXPLORATION FOR A PERIAMPULLARY TUMOR

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INTRODUCTION: Mortality due to late haemorrhage after surgery for periampullary tumors is high, especially in patients with pancreatic fistula (PF) and abdominal sepsis. Patients often require an emergency intervention (EI). Both radiological interventions (RI) and surgical interventions (SI) have been proven to be effective treatment strategies for late haemorrhage. In this study risk factors for the need of an EI and potential selection for RI or SI for late haemorrhage were identified and outcome of different treatment strategies were analyzed
AIMS&METHODS: From a prospective database including 1513 patients who underwent curative pancreatoduodenectomy or palliative bypass for periampullary tumors in the period 1992-2012, 50 patients with late haemorrhage (> 24 hours after index operation) were identified. In patients with late haemorrhage, type of intervention and outcome were analyzed. In order to identify independent predictors for the indication for an emergency intervention patient, disease specific and operation characteristics were retrieved from charts of patients with late haemorrhage. EI was defined as SI or RI in hemodynamic unstable patients
RESULTS: Of the 50 patients (3.3%) with late haemorrhage after surgical exploration for periampullary tumors, 20 patients required an EI. Postoperative PF was a risk factor for the need for EI (p=0.001). No independent predictors were identified after multivariate analysis for undergoing an EI or for type of intervention. In the EI group, 4 patients (20%) were treated primarily with SI, however 2 patients died due to persistent hemodynamic instability. The remaining patients (n=16, 80 %) were treated primarily with RI. RI was successfully in 9 patients, but failed in 7; 1 patient died due to aspiration immediately after coiling, 6 patients still required SI to manage the bleeding and stabilize their condition
CONCLUSION: For patients with late haemorrhage after surgery for periampullary tumors, the need for EI and the type of intervention is unpredictable. Mortality is still seen after both interventions due to persistent hemodynamic instability. RI is preferred due to the minimal invasive character, but an immediate change of treatment to surgery when RI is not successful is difficult. Partly due to the transportation of the patient from the RI room to the operating room. This is however possible when the RI is initially performed in the operation room. In order to perform both interventions in one setting and have all the tools to resuscitate the patient, a hybrid operation room is desirable
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Disclosure of Interest: None Declared
Keywords: emergency intervention, pancreatic surgery, postoperative haemorrhage

P1226 RISK FACTORS FOR SECOND PRIMARY PANCREATIC CANCER IN COLORECTAL CANCER PATIENTS

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INTRODUCTION: Second primary cancer in colorectal cancer (CRC) is becoming an issue as overall survival is getting improved. In this study we tried to find risk factors associated with subsequent pancreatic cancer (PC) after CRC.
AIMS&METHODS: The observed incidence rate of subsequent PC in CRC patients, obtained from Severance Hospital in Seoul, Republic of Korea, was standardized using a CRC population in the Korean Central Cancer Registry (KCCR) by National Cancer Center. The expected incidence rate of PC was obtained by assuming that these persons experienced the same cancer incidence as prevailed in the corresponding general populations in KCCR. The standardized incidence ratio (SIR) with 95% confidence interval (CI) was calculated.
RESULTS: There were 4824 CRC patients in certain age from 45 to 74 years old, providing 16,727 person-years of follow-up. Fifteen patients diagnosed subsequent PC at a median follow-up of 38.21 months, and the age-adjusted-incidence rate of subsequent PC was 13.3 per 100,000 in general; 20.4 in men and 40.7 in women. The SIR of subsequent PC in CRC patients was not significant; 0.71 (95% CI 0.41-1.19) in general and 0.88 (95% CI 0.56-1.33) in men. But the SIR significantly increased to 2.84 (95% CI 2.05-3.80) in women. Subgroup analysis of diabetes patients revealed that the SIR increased to 12.81 (95% CI 11.27-14.52). In multivariate analysis for the risk factor of second primary PC, diabetes showed higher odds ratio (adjusted odds ratio 4.218, 95% CI 1.494-11.910), but smoking history, obesity and chemotherapy showed no significant association.
CONCLUSION: The risk of second primary PC after CRC was increased in women and diabetes patients. These groups need a special attention regarding second primary PC. Further studies are needed to understand carcinogenic process of second primary cancer and build a cancer survivor screening strategy.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, pancreatic cancer, risk factors, second primary cancer

P1227 FREQUENCY OF EXCESSIVE BODY-MASS INDEX IN PATIENTS WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM OF THE PANCREAS: A SINGLE- REFERRAL CENTRE EXPERIENCE

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INTRODUCTION: Up to date no clinical reports have been able to identify any lifestyle (including excessive body weight) linked to IPMN. Elevated BMI can be a risk factor for the development of colonic polyps and colon cancer (CCR), which have been found to be one of the most frequent neoplasms associated with IPMN, thus suggesting the need for endoscopic surveillance. We estimated the frequency of excessive body mass index in patients with intraductal papillary mucinous neoplasm of the pancreas (IPMN) referred to a single tertiary centre in North-Eastern Italy
AIMS&METHODS: We reviewed all patients diagnosed with IPMN in our Centre from November 2008 to September 2012. IPMN was diagnosed by two imaging techniques (EUS and MRI) and in selected cases by EUS-guided FNA (fine-needle-aspiration)
RESULTS: There were 118 patients with IPMN, 41 males and 77 females, mean age 70 (33-90). Data on BMI were available in 109 on 118 pts with 7.5% missing. Twenty-seven patients (23%) had normal BMI (< 25), 67 (57%) were overweight (BMI ≥ 25 and < 30) and 15 (13%) were obese (BMI ≥ 30). The overall prevalence of overweight (BMI ≥ 25) was 70%. Colorectal cancer and/or colonic polyps were found in 27 patients (33%). Data on BMI were available for 26 patients on 27 with 4% missing. Four patients with CCR and/or colonic polyps (15%) had normal BMI (< 25), 18 (67%) were overweight (BMI ≥ 25 and < 30) and 4 (15%) were obese (BMI ≥ 30). The overall prevalence of overweight (BMI ≥ 25) in patients with CCR and/or colonic polyps was 82%.
CONCLUSION: Our series confirms a high prevalence of CCR and/or colonic polyps in patients with IPMN. A high proportion of our patients had excessive body weight and it becomes even higher in the subgroup with CCR and/or colonic polyps. The possible link between overweight and IPMN should require further investigation
Disclosure of Interest: None Declared
Keywords: Body mass index, Echoendoscopy, IPMN

P1228 MR BASED SCREENING PROGRAM FOR INDIVIDUALS AT RISK FOR PANCREAS CANCER

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INTRODUCTION: Ten % of all pancreatic cancers can be hereditary. A screening program for the individuals at risk (IAR) is recommended, but no defined surveillance modalities are available.
AIMS&METHODS: Aim: To analyze the frequence of findings in IAR
Methods: From 2010 to 2013, all the patients with a "genetic risk" to develop pancreas cancer and referred to the Karolinska University Hospital, were included in a MR based surveillance program. All patients were investigated for the most common genetic mutation associated with pancreas cancer.
RESULTS: Forty patients were enrolled. There were 24 female and 16 man. The mean age was 49.9. The mean length of follow-up was 12.9 (± xx) months. The number of relatives affected by pancreas cancer was 5 in 2 patients (5%), 4 in 5 (12.5%), 3 in 17 (42.5%), 2 in 14 (35%) and 1 in 2 (5%). In 4 patients (10%) a p16 mutation was found, in 3 a BRCA 2 mutation (7.5%), in 1 a BRCA 1 mutation (2.5%). In 16 patients (40%) a suspect lesion was found in the pancreas with MR. Fourteen (35%) had an IPMN and 2 (5%) a pancreas cancer. Three patients (7.5%) required surgery (two for PDCA and one for IPMN) and the remaining 37 continue with the surveillance program.
CONCLUSION: During a median follow-up of just about a year, we detected pancreatic lesions in about 40% of our patients, of which three underwent surgery. Despite the relatively short time, the surveillance program in IAR seems to be effective.
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Disclosure of Interest: None Declared
Keywords: pancreas cancer, prevention

P1229 SERUM CHROMOGRANIN-A AS A NEW DIAGNOSTIC TEST IN PANCREATIC CANCER

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INTRODUCTION: Pancreatic cancer has common diases with poor prognosis. There is still need for new, reliable serum markers for diagnosis of pancreatic cancer. Although serum Ca19-9 level are commonly used serum marker in pancreatic cancer it has low spesificity and sensitivity. Chromogranin A(CgA) is a

prohormon mainly released from neuroendocrine cells. It is commonly used for diagnosis of pancreatic neuroendocrine tumors. There is no study showing the diagnostic and prognostic significance of serum Cg A levels in pancreatic ductal adenocancer.
AIMS&METHODS: We aimed to study the diagnostic and prognostic significance of serum CgA levels in pancreatic ductal adenocancer. Seventy five patients with pancreatic adenocancer and 75 healthy controls were included to the study. Patients age, gender, age of diagnosis, stage of the disease, clinical symptoms, biochemical paremeters were recorded. Serum CgA levels were measured by ELISA method.
RESULTS: Pancreatic cancer patients has significantly higher levels of serum CgA levels then controls (299.4±460.9 vs 72.9±98.9 ng/ dl, $p < 0.001$). The cut of value of serum CgA levels over 75 ng/ml has 75% sensitivity and 79% specificity for diagnosis of pancreatic cancer (($p < 0.001$, AUC 0.79, %95 CI 3.4-17.1). Serum Cg A levels was positivly correlated with age, serum CRP and sedimantation rates while it was not correlated with serum Ca19-9 levels. Diabetes and chronic pancreatitis were independent risk factors beside pancreatic cancer that increase serum Cg A levels. Serum Cg A levels were not different with the stage of the disease and was high even in early stages.
CONCLUSION: Serum CgA level has high sensitivity and specifisity for diagnosis of pancreatic ductal cancers while it does not have prognostic significance.
Disclosure of Interest: None Declared
Keywords: chromogranin A, pancreas cancer

P1230 CHARACTERISTICS AND OUTCOME OF ASYMPTOMATIC PANCREATIC CYSTS LESS THAN 3CM - EXPERIENCE FROM A REGIONAL HOSPITAL IN HONG KONG

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INTRODUCTION: Incidental pancreatic cysts are identified more frequently. Some would have malignant potential. The natural history of incidental pancreatic cyst is not clear and the optimal imaging surveillance interval is not well established.
AIMS&METHODS: To determine the natural history of incidental pancreatic cysts less than 3cm, the predictors of cyst growth and to evaluate an optimal imaging surveillance interval.
A retrospective study on patients with incidental pancreatic cysts detected by Computed-Tomography imaging from January 2000 to December 2010. Computer search through the radiology database containing all CT exam was performed. Patients with incidental, asymptomatic pancreatic cysts less than 3cm in size at presentation with follow-up interval more than 3 months were included. Patients with history of pancreatitis, pancreatic pseudocyst and systemic cystic disease were excluded. The demographic, biochemical and radiological features of pancreatic cysts at presentation were reviewed. Outcomes include increased in cyst size, development of new cystic features, symptoms related to pancreatic cyst, malignant transformation and death related to cystic neoplasm of pancreas.
RESULTS: Ninty-nine patients were included for analysis. The mean age was 66 and male-to-female 1:1. Over 50% of patients had non-pancreatic malignancy. The most common indication for imaging that detected incidental pancreatic cyst was staging for newly diagnosed malignancy (25.3%). The initial cyst size was 14.35mm, with 66% located over pancreatic body or tail region. Septation was present in nine patients (9.1%) while no patients had mural nodules. Over a mean follow-up duration of 22.2 months, eighty-two (82.8%) patients with pancreatic cysts did not show any significant growth, development of new cystic features or new symptom related to pancreatic cysts. By using multivariate logistic regression analysis, presence of septation (p=0.024, 95% CI 1.287-33.3, OR 6.536) and radiological follow-up duration (p=0.001, 95% CI 1.021 - 1.083, OR 1.051) were independently associated with cyst progression. Among seventeen (17.2%) patients with pancreatic cysts showed significant growth, malignant IPMN with metastasis was diagnosed in one (1.0%) patient after 54 months follow-up. The remaining cases were either within surgically resectable stage or clinically benign lesions. The majority of cyst growth occured after 18 months from baseline evaluation.
CONCLUSION: Eighty percent of incidental pancreatic cysts less than 3cm did not have significant growth during 22 months follow-up. A conservative approach with regular imaging surveillance is justified. The interval of follow-up imaging at 18 months after baseline evaluation is a safe duration.
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Disclosure of Interest: None Declared
Keywords: Pancreatic cyst, pancreatic cystic neoplasm

P1231 HIGH INCIDENCE OF PANCREATIC CANCER IN PATIENTS WITH AUTOIMMUNE PANCREATITIS UNDERGOING SURGERY

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INTRODUCTION: Autoimmune pancreatitis (AIP) is a rare disease that may present with signs and symptoms mimicking pancreatic cancer. AIP is characterized by a dramatic response to corticosteroid therapy. Thus, patients diagnosed with AIP can avoid surgery and undergo immunosuppressive treatment. Only a few cases of pancreas cancer in AIP patients have so far been reported worldwide.
AIMS&METHODS: We performed a retrospective analysis of data of all patients who underwent pancreatic resection in our department for suspected cancer/focal pancreatic enlargement.
RESULTS: Two hundred and twenty pancreatic resections were performed in 153 males and 67 females (mean age 59 years, range 36-72 years). Indication for surgery was tumor suspicion based on clinical symptoms, imaging methods and laboratory findings. In 14 patients (6.4%, 9 males, 5 females), autoimmune pancreatitis was diagnosed based on histology of the resected specimen. In 5 patients, abundant IgG4 cells were present. In 3 AIP patients (21.4%, all males, one IgG4 positive), pancreatic adenocarcinoma was also present in the resected tissue. No differences were observed in the preoperative characteristics of patients with and without cancer (CT, EUS, ERCP, bile duct involvement, laboratory findings including CA 19-9). In none of the patients the diagnosis of AIP was made prior to surgery; however the diagnostic algorithm was not fully completed.
CONCLUSION: AIP patients may develop pancreatic cancer. The preoperative diagnosis of autoimmune pancreatitis in patients with focal pancreatic enlargement may not always rule out the simultaneous presence of cancer
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Disclosure of Interest: None Declared
Keywords: autoimmune pancreatitis, pancreatic cancer

P1232 ARE DIAGNOSTIC ERRORS IN CYSTIC TUMORS OF THE PANCREAS CLINICALLY RELEVANT?

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INTRODUCTION: Diagnostic errors in the preoperative evaluation of cystic neoplasm of the pancreas (CNP) are not uncommon. Only limited data is available regarding the impact of these errors on clinical management.
AIMS&METHODS: Aim:
This study aims to evaluate the clinical impact of these diagnostic errors.
Methods:
A series of 141 patients undergoing surgery for CNP at Karolinska University Hospital was retrospectively analyzed. There were 60 males; the mean age was 60.3 yrs. CT was performed in 138 patients (97.8%), MR in 85 (60.3%), and EUS in 31 (21.9%).
RESULTS: Histology confirmed the pre-operative diagnosis in 60.9% of patients. The concordance rate between pre-operative diagnosis and histology was similar for asymptomatic and symptomatic lesions (60.5% vs 61.4%; p=NS). The rate of correct diagnosis increased over time (2004-2006: 54.5%, 2007-2012: 61.7%, 2010-2012: 63.5%). Lymphoepitelial cysts (2/2) were misdiagnosed most frequently, followed by serous cystic neoplasia (24/33, 72.2%), solid pseudopapillary neoplasia (5/8, 62.5%), mucinous cystic neoplasia (7/25, 28%), and IPMN (17/56, 23.3%). Reevaluating the surgical indication in view of the histological diagnosis, surgical resection was not required in 13 patients (9.2%). There was no mortality in this patient group, and morbidity amounted to 53.8%.
CONCLUSION: The results confirm that preoperative diagnostic errors are quite common in CNP, however, the percentage of patients who unnecessarily undergo surgery is low (9.2%). The error rate is similar for symptomatic and asymptomatic patients.
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Disclosure of Interest: None Declared
Keywords: cystic tumors, pancreas

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00
ENDOSCOPY AND IMAGING III – Poster Area

P1233 THE OUTCOME OF PHARYNGEAL CANCER TREATED BY ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: Majority of pharyngeal cancer has been diagnosed in advanced stage. The standard treatment for advanced pharyngeal cancer is pharyngectomy, and the patients lost their vocal function. On the other hand, the vocal function could be kept if the patient could be treated by endoscopic submucosal dissection (ESD). However, the outcome of pharyngeal cancer treated by ESD is unknown.
AIMS&METHODS: The aim of our study is to investigate the outcome of pharyngeal cancer treated by ESD. The indication of pharyngeal ESD was epithelial (EP) and subepithelial (SEP) cancer without lymph node metastasis (LNM). CT and cervical US were done for checking LNM. 53 lesions in 36 patients treated by ESD from January 2006 to December 2012 were enrolled into this retrospective study. The median age was 67 (50-79) years, 35 were males and 1 was female. The median follow up period was 69 (5-89) months. 25 and 28 lesions were located in oropharynx and hypopharynx, respectively. 0-I, 0-IIa, 0-IIb and 0-IIc were 2, 17, 31 and 3, respectively.
RESULTS: 1. The median diameter of the resected specimens and lesions were 22 (10-90) and 3 (1-48) mm, respectively. EP and SEP cancers were 38 and 15, respectively.
2. En-bloc resection and R0 resection rate was 100% and 96% (51/53), respectively. Lateral margin was positive in 2 lesions and decided as R1.
3. Complication; There weren't severe complications such as bleeding needed blood transfusion. Delayed bleeding was occurred 2.8% (1/36), and the patient was treated by endoscopic hemostasis under tracheal re-intubation.
4. Local recurrence rate was 1.9% (1/53). The only patient was SEP cancer, and R0 resection was performed. However, local recurrence was diagnosed at 3 months after ESD. The case had lymph duct involvement.
5. LNM rate was 0% (0/24) and 8.3% (1/12) in EP and SEP groups, respectively. The only patient was SEP cancer, and neck LNM was diagnosed at 6 months after ESD. The patient was treated by LN dissection and chemo radiotherapy.

6. Distant metastasis was 0%.
7. Prognosis: No patient died of pharyngeal cancer, and 1 of 12 (8.3%) patients in SEP group died of pharyngeal cancer.
CONCLUSION: EP and SEP pharyngeal cancer is a good candidate of ESD. However, detailed follow up is recommended for SEP pharyngeal cancer.
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Disclosure of Interest: None Declared
Keywords: endoscopic submucosal dissection, pharyngeal cancer

P1234 SUBLINGUAL VERSUS ORAL ALPRAZOLAM AS CONSCIOUS SEDATION FOR ESOPHAGOGASTRODUODENOSCOPY: A RANDOMIZED PLACEBO-CONTROLLED TRIAL

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INTRODUCTION: Diagnostic esophagogastroduodenoscopy (EGD) is an uncomfortable and stressful procedure for many patients.
AIMS&METHODS: We determined the efficacy of oral and sublingual alprazolam as conscious sedation during EGD in decreasing patients' pain/discomfort, and increasing patients' compliance and satisfaction with the procedure.
In a double-blinded, placebo-controlled, randomized trial, adult patients who were candidate for EGD were allocated to four groups of oral and sublingual alprazolam and oral and sublingual placebo (n = 55 in each group). Patients received one oral dose of alprazolam 0.5 mg (or placebo) at the night before the procedure and then one oral or sublingual dose at least 30 minutes before the EGD. Procedure related pain/discomfort and patients' satisfaction were assessed by 11-point numeric rating scale. Compliance was assessed from no compliance (0) to excellent compliance (4). Duration of the procedure was also recorded.
RESULTS: Mean age was 43.4±12.6 years and 60.9% were female. The pain/discomfort score was significantly lower in the sublingual (3.2±2.0) and oral (3.4±1.6) alprazolam groups than in the oral placebo group (5.1±2.3), $P < 0.001$; but difference with the sublingual placebo group (4.1±1.8) was not significant ($P > 0.1$). Frequency of needing intravenous sedation (with midazolam) was 10.9%, 9%, 10.9%, and 12.7% in the sublingual and oral alprazolam and sublingual and oral placebo groups, respectively ($P = 0.946$). Compliance was better in the sublingual alprazolam group than other three groups ($P = 0.001$), but oral alprazolam group was not different with the placebo groups in compliance ($P > 0.1$). Satisfaction was greater in the sublingual alprazolam group (6.4±2.3), but not oral alprazolam (5.5±2.2), than in the sublingual (5.0±2.3) and oral placebo groups (4.7±2.4), $P < 0.05$. Duration of EGD (second) was also shorter in the sublingual alprazolam (271.1±33.1) than other three groups; oral alprazolam (297.5±33.6), sublingual placebo (307.4±41.5), and oral placebo (317.5±36.1), $P < 0.01$.
CONCLUSION: Although alprazolam did not reduce the need for intravenous sedation in our study, its sublingual administration reduced pain/discomfort related to EGD, reduced procedure duration, and increased patient's compliance and satisfaction with the procedure. We conclude that sublingual alprazolam is an effective conscious sedation method for EGD.
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Disclosure of Interest: None Declared
Keywords: compliance, conscious sedation, endoscopy, esophagogastroduodenoscopy, pain

P1235 CLINICAL UTILITY OF GLASGOW BLATCHFORD SCORE IN ACUTE UPPER NON VARICEAL GASTROINTESTINAL BLEEDING AS A PREDICTOR OF LOW RISK FOR THE NEED OF CLINICAL INTERVENTION.

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INTRODUCTION: Upper gastrointestinal bleeding (UGIB) is a common indication for admission in the hospital. The Glasgow Blatchford Score (GBS) is a pre-endoscopic risk scoring system for patients presenting with acute non variceal UGIB based on clinical and laboratory variables. This score has been shown to be superior to Rockall Score for predicting the risk of rebleeding or death. A GBS of zero (GBS-0) has been related with low risk patients.
AIMS&METHODS: The aim of this study is to evaluate the capacity of GBS to predict the need of clinical intervention to control bleeding (blood transfusion, endoscopic treatment or surgery).
Methods: We performed a prospective observational study in all patients with UGIB attended at the Emergency Department in our hospital from March 2010 to June 2012. Inclusion criteria included patients aged 18 to 80 with signs of UGIB such as hematemesis, coffee-ground emesis or melena, with endoscopic confirmation. Exclusion criteria included anticoagulant therapy or portal hypertension. Patients were classified in two groups, GBS-0 or GBS > 0.
RESULTS: 129 patients were included (61.2% males, mean age 50±18 years). Clinical presentation was melena in 55%, hematemesis in 31% and others in 14%. Personal history of peptic ulcer was present in 10% of patients, and 30% of patients had recently used NSAIDs. Causes of bleeding were peptic ulcer in 46.5%, Mallory-Weiss syndrome in 10.1%, erosive gastritis in 9.3%, esophagitis in 8.5% and others in 25.6%. 20 patients were classified as GBS-0 and 109 as GBS > 0. Endoscopic therapy was required to control bleeding in 3 patients with GBS-0 and in 31 patients with GBS > 0 (15 vs. 28.4%, p=0.21). No patients with GBS-0, and 3 patients in GBS > 0 group presented rebleeding (0 vs. 2.8%, p=0.45). Blood transfusion was needed in 27 patients in the GBS > 0 group whereas no patients in the GBS-0 group required blood transfusion (24.8% vs. 0%, p=0.012). No patients needed surgery to control bleeding and no deaths where registered in any group. The global median length of stay was 24 hours (IQR 13-96). 52% of all patients were discharged after a 12-hours observation period after the endoscopy, with no rebleeding in the next 30 days in any patient.
CONCLUSION: A GBS of zero is related to a very low risk of blood transfusion, surgery and mortality in nonvariceal UGIB patients. Since endoscopic treatment could be needed to control bleeding in some GBS-0 patients, upper gastrointestinal endoscopy should be performed in all patients presenting with UGIB.
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Disclosure of Interest: None Declared
Keywords: Gastroscopy, RISK-STRATIFICATION, score, upper gastrointestinal bleeding

P1236 ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR EARLY ESOPHAGEAL NEOPLASIA – EXPERIENCE IN A EUROPEAN CENTER

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INTRODUCTION: ESD experience in the western world is still limited. Especially in esophageal lesions ESD only few European data are available so far. The role of ESD in the treatment of Barretts early neolasia needs to be further defined.
AIMS&METHODS: From 08/2007 to 05/2013 ESD was performed in 82 esophageal lesions. Lesions were early Barretts cancers (n=54), Barretts with high grade intraepithelial neoplasia (n=7) and early squamous cell cancers (SCC) (n=21). Resection was judged "oncologically adequate" when invasion depth was restricted to the m2 layer for SCCs and the mm layer for Barretts lesions. Data were collected prospectively (lesions diameter, en bloc resection, R0 resectio, "oncologically adequate" resection).
RESULTS: In 79/82 cases en bloc resection was technically possible (96.3%). In three lesions ESD was impossible due to non-lifting. 5 resections were performed as circumferential resection. The following table shows the diameter of the resection specimens and the the resection rates for the different groups.

	resection specimen - diameter Ø	en bloc resection	R0 resection	resection "oncologically adequate"
LSBE(n=17)	46mm	14 / 17 (82.4%)	13 / 17 (76.5%)	13 / 17 (76.5%)
SSBE(n=44)	38mm	44 / 44 (100%)	39 / 44 (88.6%)	34 / 44 (77.3%)
Barrett total (n=61)	41mm	58 / 61 (95.1%)	52 / 61 (85.2%)	47 / 61(77%)
SCC(n=21)	35mm	21 / 21 (100%)	20 / 21 (95.2%)	13 / 21 (61.9%)
all lesions (n=82)	39mm	79 / 82 (96.3%)	72 / 82 (87.8%)	60 / 82 (73.2%)

In 79 en bloc resections R1 resection was shown in 7 specimens (3 at the basal margin, 3 at the lateral margin and one at the basal and the lateral margin). In 72 R0 resections ...high-risk"-histology was found, the resection was judged ...oncologically inadequate" and surgery was recommended (7 SCCs > m3, 5 Barretts cancers with submucosal invasion). Resection was judged "oncologically adeqate" in 60/82 lesions (73.2%). Complications: stenosis n=9, bleeding n=1, no perforation. Three recurrences: lymph node metastasis 18 months after ESD of a Barretts carcinoma G3smR0, local recurrence 11 months after ESD of an SCC G2smR0), liver metastasis 29 months after ESD of an SCC m3G3. In all three cases surgery had been refused by the patient or had not been performed due to severe comorbidity.
Mean follow-up is 22 months (1-68).
CONCLUSION: ESD of early esophageal neoplasia shows high en bloc resection rates (96.3%) and high R0 resection rates (87.8%). R0 resection rates are high for SCCs but also for Barretts early neoplasia. When oncologic limitations are noticed strictly the rate of "oncologically adequate" resection is lower (77% for Barretts and only 61.2 for SCCs).
Disclosure of Interest: None Declared
Keywords: Early esophageal cancer and precancerous lesions, ESD (endoscopic submucosal dossection)

P1237 GASTROINTESTINAL ANGIODYSPLASIA IN CHRONIC RENAL FAILURE

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INTRODUCTION: Gastrointestinal (GI) hemorrhage is a frequent and sometimes life-threatening complication of end-stage renal failure. Angiodysplasia

(AD) is the most common cause of recurrent lower-intestinal hemorrhage in patients with renal failure. Its Prevalence in chronic renal failure is 19 to 32% compared to 5% in individuals with normal renal function.
AIMS&METHODS: The aim of this study is to report the clinical, endoscopical and therapeutical characteristics of AD in these patients. All patients with chronic renal failure having angiodysplasia in endoscopy (upper digestive endoscopy, ileocoloscopy, small bowel videocapsule endoscopy) were included during 6 years.
RESULTS: Out of 411 patients with chronic renal failure, 73 patients (17.7%) had angiodysplasia. There were 45 men (61.6%) and 28 women (38,4%). Mean age was 63 years. Endoscopy was performed for anemia in 47 patients (64%), upper bleeding in 15 patients (20.5%), rectal bleeding in 8 patients (10.9%) and melena in 3 patients (4.1%). Angiodysplasia was localized in the stomach in 38 patients (52%), in the duodenum in 3 patients (4.1%), in the small bowel in 13 patients (17.8%), in the cecum in 4 patients (5.4%), in the colon in 11 patients (15%) and AD was diffuse in 4 patients (5.4%). All these patients underwent argon plasma coagulation with good clinical and biological outcome.
CONCLUSION: The Frequency of angiodysplasia as a cause of hemorrhage in chronic renal failure is 17.7% in our series. The frequent clinical sign was anemia and the predominant localization of angiodysplasia was the stomach followed by the small bowel. The diagnosis is based on endoscopy and treatment can be improved by argon plasma coagulation.
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Disclosure of Interest: None Declared
Keywords: angiodysplasia, Argon plasma coagulation, chronic renal failure

P1238 ENDOSCOPIC ASSESSMENT OF NEUROGENIC DYSPHAGIA: A NEW INSIGHT BY FUNCTIONAL ENDOSCOPY

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INTRODUCTION: Dysphagia is a frequent and early symptom in neurologic diseases. Besides disturbance during food intake and dehydration, these patients often encounter a considerable risk of aspiration pneumonia. Functional endoscopy via transnasal route provides the endosopist an insight into the deglutition of neurologic patients suffering from dysphagia.
AIMS&METHODS: Functional endoscopy applying ultrathin video endoscopes (BF-3C160, Olympus Europe) was performed in 20 patients with neurologic dysphagia - including observation of the upper esophageal sphincter in inversed position of the endoscope. Especially, the esophageal phase of deglutition may be observed which has long be considered as black box in endoscopic assessment. Furthermore, diagnostics was completed by kinematography, high-resolution endoscopy and fiberoptic endoscopic evaluation of swallowing.
RESULTS: A varity of disorders was documented by functional endoscopy: Clearance disturbance of tubular esophagus, incomplete closure of the upper esophageal sphincter, bolus leakage, delayed swallowing reflex, and residues in valleculae and piriformes, esophageal hyperperistalsis and aspiration during food intake.
CONCLUSION: By interdisciplinary cooperation (gastroenterology, neurology and ENT) with additional assessment of the esophageal phase of deglutition using functional endoscopy, the diagnostic of neurologic disorders including dysphagia may tremendously be improved. Consequently, the clinical understanding of complex dysfunctional patterns is improved. Because primary and secondary opening disorders of the upper esophageal sphincter may often be observed in neurogenic dysphagia, this diagnostic comprehensive approach may be helpful to apply focussed prophylactic and therapeutic actions.
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Disclosure of Interest: None Declared
Keywords: endoscopy, functional gastrointestinal disorders

P1239 RELATION OF DISTANCE BETWEEN TWO FREE ENDS OF RING ENDS AFTER PERORAL ENDOSCOPIC MYOTOMY AND ACHALASIA SYMPTOM

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INTRODUCTION: Peroral endoscopic myotomy (POEM) is a new-developed minimally invasive endoscopic technique, expected to be the first choice for treating achalasia (AC). The relation of distance between two free ends of ring muscules after peroral endoscopic myotomy and achalasia symptom has not been reported. The aim of our study was to investigate the relation of distance between two free ends of ring muscules after peroral endoscopic myotomy and achalasia symptom
:EN-US;mso-fareast-language:ZH-CN; mso-bidi-language:AR-SA'>achalasia (AC).
AIMS&METHODS: To study the relation of distance between two free ends of ring muscules after peroral endoscopic myotomy and achalasia symptom. Fourty-six patients (male 28, female 18, age 16-63, mean±SD 40.6±13.0) with achalsia undergoing POEM during December 2010 to December 2012 was studied. According to the distance between two free ends of ring muscules after POEM, the fourty-six patients was divided into two groups. Preoperative and postoperative Eckardt scores of achalsia was compared between two groups.
RESULTS: Postoperative symptom Eckardt scores (6~9, mean 7.5) was significant lower than preoperative symptom scores (0-6, mean 2.6). The decreaing extent of Eckardt scores in achalsia with big distance between free ends of ring muscules was greater than that with small distance(7.1 vs 4.2 respectively, $P < 0.05$).
CONCLUSION: Peroral endoscopic myotomy is an effective method for achalasia, and the distance of two free ends of ring muscules after peroral endoscopic myotomy was positively associated with relief of achalsia symptom.
Disclosure of Interest: None Declared
Keywords: achalasia, POEM, ring muscules

P1240 DOUBLE PERORAL ENDOSCOPIC RESECTION OF GASTRIC SUBEPITHELIAL TUMORS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) and surgery is efficacious technique for superficial gastrointestinal neoplasms. However, the procedure is long, complex, and associated with higher complication rates.
AIMS&METHODS: To evaluate the feasibility and efficacy of endoscopic resection of gastric subepithelial tumors originated from the muscularis propria layer with double peroral endoscopes. In this study 4 patients who presented with gastric subepithelial tumors were enrolled. Endoscopic resection was performed using preoral endoscopes. The four gastric subepithelial tumors were removed integrally and incision of muscularis propria layer were closed firmly by metal clips when ancillary endoscopy draw tumors or muscularis propria layer.
RESULTS: The four gastric subepithelial tumors originated from the muscularis propria layer were removed integrally, which were diagnosed pathologically as gastrointestinal stromal tumor and leiomyoma. The diameter of tumors were 22 mm. The mean procedure time was 48 minutes. No complications as perforation or bleeding occurred in all cases after the operation, who received successful closure with metal clips. The mean hospitalization time was 7 days.
CONCLUSION: Double peroral endoscopic resection, an efficacious and safe endoscopic surgical procedure to resect gastric subepithelial tumors originated from the muscularis propria layer integrally and close the incision of muscularis propria layer, is able to achieve the efficacy equivalent to ESD or surgery .
Disclosure of Interest: None Declared
Keywords: double endoscopes, endoscopic resection, peroral, subepithelial tumors

P1242 CONTRIBUTION OF UPPER DIGESTIVE ENDOSCOPY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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INTRODUCTION: Digestive disorders are more common in kidney failure.
AIMS&METHODS: The aim of this study is to analyze the frequency and different types of endoscopic lesions in patients with chronic kidney disease.
We included all patients with chronic kidney failure at the stage of hemodialysis or not between January 2007 and April 2013. Endoscopy is systematically realized in patients planned for kidney transplantation. Other indications are represented by dyspepsia in 97 patients (26%), upper gastrointestinal bleeding in 58 patients (15.6%) and iron-deficiency anemia in 42 patients (11.3%).
RESULTS: Out of 12580 Upper digestive endoscopy performed, 372 (3%) patients have a chronic kidney failure. 204 are men and 168 are women with a sex ratio of 1,2. The mean age is 44.7 years.
The Upper digestive endoscopy objectified lesions in 313 cases (84%), it's a congestive gastritis in 156 patients (42%), ulcerative gastritis in 58 patients (15.6%), angiodysplasia in 43 patients (11.5%), peptic esophagitis in 26 patients (7%), signs of portal hypertension in 20 patients (5.4%), peptic ulcer in 18 patients (5%) and a hiatal hernia in 8 patients (2.1%). 59 patients (16%) have normal Upper digestive endoscopy.
CONCLUSION: Upper digestive lesions are common in patients with chronic kidney failure. 84% of these patients have lesions in our series. They are dominated by congestive and ulcerative gastritis followed by angiodysplasia.
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Disclosure of Interest: None Declared
Keywords: angiodysplasia, chronic kidney disease, Gastritis, upper digestive endoscopy

P1243 TREATMENT OF ZENKER'S DIVERTICULUM WITH FLEXIBLE ENDOSCOPE: RESULTS AND TECHNICAL ASPECTS

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INTRODUCTION: In our country the Zenker's diverticulum is an entity known as heritage of surgery. In 1995, Ishioka and Mulder publish their experiences using flexible endoscopes.
AIMS&METHODS: To report our results and techniques modifications. We reviewed the database of 51 patients (33 men) with a mean age of 72.14 years (range 37-98 years) with symptomatic Zenker's diverticulum who underwent endoscopic myotomy between december 1997 and april 2013. All procedures were performed in our service by the same endoscopist (H. M.). The most common symptom was oropharyngeal dysphagia (96.1%), which was recorded by a 0-4 score (0 = no dysphagia, 1 = for solids, 2 = semisolids, 3 = liquid, 4 = saliva). First ten cases were done exposing the septum with a nasogastric tube and the others patients were performed with soft diverticuloscope. All procedures were performed under deep sedation by anesthesiologist then a myotomy was done in all cases with needle-knife using pure coagulation to prevent bleeding. Clips were placed to close mucosal flaps.
RESULTS: Sixty-four procedures were performed in 51 patients. The 95.83% of the patients had dissapearence or improvement of dysphagia score at 30 days.

Two patients with only regurgitation were completely resolved. Mean follow up was 31 months (1-99 months). Thirty-five patients were followed at least for 1 year and 97,1% had good outcome. In 13 cases (24.5%) a reintervention was needed. Bleeding ocurred in one patient (1,96%) who required surgery. Other patient required surgical intervention due to technical issues. There were no perforations or infections.

CONCLUSION: The treatment of Zenker's diverticulum with flexible endoscope is a safe and effective option, with good long-term results.

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Disclosure of Interest: None Declared

Keywords: Complications, flexible endoscope, myotomy, Outcomes, treatment, ZENKER DIVERTICULUM

P1244 CAN SHORT LENGTH TRAINING PERIOD IN A JAPANESE SPECIALIZED CENTER IMPROVE THE DIAGNOSTIC YIELD OF EARLY GASTRIC CANCER IN WESTERN COUNTRIES?

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INTRODUCTION: Intensive training in early gastric cancer (EGC) detection improves detection of these lesions1.

AIMS&METHODS: We evaluated the diagnostic impact in a western population of a training period undergone by a western endoscopist (WE) in a japanese endoscopy unit specialized in the detection and treatment of EGC. In April 2012 a WE received intensive training in detection of EGC and endoscopic submucosal dissection (ESD) in a japanese reference unit. All gastroscopies performed by WE in his original hospital after that stay (IV/2012-IV/2013) were prospectively recorded (Case Group). The detection rate of EGC and precancerous lesions in this group was compared to a Control Group consisting in the same number of gastroscopies performed by WE prior to the stay (IV/2010-III/2012). Topical pharyngeal anaesthesia or conscious sedation were used. The technique varied from the Control Group (full evaluation of the stomach with lavage of the gastric wall when contents covered most of it) to the Case Group (thorough washing, distention, aspiration of gastric contents and observation of the mucosal surface). Therapeutic and urgent gastroscopies were excluded. Student t and chi-square test were used for comparison.

RESULTS: 254 patients were included in each group. There were no differences in age or sex distribution ($p > 0.05$). Sedation was more frequently used in Control Group (79vs104, p=0.006) and consequently tolerance was significantly better (p=0.03). Detection of gastric mucosal lesions in the Case Group was significantly higher [100(39.37%)vs32(12.59%), $p < 0.0001$]. These lesions included 7 advanced gastric cancers in the Case Group vs 4 in the Control Group (2.75%vs1.57%, $p > 0.05$). Of the 93 remaining lesions detected in the Case Group, 67 were Paris 0-II and only 11 in the Control Group (72%vs34.3%, p=0.002). Taken together, the diagnosis of precancerous lesions and EGC was not significantly different in both groups: 1 hyperplastic polyp > 3 cm, 1 adenomatous polyp and 11 EGC vs 4 adenomatous polyps and 1 EGC (p=0.1). EGC detection was significantly higher in the Case Group [11 (4.33%) vs 1 (0.39%), p=0.003]. These lesions were treated by means of ESD, endoscopic resection, surgery or medical treatment. The remaining mucosal lesions corresponded to inflammatory lesions, small hyperplastic polyps and mild dysplasia.

CONCLUSION: Training of a WE in a specialized center significantly improves the diagnostic rate of EGC in a western population by means of improving detection of subtle Paris type 0-II lesions, and allows curative endoscopic treatment.

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Disclosure of Interest: None Declared

Keywords: Early Gastric Cancer, Endoscopic submucosal dissection (ESD), Western countries

P1245 PREDICTING RISK FACTORS FOR EARLY BLEEDING INCLUDING ASYMPTOMATIC EVENTS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC NEOPLASMS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been reported to be associated with a higher bleeding rate than conventional endoscopic mucosal resection. Bleeding is one of the major complications of endoscopic submucosal dissection (ESD). Previous reports focused on patients with symptomatic bleeding. There was no study clarified on the risk factors for early bleeding included patients with asymptomatic bleeding after ESD.

AIMS&METHODS: The aim of this study was to identify the risk factors for early bleeding associated with ESD for gastric neoplasms. This retrospective study was performed in a single tertiary referral medical center. The medical records were retrospectively reviewed 768 lesions in 703 patients who were underwent endoscopic submucosal dissection (ESD) for gastric neoplasm from February 2008 to August 2011. A total of 750 gastric neoplasms in 698 consecutive patients were included in the analysis.

RESULTS: The mean age of the patients was 64.2+10.0 years and 534 (76.5%) were male. The mean size of the resected specimens was 31.1+10.1 mm. The most common longitudinal and horizontal location was lower third (632/750, 84.3%) and lesser curvature (259/750, 34.5%) in included cases. The number of cases who were planned second look endoscopy (SLE) on the next day after ESD (pSLE group) were 576, and the npSLE group (who did not planned SLE) were 174 cases. There were more high occurrence of symptomatic early bleeding (within 24 hours after ESD) in the pSLE group (2.3% vs. 0%, p=0.045). In the pSLE group, early bleeding after ESD occurred in 78 cases (13.5%) including asymptomatic bleeding in 65/78 cases (83.3%). In all cases except for one case of early bleeding, immediate hemostatic therapy was successful. In multivariate analysis, the significant factors predicting early bleeding after ESD were resectecd specimen over 30 mm in size (odds ratio [OR], 1.796; 95% confidence interval [CI], 1.101–2.927) and young age (< 65 years) (OR, 1.692; 95% CI, 1.040–2.753).

CONCLUSION: It seems to be no need planed routine SLE on the next day after ESD in patients with gastric neoplasm However, the SLE on the next day after ESD may be beneficial for selected patients with risk factors of early bleeding such as large resected specimen (>30mm) and young age (< 65 years).

Disclosure of Interest: None Declared

Keywords: Bleeding, Dissection, Endoscopy, Risk factors, Stomach neoplasms

P1246 ARE HIGH DOSE SYSTEMIC STEROIDS EFFECTIVE IN PREVENTING LUMINAL STRICTURES AFTER LARGE ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) FOR OESOPHAGEAL NEOPLASIA?

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INTRODUCTION: ESD is effective for treatment of superficial oesophageal cancers. However, circumferential or large ESDs often induce luminal strictures, requiring repeated endoscopic dilations. Recently, literature reports suggested that systemic steroids could prevent such stenoses (Yamaguchi et al. GIE 2011). The aim of the present study was to evaluate the efficacy of systemic steroids in this indication and determine the best daily dose and administration protocole.

AIMS&METHODS: From 11/2009 to 07/2012, all patients referred for treatment of an early oesophageal cancer –squamous cell carcinoma or Barrett adenocarcinoma– were included and distributed over time in 3 treatment groups:

Group A was made of patients treated from 11/2009 to 06/2011, by repeated endoscopic dilation; Group B included patients treated from 07/2011 to 08/2011 who were prescribed oral prednisolone 10-30mg daily for more than 8 weeks; Group C included patients treated after 08/2011 who received IV prednisolone 100-150 mg daily followed by progressive discontinuation for at least 8 weeks. Primary outcome was the need for endoscopic dilations and the number of dilation attempts. Groups were compared by chi2 test.
RESULTS: 28 patients (21 men, 7 women, mean age 64 years) underwent large or circumferential ESD for Barrett early cancer/HG-IEN (n=18) or squamous cell carcinoma/HG-IEN (n=10). In Group A (n=13), a stricture developed in 10 (76.9%) and was treated by dilation. 4 patients (25%) had a temporary stent. In Group B (n=4) on oral prednisolone 10-30mg daily up to 8 weeks, a stenosis occurred in 3 patients (75%) and was treated by dilation. In Group C (n = 13) on oral prednisolone 100-150mg daily up to 8 weeks, no stricture was observed. The incidence of oesophageal stricture was significantly lower in group C as compared to Groups A and B (chi2 = 14.00; P = 0.0002). 3 complications occurred in Group A: 2 aspiration pneumonia and 1 bleeding, all resolving under medical treatment. In Groups B and C, 1 patient had reactivation of pulmonary tubreculosis, 1 a spinal fracture in context of osteoporosis and 15 (88.2%), monilial oesophagitis.
CONCLUSION: Systemic high dose steroids significantly reduced the occurence of strictures after circumferential ESD. Our results show that early high daily doses of steroids are more effective but side effects must be monitored and prevented (diabetes mellitus, osteoporosis, tuberculosis quantiferon test, systematic treatment by Fluconazol). Further evaluations in larger series are needed to validate this therapeutic option.
Disclosure of Interest: None Declared
Keywords: corticosteroids, Endoscopic submucosal dissection (ESD), Oesophageal carcinoma, oesophageal stenosis

P1247 COMPARISON OF SUPERFICIAL GASTRIC NEOPLASIA DIAGNOSIS WITH A PROBE BASED CONFOCAL LASER ENDOMICROSCOPY (CLE) BETWEEN GASTROENTEROLOGY FELLOWS AND EXPERT ENDOSCOPISTS WITHOUT ANY CLINICAL EXPERIENCE OF CLE AFTER A BRIEF WEB-BASED TRAINING

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INTRODUCTION: Confocal laser endomicroscopy (CLE) provides real-time histologic images of GI superficial lesions. However, it is surmised that the morphological interpretation of unstable ''super'' magnified images could be challenging especially for beginners. CLE has not been approved for clinical use in Japan yet. Our institution introduced a probe based CLE system for clinical researches in January, 2013.
AIMS&METHODS: Aims of this study were to compare CLE diagnosis of gastric superficial lesions between gastroenterology fellows and expert endoscopists without any clinical experience of CLE . Overall 27 video clips of a probe based CLE images (CellVisio, Maunakea technology, Paris) obtained from 5 patients with 10 adenocarcinomas and 1 adenoma in the stomach were studied. After an approximately 20 min web-based training of the CLE diagnosis (Cellvisio.net) of gastric lesions, demonstratives video clips of CLE obtained from either neoplastic mucosa (n=11) or non-neoplastic background mucosa (n=16) edited by CLE experts were reviewed by blinded 5 gastroenterology fellows and also blinded 5 staff endoscopists without any clinical experience of CLE. The reviewers made diagnosis of neoplasia or non-neoplasia while reviewing every movie clip less than 1 min. The results of the CLE diagnosis were compared with the corresponding histological diagnosis of biopsy specimens sampled from the studied sites.
RESULTS: The accuracy of CLE neoplastic diagnosis between the fellows and the staff endoscopists were not significantly different (85.9% 116/135 vs 88.9% 120/135, p=0.56). Overall Sens, Spec, PPV and NPV were 91.8%, 84.4%, 80.2% and 93.8% respectively. Metaplastic mucosa was misdiagnosed as neoplastic more frequently than non-metaplastic, non-neoplastic mucosa was so (17/80 and 8/80 respectively, p=0.05).
CONCLUSION: The results of this preliminary study conducted in the run-in period demonstrated that the knowledge base for on-site interpretation of mobile gastric CLE images could be established quickly with the brief web-based training regardless of readers' basal endoscopic experiences and pathological knowledge. However, further prospective studies are necessary to elucidate the true accuracy.
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Disclosure of Interest: None Declared
Keywords: confocal endomicroscopy, gastric neoplasia, web based training

P1248 ESOPHAGEAL „OUTLET PATCHES": ENDOSCOPIC, HISTOLOGIC AND ELECTRONMICROSCOPIC DESCRIPTION OF NEW LESIONS (SMALL VESICLES CONTAINING GASTRIC METAPLASIA AND SUBMUCOSAL GLANDS) AT THE GASTROESOOPHAGEAL JUNCTION

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INTRODUCTION: The gastroesophageal junction (GEJ) is still an ill-defined, physiologically and pathologically highly active transition zone connecting the esophagus to the stomach. Although several endoscopic and histologic aspects such as the Z-line, cardia, tongues of zylindrical and/or tiny islands of zylindrical epithleium have been well described, we have often observed the presence of small yellow vesicles or tiny submucosal cysts above the Z-line in a significant number of patients. These lesions have not been described in the literature.
AIMS&METHODS: To evaluate the incidence of these lesions and characterize them endoscopically and histolgically.
200 patients were prospectively and consecutively enrolled. The endoscopies were performed using standard and high-definition white light endoscopes with magnification (up to x 110) capability (Olympus, Q160Z, Hamburg, Germany). Histology was performed using H&E. In 10 patients we also performed electron microscopy with magnification up tp 7000x (Phillips, Holland). All potential physiologic and pathologic lesions found in the esophagus and stomach were carefully searched and described for (e.g. inlet patches, glycogenic acanthosis, zylindrical epithelia, gastritis, atrophy, metaplasia, etc). The occurrence of these yellow vesicles was analyzed in the context of these lesions using univartiate and multivariate analysis, Mann-Whitney and Student t-test.
RESULTS: A total 197 were included (102 women and 95 men, mean age 55,5, SD+15) (thrre patiens were excluded). The incidence of yellow vesicles was30% of EGDs. Some lesions had a shape of a . . .volcano'' with zylidrical epithelium on its tip. Their sizes ranged from 3 mm to 10 mm. These yellow vesicles had a significant correlation with zylindrical esophageal epithelium (including Barrett esophagus) (p = 0,009) and inverse correlation with erosive esophagitis (p = 0.024) and female sex (p = 0,011). Histology and elctron microscopy demonstrated submucosal glands and zylindrical epithelium, including pancreatic and gastric metaplasia (the patholgist blinded to the study called these lesions . . .inlet patches'').
CONCLUSION: Yellow vesicles in the distal esophagus are found in 30% of patients undergoing EGD for clinical symptoms. Yellow vesciles are inversely associated with columnar lined epithelium (Barrett esophagus) and positively associated with female sex and less erosive esophagitis, suggesting a protective mechanism tof the GEJ. These lesions contain glands and gastric metaplasia and could be thus considered esophageal . . .outlet patches''.
Disclosure of Interest: None Declared
Keywords: inlet patch, metaplasia

P1249 MULTIPURPOSE USE OF THE "BEAR CLAW" (OVER-THE-SCOPE-CLIP, OTSC-SYSTEM) TO TREAT ENDOLUMINAL GASTROINTESTINAL DISORDERS

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INTRODUCTION: The ''bear-claw'' or over-the-scope clip system, OTSC (Ovesco Endoscopy, Tübingen, Germany) is a new clipping device developed for closure of large luminal gastrointestinal (GI) defects.
AIMS&METHODS: To evaluate the clinical outcomes of patients treated with the OTSC.
Observational, open-label, retrospective, single-arm case series conducted at two hospitals with tertiary care endoscopy. This study involved 26 clip applications in 22 patients patients (median age 64.3 years [range 28-90 years], 7 women) with GI defects from fistulas and anastomotic dehiscence and peptic ulcer bleeding.
RESULTS: The range of indications included gastrointestinal bleeding (n = 8), gastrocutaneous fistulas (n = 4), esophagotracheal and/or esophagopleural fistulae (n = 3), resection of submucoal tumors (n = 3), gastrocolonic fistulae (n=1), gastro-gastric fistula after gastric bypass (n = 1), stent fixation (n=1), and anastomotic leak after esophagectomy (n=1). The overall success rate for the OTSC device was 76% (17 out of 21 patients). The overall per procedure success rate was 80% (21 of 26 applications). There were no complications (0%) related to endoscopy, sedation or application of the clipping device.
CONCLUSION: The OTSC system is a useful device in a variety of clinical scenarios including the management of larger GI leaks, complex GI fistulas, GI bleeding and stent anchoring, even in very old and frail patients.
Disclosure of Interest: None Declared
Keywords: fistula, OTSC (over-the-scope clip)

P1250 A RETROSPECTIVE STUDY OF THE SALVAGE SURGERY FOR EARLY GASTRIC CANCER UNCURED BY POST ESD PATHOLOGICAL ASSESSMENT

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INTRODUCTION: After many discussions about indication of ESD, it has been revealed that radical resection by ESD is expected up to so-called an extended indication lesion. Although standards of additional resection are based on the guidelines, a case of additional resection is not discussed adequately. Here, we compared each factor for an additional surgery by final diagnosis with pathological findings about additional resection, and examined problems of additional resection as a non-indication lesion by pathologic final diagnosis after ESD.
AIMS&METHODS: From December 2003 to April 2013, there were 957 cases and 1036 lesions which had ESD while aiming at the absolute cure of gastric cancer in our institution. From them, there were the actual additional surgery 79 non-indication lesions, positive stumps in deep part and positive vascular invasions, according to the pathological diagnosis after ESD classified by guidelines for Diagnosis and Treatment of Carcinoma of the Stomach 2004 edition edited by the Japanese Gastric Cancer Society Each factor which had required additional surgery was examined by comparison to the surgical pathology.
RESULTS: The details of target lesions are, as non-indication, (1) cancer deeper than 'sm2'or 'positive vertical stumps': 'sm2' 50 lesions, 'mp' 1 lesion, enclosed

VT(+) 10 lesions. (2) undifferentiated dominant cancer, 'm', over 2cm, sig mixed 1lesion, 'por' mixed 3 lesions, (3) positive vascular invasion: 'ly' single positive 16 lesions, 'v' single positive 7 lesions, 'ly v' co-positive 5 lesions. In the above, the additional surgery specimen for each factor had the local residual (%) of resected area / the positive vascular invasion (%) of local ESD / the positive lymph node metastasis (%); those were (1)5/5/6, (2)25/0/0, (3)0/4.3/8.7. As for (1), it was the vertical margin positive lesion at the time of ESD at 'mp' invasion, and the residual of local resection and 'ly' of the surrounding area of resection were positive. As for (3), one case of advanced stomach cancer complication was included, and there was a possibility of increased positive lymph node ratio.
CONCLUSION: In 'sm2', there is no local residual, there were significantly many cases in which invasion finding could not be obtained from the resected specimens even if they had been the vascular invasion positive at the time of ESD. The indication of additional resection as the definitive diagnosis of ESD needs reexamination, additional resection should be considered with exception for non-indication, and it is preferable to treat them as individual.
Disclosure of Interest: None Declared
Keywords: ESD (endoscopic submucosal dossection), Gastric cancer, Salvege surgery

P1251 ACETIC ACID CHROMOENDOSCOPY FOR JUDGING THE EXTENT OF GASTRIC INTESTINAL METAPLASIA

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INTRODUCTION: The diagnosis of gastric intestinal metaplasia is currently possible with the histological assessment of multiple endoscopic biopsies or chromoendoscopy with methylene blue. But, both method is not practical; limited by accessibility or cost-effectiveness.
AIMS&METHODS: The acetic acid (vinigar) chromoendoscopy has not been used for this purpose. Therefore, we wanted to assess the diagnostic accuracy of acetic acid chromoendoscopy for detecting the extent of gastric intestinal metaplasia and interobserver variability of this chromoendoscopy. Consecutive 126 patients were enrolled. The participants underwent screening EGD with 1.5% acetic acid for detection of acetowhitic reactions. And targeting biopsies were performed subsequently at the five standardized intra-gastric locations according to the updated Sydney System. The accuracy of acetic acid chromoendoscopy was evaluated with biopsy report as the reference. Two endoscopists judged the presence or absence of acetowhitic reactions, blinded to the other physician's result.
RESULTS: There was substantial inter-observer agreement between the two endoscopists (k index =0.808, $P<0.01$). The diagnostic accuracy of acetic acid chromoendoscopy was 86.5% and 86.3%, respectively by two endoscopists . The overall sensitivity, specificity, positive predictive value and negative predictive values were 74.6%, 91.7%, 79.9% and 89.1%, respectively. The specificity of gastric body was over 92%. Bile stained gastric muocsa was 1.94(1.06-6.56) fold inaccurate using this chromoendoscopy.
CONCLUSION: The acetic acid chromoendoscopy is a valid tool for evaluating the extent of gastric intestinal metaplasia. It may serve as a practical method to discriminate population with high risk of gastric cancer.
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Disclosure of Interest: None Declared
Keywords: acetic acid, chromoendoscopy, intestinal metaplasia

P1252 DEVELOPMENT AND EXPERIENCE WITH USING A PERIPHERALLY INSULATED SCISSOR-TYPE FORCEPS (SB KNIFE)

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INTRODUCTION: Although knife-type instruments are primarily used to make incisions during ESD at present, it is necessary to be proficient in the procedure to perform endoscopic procedures simultaneous to electrification and incision. Scissor-type forceps are comparatively easy to manipulate. We have fabricated a scissor-type forceps (SB knife, SUMITOMO BAKELITE CO.) in which the periphery is coated with an insulator, and have used this device in clinical applications.
AIMS&METHODS: The periphery of rotatable monopolar scissors was coated with an insulator, the tips were smoothened and isolated from the electrodes, and only the central electrode portion was allowed to be electrified. Raising the tips and central electrified portion above the level of the base prevented pinching of the muscular layer, and cutting force was enhanced by centralizing the current. In addition, the overall shape is a pean type having a gentle curvature to facilitate penetration of the submucosal layer, and the tip shape is an L-shape having a thick hook on one side to avoid catching the muscular layer with the tip.
RESULTS: This developed scissor-type forceps was used on 98 gastric lesions. Although it was primarily used to detach the submucosal layer, it was also possible to cut away surrounding mucosa. There was no incidental occurrence of muscular layer damage or bleeding observed. The procedure itself was comparatively easy, and was particularly effect at distal sites, sites subjected to strong respiratory fluctuations and sites containing blood vessels where conventional devices encounter difficulties. There was no pinching of the muscular layer observed even if certain parts of the procedure had to be performed blindly due to the smooth shape. Although the procedure was basically performed with an incision wave, at sites containing blood vessels, the procedure was able to be performed with little bleeding by initially inserting a coagulant. There was also little thermal damage to surrounding tissue due to the insulating treatment that included the base of the instrument.
CONCLUSION: This peripherally insulated scissor-type forceps (SB knife) contributed to greater ease of the procedure was determined to be an effective device for ESD.
Disclosure of Interest: None Declared
Keywords: ESD (Endoscopic submucosal dissection), SB Knife

P1253 CLINICOPATHOLOGICAL PREDICTIVE FACTORS ASSOCIATED WITH LYMPH NODE METASTASIS IN INTRAMUCOSAL EARLY GASTRIC CANCER

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has been introduced as a curative treatment option for early gastric cancer (EGC). However, the potential major limitation of ESD is its disability of sweeping away the lymph node radically. Because lymph node metastasis of EGC is the most important factor that causes recurrence or distal metastasis, how to predict the metastasis, especially in intramucosal gastric cancer, is now becomes the restriction for the widely application of ESD in EGC.
AIMS&METHODS: 498 patients underwent radical gastrectomy and were histologically confirmed intramucosal gastric cancer from June 2006 to October 2011. Retrospectively collected the clinicopathological data of ruled-in patients, including gender, age, location, tumor size, histological type, depth of invasion, presentation of ulceration and vascular invasion. All the patients were divided into positive group or negative group according to the metastasis condition of the lymph node microscopically. Cox univariate and multivariate analysis were applied to determine the independent predictors of lymph node metastasis in EGC.
we aim to investigate the prediction factors of lymph node metastasis in intramucosal early gastric cancer and provide reference for treatment choice of early gastric cancer.
RESULTS: Forty-three of 498 patients (8.6%) had lymph node metastasis. There was no significant difference between positive group and negative group in patient characteristics, tumor location and vascular invasion. According to the multivariate analysis, lymph node metastasis is related to tumor size ($\leq$ 20mm vs. $>$20m and $\leq$30mm vs. $>$30mm; HR (95% CI), 1.525(1.040-2.236); P=0.042), histological type (severe dysplasia with focal canceration vs. well-differentiated adenocarcinoma vs. moderate-differentiated adenocarcinoma vs. undifferentiated adenocarcinoma; HR (95% CI), 1.656(1.158-2.368); $P<0.001$) and depth of invasion (confined into epithelium vs. confined into lamina propria vs. invasion to muscularis mucosae; HR (95% CI), 8.149(1.770-37.513); $P<0.001$). Particularly, no lymph metastasis occurred in 97 cases with lesions confined into lamina propria, no bigger than 20 mm, and well-differentiated.
CONCLUSION: Tumor size, histological type, and depth of invasion were the independent factors for the prediction of lymph node metastasis in EGC. ESD can be adopted as a curative treatment of choice only for the well selected patients.
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Disclosure of Interest: None Declared
Keywords: early gastric cancer, lymph node metastasis, Endoscopic submucosal dissection

P1254 AN ASSESSMENT OF FOUR WATER-JET TOOLS IN SUBMUCOSAL CUSHION FORMATION FOR ENDOSCOPIC SUBMUCOSAL DISSECTION

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INTRODUCTION: One of the most difficult steps of endoscopic submucosal dissection (ESD) is dissection of a lesion in the submucosal plane. Repeated submucosal cushions are required to allow safe dissection through the submucosa whilst ensuring the muscularis layer remains intact. A submucosal cushion is created by injecting lifting solution (e.g. normal saline) into the submucosal layer. Relatively recently a number of water-jet tools have been introduced making this step quicker, easier and more effective. Four water jet tools are reviewed in this study, the primary outcome is the time required to create a submucosal cushion. Secondary outcomes include the volumes of lifting solution used to create a submucosal cushion and subjective measurements of the four water-jet tools from six endoscopists.
AIMS&METHODS: Simulated gastric lesions were created by marking 2 x 2cm lesions in porcine gastric body and antral specimens. Porcine upper gastrointestinal specimens were placed into a validated endoscopic surgery simulator tray (EASIE-R, ENDOSIM). Six endoscopists used the ERBE Hybridknife, T-type and I-type, Fuijinon Flush Knife and Pentax Splash needle to raise three simulated lesions with each tool. The lifting solution used was a litre of normal saline with 5 millilitres of methylthioninium chloride. Finally, a survey was completed by the endoscopists once they had finished using the four tools.
RESULTS: The average time taken to lift a 2 x 2cm gastric lesion was 3.0 seconds, 2.9 seconds, 3.8 seconds and 4.5 seconds using the Hybridknife, T type, Hybridknife I-type, Flush knife and Splash needle respectively. 5, 4,7 and 5 millilitres of lifting solution were needed to lift lesions using a Hybridknife, T-type, Hybridknife I-type, Flush knife and Splash needle respectively.
The Hybrid knife, I-type was considered the best water-jet tool to use overall by four out of the six endoscopists. Table 1 shows the average Likert scale scores for four qualities of the tool.

	HybridKnife, T-type	HybridKnife, I-type	Flush Knife	Splash Needle
Ease of insertion	4.7	5	4.8	5
Ease of cushion formation	4.2	4.7	3.7	4.2
Quality of cushion formation	4.7	4.7	3.7	4.2
Ease of use of the distal tip	3.8	4.7	3.3	4.5

Table 1: average Likert scores for the four water-jet tools (1 - easiest/fastest,5- most difficult/slowest) for six endoscopists

CONCLUSION: All water-jet tools were shown to create a quick and adequate submucosal cushion. The Hybridknife, I-type was shown to produce the quickest submucosal cushion with the lowest volume of lifting solution and was also deemed to be the easiest to handle generally. Comparison studies in humans are warranted to further review water-jet tools enabling safe and effective ESD.

Disclosure of Interest: None Declared

Keywords: cancer, Endoscopic submucosal dissection (ESD), water jet system

P1255 THE INTRAGASTRIC BALLOON FOR PRE-OPERATIVE WEIGHT LOSS IN LAPAROSCOPIC GASTRIC BYPASS

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INTRODUCTION: INTRODUCTION: Intragastric balloon (IGB) is indicated as a temporary treatment for weight loss, in super-obese patients (body mass index, BMI $>50Kg/m^2$), who are candidates for bariatric surgery to lose weight and to reduce their surgical and anesthetic risks. We evaluated the potential benefit of preoperative IGB on the outcome of laparoscopic Roux-en-Y gastric bypass (LGB) in super-obese patients.

AIMS&METHODS: Aims & Methods: Retrospective analysis, case-control, of 80 consecutive super-obese patients submitted to a LGB between 2008 and 2012, with preoperative IGB (cases) or without (controls). Clinical success of IGB was defined as a weight loss (WL) $\geq$10%, and clinical success of LGB as an excess weight loss (EWL) $\geq$25%. The anesthetic risk was assessed by ASA physical status classification system. Adverse event was categorized as the need for conversion to laparotomy, hospitalization $>$15days or ICU admission.

RESULTS: Results: 80 patients were included (80% women; average age of 45,7years old), 18 cases and 62 controls. 81,3% presented comorbidity. The initial mean BMI and overweight was $57.4Kg/m^2$ and 84.6kg for cases versus (Vs) $53.1Kg/m^2$ and 71.1kg for controls ($p<0.001$). In case group, the IGB was inserted for a mean time of 191.3 days, obtaining a 100% success in its placement and removal. IGB induced a mean reduction of 9.1 kg/m^2 in BMI, mean WL of 26.4Kg, and EWL of 29%, achieving clinical success in 83.3% and improvement of ASA and comorbidities in 22.2% of cases. The mean time between IGB removal and LGB was 133.8 days, resulting in mean weight gain of 5.4kg. Mean operative time was lower in the cases group (118.94 Vs 142.6 minutes; $p<0,05$). Clinical success of LGB was achieved in 100% of patients without adverse events. The mean EWL on follow-up at 6, 12, 18 and 24 months, in cases Vs controls was: 57.1% Vs 51.9% ($p>0.05$); 55.5% Vs 67.8% ($p<0.05$); 54.2% Vs 70.9% ($p<0.05$); 57.1 Vs 70.9% ($p<0.05$).

CONCLUSION: Conclusion: IGB prior to LGB is a safe and effective temporary treatment for weight loss in super-obese patients, improving comorbidities, reducing anesthetic risk and operative time.

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Disclosure of Interest: None Declared

Keywords: INTRAGASTRIC BALLOON, LAPAROSCOPIC GASTRIC BYPASS

P1256 CHROMOENDOSCOPY WITH METHYLENE BLUE IS A USEFUL TOOL IN THE DIAGNOSIS OF ESOPHAGEAL CANDIDIASIS

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INTRODUCTION: *Candida* species are the most common cause of infective esophagitis. Currently, the diagnosis of esophageal candidiasis is based on the endoscopic examination combined with histopathological and/or direct microscopic examination of the specimens taken from pathologically changed areas. Aside from chromoendoscopy, staining with methylene blue (MB) is used to identify fungal structures on microscopic preparations. However, the usefulness of chromoendoscopy with MB in the diagnosis of esophageal candidiasis has not been determined yet.

AIMS&METHODS: Evaluation of the usefulness of endoscopy with MB staining in the diagnosis of esophageal candidiasis.

Patients with suspected candidiasis on the basis of endoscopic examination as well as patients with suspected oral candidiasis with accompanying dysphagia and odynophagia were recruited to the study. All patients underwent endoscopy with two biopsies (for histology and microbiology) taken from suspicious areas prior to staining and two additional biopsy samples obtained from sites positively stained with MB. Direct preparations were stained with Gram's method. Identification of cultured fungi and susceptibility tests were performed on the Vitek analyzer (bioMérieux). Histological preparations were stained using H&E and Grocott's method.

RESULTS: To date 21 eligible patients were enrolled to the study. Among 21 patients with endoscopic suspicion of candidiasis, esophageal candidiasis was confirmed by histology and microbiology in 14 patients (66%). Chromoendoscopy was positive in 19/21 patients. Methylene blue staining was positive in all patients with confirmed candidiasis. In patients with positive chromoendoscopy, in whom candidiasis was not confirmed by histopathology or on the basis of examination of direct microscopic preparations (5/19), *Candida* colonization was confirmed by isolation of fungi. In one patient, the presence of *Candida* colonies has been detected only by means of MB chromoendoscopy and subsequently confirmed by microbiology. In two patients with candidiasis suspected on the basis of classic endoscopy with a negative result of chromoendoscopy esophageal candidiasis was excluded. Fungi were isolated in 76% of cultures of biopsy material taken before staining and in 82% of cultures of biopsy samples taken from stained areas (NS).

CONCLUSION: The preliminary results of our study suggest that chromoendoscopy with MB is a quick and sensitive test confirming endoscopic diagnosis of *Candida* infection or colonization.

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Disclosure of Interest: None Declared

Keywords: chromoendoscopy, esophageal candidiasis, Methylene Blue

P1257 CARDIAC SAFETY OF RADIOFREQUENCY ABLATION IN THE ESOPHAGUS

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INTRODUCTION: Radiofrequency ablation (RFA) can be a therapeutic option in the treatment of several medical conditions. It can be used for instance in the treatment of gastrointestinal neoplasia but also in the treatment of atrial fibrillation. RFA has proven to be an effective method for the treatment of neoplastic changes in the esophagus, mainly in Barrett's esophagus (BE), with low complications rate. Some patients may suffer chest pain after esophageal RFA, so the question naturally arises whether esophageal RFA can induce heart injury?

AIMS&METHODS: Consecutive patients who underwent esophageal RFA at 2 tertiary hospitals were included. Blood troponin T and proBNP levels were assessed before and 24 hours after RFA. The delivered energy in the ablations were either 10 or 12 Joule/cm2. Symptoms assessment was performed in each patient at the 24 hours control. Chest pain after treatment was graded as none, moderate or severe.

RESULTS: Twenty one patients were invited to paticipate, being 3 excluded due to incomplete sampling protocol. Eighteen patients were included (15 men), with avarage age of 64.4 years-old. Three patients had a previous history of myocardial infarct. After RFA, 5 patients suffered moderate pain and 1 severe pain. Three patients had a mild increase in the Troponin T level after treatment (5-12 units), being this increase not pathological and not related to chest pain nor to the delivered energy. None of the patients with elevated cardiac enzymes had a history of heart disease.

CONCLUSION: In this prospective study, esophageal RFA did not induce significant cardiac injury in any patient. This can be useful since some patients seek emergency with chest pain after RFA. Cardiac enzymes increase was not pathological in any patient and did not correlate to patients background. RFA in the esophagus seems a safe procedure in terms of cardiac injury.

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Disclosure of Interest: None Declared

Keywords: cardiac safety, Esophagus, radio frequency ablation

P1258 THE USE OF TISSUE-ENGINEERED CELL SHEETS TO IMPROVE HEALING AFTER RADIOFREQUENCY ABLATION (RFA) IN THE ESOPHAGUS.

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INTRODUCTION: RFA has proven to be a safe method to eradicate Barretťs esophagus. However some patients do not heal properly with squamous cell epithelium after RFA. The patients, sometimes reffered to as "poor healers", are usually patients with long Barretts segments and hiatus hernias. Transplantation of tissue-engineered autologous oral mucosal epithelial cell sheets in the esophagus has shown to be able promotes re-epithelialization of the esophagus after ESD. We wanted to investigate if cellsheets could improve the healing RFA as well.

AIMS&METHODS: The first patient selected was a 71 year old male with a C8M10 Barretís esophagus according to the Prague classification. He had intestinal metaplasia but no dyplasia. 24 hour manometry and pH-metry showed a severe reflux with reduced clearance of the distal esophagus. The second patient was a 72 year old female with initially a 11 cm long Barretís esophagus with recurrent high grade dysplasia (HGD). The patient had previously been treated three times with endoscopic resection (ER) and six times with RFA but did still have four cm long, almost circumferential area with columnar lined epithelium containing HGD but no visible lesion. 24 hour manometry and pH-metry showed mild reflux but hypoperistaltic movements. We collected specimens of oral mucosal tissue from the patients and the epithelial cells were cultured for 16 days on temperature-responsive cell culture surfaces. At the day of the RFA a temperature reduction released the cellsheets that endoscopically transplanted to the raw surfaces. All patients were monitored by endoscopy and confocal microscopy once a week for a four week period.
RESULTS: During the four week period the first patient had complete re-epithelialization. He experienced no dysphagia nor any stricture or other complications. The second patient is just recently treated but so far there has been no complications.
CONCLUSION: Transplantation of tissue-engineered autologous oral mucosa-lepithelial cell sheets in the esophagus after RFA seems topromote re-epithelialization. Further studies are needed to show if this could be a procedure to treat patients with poor healing after RFA.
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Disclosure of Interest: None Declared
Keywords: cell sheet, Esophagus, radio frequency ablation

P1259 ENDOSCOPIC RESECTION OF DUODENAL ADENOMAS : EVOLUTION OF A HYBRID EMR-ESD TECHNIQUE IN 2 UK CENTRES

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INTRODUCTION: Sporadic duodenal adenomas (SDAs) have traditionally been managed by radical or local surgical resection, but these techniques carry substantial mortality and morbidity risks. Recent series have shown EMR of SDAs to be an effective treatment but with a risk of delayed bleeding within 48 hours. ESD of SDAs carries very high risk of perforation (22-50%).
AIMS&METHODS: All ER procedures for SDAs at both centres for the period Jan 2005 – Dec 2012 were recorded in a prospective database which was analysed. Demographic data, histology, procedure success, long-term outcome and complications were assessed.
RESULTS: 34 patients were identified, of which 18 were male and 16 female. The mean age was 69 years (range 48-87). Mean adenoma size was 25mm (range 6-80mm). The majority of SDAs (71%) were located in the second part of the duodenum. Additional staging investigations (EUS/CT) were performed in 13 of the 34 cases. 21 cases were performed by traditional piecemeal-EMR, 1 by full ESD and 12 by a hybrid EMR-ESD technique combining circumferential mucosal incision by ESD, with en bloc or piecemeal snare resection. En bloc resection was achieved in 50% of cases and adjunctive use of APC was used in 68%. Successful resection was achieved in 97% of cases in a single ER session. Histology showed adenoma with low grade dysplasia in 22 cases and adenoma with high grade dysplasia in 12. There were no cases of invasive malignancy.
Mean duration of follow-up was 38 months. Recurrence of adenomatous tissue was detected in 10 (29%) of cases. This was successfully treated in 8 cases with APC or further ER. One patient is awaiting further treatment and one patient developed an unrelated malignancy and therefore no further treatment is planned.
No perforations occurred in these 2 series. There were 3 episodes (7.5% of ER procedures) of significant late bleeding occurring 1, 12 and 18 days respectively after ER. 2 of the 3 cases required endoscopic therapy to achieve haemostasis. The risk of delayed bleeding was significantly higher following resection of lesions of 30mm or larger compared to those under 30mm (33% vs 0%, P=0.003). Risk of delayed bleeding was not significantly related to ER technique used (EMR = 9.5%, ESD/Hybrid = 7.7%, P=0.855).
CONCLUSION: Endoscopic resection is an effective treatment for duodenal adenomas. Appropriate case selection can be made on the basis of endoscopic assessment without need for EUS/CT. Hybrid ESD-EMR technique is a promising new endoscopic treatment option. There is substantial risk of delayed bleeding which in contrast to other series can occur up to 2-3 weeks after the index procedure.
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Disclosure of Interest: None Declared
Keywords: Complications, duodenal adenoma, endoscopic resection, ESD

P1260 HIGH-MAGNIFICATION ENDOSCOPY (HME) FOR NEOPLASTIC AND NON-NEOPASTIC GASTRIC LESIONS: DIFFERENTIATION, HISTOLOGY PREDICTION AND CANCER RISK ASSESSMENT

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INTRODUCTION: HME combined with narrow-band imaging (NBI) provides effective detection and precise characterization of gastric lesions due to the ability of observing microvascular (MV) and microsurface (MS) patterns [1]. However, the diagnostic standards have not been established yet and their clinical application requires a high level experience of medical experts for making a correct diagnosis.
AIMS&METHODS: The aim was to evaluate the diagnostic accuracy of MV and MS criteria for differentiation of neoplastic and non-neoplastic gastric lesions and to create cancer risk assessment system. 128 gastric lesions in 106 patients (mean age 51.3 years, SD=12.1) were observed with HME-NBI (GIF-H190, Q260Z, Q160Z, Olympus endoscopes). MV and MS patterns were assessed independently: regular (RV, RS), irregular (IV, IS), absent (AV, AS) and compared with histology.
RESULTS: From 128 gastric lesions there were 69 with RV+RS, 7 with AV+RS, 11 with IV+IS and 33 with IV+AS. The data are summarized in the table. Combination of RV+RS and AV+RS was found as a low cancer risk group with sensitivity, specificity, positive predictive value and negative predictive value 91.6%, 100%, 100% and 86.5% respectively for non-neoplastic lesions. Combination of IV+IS, IV+AS and AV+IS was found as high-risk group with sensitivity, specificity, positive predictive value and negative predictive value 100%, 91.6%, 86.5%, 100% respectively for neoplastic lesions.
Table. Results of the study

	RV	IV	AV
RS	Benign – 64 (92.8%) LGD – 5 (7.2%)	n.i.	Benign – 4 (57.1%) LGD – 3 (42.9%)
IS	n.i.	LGD – 2 (18.2%) HGD – 3 (27.2%) AC – 6 (54.6%)	Benign – 2 (25%) HGD – 1 (12.5%) AC – 5 (62.5%)
AS	n.i.	Benign – 3 (9.1%) HGD – 2 (6.1%) AC – 28 (84.8%)	n.i.

n.i. – not identified;, benign conditions included chronic gastritis, intestinal metaplasia, hyperplasia; LGD – low-grade dysplasia; HGD – high-grade dysplasia; AC – adenocarcinoma
CONCLUSION: The results of the study showed good correlation of MV and MS criteria with histology. These criteria can be included into cancer risk assessment system for histology prediction and differentiation of non-neoplastic and neoplastic gastric lesions.
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Disclosure of Interest: None Declared
Keywords: Gastric cancer, magnifying endoscopy with narrow-band imaging, RISK-STRATIFICATION, Stomach Neoplasms

P1261 THE EFFICACY AND SAFETY OF 0.4% SODIUM HYALURONATE SOLUTION IN ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC NEOPLASM

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INTRODUCTION: Background: A sufficient amount of submucosal fluid cushion is one of the important requisites for endoscopic submucosal dissection. The ideal injection agent should provide a long lasting submucosal cushion. Sodium hyaluronate produces long lasting mucosal elevation.
AIMS&METHODS: To evaluate the efficacy and safety of sodium hyaluronate solution in endoscopic submucosal dissection for gastric neoplasm. A prospective multicenter randomized, double-blind, controlled trial was designed in this study. A total of 76 patients with 5~20mm sized gastric neoplasms were enrolled at three academic hospitals in Korea from June 2011 to October 2011. Patients were randomly assigned to the 0.4% sodium hyaluronate or control groups. All lesions underwent endoscopic submucosal dissection. Endoscopic submucosal dissection was performed with 0.4% sodium hyaluronate and normal saline solution for submucosal injection. The efficacy was assessed by en-bloc resection and the number of additional injections. The secondary evaluation variables were the

volume of injection material, steepness of mucosal elevation, bleeding rate, procedural time and operator satisfaction. The safety was assessed by analyzing adverse events during the study.
RESULTS: The usefulness rate in 0.4% sodium hyaluronate group and the controlled group was 90.90% and 61.11%, respectively, a statistically significant difference (p=0.0041). Depending upon the secondary evaluation variables, volume of injection material and operator satisfaction differed significantly between groups ($p < 0.05$). The safety of the solution did not differ between the groups (p=0.47).
CONCLUSION: 0.4% sodium hyaluronate solution gives gastric mucosa long lasting lifting compared to normal saline, thereby endoscopic submucosal dissection is more effective compared to the control group. The solution is safe when comparing adverse events to the normal saline group. 0.4% sodium hyaluronate is a useful agent for submucosal injection during endoscopic submucosal dissection.
Disclosure of Interest: None Declared
Keywords: ESD, gastric neoplasm, Sodium Hyaluronate

P1262 RISK FACTORS FOR COMPLICATIONS ASSOCIATED WITH ENDOSCOPIC REMOVAL OF INGESTED FOREIGN BODY IN UPPER GI TRACT

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INTRODUCTION: There are few reports about ingested foreign bodies of upper GI(gastrointestinal) tract. We aimed to investigate the status of foreign bodies in upper GI tract and to determine the predictive risk factors associated with complications of endoscopic removal of foreign bodies.
AIMS&METHODS: Eighty-nine cases with endoscopically confirmed foreign bodies in the upper gastrointestinal tract were retrospectively investigated. A review of the medical records of the patients who underwent endoscopic foreign body removal at Myongji hospital between January 2004 and August 2012 was performed. Patients' demographic data including sex, age and presence of esophageal stricture were collected, and data about foreign body, such as, type, size, sharpness, location of impaction and radio-opacity were investigated. Values associated with endoscopic foreign body removal were duration of foreign body impaction, endoscopic removal duration time, removal method, the presence of complication, hospitalization after the procedure, operation related to endoscopic foreign body removal.
RESULTS: The types of upper gastrointestinal foreign bodies included fish bone (25.8%), food and drug (16.9%), metal (12.4%), stone (12.4%), shell (11.2%). The location of impaction was pharynx (4.5%), upper esophagus (40.4%), mid esophagus (32.6%), lower esophagus (3.4%), stomach (19.1%). The proportions of foreign body size were 42.7% (larger than 3cm) versus 57.3% (smaller than 3cm). Successful endoscopic foreign body removal without operation or endoscopy under general anesthesia was achieved in eighty-five patients. The development of complication after endoscopic removal was 37 cases (41.5%) including laceration with minor bleeding(20.2%), erosion and ulcer (19.1%), perforation (1.1%), abscess (1.1%). There was only one case of massive bleeding after foreign body removal. Cases of operation related to foreign body were 7 cases (7.9%). Multivariate analysis showed that age (HR 1.04, CI 1.01-1.07, p=0.013), size larger than 3cm (HR 3.83, CI 1.25-11.72, p=0.019), sharpness (HR 3.50, CI 1.07-11.40, p=0.038), and longer than 4 hours of duration of impaction (HR 4.61, CI 1.50-14.16, p=0.008) were significant independent risk factors associated with the development of complications in patients with upper gastrointestinal foreign bodies.
CONCLUSION: Fish bone was most common foreign body of upper gastrointestinal tract. Complication rate related to endoscopic foreign body removal was 41.5%, and the risk factor were increased with age, sharpness, larger size (larger than 3cm), and longer duration of impaction time (longer than 4 hours).
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Disclosure of Interest: None Declared
Keywords: Foreign body, risk factors, Upper GI tract

P1263 POSTBANDING ULCER HEMORRHAGE AFTER ENDOSCOPIC BAND LIGATION - PREDICTORS OF A RATHER STUDIED ENTITY

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INTRODUCTION: The endoscopic band ligation (EBL) is the preferred treatment for acute variceal hemorrhage, and also used in primary and secondary prophylaxis. Complications after EBL include esophageal stricture, infection and recurrence of bleeding by postbanding ulcers. Postbanding ulcer hemorrhage (PBUH) is a significant cause of morbidity and mortality, which studies are limited to date.
AIMS&METHODS: AIM: To evaluate the incidence of PBUH in our institution, identify predictors of its occurrence and evaluate the treatment strategies to manage PBUH.
MATERIAL & METHODS: Retrospective analysis of all patients included in an EBL program in our department, for 3 consecutive years. Collected data: demographic, clinical, analytical (CBC, liver function tests, renal and coagulation - calculated scores MELD and Child-Pugh) and endoscopic (urgent/elective indication, number of ligation bands placed at each EBL session) and eventual complications. PBUH was confirmed endoscopically
RESULTS: Included 112 patients, a total of 505 primary prophylaxis sessions (n=37), secondary (n=430) and treatment (n=38) of variceal bleeding. EBL was performed in 40% (n=202), identifying PBUH in 13/202 (6.4%). PBUH occurred more frequently after urgent EBL for active bleeding (n=8) than after prophylactic EBL (n=5), with a mean time period of 9.2 days after the procedure. In comparative analysis, patients who suffered PBUH had lower platelet count and higher MELD and SCP scores, a statistically significant difference ($p < 0,05$). Endoscopic therapeutic performed: EBL (n=5), sclerosis (n=2) and conservative (n=6). There was no 30-day mortality in our patient sample.
CONCLUSION: In our study, postbanding ulcer hemorrhage occurred in 6.4% of cases, most often after EBL for variceal hemorrhage, in patients with advanced liver dysfunction (with higher MELD and Child-Pugh scores).
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Disclosure of Interest: None Declared
Keywords: CIRRHOSIS, postblanding ulcer hemorrhage, Variceal bleeding, variceal ligation

P1264 DUODENAL BIOPSIES FOR DIAGNOSIS OF COELIAC DISEASE – A 5-YEAR EXPERIENCE

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INTRODUCTION: Duodenal biopsies are indicated for patients having gastroscopies for anaemia, diarrhoea, weight loss and other autoimmune conditions to diagnose Coeliac Disease (CD). There is a low threshold for taking duodenal biopsies in patients as CD can present with a variety of symptoms and subtle endoscopic appearances. However, there are no large studies to show the efficacy of this practice for diagnosing CD.
AIMS&METHODS: Our study sought to evaluate the diagnostic yield of duodenal biopsies in patients having a gastroscopy and to calculate the cost of analysing tissue samples for diagnosis of CD.
A retrospective study was performed on patients who had endoscopic duodenal biopsies over a 5-year period between 2007 and 2011. Symptoms, serology, endoscopy and histology findings of the abnormal biopsies were collated. An estimate of the pathology cost for diagnosing a patient with CD on biopsy (not including endoscopy cost) was calculated.
RESULTS: Of 4410 duodenal biopsies, 4238 (96%) were normal and 162 (4%) were abnormal. 93 (58%) patients were males (mean age 64, range 18 - 95). Of the abnormal biopsies, 30% were from duodenal bulb and 70% from second part of duodenum. Only 11 (7%) patients were positive for anti-tissue transglutaminase (anti-TTG) and 4 (3%) were positive for anti-endomysial antibody (EMA). On endoscopy, 6 (4%) cases were suspected to have CD. Histology showed non-specific duodenitis in 85%, CD in 13% and ulceration in 3%.
In the CD group, there were 11 males and 10 females, (mean age 61, range 21 – 90). Presenting symptoms were abdominal pain in 9 (43%), diarrhoea in 7 (33%), unexplained gastrointestinal symptoms in 5 (24%), anaemia in 5 (24%), weight loss in 2 (10%) and prolonged fatigue in 1 patient. 6 (28%) were only anti-TTG positive, 5 (24%) were positive for both anti-TTG and EMA, neither test was performed in 4 (19%), 3 (14%) were negative for both and 1 patient was only EMA positive. On endoscopy, duodenum was normal in 9 (43%), 5 (24%) were suspected CD, 1 patient (5%) each had duodenitis and an ulcer, 5 (24%) reports could not be traced. On histology, 9 patients (43%) each were classified as Marsh IIIA, IIIB and 3 (14%) as Marsh IIIC. There was one case each of hypothyroidism and type 1 diabetes. Of the 4410 biopsies, only 21 cases (0.5%) were diagnosed with CD. The cost of analysing and reporting biopsies costs about £50 each thus totalling to £220,500 and averaging £10,500 for diagnosing each case of CD.
CONCLUSION: Taking routine duodenal biopsies at gastroscopy has a low diagnostic yield. It is not a cost effective way of diagnosing CD. Endoscopic duodenal biopsies should be taken if clinical suspicion is high with a negative serology or there are endoscopic findings suggestive of CD.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, cost-effectiveness, Endoscopy

P1265 EFFICACY OF ENDOSCOPIC VARICEAL LIGATION FOR TREATMENT OF EARLY GASTRIC VARIX BLEEDING.

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INTRODUCTION: Gastric varix (GV) occurs in about 20% of patients with portal hypertension. GV are one of the most serious complications of portal hypertension. Endoscopic variceal obliteration (EVO) and endoscopic variceal ligation (EVL) are commonly used to manage gastric variceal bleeding. The aim of this study is to evaluate the efficacy of EVL compared to EVO for patients with early GV.
AIMS&METHODS: Sixty-nine patients with grade F1 or grade F2 GV were enrolled between June 2006 and May 2012. We retrospectively reviewed patient's medical records. Nineteen patients underwent EVO and fifty patients underwent EVL. Rebleeding was defined as newly-development hematemesis, hematochezia, melena, or endoscopically proven bleeding. Kaplan-Meier method and Cox regression analysis were used to examine the efficacy of EVL.
RESULTS: During follow-up period, rebleeding has occurred in eleven patients (4 EVO and 7 EVL) and twenty-five patients have died (5 EVO and 20 EVL). The median event-free survival for EVO and EVL were 248 (range 2~2105) and 458 (range 1~2179) days, respectively (p=0.332). The median overall survival were 368 (range 6~2195) and 647 (16~2179) days, respectively (p=0.360).

CONCLUSION: There were no differences in efficacy between EVO and EVL for treatment of grade F1 or F2 GV with bleeding. Further prospective, large-scale studies are needed.
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Disclosure of Interest: None Declared
Keywords: endoscopic variceal ligation, Gastric varices, Variceal bleeding

P1266 DEVELOPMENT OF NEW TECHNIQUE FOR ENDOSCOPIC SUBMUCOSAL DISSECTION USING CARBON DIOXIDE LASER

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INTRODUCTION: Recently, endoscopic submucosal dissection (ESD) has increasingly been applied as a less-invasive treatment method for early gastrointestinal cancers. In ESD procedure, a solution such as saline and sodium hyaluronate solution is injected into the submucosa layer to lift the lesion and to avoid the risk of perforation. However, the process of ESD using electrosurgical knives is highly skilled and has a risk of perforation because of unexpected incision for muscularis propria. On the other hand, carbon dioxide (CO_2) laser with a wavelength of 10.6 μm is suitable for incision, coagulation, ablation, and hemostasis of soft tissues and has widely been used in clinical treatments. Furthermore, CO_2 laser has the character in which water is easy to be absorbed.
AIMS&METHODS: To assess the feasibility of ESD using CO_2 laser in porcine model.
A porcine stomach was used as a sample for an *in-vitro* experiment of safe ESD. A carbon dioxide laser (J. MORITA Mfg. Corp.) with a wavelength of 10.6 μm was delivered to the sample with a hollow optical fiber with an inner diameter of 700 μm. The carbon dioxide laser was operated in the continuous wave mode, and the output power from the hollow optical fiber was up to 15 W. The laser was irradiated normal to the surface of mucosa from a distance of 2 mm.
RESULTS: Although perforation was observed without submucosal injection, the muscle layer was not damaged when saline was injected into the submucosa in spite of the same laser irradiation condition.
CONCLUSION: In these studies, ESD using CO_2 laser with submucosal laser absorber may be feasible and safe methods for the treatment of early gastrointestinal tumors. Further results including *in-vitro* experiments of submucosal dissection and *in-vivo* laser ESD experiments will be presented at the conference.
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Disclosure of Interest: None Declared
Keywords: CO2 laser, ESD (Endoscopic submucosal dissection)

P1267 THE FREQUENCY AND CLINICAL CHARACTERISTICS IN THE CARCINOMA DERIVED FROM SESSILE SERRATED ADENOMA/ POLYP (SSAP).

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INTRODUCTION: New classification to sessile serrated adenoma/polyp (SSAP), traditional serrated adenoma (TSA), classical hyperplastic polyp (HP) was proposed in serrated polyps (SPs) from WHO 2010. SSAP come to be recognized as neoplasm having malignant potential such as serrated neoplastic pathway, more overe suspected as the prodromal lesion of MSI-H colon cancer so that it is concerned about having high malignant potential. However, since changing pathological classification there are few reports in the frequency of the carcinoma derived from SSAP.
AIMS&METHODS: This study is clinical examination about the frequency in the carcinoma derived from SPs and is going to compare with coexisted cancer with CAD. In our hospital during the period from March 2005 to December 2011 cases were removed by endoscopic resection and diagnosed SSAP or TSA or HP, there were 1,673 lesions. The indication of endoscopic treatment for colorectal tumors is the neoplastic lesion more than 5mm, in other words including the lesion in proximal or the large size lesion even if it is diagnosed classical HP by endoscopy. In the way of endoscopic resection we assumed polypectomy and mucosal resection (EMR) but deleted the case by hot biopsy or only biopsy forceps. The extracted lesion was reevaluated to of each SPs with new classification by one pathological leader. Characteristic histological features of SSA/P recognized the crypts showed dilation, serration, irreguraly branching and horizontally arranging(L-shaped, inverted T-shaped or anchor shaped) at the base. Moreover, the mixed lesion which included different SPs more than two kinds was omitted. And we examined the frequency of coexisted cancer with CAD into all of the CAD lesion resected during same period.
RESULTS: The total number of extracted lesion and coexisted early cancer is following that, in HP extracted lesions is 1,001 and coexisted cancer with HP is one (0.1%), in SSAP is 492 and coexisted cancer with SSAP is five (1%), in TSA is 180 and coexisted cancer with TSA is two (1%), in CAD is 18,683 and coexisted cancer with CAD is 1,146 (6%), respectively. In cancer coexisted with SSAP there was no significant difference about gender and age (average; 68-year-old), the median of the tumor diameter is 17 SD8mm (SD; standard deviation), all five cases recognized in proximal colon.
CONCLUSION: This examination in the malignancy such as progress speed was not included and it was only for early colorectal cancer, however, in practically resected lesion during the same period that frequency of coexistence cancers with SSAP was 1% it was lower than frequency for 6% of CAD and was rare with 0.1% in the HP.
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Disclosure of Interest: None Declared
Keywords: hyperplastic polyp, serrated lesion, serrated pathway, serrated polyp cancer, sessile serrated adenoma/polyp

P1268 CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION FOR SUBMUCOSAL INVASIVE COLORECTAL CARCINOMA.

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INTRODUCTION: Endoscopic resection (ER) for early colorectal carcinoma has been recently performed more and more often. However, only little is known about treatment outcomes of ER for submucosal(SM) invasive colorectal carcinoma.
AIMS&METHODS: The aim of this study is to evaluate clinical outcomes of ER for SM invasive colorectal carcinoma(CRC). We checked electronic medical chart and extracted data on ER for SM CRC at NTT Medical Center Tokyo. Our treatment strategy followed Japanese colorectal cancer treatment guideline. Meeting all the following conditions means no need for additional operation after ER: SM invasion $< 1000\mu$m, budding grade 1 or 2, marginal involvement negative, and no lymphatic or vascular invasion. We collected data on patients' characteristics and pathological features of resected cancers, and investigated clinical courses.
RESULTS: From January 2000 through September 2012, ER was carried out for 138 SM cancers at our institution. 77 cases (55%) were followed up without additional treatment (44 males, 33 females, mean age 66.1yr), and 61 cases(45%) were performed additional treatment after ER. We next investigated 77 follow-up cases. 46 cancers were in colon and 31 were in rectum . macroscopic types were 38 protruded tumors and 39 laterally spreading tumors. Out of 77 cases without additional treatment after ER, 61 cases met guideline criteria, and as to the 61 cases there was no recurrence during follow-up period (47 ± 14.2 mths). 16 cases were outside the guideline criteria (13 lesions were $>$ SM 1000μm, 10 lesions were budding grade3, 3 lesions were positive margin, 5 lesions were lymphatic or vascular invasion, overlapped), but additional treatment was not performed. The reasons for not performing additional treatment were the risk of operation (4 cases), and patients' rejection (9 cases). Out of the 16 cases, 2 cases of recurrence (1 local recurrence/1 liver metastasis) occurred during follow-up period (42 ± 28.6 mths). 1 local recurrence subject developed multiple lymph node and liver metastasis rapidly, and 1 liver metastasis subject died 22month after ER.
CONCLUSION: In our study, as to SM CRC, outside the Japanese guideline criteria, recurrence occurred at a rate of 12.5 %. Once tumor recurrence happened, it is very difficult to control disease progress. So we must be careful when we choose not to perform additional treatment after ER for CRC with SM invasion $> 1000\mu$m.
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Disclosure of Interest: None Declared
Keywords: clinical outcome, endoscopic mucosal resection, Endoscopic submucosal dissection (ESD), submucosal invasive colorectal carcinoma

P1269 PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY IN COLONOSCOPIC SURVEILLANCE OF PATIENTS WITH PSC-IBD.

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INTRODUCTION: Primary sclerosing cholangitis related inflammatory bowel disease (PSC-IBD) represents a specific phenotype characterized by extensive colitis, low inflammatory activity, right-sided and patchy colonic inflammation and a high risk of cancer. Surveillance colonoscopies with targeted and random biopsies for detection of premalignant lesions have doubtful efficiency and are time-consuming
AIMS&METHODS: . The aim of the study is to evaluate the efficacy of probe-based Confocal Laser Endomicroscopy (pCLE) as a complement to high definition endoscopy (HDE) for the detection of colonic dysplasia in patients with PSC-IBD.
Methods: Twenty-five patients with PSC-IBD underwent colonoscopy in two steps. On the way from rectum to caecum the mucosa was evaluated with HDE with random biopsies taken according to the routine standards. On the way from caecum to rectum fluorescein-enhanced pCLE was performed and biopsies of all macroscopic and microscopic lesions were taken. All regions, where random biopsies were taken, were also examined with pCLE. Three investigators, blinded to histology and endoscopy, analyzed all pCLE videos.
RESULTS: PCLE revealed crypts irregularity in 70/243 biopsied regions and dysplasia suspected lesions in 13/70 biopsies. Histology confirmed the presence of low-grade dysplasia in 8/13 cases. Sensitivity, specificity and kappa index of pCLE versus histology in detecting dysplasia were 100%, 45% and 1.0 and in detecting crypts irregularity 90%, 100% and 0.922. The kappa index for HDE versus histology was 0.861 for dysplasia and 0.549 for crypts irregularity.
CONCLUSION: pCLE in PSC-IBD surveillance has high diagnostic accuracy that is superior to HDE alone. Future studies need to evaluate if real-time pCLE could replace random taken biopsies in PSC-IBD surveillance.
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Disclosure of Interest: None Declared
Keywords: endomicroscopy, PSC-IBD, surveillance

P1270 PATIENT-CONTROLLED SEDATION DURING COLONOSCOPY: RESULTS FROM A PROSPECTIVE RANDOMIZED CONTROLLED STUDY.

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INTRODUCTION: Propofol is often associated with deep sedation and decreased maneuverability, so that, in Tunisia, sedation for colonoscopy is usually limited to intolerant patients. Patient-controlled sedation (PCS) with propofol has been advocated as a method for dealing with the narrow therapeutic window for moderate sedation, and is gaining increasing popularity for gastrointestinal endoscopy. This study was carried out to determine the feasibility, effectiveness and safety of PCS during colonoscopy.
AIMS&METHODS: Sixty American Society of Anesthesiologists (ASA) physical status class I to II adults, aged from 18 to 80, scheduled for elective colonoscopy were enrolled. Patients were prospectively randomized to receive either target-controlled infusion (TCI control group, n=30) or patient-controlled sedation (PCS group, n=30). Patients in the PCS group were connected to an infusion pump containing propofol and self-administered 10-mg boluses as often as they required. In the TCI group, sedation was initiated with propofol to obtain an effect-site concentration (Ce) of 1μg/ml. An anesthetist was present throughout the procedure. Primary endpoints included patient satisfaction and level of sedation according to the OAA/S scale. Other outcome measures assessed were clinician satisfaction, oxygen desaturation and patient recovery time.
RESULTS: During the study period, 234 patients underwent elective colonoscopy, 60 of them were eligible and were asked to participate in the study. All of them gave their informed consent and were prospectively randomized. The patients' mean satisfaction scores were not statistically different between the two groups. Clinician satisfaction was greater with PCS. Mean doses of propofol (0.072 vs. 0.128 mg/Kg/min; $p < 0.0001$), depth of sedation (4.58 vs. 3.97; $p < 0.001$) and time before discharge were significantly lower for patients in the PCS group. There were no statistically significant differences between the two groups regarding oxygen desaturation, duration of colonoscopy (26.46 min in the PCS group vs. 22.83 min in the control group) difficulty and therapeutic procedures (biopsy or polypectomy).
CONCLUSION: PCS with propofol is an effective and very well accepted form of sedation for coloscopy. However, combining patient-maintained sedation with target-controlled infusion could be the best technique.
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Disclosure of Interest: None Declared
Keywords: Colonoscopy, sedation

P1271 COLD BIOPSY VS. COLD SNARE FOR THE RESECTION OF DIMINUTIVE AND SMALL COLORECTAL POLYPS: PRELIMINARY RESULTS

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INTRODUCTION: There are several endoscopic techniques for treating diminutive and small polyps; however the optimal technique for removing these polyps is unknown.
AIMS&METHODS: This study was perfomed to compare the complete resection rate, complication rate, and tissue retrieval rate of cold biopsy polypectomy (CBP) versus cold snare polypectomy (CSP) for diminutive and small colorectal polyps. The patients with colorectal polyps 7 mm or smaller were randomly allocated to either CBP or CSP group. In CBP group, polyps were removed by the biopsy forceps until no residual tissue was observed. In CSP group, polyps were resected using the mini oval snare without electrocautery. Thereafter, in both groups, the base of the polypectomy site was excised with a 1-2 mm clear margin using EMR technique. After the EMR specimen was fixed on a plate, the most probable residual portion was marked with a pen under stereoscopy. Then the marked portion was cut into sections for histologic evaluation of incomplete resection.
RESULTS: A total of 101 polyps in 96 patients were removed by CBP (n=52) and CSP (n=49), and 85 (84.2%) of the polyps were adenomas. The incomplete resection rate of CBP and CSP for adenomas was 10.9% and 5.1%, respectively (P=0.445). In subgroup analysis, the incomplete resection rate of CBP and CSP for adenomas 5 mm or smaller was 2.8% and 3.4% (P=1.000) while the incomplete rate of CBP and CSP for adenomas 6-7 mm was 40.0% and 10.0%, respectively (P=0.303). A case of delayed bleeding occurred in each group; however the association between the bleeding and the polypectomy could not be concluded because additional EMR was performed for the polypectomy site. Tissue retrieval failure rate of CBP and CSP was 0.0% and 6.1%, respectively (P=0.111).
CONCLUSION: Cold snare tends to be superior to cold biopsy for complete resection of adenomas 6-7 mm in size. For adenomas 5 mm or smaller, complete resection rates of the two methods were comparable. Cold snare polypectomy may be associated with more tissue retrieval failure. Additional study results from more patients will be followed. (NCT01665898)
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Disclosure of Interest: None Declared
Keywords: Cold biopsy polypectomy, Cold snare polypectomy, Colorectal polyps, Diminutive polyps, Small polyps

P1272 A META-ANALYSIS OF COLON CLEANSING WITH PEG COMPARED TO OTHER BOWEL PREPARATIONS.

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INTRODUCTION: Different regimens of colon preparation are available for colonoscopy, they primarily include polyethylene glycol (PEG), sodium phosphate (NaP), picosulfate (PICO) or oral sulfate solution (OSS).
The objective of this meta-analysis is to evaluate the efficacy, safety and patient satisfaction of PEG versus any comparator, NaP, PICO, and OSS.
AIMS&METHODS: Systematic searches were completed querying MEDLINE, EMBASE, Scopus, CENTRAL and ISI Web of knowledge from January 1980 to September 2012. All fully published randomized controlled trials with colon preparation for colonoscopy were included. Populations including pediatric, sole inpatients or sole IBD patients were excluded. The primary outcome measure was the efficacy (excellent/good) of colon cleansing. Secondary outcomes included side effects or complications, procedural outcomes and patient satisfaction.
A meta-analysis was conducted with results reported as odd-ratios (OR) with 95% confidence intervals. Heterogeneity and publication bias were assessed and quantified.
RESULTS: From an initial 2033 citations, 68 trials fulfilled the inclusion criteria (15262 patients). When PEG was compared to all types of colon preparations, it did not show a significant difference in efficacy; OR(random)=1.15(0.92;1.44). Willingness to repeat was lower in the PEG group OR(random)=0.48 (0.29;0.22) as was fainting or dizziness OR(random)=0.76 (0.59;0.98), Headaches were increased with PEG; OR(fixed)=1.33 (1.01;1.74). Forty-seven trials included the comparison PEG versus NaP (10795 patients); PEG did not show a difference in efficacy; OR(random)=0.90(0.67; 1.20); willingness to repeat was decreased; OR(random)= 0.36(0.20; 0.64) as well as fainting or dizziness OR(fixed)=0.63(0.49;0.80). Six trials included the comparison PEG versus PICO (1208 patients). PEG did not show a difference in efficacy; OR(random)=1.03(0.43;2.48). Fainting or dizziness was decreased in the PEG group OR(fixed)=0.63(0.49;0.80). Two studies compared PEG to OSS. PEG was not different in efficacy; OR(random)= 0.74(0.47,1.15).
CONCLUSION: PEG provides similar bowel cleansing efficacy to different types of colon preparations. Willingness to repeat was significantly lower with PEG when compared to all types of preparation and NAP. With PEG, more patients reported headaches but less experienced fainting or dizziness compared to all types of preparations, NaP, and PICO.
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Keywords: colon cleansing, colon preparation, colonoscopy, Meta-analysis

P1273 A META-ANALYSIS OF SPLIT VERSUS NON-SPLIT COLON PREPARATIONS

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INTRODUCTION: Different regimens of colon preparation are available for colonoscopy, they primarily include polyethylene glycol (PEG), sodium phosphate (NaP), picosulfate (PICO) and oral sulfate solution (OSS).
The objective is to evaluate the efficacy, safety and patient satisfaction of split versus non-split regimens for the same comparator and across all preparation and amongst a same type; split versus non-split PEG, split versus non-split NaP, split versus non-split PICO, and split versus non-split OSS.
AIMS&METHODS: Systematic searches were completed querying MEDLINE, EMBASE, Scopus, CENTRAL and ISI Web of knowledge from January 1980 to September 2012. All fully published randomized controlled trials with colon preparation for colonoscopy were included. Populations including pediatric, sole inpatients or sole IBD patients were excluded. The primary outcome measure was the efficacy of colon cleansing. Secondary outcomes included side effects or complications, procedural outcomes and patient satisfaction.
A meta-analysis was conducted with results reported as odd-ratios (OR) with 95% confidence intervals. Heterogeneity and publication bias were assessed and quantified.
RESULTS: From an initial 2033 citations, 16 trials fulfilled the inclusion criteria for split dosing (4253). Compared to the latter, split-dose regimen significantly increased efficacy OR(random)= 4.08(2.86;5.82), willingness to repeat OR(random)=1.95(1.11;3.45), fainting or dizziness OR(fixed)=1.86(1.14; 3.03), and perianal irritation OR(fixed) = 2.39(1.35; 4.22). Eleven trials compared split versus non-split PEG (2971 patients). Efficacy was increased in the split PEG group OR(random)=3.88 (2.47;6.10), whereas nausea or vomiting was lower OR(random)=0.65 (0.52;0.81). Four trials compared split NaP versus NaP (1046 patients). Efficacy was significantly increased with split NaP OR(random)= 3.22(2.06;5.03); willingness to repeat was increased: OR=2.38(1.07,5.33) as well as fainting or dizziness OR=2.59(1.37,4.87), headache=2.49 (1.30,4.75) and perianal irritation OR=2.65(1.43,4.89). One trial

compared split versus non split PICO (236 patients), efficacy was increased with split PICO; OR=8.00(3.40,18.81). No trial with head-to-head comparison for split versus non-split OSS is currently published.
CONCLUSION: Split dosage regimen increase the quality of colon cleansing across all type of preparation with, in the case of PEG, improved symptoms and is the preferred method.
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Keywords: colon cleansing, Colonoscopy, Meta-analysis, split and morning preparation

P1274 OPTIMAL TREATMENT OF PERFORATION DURING COLONOSCOPY : A REVIEW OF 46,138 PATIENTS

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INTRODUCTION: In the past, patients with colonoscopic perforation have been treated surgically, but surgery was associated with significant morbidity and mortality. These days, conservative treatment including endoscopic clip closure or laparoscopic repair has been used to treat colonoscopic perforations. Colonoscopic perforation represents one of the most frequent causes of malpractice claims for endoscopy. Choice of effective and less invasive treatment may reduce claims.
AIMS&METHODS: This study aimed to suggest the guideline for choosing optimal treatment of perforations that occurred during colonoscopy by analyzing our institutional data.
We conducted a retrospective review of medical records of patients who had been treated for colonoscopic perforation from January 2004 to March 2013 at Bundang CHA hospital in Korea.
RESULTS: A total of 46,138 patients underwent either a diagnostic or therapeutic colonoscopy procedure. A total of 35 (including 12 referred patients from outside institution) patients were treated due to colonoscopic perforation. The overall perforation rate was 0.05%. Most common perforation sites were sigmoid colon (40%) and rectum (17%). Twenty patients underwent surgery for perforation (13 laparotomy, 7 laparoscopic surgery) and fifteen patients underwent medical treatment (9 conservative, 6 endoscopic clip closure). Conservative treatment was safe in patients who had microperforation and were hemodynamically stable with or without peritoneal irritation sign on examination. Endoscopic clip closure was successful if perforation size was less than 10mm and patients had no aggravation of peritoneal irritation. Among the patients who underwent surgery, there were no significant differences in duration of fasting (4 vs. 6 mean days), perforation size (7 vs. 15 mean mm), the length of time from diagnosis to operation (3 vs. 4 mean hours) and mortality (0) between laparoscopic surgery group and laparotomy group. But, the length of hospital stay was significantly short at laparoscopic surgery group (8 vs. 14 mean days, p=0.006). No perforation-related major morbidity or mortality occurred in both conservative group and surgical group.
CONCLUSION: Conservative treatment including endoscopic clip closure may be effective if perforation size is small (microperforation or less than 10mm) and patients are hemodynamically stable regardless of peritoneal irritation sign. Otherwise, surgical treatment is recommended. Especially, laparoscopic surgery seems superior to laparotomy in hospital stay with non-inferior outcomes.
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Disclosure of Interest: None Declared
Keywords: Colonoscopic perforation, Colonoscopy, Treatment

P1275 FACTORS AFFECTING THE CHARACTERISTICS OF COLORECTAL ADENOMA IN DIABETIC MELLITUS

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INTRODUCTION: It has been reported that type 2 diabetes mellitus (DM) is associated with higher relative risk for colorectal cancers. Hyperinsulinemia associated with DM may lead to carcinogenesis through increased level of insulin-like growth factor-1.
AIMS&METHODS: The aim of this study is to evaluate the factors affecting the incidence of colorectal adenoma known as precancerous lesion in diabetic patients.
We retrospectively analyzed the data of patients who have type 2 DM and had a colonoscopy from august 2008 to august 2012. After having a colonoscopy, patients were divided into 2 groups with or without colorectal adenoma by pathologic findings and then the data from the both groups were analyzed by multivariate logistic regression analysis. The cases of incomplete study, familial polyposis, inflammatory bowel disease, prior colon cancer and other malignancy were excluded.
RESULTS: 72 patients were excluded in 383 enrolled patents from the study by exclusion criteria and the adenomas were found in 134 patents (43%). Higher incidence of adenoma was shown in the males (odds ratio=1.950, 95% CI 1.021-3.724, p=0.043) in multivariate analysis. Sulfonylurea was significantly related to the more than 10 mm sized adenoma (odds ratio=2.883, 95% CI 1.056-7.871, p=0.039). There was no relationship between the level of HbA1c and colorectal adenoma incidence.
CONCLUSION: The incidence of colorectal adenoma was higher in the male diabetic patients. The users of sulfonylurea showed a tendency to have a large colorectal adenoma. Further evaluation with more patients will be needed.
Disclosure of Interest: None Declared
Keywords: Colorectal adenoma, Diabetes mellitus

P1276 MULTICENTRIC AND PROSPECTIVE EVALUATION OF LARGE COLORECTAL ENDOSCOPIC MUCOSAL RESECTION (EMR) AND POLYPECTOMY FOR PATIENTS UNDER CHRONIC ASPIRIN THERAPY: THE "OPERA" STUDY

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INTRODUCTION: ESGE guidelines allow continuation of aspirin for polypectomy but not for EMR. The aim of the study was to evaluate the risk of bleeding after large colorectal EMR/polypectomy for patients under chronic aspirin therapy.
AIMS&METHODS: This was a multicentric and prospective study conducted from Jan 2010 to Oct 2012. Patients with high thrombotic risk under aspirin were included when colorectal EMR/polypectomy was scheduled. Patients using others anti platelets agents, anti coagulation, presenting disorders of coagulation/hemostasis, liver or renal insufficiency were excluded. The technique of resection was standardized. Preventive mechanical (loop, hemoclip) methods were allowed. Aspirin was also continued the day of procedure. The main objective was to determine the rate of delayed (DPB) and severe (SPB) colorectal post EMR/polypectomy bleeding. Secondary endpoints were to evaluate the incidence of immediate bleeding, the effectiveness of endoscopic hemostasis, the morbi/mortality induced and to identify predictive factors of bleeding. The follow-up was clinical during one month.
RESULTS: A total of 570 lesions were treated among 317 patients included in the study (248 men, mean age 68.8 ± 10.3 years [34-90]). Technique of resection was EMR (55%) or polypectomy (45%) using a piecemeal approach in 19% of cases. Mean size of polyps was 12.3 ± 10.2 mm [1-70] with 191 lesions (33.5%) ≥ 15 mm. Preventive mechanical techniques were used in 25% of cases. The immediate bleeding rate per patient was 9.7% (37/317) and per lesion 5.6% (37/570). The rate of DPB per patient was 1.9% (6/317) and per lesion 1% (6/570). The rate of SPB per patient was 5.6% (18/317) and per lesion 3.1% (18/570). In all cases of hemorrhage the endoscopic hemostasis was efficient except in an immediate one requiring surgery (technical success of 98%). Mean time of delayed bleeding occurence was 4.7 ± 3.8 days [1-10]. Blood transfusion and hospitalization (mean duration of 2.4 ± 2.3 days [1-10]) were required in 1.5% and 5% of cases respectively. No fatal evolution was recorded.
CONCLUSION: Immediate, delayed and severe bleeding risk after colorectal large EMR/polypectomy are low and acceptable.
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Disclosure of Interest: None Declared
Keywords: Aspirin, Bleeding, colon, EMR, polypectomy

P1277 HIGH DEFINITION PLUS COLONOSCOPY WITH I-SCAN VS STANDARD COLONOSCOPY: A RETROSPECTIVE STUDY OF A SINGLE CENTRE

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INTRODUCTION: Colonoscopy is widely considered the gold standard for the detection of colorectal cancer and adenomatous lesions.
AIMS&METHODS: The aim of this retrospective study was to compare high-definition plus (HD+) colonoscopy (series EC-3890Fi, Pentax Ltd., Tokyo, Japan) with i-Scan functionality (electronic staining) vs. standard definition white-light colonoscopy (SDWL- series EC 380 FKp/EC 3885 FK/EC 3890 FK, Pentax Ltd., Tokyo, Japan). Adenoma detection rate was the primary endpoint, whereas the total number of polyps detected and number of patients with at least one hyperplastic lesion were the secondary endpoints. All the patients were referred for a screening colonoscopy within colon cancer screening program (based on Immunochemical Fecal Occult Blood Tests), for individual positive occult blood test and for individual prevention. All the colonoscopies were performed by five expert endoscopists.

RESULTS: A total of 2856 patients were included (1470 F/1386 M; median age 60 years) who underwent their first colonoscopy from January 2006 to December 2011; 1305 received HD+ colonoscopy and 1551 received SDWL colonoscopy. Number of procedures performed and proportion of each imaging technique used were not significantly different among endoscopists. Detected colorectal lesions were classified according to Paris classification and divided as follows: 0-5 mm, 6-9 mm, 10-19 mm, ≥20 mm. For each lesion, histological diagnosis was collected. The detection rate of any size adenoma and the total number of polyps detected were not significantly different between HD+ and SDWL, being 46 % vs 50% (p= 0.2) and 1799 vs 2731 (p= 0.9), respectively. However, the detection of IIb type lesions was higher with HD+ compared to SDWL (0.66% vs 0.14%, $p<0.05$); conversely the number of patients with at least one hyperplastic lesion was higher in the standard colonoscopy group (0.34% vs 0.27%, $p<0.05$).
CONCLUSION: The colonoscopy HD+ does not increase the adenoma detection rate in expert endoscopists with a adenoma detection rate already high, however it would improve the identification of completely flat lesions. The ability of endoscopists to accurately differentiate neoplastic from non-neoplastic lesions could explain the lower number of patients with at least one hyperplastic polyp removed in the HD+ group.
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Disclosure of Interest: G. De Roberto: None Declared, G. Fiori: None Declared, D. Tamayo: None Declared, A. de Leone: None Declared, D. Ravizza: None Declared, C. Trovato: None Declared, I. Bravi: None Declared, C. Crosta Other: teacher at the Milan Pentax Medical Education Center
Keywords: adenoma detection rate, high-definition colonscopy

P1278 PRACTICABILITY OF BREATH MONITORING WITH A NEW RESPIRATORY RATE COUNTING DEVICE IN PATIENTS UNDERGOING ELECTIVE COLONOSCOPY UNDER PROPOFOL SEDATION

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INTRODUCTION: In many European countries (e.g. Switzreland) propofol is the most often used sedative in GI endoscopic procedures and is mostly used by the endoscopist or the endoscopy nurse without assistance of an aneasthesiologist. In some studies capnography has been suggested to increase detection of adverse respiratory events. However capnography is expensive and its use mainly relies on the observation of the breath curve.
AIMS&METHODS: Aim of this pilot study was to determine whether breath monitoring with a newly developed respiratory monitoring device could be a practical and accurate way of monitoring ventilatory response under sedation with propofol in addition to standard monitoring with pulse oximetry.
All patients (American Society of Anesthesiologists Classification (ASA) I-III) scheduled for elective colonoscopy under propofol sedation were monitored with a new monitoring device measuring respiratory rate based on humidity in expired air (respiR8™) in addition to standard monitoring with pulse oximetry. Detection of apnea longer than 30 seconds induced withholding propofol and stimulation of patients as loud speaking or chin lift maneuver. Apnea was defined as cessation of breathing for a minimum of 10 seconds . Significant apnea was defined as cessation of breathing for more than 30 seconds. Hypopnea was defined as reduction in respiratory rate below 6/Min. during a minimum of 10 seconds. The primary endpoint was detection of all respiratory events. Secondary end point included correlation of apnea or hypopnea with hypoxemia (measured as fall in oxygen saturation (SaO2) of at least 5% from baseline or less than 90%) or severe Hypoxemia (SaO2 <85%).
RESULTS: A total of 76 Patients (51 Female and 25 Male) were monitored with Respir8 during colonoscopy under propofol sedation. 37 patients (48.7%) developed at least one respiratory event. There were a total of 73 respiratory events ranging from one to 6 events in a single patient. Significant apnea > 30 sec occurred in 5 patients (6%). Only one apnea led to a relative SaO2 reduction (from 98 to 93%) after 50 seconds lag time. No event requiring immediate intervention such as assisted ventilation recorded.
CONCLUSION: Additional monitoring of ventilatory activity with Respir8 detects apnea or hypopnea earlier as compared to pulse oximetry and could therefore provide early warning of impending respiratory abnormality. The clinical impact of breath rate monitoring remains indetermined.
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Disclosure of Interest: None Declared
Keywords: monitoring, Propofol sedation, sedation by the gastroenterologist

P1279 THE LEARNING CURVE OF ENDOSCOPIC SUBMUCOSAL DISSECTION IN THE COLORECTUM

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INTRODUCTION: Endoscopic submucosal dissection (ESD) for colorectal neoplasms is still a big challenge for most endoscopists even in Japan. The technique was introduced to and started in our institute in the year 2010. The aim of this study is to analyze the learning curve of colorectal ESD procedures for the first 3 years.
AIMS&METHODS: The aim of this study is to analyze the learning curve of colorectal ESD procedures for the first 3 years. The subjects are 121 consecutive lesions in 111 patients which were treated with ESD technique. The indications for ESD in our hospital are; 1. Neoplasms larger than 20mm but confined to the mucosa or invading minimally to the submucosal layer, 2. Those smaller than 20mm but unable to be lifted by injection due to fibrosis. The instruments used are PCF-Q260AZI or JI (Olympus), Short ST Hood and Flush Knife (Fujifilm) and VIO 400 or ICC200 (Erbe).
RESULTS: Male: female ratio was 56: 55 and the average age was 68.5 (44-90) years old. The final pathological diagnosis was SSA/P in 2, adenoma in 33, mucosal carcinoma in 69, minimally invasive (SM1) in 13 and deeply invasive (SM2) in 4. The average diameter was 35.5(7-80) mm and the gross appearance of the lesions was IIc in 2, Is in 3 and laterally spreading tumor (LST) in 116. The major site of each subgroup of LST was the cecum in 40 homogeneous granular-type (LST-GH), the rectum in 25 mixed-nodular type (LST-GM), the ascending colon in 23 flat-elevated type (LST-NGF), and the transverse colon in 28 pseudo-depressed type (LST-NGPD). The average size in LST-GH, LST-GM, LST-NG and LST-NGPD was 41.2mm, 42.8mm, 32.3mm and 25.7mm, respectively. The outcomes were evaluated after dividing the subjects into the first 50 lesions, the second 50 lesions and the following cases up to present. The en bloc resection rate was 78%, 88% and 95% in the 1st, 2nd and 3rd period. Post-procedure bleeding occurred in 1 case (0.9%) in the 1st period. Minor intra-procedure perforation was encountered in 6%, 2% and 0% of the cases in each period but emergency operation was not necessary. Delayed pneumoperitoneum was witnessed in one case of the 1st period, but it was attributable to the ileus caused by anal stricture. Two of the 4 cases with deep invasion were treated surgically afterwards. Local recurrence was witnessed in 3 cases where the ESD procedure had resulted in piecemeal resection, but the recurrent lesions were all treated endoscopically.
CONCLUSION: A learning curve was confirmed in the colorectal ESD procedures. The more cases are experienced, the higher the en bloc resection rate and the lower the complication rate got.
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Disclosure of Interest: None Declared
Keywords: Colorectal neoplasms, Endoscopic submucosal dissection (ESD), laterally spreading tumor

P1280 "PICO-BELLO-KLEAN STUDY": EFFECTIVENESS AND PATIENT TOLERABILITY OF BOWEL PREPARATION AGENTS PICOPREP® AND KLEANPREP® BEFORE COLONOSCOPY. A SINGLE-BLINDED RANDOMIZED TRIAL.

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INTRODUCTION: Adequate bowel preparation is an important condition for an effective colonoscopy. Polyethylene glycol solution (Kleanprep®) and sodium picosulphate solution (Picoprep®) are bowel cleansing agents both registered and available for this purpose. Reliable conclusions in the comparison of effectiveness between these agents can not be made based on previous research, due to the heterogeneity in study designs and subjective outcome assessments.
AIMS&METHODS: To compare the cleansing agents Kleanprep® and Picoprep®, primarily assessing effectiveness by degree of colon cleansing and secondarily determining patient tolerability.
In this single-blinded randomized controlled trial all patients referred for an outpatient colonoscopy received either Kleanprep® (n=88) or Picoprep® (n=85), stratified by two age groups: 18-64 and 65-80 years. Both Picoprep® and Kleanprep® were administered in a split-dose regimen, while fluid intake was monitored and registered. Effectiveness was measured by assessing bowel cleansing using the Boston Bowel Preparation Score. Patient tolerability was measured with a patient questionnaire. An intention-to-treat-analysis was performed.
RESULTS: There was no difference in level of bowel cleansing according to the Boston Bowel Preparation Score considering treatment arms. The overall cleansing score between Kleanprep® and Picoprep® was not significantly different (p=0,182). Reviewing segment scores, there were also no significant differences between Kleanprep® and Picoprep® (right colon p=0,051, transverse colon p=0,563 and left colon p=0,352). The minimum warranted level of cleansing (BBPS ≥ 6) is achieved with a percentage > 90% by both agents. Patients using Picoprep® scored significantly better on the aspects convenience and flavour of the preparation agent, compared to patients using Kleanprep® (p-value <0,001). Side effects like nausea, vomiting, headache and bloating were significantly less experienced by patients using Picoprep®. Side effects like abdominal pain and dizziness were similar between treatment arms.
CONCLUSION: The present study did not demonstrate a difference in effectiveness of bowel cleansing between Kleanprep® and Picoprep®. Both showed to be adequate bowel preparation agents, ensuring a good visibility of the colon during colonoscopy. Picoprep® was significantly better tolerated than Kleanprep®.

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Disclosure of Interest: None Declared
Keywords: Bowel preparation, Effectiveness, Endoscopy, patient satisfaction, randomised controlled trial

P1281 DOES THE ENDOSCOPIST FATIGUE PLAY ANY ROLE ON COLONOSCOPIST RESULTS?

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INTRODUCTION: Contradictory results have been published concerning the possible effect of endoscopist fatigue on colonoscopies findings, especially in relation to neoplastic polyp detection.
AIMS&METHODS: AIMS: To analysed possible differences in the diagnostic and therapeutic capacity of colonoscopies, depending if they were performed at the beginning or at the end of every working day.
METHODS: 1000 ambulatory and consecutive colonoscopies, sedated with propofol iv. were reviewed. The explorations were divided into 2 groups: A.- Early (The first 4 colonoscopies of each day, n = 569) and B.- Late (the rest of the session, n= 431). Possible differences between 2 groups concerning patients characteristics, incomplete colonoscopies, frequency, number, size of the bigger polyp, histology, and resection and recovery polyp rates were analysed.
RESULTS: Colonoscopies performed at the beginning and at the end of the working day were similar when comparing gender, age, colonoscopy indication, personal and familial history of colorectal polyps (p = n.s.). No significant differences were registered between both groups related to endoscopic findings: Incomplete colonoscopy: A (Early) = 1.3%, B (Late)= 1.2% (p = 0.99); Polyp detection rate: A = 46.2%, B = 42.4% (p = 0.97); Multiple polyps: A = 26%, B = 23.9% (p = 0.45); polyps <5mm: A = 26.7%, B = 22.9% (p = 0.18); Cases with all polyps resected: A = 95%, B = 95,6% (p = 0,79); cases with all polyps recovered: A = 86.9%, B = 91.7% (p = 0.12); Histology: hyperplastic polyps: A = 11.2%, B = 9.3% (p = 0.31); simple adenomas: A = 26.4%, B = 23.9% (p = 0.37); advanced adenoma: A = 7.7%, B = 9% (p = 0.46); carcinoma: A = 3.2%, B = 4.4% (p = 0.30).
CONCLUSION: 1.- Endoscopist fatigue at the end of the day does not influence on incomplete colonoscopies rate in our series.
2.- There are no differences in number of neoplastic detected lesions, macroscopic and histologic neoplasms characteristics or resection and recovery rates between colonoscopies performed at the beginning or at the end of the working day.
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Disclosure of Interest: None Declared
Keywords: Colonoscopy performance, fatigue, polyps colon

P1282 BLUE LASER IMAGING: APPLICATION FOR COLON POLYP CHARACTERIZATION

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INTRODUCTION: Lasers produce light through optical amplification based on the stimulated emission of photons. The emitted light is notable for its high degree of spatial and temporal coherence. Recently, a new image enhanced endoscopy system using laser light (now designated Blue Laser Imaging, BLI) is being used in Japan. In BLI, 2 monochromatic lasers (410nm and 450nm) are applied instead of xenon light. A 410nm laser visualizes small vessels on the mucosal surface because its wavelength represents the absorption spectra of vessels, and a 450nm laser provides white light by excitation. BLI is also equipped with a zoom apparatus for polyp characterization.
AIMS&METHODS: In this study, we aimed to evaluate the use of BLI for polyp characterization. Since November 2012 in our institution, colonoscopy has been primarily performed with BLI. Colorectal polyps were observed with BLI and resected/biopsied by experienced colonoscopists. With BLI, the polyp vascular pattern as well as surface pattern are clearly visualized, similar to narrow band imaging (NBI). Therefore, we applied the Sano classification frequently used in NBI.
RESULTS: BLI allowed clear visualization of vessel architecture even with a distant view, and without the need for dye application. To date, 381 lesions including 20 inflammatory polyps, 13 hyperplastic polyps, 307 adenomas, 23 mucosal cancers (adenomas with high grade dysplasia) and 18 submucosally invasive cancers were studied. Hyperplastic polyps revealed type 1 vascular pattern in 85%. Adenoma showed type II in 97%. 23 mucosal cancers showed type II in 52% and type IIIA in 48%. 18 submucosal cancers demonstrated type IIIA in 30% and type IIIB in 50%. These results are consistent with previous reports using NBI.
CONCLUSION: BLI provided useful information for polyp characterization, without dye application. Further prospective evaluation of the performance characteristics of the BLI system for polyp characterization is required.
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Disclosure of Interest: None Declared
Keywords: colonoscopy, image enhanced endoscopy, laser, Polyp

P1283 COMPARISON OF ENDOSCOPIC SUBMUCOSAL DISSECTION AND ENDOSCOPIC MUCOSAL RESECTION TO LATERALLY SPREADING TUMORS

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INTRODUCTION: Laterally spreading tumors (LSTs) are usually benign in spite of their large diameter and therefore, good indication for endoscopic treatment.
On the other hand, Endoscopic submucosal dissection (ESD) enables en bloc resection for colorectal neoplasms regardless of their localization or diameter, and has been developed more popular as a treatment in Japan. However, the ESD procedures are difficult and associated with more risk of complications compared to conventional endoscopic mucosal resection or endoscopic piecemeal mucosal resection (EMR/EPMR).
AIMS&METHODS: The aim of this study is to evaluate the outcomes of treatment for LSTs, and to clarify indications for EMR/EPMR and ESD.
We retrospectively assessed all patients who underwent endoscopicaly or surgically treatment from April 2001 to December 2012. 17802 colorectal adenomas and early cancers were treated, and among them 2002 lesions were so-called LSTs. There are two subtypes of LSTs; non granular type (LST-NG) and granular-type (LST-G). We analyzed features of LST-NG and LST-G, and investigated the rate of en bloc resection, residual tumor/recurrence and complications between EMR/EPMR and ESD in LSTs.
RESULTS: The lesions which were treated by EMR/EPMR technique were 1437 in number and those treated by ESD technique were 485. The rate of submucosal invasion was significantly higher in LST-NG than in LST-G (15.7% vs 9.2%: $p<0.01$), and especially LST-NG over 20mm in diameter showed the very high rate of submucosal invasion (24.3%). The en bloc resection rate over 20mm in diameter of LSTs was 30.9% (197/637) in the EMR group(20 mm or more less than 30 mm LST-G was 40.8%, and LST-NG was 43.4%. LST-G of 30 mm or more was 10.4%, and LST-NG was 21.1%). 97.2% (432/444) in the ESD group. Residual tumor/recurrence was observed in 119 (8.3%) of the EMR group, but The prognosis of the residual tumor / recurrence of EPMR of mucosal carcinoma and an adenoma was not bad. there was no case with recurrence in the ESD group. With regards to complications over 20mm in diameter, there was no significant difference in the rates of post-treatment bleeding (2.6%vs.1.6%) and perforation (1.4%vs2.7%) between EMR/EPMR and ESD, In summary, LST-NG over 20mm in diameter should be removed en bloc with ESD technique because of its higher potential for submucosal invasion.
CONCLUSION: It is important to classify LSTs into LST-NG and LST-G in diagnosis.
ESD is feasible treatment for LST-NG especially more than 20 mm which is hard to be resected by EMR technique.
Disclosure of Interest: None Declared
Keywords: EMR, ESD, LST

P1284 IS THE PROGNOSIS OF THE COLORECTAL CANCER IMPROVED WHEN THE OUTPATIENTS WITH NEGATIVE FIT UNDERGO COLONOSCOPY?

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INTRODUCTION: In Japan, the colorectal cancer morbidity has been increasing year by year. Therefore, screening examination is essential for early detection of the colorectal cancer (CRC). Fecal immunochemical test (FIT) is a simple, low cost and non-invasive method. Furthermore, there has been firm experimental evidence that FIT reduces the risk or CRC mortality. Therefore, FIT is recommended as a population-based CRC screening in Japan. However, some of CRC are negative for FIT. The endoscopic features of the CRC with false-negative FIT are not well known because colonoscopy is not generally performed in the FIT-negative examinees.
AIMS&METHODS: This follow-up study was designed to compare the prognosis of the FIT-negative CRC with the FIT-positive one. From January, 2007 to December, 2009, we performed 1-day FIT before endoscopy for 1592 outpatients who consented for the purpose of colonoscopy in our hospital. And we compared the FIT-negative group with the FIT-positive group about endoscopic findings and the three years overall survival (3ys OS).
RESULTS: Of 1592, 983 patients were in FIT-negative groups, and 609 were in the FIT-positive group. A significant difference was not seen in the sex between both groups. Of 983, 336 FIT-negative patients had neoplastic lesions, and the number of them was 566 (9: invasive cancer, 26: high grade dysplasia, 531: low grade dysplasia) while 690 (81: invasive cancer, 58: high grade dysplasia, 551: low grade dysplasia) in the FIT-positive group. The average age of the FIT-negative group was significantly younger than that of the FIT-positive group (58.3 ± 13.9 vs. 61.4 ± 13.8: $P<0.01$). The average tumor diameter in the FIT-negative group was significantly smaller than the FIT-negative group (4.72 ± 6.27 mm vs. 9.75 ± 12.1 mm: $P<0.01$). The detection rate of invasive cancer was lower in the FIT-negative group than the FIT-positive group (0.92% vs. 12.5%: $P<0.01$). As for advanced neoplasia, the detection rate was also lower in the FIT-negative group than the FIT-positive group, significantly (5.60% vs. 29.1%: $P<0.01$).

Furthermore, there were no distant metastasis cases in the FIT-negative group while 15 cases in the FIT-positive group. As for the 3ys OS of patients with invasive cancer, the FIT-negative group was 100% while the FIT-positive group was 92.4%.

CONCLUSION: The FIT is an excellent screening test, however the prognosis of CRC might be improved if the outpatients with negative FIT undergo colonoscopy.

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Disclosure of Interest: None Declared

Keywords: colonoscopy, colorectal cancer screening, CRC, fecal immunochemical test, FIT-negative screening cancer

P1285 IN VIVO TARGETING OF COLONIC NEOPLASIA BY MMP DIRECTED FLUORESCENCE ENDOSCOPY

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INTRODUCTION: Patients with ulcerative colitis are at increased risk for colorectal cancer (CRC). Therefore, endoscopic surveillance programs have been established, however their diagnostic yield is still not satisfying yet. Matrixmetalloproteinases (MMP)-2/-9 are key enzymes in metastatic processes of CRC and high expression levels can be observed in affected mucosa. Aim of this study was to evaluate molecular imaging by MMP-2/-9 guided fluorescence endoscopy (FE) for early tumor detection in a murine model of colitis associated CRC.

AIMS&METHODS: Colorectal cancer in C57Bl/6 WT mice (n=15) was induced by single i.p. injection of azoxymethane (AOM) and cyclic administration of dextran sodiumsulfate (DSS). A nonpeptidic, Cy5.5-labeled MMP-selective tracer (Cy5.5-AF443) was intravenously injected 24 hrs before endoscopic examination. Tumor development was assessed *in vivo* by white light endoscopy and FE applying a bandpass filter system. Murine colons were examined by fluorescence reflectance imaging (FRI) to measure tracer uptake *ex vivo*. *Ex vivo* tumors were enumerated stereomicroscopically and graded by HE staining and Ki67-immunhistochemistry. The expression and activity of MMP-9 in colorectal tumors was assessed by immunochemistry, western blot analysis and zymography.

RESULTS: By applying our MMP photoprobe a significant higher contrast of colonic adenomas as compared to the adjacent non-malignant mucosa could be achieved during fluorescence endoscopy (75.9 ± 8.7 vs. 66.5 ± 7.4, mean gray values, $P<0.001$). FRI detected significantly higher tracer uptake in colorectal adenoma as compared to healthy mucosa (Average Radiant Efficiency: 1.41 E+12 ± 0.75 E+12 vs. 0.62 E+12 ± 0.44 E+12 [p/s/cm≤/sr] / [μW/cm≤], $P < 0.001$) and revealed a tumor size dependent increase ($P < 0.05$). Proliferation rate in tumors was significantly increased as assessed by Ki67 positive cells per 10 high-power fields (25.7 ± 14.2 % vs. normal mucosa 11.8 ± 5.7 ($P < 0.01$). Standard histology revealed colorectal adenomas up to high-grade dysplasia and pT1 carcinomas.

Immunhistochemistry for MMP-9 proved markedly increased expression in high-grade dysplasia and pT1 tumors as compared to non-malignant mucosa and western blot analyses and zymography indicated higher levels of active MMP-2/-9 and its pro-enzymes in colorectal dysplasia.

CONCLUSION: Mucosal MMP-9 expression was significantly increased in colorectal high-grade dysplasia and pT1 tumors. Specific targeting of MMP was feasible to detect colonic dysplasia during fluorescence endoscopy and might facilitate the detection of human early colorectal cancer in the future.

Disclosure of Interest: None Declared

Keywords: Colonoscopy, Colorectal cancer, molecular imaging

P1286 ORAL SULFATE SOLUTION PROVIDES SUPERIOR BOWEL CLEANSING TO SPLIT-DOSE SODIUM PICOSULFATE AND MAGNESIUM CITRATE

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INTRODUCTION: Split-dose bowel preparation has been shown to produce superior cleansing to evening only bowel preparation in patients undergoing colonoscopy. This study seeks to determine if differences in efficacy can be detected when an oral sulfate (OS) preparation and sodium picosulfate and magnesium citrate (P/MC) preparation are both given in a split-dose (PM/AM) administration.

AIMS&METHODS: Adult outpatients scheduled for colonoscopy were enrolled into this single-blind, multi-center study and were administered either an OS preparation (SUPREP®, Braintree Laboratories) or P/MC preparation (Prepopik™, Ferring Laboratories). Both preparations followed their approved labeling for a split dose (PM/AM) regimen. Colonoscopies were performed by investigators blinded to treatment assignment. Cleansing was graded using a 4 point scale (Excellent - no more than small bits of adherent feces/fluid, Good - small amounts of feces or fluid not interfering with exam, Fair - enough feces or fluid to prevent a completely reliable exam, Poor - large amounts of fecal residue, additional cleansing required) where scores of Good or Excellent were considered "successful". Patients with scores of Fair and Poor were considered failures, as well as those unable to undergo colonoscopy due to ineffective preparation.

RESULTS: Ninety-five percent of patients had successful preparation with OS, compared to 86% of P/MC patients ($p = 0.006$). Twice as many sulfate preparations (55%) were graded as Excellent by the colonoscopist, as compared to P/MC (26%, $p < 0.001$). All OS patients underwent colonoscopy. Five P/MC patients (3%) could not undergo colonoscopy after taking the preparation and needed to be rescheduled or receive an additional cleansing agent.

Preparation Success	Sulfate Solution (n=168)	Picosulfate (n=169)	p value
% Success	94.6	85.8	0.006
% Failure	5.4	14.2	
Cleansing by Grade	Sulfate Solution (n=168)	Picosulfate (n=164)	p value
% Excellent	54.8	26.0	< 0.001
% Good	39.9	59.8	
% Fair	3.6	7.7	
% Poor	1.8	3.6	

CONCLUSION: Oral sulfate solution provides superior bowel cleansing compared to sodium picosulfate and magnesium citrate when both are given as split-dose regimens. This result was seen in the global efficacy assessment, as well as in the proportion of Excellent preparations achieved. The high level of efficacy confirms results seen in prior studies, and adds greater support to the efficacy of split-dosing, especially when an oral sulfate solution is used.

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Disclosure of Interest: J. Mcgowan Other: Employee of Braintree Laboratories, M. Cleveland Other: Employee of Braintree Laboratories, J. Di Palma Lecture fee(s) from: Braintree Laboratories, Other: Medical Director - Braintree Laboratories, D. Rex Lecture fee(s) from: Braintree Laboratories, Ferring Laboratories

Keywords: bowel preparation, colonoscopy

P1287 CLINICAL IMPACT OF ENDOSCOPY POSITION DETECTING UNIT (UPD-3) FOR COLONOSCOPY IN NON-SEDATED PATIENT.

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INTRODUCTION: Achievement of high cecal intubation rate and patient's comfort depend on insertion shape of scope during examination. And insertion shape of scope during examination depends on experience.

AIMS&METHODS: This study aims to evaluate whether endoscopy position detecting unit (UPD-3) can improve cecal intubation rate regardless of experience of colonoscopy. A total of 240 patients enrolled from February 2012 through June 2012 were randomly divided into UPD-3 guided group or conventional group (no UPD-3 guidance). All colonoscopies were performed by experts (more than 500 colonoscopies) and trainees (less than 100 colonoscopies). Cecal intubation rate, procedure time, insertion methods (straight insertion: shortening the colonic fold through bending technique/ roping insertion: right turn shortening technique) and patient discomfort were assessed. Patient discomfort during scope insertion was scored by Visual analog scale (VAS) in 5-steps degree. CF-Q260DI (12.4mm in diameter) was used in UPD-3 guided group. CF-Q260AI (12.2mm) were used in conventional group. Patients with any abdominal operation in the past were excluded. CO2 insufflation was available in all procedures.

RESULTS: In conventional group (n=122), 77 and 45 procedures were performed by experts (E) and trainees (T), respectively. In UPD-3 guided group (n=118), 77 and 41 procedures were operaded by experts (UE) and trainees (UT), respectively. Intubation times were 8.1 minutes in E, 20.7 in T, 9.1 in UE and 19.5 in UT. It showed a significant difference between E and T ($p < 0.05$). The intubation time in UPD-3 guided group was not significantly shorter than that without UPD-3. As for straight insertion technique, its rate in UT (537%) was significantly improved rather than that in T (33.3%) ($p < 0.05$). VAS scale in UT was also getting better from 2.6 in T to 1.9 ($p < 0.05$).

CONCLUSION: Though UPD-3 could not contribute to shorten the intubation time both in expert and trainee, the rate of the straight insertion and the reduction of patients' pain during colonoscopy were significantly improved in trainees. Thus, this equipment should be clinically applied.

Disclosure of Interest: None Declared

Keywords: colonoscopy performance, UPD-3

P1288 A RISK SCORE TO INDENTIFY SUBJECTS AT HIGH-AVERAGE RISK OF ADVANCED COLORECTAL NEOPLASIA

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INTRODUCTION: The risk of advanced colorectal neoplasia is not evenly distributed throughout the screening population.

AIMS&METHODS: This study aimed to develop and validate a model to quantify the individual risk of advanced colorectal neoplasia in Caucasian subjects useful for health counselling.

We performed a cross-sectional analysis of database records for 40- to 66-year-old subjects who entered a national primary colonoscopy-based screening program for colorectal cancer in 73 centres in Poland in the single year of 2007. We used multivariate logistic regression to investigate the associations between clinical variables and the presence of advanced neoplasia in a randomly selected test set, and confirmed the associations in a validation set. We used model coefficients to develop a risk prediction score for advanced colorectal neoplasia.

Table: P1290

Variable	Pooled difference in means (95% CI)	p values
All polyps	0.132 (-0.064 to 0.328)	0.188
All adenomas	0.033 (-0.056 to 0.122)	0.468
Flat adenomas	0.077 (-0.099 to 0.254)	0.389
Hyperplastic polyps	0.104 (-0.072 to 0.280)	0.248

Characterisation	Of polyps	using	FICE			
Variables	**Pooled sensitivity (95%CI)**	**Pooled specificity (95%CI)**	**Pooled Positive Likelihood ratio (95%CI)**	**Pooled Negative Likelihood ratio (95%CI)**	**Pooled diagnostic Odds ratio (95%CI)**	**Pooled area under the ROC (95%CI)**
Polyps < 5mm	85.9% (81.1 to 89.9)	85.5% (79.3 to 90.4)	5.4 (3.75 to 7.77)	0.17 (0.113 to 0.255)	32.81 (16.74 to 64.33)	0.914 +/- 0.017
Polyps <10mm	91.3% (88.4 to 93.7)	74.7% (68.5 to 80.2)	3.86 (2.37 to 6.30)	0.115 (0.07 to 0.19)	37.08 (16.01 to 85.85)	0.902 +/- 0.08
All polyps	90.4% (88.3 to 92.2)	86.9% (83.8 to 89.5)	5.96 (2.32 to 15.32)	0.135 (0.08 to 0.225)	45.56 (15.13 to 137.15)	0.945 +/- 0.025

RESULTS: Advanced colorectal neoplasia was detected in 2,544 of the 35,918 included participants (7.1%). In the test set, a logistic-regression model showed that independent risk factors for advanced colorectal neoplasia were: age, sex, family history of colorectal cancer, cigarette smoking ($P<0.001$ for these four factors), and body mass index ($P=0.033$). The model was well calibrated in the validation set (ratio of expected to observed risk of advanced neoplasia: 1.00 (95% CI, 0.95-1.06)). The concordance statistics of the model were 0.64 for the test set and 0.62 for the validation set. We developed a risk score that quantified the risk of advanced neoplasia in the whole data set, from 2.49% for subjects scoring 0, to 19.44% for subjects scoring 7-8.
CONCLUSION: Developed and validated risk score consisting of simple clinical factors successfully quantifies the risk of advanced colorectal neoplasia in asymptomatic Caucasian subjects. This scoring system may be useful for counselling purposes or designing primary prevention studies.
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Disclosure of Interest: None Declared
Keywords: advanced neoplasia, risk factor, Screening colonoscopy

P1289 THE MALIGNANT POTENTIAL OF NONPOLYPOID COLORECTAL LESIONS IN PATIENTS WITH LYNCH SYNDROME

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INTRODUCTION: Patients with Lynch syndrome (LS) are at risk for developing colorectal cancer (CRC). Thus, an intensive colonoscopic surveillance program is recommended for them in order to reduce the mortality associated with CRC. However, there are still uncertainties about which type of lesion is more accurately detected and whether complete removal of all colorectal lesions should be considered during surveillance colonoscopy.
AIMS&METHODS: The aim of this study was to compare the endoscopic appearance and size of early colorectal lesions with 3 different mutations: MLH1, MSH2, and MSH6. The study included 88 Lynch syndrome patients with identified mutations in one of the DNA mismatch repair genes (MLH1, 29; MSH2, 52; MSH6, 7). For all LS patients who underwent at least one surveillance examination from January 2001 to March 2013 at the Cancer Institute Hospital, the colonoscopic finding of lesions and the histopathological diagnosis of the 3 different mutations were retrospectively analyzed. Advanced histology (AH) was defined as the presence of high-grade dysplasia or early cancer (invasion into the submucosa).
RESULTS: A total of 235 lesions were detected in the LS patients (49 MLH1 lesions, 166 MSH2 lesions, 20 MSH6 lesions); the average size of the lesions was 5.9 ± 4.0 mm (mean $\pm$ standard deviation, SD) and 51.5% of them were nonpolypoid. The histopathological diagnoses were low-grade dysplasia and serrated adenoma in 132 lesions (56%), high-grade dysplasia in 21 lesions (9%), and early cancer in 23 lesions (10%).
Among the nonpolypoid lesions of <10 mm in size, a significantly higher accuracy in detection of the adenoma was noted in MLH1 mutation carriers (87%) as compared to MSH2 mutation carriers (59%) ($p<0.05$). Among the nonpolypoid lesions of <5 mm in size, a significantly higher accuracy in detection of the adenoma was noted in MLH1 mutation carriers (83%) as compared to MSH2 mutation carriers (51%) ($p<0.05$). Among the lesions of <5 mm in size, the tendency of accurate detection of AH was higher in MLH1 mutation carriers (20.8%) than in MSH6 mutation carriers (9.6%).
CONCLUSION: Nonpolypoid lesions of <10 mm in size should be carefully evaluated, and complete removal of all colorectal lesions in patients with a MLH1 mutation is recommended. Nonpolypoid lesions in patients with a MLH1 mutation may have a high malignancy potential, despite a small size (<5 mm).
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Disclosure of Interest: None Declared
Keywords: colon cancer screening, Lynch syndrome

P1290 META-ANALYSIS OF FLEXIBLE SPECTRAL IMAGING COLOUR ENHANCEMENT (FICE) IN DETECTION AND CHARACTERIZATION OF COLORECTAL POLYPS.

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INTRODUCTION: Several endoscopic innovations have been developed recently to improve detection and characterization of colorectal polyps. Flexible spectral imaging colour enhancement (FICE) is a form of image enhanced endoscopy which enhances the visualization of mucosal structures and microcirculation by the selection of spectral transmission with a dedicated wavelength.
AIMS&METHODS: We aim to perform a meta-analysis to look at the effect of FICE on detection and characterisation of colorectal polyps.
Various electronic databases were searched for articles reporting on detection and characterization of colonic polyps comparing standard while light endoscopy and FICE. The pooled mean differences in total numbers of polyps, adenomatous polyps, flat adenomas, and hyperplastic polyps detected was calculated. Additionally, pooled sensitivity, specificity, positive and negative likelihood ratio, diagnostic odds ratio and pooled area under the receiver operating curve was calculated.
RESULTS: 5 studies/2150 patients and 11 studies/ 2425 patients were included in the analysis for detection of polyps and polyp characterization respectively. There were no differences between FICE and standard colonoscopy for the detection of all polyps, adenomatous polyps, flat adenoma or hyperplastic polyps. Pooled diagnostic accuracy for FICE is listed in table.
Table: Detection of Polyps
CONCLUSION: FICE does not seem to improve the detection rate of adenomatous polyps during screening colonoscopy. These results may partially be due to the small number of studies done so far using FICE. The pooled sensitivity and specificity of FICE does not meet the currently accepted criteria of the ASGE PIVI committee for use in routine clinical practice.
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Disclosure of Interest: None Declared
Keywords: colon, FICE, polyps

P1291 LOW-VOLUME ORAL SULFATE SOLUTION VERSUS HIGH-VOLUME POLYETHYLENE GLYCOL SOLUTION: ACHIEVING A CLEAR VIEW

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INTRODUCTION: INTRODUCTION: The poor quality of bowel preparation remains one of the great difficulties of colonoscopy. We compared the adherence, tolerability and efficacy of a low-volume oral sulfate solution (LV-OSS) with a high-volume sulfate-free (standard 4-L polyethylene glycol) electrolyte lavage solution (HV-SFS) as bowel preparation for colonoscopy.
AIMS&METHODS: Aims & Methods: Prospective analysis in patients undergoing colonoscopy, in an outpatient setting, between January and December 2011. Patients were randomized to receive LV-OSS in equally divided doses, at 4pm and 10pm, the day before of colonoscopy versus (Vs) HV-SFS given the night before colonoscopy. The efficacy of the bowel preparation was assessed by the Ottawa bowel preparation scale. The scale is applied to each colon segment: right colon, mid colon and the rectosigmoid colon. The fluid quantity is a global value for the entire colon. The score is calculated by adding the 0 to 4 ratings for each colon segment and the 0 to 2 fluid quantity rating. The scale has a range from 0 (perfect) to 14 (solid stool in each colon segment and lots of fluid, completely unprepared colon). Preparations with ≥ 8 points were considered unsatisfactory.
RESULTS: Results: 416 patients were included (52.2% men; average age of 64,3years old. 209 patients received HV-SFS and 207 LV-OSS. 8.7% did not complete the intake of the preparation (77.8% HV-SFS Vs 22.2% LV-OSS; $p<0.001$). Incomplete progression occurred in 5.3% due to completely unprepared colon (54.5% LV-OSS Vs 45.5% HV-SFS; $p>0.05$), 31.8% did not complete the intake of the preparation. 35.6% revealed bad taste (77% HV-SFS Vs 23% LV-OSS; $p<0.001$). 21.9% had nausea (64.8% HV-SFS Vs 35.2% LV-OSS;

p<0.05). 7.9% had vomiting (63.6% HV-SFS Vs 36.4% LV-OSS; p<0.05). 42.1% had abdominal pain (50.3% HV-SFS Vs 49.7% LV-OSS; p>0.05). 14.4% had unsatisfactory bowel preparation (53.3% LV-OSS Vs 46.7% HV-SFS; p>0.05). The mean total score in the Ottawa scale to the LV-OSS Vs HV-SFS was 4.37±2.96 Vs 4.74±2.94 (p>0.05). Fluid quantity rating 1-2 occurred in 42.3% (52.6% HV-SFS Vs 47.4% LV-OSS; p>0.05).
CONCLUSION: Conclusion: The HV-SFS was associated with statistical significance of incomplete intake of the preparation, bad taste and the presence of nausea and vomiting, thus presenting lower adherence and tolerability. The LV-OSS was more effective, but without statistical significance.
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Disclosure of Interest: None Declared
Keywords: BOWEL PREPARATION, ORAL SULFATE SOLUTION, POLYETHYLENE GLYCOL

P1292 CHARACTERISTICS OF THE ENDOSCOPISTS THAT INFLUENCE QUALITY OF COLONOSCOPY

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INTRODUCTION: The main objective of screening colonoscopy is the detection of premalignant lesions. Several factors are directly related to colonoscopy quality, but scarce information exists about the characteristics of the endoscopists that influence detection of lesions
AIMS&METHODS: Fifty endoscopists participant in the study COLONPREV (a randomized trial aimed to compare screening by direct colonoscopy vs FIT) performed at least 20 procedures in the colonoscopy arm of this study, with a total of 3.838 colonoscopies. Evaluated factors related to colonoscopy quality were: adenoma detection rate (ADR), advanced ADR, proximal and distal ADR and adenoma rate. Evaluated characteristics of endoscopists were: age, sex, exclusive dedication to endoscopy, especialty, years as physician, years as especialist, total longlife number of colonocopies, number of colonoscopies last year, weekly hours dedicated to endoscopy and number of formative activities in the last year.
RESULTS: Mean age of endoscopists was 39.7 years. There were 31 men (62%). A 20.8% had exclusive dedication to endoscopy. All but one endoscopists were gastroenterologists. Age, sex, years as physician or as especialist did not show any relationship with the studied quality indicators. Endoscopists with exclusive dedication had a higher proximal ADR (19.3% vs 14.4%; p=0.04). Endoscopists with a total number of colonoscopies higher than 6.000 procedures showed a higher adenoma rate (0.66 vs 0.51; p=0.04). However, the weekly mean number of hours dedicated to endoscopy was not associated with any quality indicator. Performance of more than 300 yearly colonoscopies was associated with a better ADR (33.1% vs 27.5%; p=0.04) and adenoma rate (0.63 vs 0.41; p=0.0001). Finally, the endoscopists that assisted to at least 3 formative activities during the last year showed also higher ADR (35.2% vs 27.9%; p=0.02), adenoma rate (0.66 vs 0.49; p=0.03) and distal ADR (17.7% vs 13.6%; p=0.04).
CONCLUSION: The endoscopists characterisitics that are more associated to better quality indicators are the performance of more than 300 colonoscopies/year and the assitance to a higher number of formative activities.
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Disclosure of Interest: None Declared
Keywords: Quality of colonoscopy, Screening colonoscopy

P1293 SCREENING COLONOSCOPY WITH DYEING OF PROXIMAL COLON VERSUS TOTAL CHROMOCOLONOSCOPY USING INDIGO CARMINE: FIRST REPORT

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INTRODUCTION: The adenoma–carcinoma sequence developed is accepted in principle for colorectal cancer. The early detection and completely removal of colon adenoma is essential.
AIMS&METHODS: The aim of our study was to assess the detection rate of colorectal lesions by comparing total chromocolonoscopy and proximal chromocolonoscopy. In one institution, 183 asymptomatic patients (mean age 52,5) participated in study of screening video colonoscopy, performed by a single endoscopist. Informed consents were obtained in all cases. Patients were excluded if the bowel preparation was inadequate, if they had an earlier diagnosed colorectal neoplasia or inflammation, or if they were receiving anticoagulant medication. Patients received intravenous propofol prior to intubation of the colonoscope. Complete colonoscopy was performed in 183 (100%) cases. A total chromocolonoscopy using 0,2% indigo carmine solution was performed in 92 patients. A further 91 patients were examined with dyeing of cecum, ascending and transversal colon only. All lesions identified during screening colonoscopy in both groups were removed completely by cold forceps or snare polypectomy. The two groups were similar with regard to age, gender and rate of complete colonoscopy. Mann-Whitney U Tests were used to determine differences between groups.
RESULTS: There was not anything complications after colonoscopy. Results of colorectal lesions detection are shown in Table, the difference between two groups was insignificant (p value more than 0.05).

	Patients with colorectal adenoma	Patients with proximal adenoma	Patients with distal adenoma	Distal adenoma/patients
Total chromocolonoscopy	51,7%	37,4%	29,7%	0,53
Proximal chromocolonoscopy	53,8%	38,5%	31,9%	0,46

CONCLUSION: The results of our study show that proximal chromocolonoscopy can be recommended for improving adenoma detection rate instead of total chromocolonoscopy.
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Disclosure of Interest: None Declared
Keywords: adenoma detection rate, chromoendoscopy, Screening colonoscopy

P1294 PREOPERATIVE EVALUATION WITH ENDOSCOPIC ULTRASONOGRAPHY AND ENDOSCOPIC SUBMUCOSAL DISSECTION FOR NEUROENDOCRINE TUMORS OF THE RECTUM

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INTRODUCTION: Neuroendocrine tumors (NETs) of the Rectum are rare but are increasing in incidence as a result of increases in screening endoscopy of the colon and rectum. Eighty percent of rectal NETs are less than 1cm, limited to submucosa and have no metastasis; therefore endoscopic treatment is selected as minimal invasive therapy for small rectal NETs. However, incomplete resection of tumors sometimes occurs and in such cases, additional operation should be often required. Endoscopic submucosal dissection (ESD) is a developed EMR technique for reliable en bloc resection of large superficial lesions and is expected to enable expansion of the criteria for endoscopic treatment.
AIMS&METHODS: The objective of this study was to determine the efficacy and safety of ESD for rectal NETs. Thirty six patients (38 lesions) with rectal NETs treated endoscopically at Nanpuh Hospital between June 2002 and July 2012 were assessed. These patients were classified into two groups according to the endoscopic procedure ; EMR group (15 patients 15 lesions) and ESD group (21 patients 23 lesions). Endoscopic findings and Endoscopic ultrasonography (EUS) findings, rate of the en-bloc resection, rate of the complete resection, incidence of complications, length of hospitalization were evaluated.
RESULTS: There were no significant differences in age, gender, tumor size and location of the tumors. Macroscopically, all of the tumors appeared as dome-shaped or flat elevation and central depression was found in four lesions. Most of the lesions were detected as homogenous hypoechoic tumors with sharp border by EUS. However in three lesions the border was unclear and histological examination confirmed that tumor cells spread laterally in submucosal layer without mucosal elevation. The rates of en-bloc resection were 100% in both groups. The rate of complete resection of the ESD group was significantly higher than that of the EMR group (p=0.003). Perforations did not occur in either group. Postoperative bleeding occurred in one EMR case and one ESD case and these were endoscopically managed. The average hospitalization period after treatment was 3.3 days in EMR group and 5.1 days in ESD group (N.S.).
CONCLUSION: Endoscopic submucosal dissection appears to be safe and reliable treatment procedure for rectal NETs, especially when the border of the tumor is unclear by preoperative evaluation with EUS.
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Disclosure of Interest: None Declared
Keywords: ESD, EUS, neuroendocrine tumors of the rectum

P1295 WHO SHOULD HAVE A COLONOSCOPY AMONG PATIENTS WITH INCIDENTAL COLON UPTAKE ON PET-CT?

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INTRODUCTION: It is a clinical dilemma whether patients with incidental colonic uptake (ICU) identified on positron emission and computed tomography (PET-CT) should undergo colonoscopy.
AIMS&METHODS: AIM: To identify the optimal cut-off value of maximum standard uptake value (SUVmax) for colorectal neoplasms and suggests for whom further colonoscopy is recommended in patients with ICU on PET-CT. METHODS: 691 consecutive patients who had a colonoscopy within 3 months after PET-CT between January, 2009, and December, 2009. Per-patient and per-lesion diagnostic performance measure of PET-CT for detecting colonic neoplasms were obtained in 306 patients. In addition, per-lesion sensitivity and positive predictive value (PPV) of various SUVmax criteria for detecting colorectal malignancy and high-grade dysplasia were determined. Receiver operating characteristic (ROC) analysis was used to identify the best positive likelihood ratio (PLR) for diagnosing malignancy and high-grade dysplasia.
RESULTS: Both per-patient and per-lesion PET-CT detection sensitivities for malignancy were 93.3% (28/30; 95% CI 76.5% to 98.9%) and 93.5% (29/31, 95% CI 77.2% to 98.9%) respectively and for high-grade dysplasia were 90.0% (9/10; 95% CI 54.1% to 99.5%). Per-patient negative predictive value (NPV) of malignancy and high-grade dysplasia were 99.1% (216/218; 95% CI 96.4% to

99.8%) and 99.5% (217/218; 97.1% to 99.9%). A SUVmax more than 2.5 as the criteria to specifically detect both malignancy and high-grade dysplasia yielded 92.3% per-lesion sensitivity and 42.9% per-lesion PPV. There is no missing malignancy or high-grade dysplasia among ICUs on PET-CT above the SUVmax=2.5. In the ROC curve analysis, a cut-off value of SUVmsx=5.8, at which the sensitivity, specificity, and PLR for diagnosing malignancy and high-grade dysplasia were 77.8%, 87.5%, and 6.2, respectively.

CONCLUSION: PET-CT is highly sensitive in detecting malignancy and high-grade dysplasia. In negative PET-CT, malignancy and high-grade dysplasia are highly excluded. In order not to miss the malignancy or high-grade dysplasia, it is preferable to perform the colonoscopy in all patients with ICU on PET-CT even in low SUVmax value. A cut-off value using ROC curve has limited capability in screening all malignancy and high-grade dysplasia, however this compromises best positive likelihood ratio with valuable predictive criteria for distinguishing from low-grade dysplasia or inflammatory process.

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Disclosure of Interest: None Declared

Keywords: colonoscopy, colorectal neoplasms, maximum standard uptake value, PET-CT

P1296 FEASIBLE INDICATION FOR COLORECTAL ESD: A PROPOSAL FROM TREATMENT OUTCOME IN A SINGLE CENTER ANALYSIS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is now covered by Japanese health insurance for the treatment of ''early colorectal cancers or adenomas with a maximum diameter of 2 to 5 cm'' regardless of tumour morphology and histological staging.

AIMS&METHODS: [Aim] This case-series study is aiming to reevaluate the clinical feasibility of colorectal ESD from the treatment results.

[Subjects & Methods]

Clinical records of 200 colorectal tumours which treated by ESD from June 2007 to March 2012 were reviewed. Tumours were classified into 3 groups according to the tumour size (<20, 20-50,51≦(mm)), then following clinical outcomes; tumour morphology, histology, procedure time, en-bloc resection rate and complications, were evaluated. ESD was indicated for the following lesions in accordance with the Working Group of ESD Standardization for Colorectal Tumors in Japan

RESULTS: Lesions <20mm (n=19) were macroscopically divided into IIa;2, LST-NG:8, LST-G:1, remnant tumour;8. As for histopathological assessment, 4 were adenoma (21%), 15 were cancer (79.0%), including 1 SM cancer (5.3%). Macroscopic type of lesions 20-50mm in size (n=161) were classified in to Is/Isp;10, IIa/IIa+IIc;3, LST-NG;67, LST-G;79, remnant tumour;2. 27 adenoma (16.8%), 124 cancer (77.0%), and 22 SM cancer (19.8%).

20 lesions which more than 50mm in size were classified in to LST-NG;1, LST-G;19. 15 intramucosal cancer (75%) and 5 SM cancer (25%).

The mean procedure time was 56.6 minutes, 96.2 and 171.5 each in 3 groups, respectively. Complete en-bloc resection rate was 94.7%, 88.8% and 90.0% in each group. By the location were C-T/D–S/R: 83.5 / 100 / 100,85.9 / 90.1 / 92.7, 85.9 / 90.1 / 92.7 respectively. There were no significant differences of en-bloc resection rate according to the tumours locations, but the mean procedure time was significant longer in large size tumor group.

Though postoperative bleeding and perforation was found in 4 (2%), in 5 (2.5%), all complications could be endoscopically managed. The rate of cacer becomes high as the tumor size becomes large. And SM cancer were included 25% in tumor size >50 mm..

CONCLUSION: Considering histological staging causing curability of the treatment, clinical indication of colorectal ESD should be feasible for the tumours less than 50mm.

Disclosure of Interest: None Declared

Keywords: Colorectal cancer, Colorectal endoscopic submucosal dissection

P1297 COMPARISON OF CLINICAL OUTCOMES OF LOCAL EXCISION FOR LOWER RECTAL NEOPLASMS -ESD VS TRANSANAL RESECTION (TAR)-

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INTRODUCTION: Endoscopic submucosal dissection for lower rectal neoplasm is technically easy procedure comparing with other parts of colorectum. To elucidate the clinical outcomes of local excision for lower rectal neoplasms on using endoscopic submucosal dissection (ESD) and transanal resection (TAR).

AIMS&METHODS: We considered all patients who underwent ESD or TAR for lower rectal neoplasms from 1999 to 2012 at the National Cancer Center Hospital, Tokyo, for inclusion in this retrospective study. Patients were excluded if their lesions were histologically diagnosed as deep invasive submucosal cancer (≥1,000 μm) or if lymphovascular invasion was noted. In addition, patients who did not receive surveillance colonoscopy were excluded. Clinical outcomes, including the rate of complete en bloc resection and local luminal recurrence, were analyzed and compared between the ESD and TAR groups. Lesion size, macroscopic type, and extension to the dentate line were evaluated for association with the presence of local luminal recurrence in the TAR group.

RESULTS: A total of 96 lesions in 90 patients were eligible for the present study. ESD was performed on 77 lesions in 75 patients, and TAR was performed on 19 lesions in 15 patients. For the patients who underwent ESD, the median follow-up period was 11 months (range: 3–108 months) and the median lesion size was 3.8 cm (range: 2–12 cm). Macroscopically, 6 lesions were protruding (0–I), 63 lesions were laterally spreading tumors (LST), and 8 lesions were recurrent or residual tumor. In contrast, for the patients who underwent TAR, the median follow-up period was 22 months (range: 6–131 months) and the median lesion size was 3.7 cm (range: 1.2–10 cm). Macroscopically, 7 lesions were 0–I, 8 lesions were LST, and 4 lesions were recurrent or residual tumor. The rate of complete en bloc resection in the ESD and TAR groups were 88% and 53%, respectively ($p<0.001$). Local luminal recurrence was observed in 4% of patients in the ESD group and in 42% of patients in the TAR group ($p<0.001$). With regard to the parameters assessed in the TAR group, LST and recurrent lesions were relatively more frequent in cases of local luminal recurrence (75% and 45%, respectively); however, this difference was not statistically significant.

CONCLUSION: ESD is an excellent treatment option for lower rectal lesions indicated for topical treatment, considering the high success rate of en bloc resection and low rate of local luminal recurrence. Importantly, in cases of LST or recurrence in which it is difficult to recognize the lateral margin of the lesions, ESD should be performed.

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Disclosure of Interest: None Declared

Keywords: Endoscopic submucosal dissection (ESD), lower rectum, transanal resection

P1298 AUTOMATIC CLASSIFICATION OF COLORECTAL LESIONS BASED ON TEXTURE ANALYSIS OF CONFOCAL LASER ENDOMICROSCOPY IMAGES

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INTRODUCTION: Confocal laser endomicroscopy (CLE) enables in vivo optical biopsies providing real-time diagnosis of colorectal lesions. It can differentiate between normal mucosa, neoplastic and inflammatory changes based on the examiner's interpretation of crypts architecture and vascular pattern during ongoing colonoscopy. Texture analysis has been used for interpreting and classifying medical images, with initial studies including radiology and ultrasound images.

AIMS&METHODS: Thus our aim was to determine if measurements resulting from gray level co-occurrence matrices can be employed as classifiers for colonic lesions imaged by CLE. Patients with neoplastic and inflammatory colonic lesions underwent CLE examination with a dedicated endomicroscopy system (EC-3870 CIFK, Pentax, Tokyo, Japan). Images of each lesion and corresponding normal mucosa were recorded for later analysis. A total of 472 images were analyzed as follows: 107 CLE images of colorectal cancer, 183 images of colitis, 30 images of colorectal polyps and 152 control images from normal mucosa. Analysis was performed using the public domain image processing tool ImageJ (Bethesda, USA) and the GLCM texture analyzer plug-in (Cabrera, USA). Five

texture parameters (contrast, entropy, correlation, angular second moment - ASM and inverse difference moment - IDM) were calculated for each image. We used these parameters in a support vector machine (SVM) for automatic classification of the lesions.
RESULTS: In a preliminary analysis, we found statistically significant differences between the mean values of all parameters (ANOVA test, $p<0.001$), while applying Bonferroni's multiple comparisons test we found that only ASM and IDM were different between all groups. We included these two parameters in the SVM as main classifiers, obtaining high classification rates for all pathologies (101/107 colorectal cancer, 170/183 colitis, 21/30 polyps and 148/151 control images).
CONCLUSION: This is, to our knowledge, the first attempt to use texture analysis for classifying colorectal lesions based on CLE imaging. Such computer aided analysis could enhance the diagnosis yield and reduce the intra- and interobserver variability of CLE examinations. Inclusion of automatic algorithms of diagnosis could thus offer support for evidence based clinical decisions in real-time while significantly decreasing the time for analysis of hundreds of images obtained during the examination.
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Disclosure of Interest: None Declared
Keywords: colitis, colon, colorectal cancer, confocal laser endomicroscopy, texture image analysis

P1299 OVER THE SCOPE FULL THICKNESS CLIP FOR THE CLOSURE OF ENTERO-CUTANEOUS FISTULAS

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INTRODUCTION: Post surgery leakage of the gastrointestinal tract is a significant source of morbidity in clinical practice. It seems that Over-The-Scope Clip (OTSC) has been promising lately in the management of gastrointestinal complications such as bleeding, perforations, and fistulas closure where surgery has been traditionally the standard of care.
AIMS&METHODS: The aim of this study was to present the therapeutic results of OTSC in two cases with post surgical entero-cutaneous fistulas. The first case is a 37-year old female who presented with entero-cutaneous fistula after sigmoidectomy and the second is a 68-year old female with pouch-cutaneous fistula after total colectomy with IPAA for ulcerative colitis. They were investigated with endoscopy, CT- scan, pouchography, bowel contrast enema and treatment was planned according to the results and co-morbidities.
RESULTS: In both cases leakage and fistula formation was chronic (1 month and 22 years post operatively). Primary technical success was achieved in both cases. In the first case complete closure of the fistula was achieved in 6 weeks after clip placement in combination with external drainage and no additional surgery was needed. In the second case apart from external drainage and the clip, a loop ileostomy was performed and it came to complete closure after 4 weeks with no need of ileal pouch revision. Median follow up time was 4,2 months. No adverse events related to the use of clip were noted.
CONCLUSION: OTSC seems to be an effective and safe method for the management of post operative entero-cutaneous in combination with other methods especially in cases where major surgical procedures could be deleterious. Further experience and technical improvement is needed for better and permanent results.
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Disclosure of Interest: None Declared
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P1300 CONDITIONS OF USE AND SAFETY OF SODIUM PHOSPHATE TABLETS FOR BOWEL PREPARATION IN FRANCE

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INTRODUCTION: The primary objective was to describe the conditions of use and safety of sodium phosphate (NaP) tablets in France.
AIMS&METHODS: Prospective, longitudinal observational study carried on by French private and public hospital gastroenterologists (GE) in routine medical practice. GE were randomly selected from a national database. Thousand consecutive patients likely to receive NaP tablets as bowel preparation should be included. The data collection was based on two questionnaires filled in by each GE and patient, focused on patient characteristics, use, safety, acceptability and quality of bowel preparation. This study was monitored throughout by an independent Safety Committee.
RESULTS: From September 2011 to March 2012, 1048 patients have been enrolled by 108 GE. Data were available for 996 patients. Both populations (GE and patients) were representative. The patients age ranged from 18 to 81 years (m±SD: 54.6 ±11.8), 20 were over 75 years. At baseline, 46% of patients had comorbidities, mainly cardiovascular, endocrine / metabolic and gastrointestinal conditions. Concomitant treatments were mainly cardiovascular drugs (39%). 55% of patients had a previous colonoscopy with PEG prep in 71% of them.98% of patients received appropriate and sufficient information on how to prepare. 84% of patients had a Boston BPS score ≥ 2 (preparation of good to excellent quality) in each colonic segment. Failure of colonoscopy was reported for 17 patients (1.7%) including only 7 for poor bowel cleansing. 310 patients (31%) reported an adverse event (AE). 6 patients stopped the study drug and only one patient had three serious AEs unrelated to the prep. The most common reported AE were bloating (26%), digestive discomfort (23%) and anal irritation (24%). Only 9.8% of patients experienced vomiting. Among the 360 upper GI endoscopies simultaneously performed, 201 showed superficial gastric lesions. The Safety Committee considered these lesions as likely NaP related in 19 patients (5%). Neither electrolytic disorders nor acute renal failure have been reported. Among the 520 patients who had previous colonoscopy, NaP tablets were preferred, designated as easier to take and more tolerable for 76%, 69%, 58% of patients, respectively and 72% of them were willing to take again the same preparation for a future colonoscopy.
CONCLUSION: The results of this observational study are consistent with those previously reported in controlled clinical studies and highlighted the safety, quality and acceptability of NaP tablets bowel prep in routine practice.
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Keywords: bowel preparation, conditions of use, NaP tablet, routine medical practice, safety

P1301 CAN ENDOSCOPIC SUBMUCOSAL DISSECTION OF COLORECTAL NEOPLASM GREATER THAN 50 MM SIZE BE SAFELY PERFORMED IN A GENERAL HOSPITAL?

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is minimally invasive treatment and enables en-block resection for early colorectal neoplasm. However, it is not widely used in the large neoplasm lesions because of technical difficulty and complications. It has been reported that tumor size of 50 mm or larger was an independent risk factor for complications.
AIMS&METHODS: We aimed to examine the safety, efficacy and complications (perforation and delayed bleeding) of ESD for large colorectal neoplasm in a nonacademic hospital in Japan. All cases were carried out with 1 expert and/or 5 novice endoscopists who had performed under expert's supervision. We have treated 608 cases of colorectal neoplasms (size$\geq$20mm) from July 2007 to December 2012. We devided the cases into two groups by size :Group A (lesion size,20-49mm) and Group B (lesion size$\geq$50mm).
RESULTS: For the 608 cases, 511 cases (84.0%) were assigned to Group A and 97 cases (16.0%) were assigned to Group B. The average age, lesion size and procedure times were 67.4 years, 30.0 mm, 60.0 min in group A, and 67.1 years ($P=0.41$), 64.2mm, 119.6min ($p<0.001$), respectively, in Group B. En bloc resections rate ware 99.2% and 99.0% ($P=0.80$) and complication rate were 4.1% and 9.9% ($p=0.03$). Complications in Group A were 14 perforations, 6 bleeding and 1 ischemic colitis. In group B were 8 perforations and 1 bleeding. Emergency operations were performed two cases in Group A, but none in Group B.
CONCLUSION: ESD was expected to be more complicated for colorectal lesions greater than 50mm in size. However, if it is performed under expert's supervision even if it is a general hospital, ESD for colorectal neoplasm greater than 50 mm in size has become a safe therapeutic method.
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Disclosure of Interest: None Declared
Keywords: Colorectal endoscopic submucosal dissection, Endoscopic submucosal dissection (ESD), Large Lesions

P1302 COMPLEX ENDOSCOPIC RESECTION OF GIANT (>4CM) SESSILE/FLAT COLONIC POLYPS: TECHNIQUES AND OUTCOMES.

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INTRODUCTION: Giant, sessile/flat colon polyps (>4cm) are challenging to remove endoscopically and many lesions are still treated with laparoscopic or open segmental resection. However compared to surgery, complex endoscopic

resection can provide reduced procedure morbidity, significant lower cost and is generally preferred by patients.
AIMS&METHODS: We conducted a prospective analysis of all tertiary cases referred to our academic center for endoscopic assessment and complex resection of giant (>4cm) sessile/flat colon polyps over a 2½ year period (January 2010 - August 2012). Completion rates, adverse events and recurrence rates were recorded.
RESULTS: 107 consecutive patients [mean age 69 years) with 109 colon polyps underwent complex polypectomy. Mean polyp size was 52mm. 31% of polyps were proximally distributed and 69% distal. Primary reasons for referral were polyp size, submucosal fibrosis (SF) and difficult endoscopic access. ASA status of the patients were: ASA I/35%, ASA II/55% and ASA III/10%.
The majority of polyps (n=90) were resected by piecemeal Endoscopic Mucosal Resection (P-EMR). Endoscopic Mucosal Ablation(EMA)-assisted polypectomy (n=19) and Spiral-snare (n=29) were utilized in cases of moderate to severe SF. Supplementary techniques were employed to augment endoscopic access in 3 cases: two Endocuff-assisted polypectomy and one Laparoscopic-assisted polypectomy.
Complex polypectomy was successful in 94.5% in a single session with mean procedure time 43min. Immediate adverse events included controlled intra-procedural bleeding (13.7%), self-limiting vasovagal episodes (8.2%) and one deep submucosal tear (0.9%) treated with endoclips. Eight patients (7.4%) required hospitalization due to delayed post-polypectomy bleeding with one requiring emergency laparotomy. No mortality was noted.
92 patients attended for follow up at 3/6 months, with no recurrence in 45% of cases (n=41). <10mm recurrence (benign and easily treatable) was found in 42% (n=39) of cases and >10mm recurrence in 13% (n=12). One patient with large rectal recurrence had a TEMS procedure and two patients with histology showing malignancy had segmental resections. Further follow up at 9/15 months was performed in 40/92 patients with no recurrence in 70% (n=28), <10 mm benign recurrence in 28% (n=11) and one >10mm benign recurrence 3% (n=1).
CONCLUSION: Complex endoscopic resection of giant (>4cm) sessile/flat colon polyps demands a multi-modality approach, but good medium term outcomes can be achieved with most patients spared surgery. Minor recurrence occurs frequently but can be successfully managed with close surveillance.
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Disclosure of Interest: None Declared
Keywords: Endoscopic resection, giant polyps, polypectomy,

P1303 EFFECT OF RECTAL INDOMETHACIN FOR PREVENTION OF POST-ERCP PANCREATITIS: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL

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INTRODUCTION: Two problems of endoscopic retrograde cholangiopancreatography (ERCP) compromise the clinical benefits of endoscopic biliary therapy: failure of selective biliary cannulation and post-ERCP pancreatitis (PEP). Unsuccessful biliary cannulation may occur in up to 15 - 35% of cases. PEP remained the most common major complication of ERCP, its frequency was reported between 5 and 10 % generally, but it can increase at high risk procedures in high risk patients up to 42 %. On time interruption of unsuccessful attempts for cannulation seems to be important: after many unsuccessful attempts the risk of PEP rises and complete failure becomes inevitable.
AIMS&METHODS: To evaluate the efficacy of rectal indomethacin for prevention of PEP, while success rate of therapeutic ERCP was maximised. 539 patients selected for biliary endoscopic therapy were randomized in a prospective, double-blind clinical trial: 270 patients were given rectal 100 mg indomethacin and 269 patients received placebo within 1 hour before ERCP. Patients (with papillectomy, previous serious PEP, cannulation of minor papilla) receiving pancreatic stents were excluded. Wire-guide cannulation (WGC) was planned after 5 unsuccessful attempts, if 5 WGCs were unsuccessful, precut was performed.
RESULTS: The 2 groups were comparable in age, sex, analytical parameters, indications for ERCP, procedure and disease characteristics. Successful ERCP was performed in 529 patients (98.1%), ''simple'' diagnostic ERC was performed in 16 patients (2.6%), endoscopic biliary therapy was achieved successfully in 513 patients (95.2%). PEP occurred in 55 patients (10.2%), 18 patients (6.7%) in indomethacin group and in 37 patients (13.7%) in placebo group (p=0.007). Prophylactic effect of indomethacin was detected more definitely in patients having high risk procedure-related factors (13.8% in indomethacin group versus 28.3% in placebo group, p=0.028) and high risk patient-related factors (7% in indomethacin group versus 16.5 % in placebo group, p=0.004). No adverse event attributable to indomethacin was observed.
CONCLUSION: On time interruption of unsuccessful attempts for selective biliary cannulation and early implementation of precut can confer high success rate of biliary endoscopic therapy. Prophylactic 100 mg rectal indomethacin is effective for prevention of PEP, particularly in high risk patients and at high risk procedures.
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Disclosure of Interest: None Declared
Keywords: ERCP, high success rate of biliary cannulation, indomethacin, post-ERCP pancreatitis, prospective, randomized, double-blind, placebo-controlled clinical trial

P1304 NEEDLE-KNIFE SPHINCTEROTOMY OVER A PANCREATIC STENT (NKPS) IN DIFFICULT BILIARY CANNULATION BUT INCIDENTAL SELECTIVE PANCREATIC DUCT (PD) CANNULATION.

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INTRODUCTION: The rate of post-ERCP pancreatitis (PEP) increases when cannulation is difficult. Precut biliary endoscopic sphincterotomy (precut ES) has been used to improve the success rate of biliary cannulation; however, precut ES is an independent risk factor for PEP. There are a few reports that the pancreatic stent helps guide the precut ES improving the safety of the technique.
AIMS&METHODS: This was a prospective observational study of difficult biliary access and incidental selective PD cannulation that assessed effectiveness and safety of NKPS in this high risk situation for PEP. Between Jan. 2012 and Mar. 2013, consecutive patients who underwent ERCP with a clear indication for biliary access in Jeju National University Hospital were enrolled. All ERCP procedures were performed by one endoscopist. When bile duct cannulation was difficult and incidental PD cannulation was achieved, PD stent was placed using a 0.018 guidewire (Cook Endoscopy, Winston-Salem, NC) and 3F unflanged single pigtail plastic stent (4 to 8 cm, Zimmon; Cook Endoscopy). Using the PD stent as a guide, precut ES was performed by cutting cephalad in the 12-o'clock position beginning at the papillary orifice with needle-knife sphincterotome. Selective biliary cannulation was then attempted. The PD stent was left in place. This group of patients was classified as NKPS group and compared to the rest of patients, called routine group. ERCP-related complications were classified and graded according to consensus guidelines. Statistical analyses were performed by Fisher's exact test and Mann–Whitney U test using SPSS version 17.0 (SPSS, Inc., Chicago, IL).
RESULTS: Among 306 ERCP during this period, 175 patients with naïve papilla (M=89, F=86) for biliary indication were prospectively enrolled. Of those 175, 16 (M=9, F=7) were included in the NKPS group. The mean age was 64 in both groups. Successful biliary cannulation was achieved in all NKPS patients. PEP was developed in 8 of 159 (5%) in routine group and 2 of 16 (12.5%) in NKPS group (p=0.229). Bleeding was developed in 9 of 159 (5.7%), 1 of 16 (6.3%), respectively (p=1.000). Mean (SD) serum amylase levels after ERCP were 194.9 (377.5) U/L and 438.2 (474.6) U/L, respectively (p<0.001). All the PEP was mild in NKPS group. All PD stents were dislodged spontaneously within 7 days.
CONCLUSION: Even though NKPS group was high risk for PEP, the incidence of PEP was comparable to the routine group. If biliary cannulation is difficult and incidental PD cannulation is achieved, NKPS would be safe and feasible with a lower rate of post-procedure complications.
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Disclosure of Interest: None Declared
Keywords: pancreatic stent, post ERCP pancreatitis, precut sphincterotomy

P1305 FEASIBILITY OF AN ENDOSCOPIC PORCINE MODEL OF BILIARY OBSTRUCTION USING OVER-THE-SCOPE CLIPS. EVALUATION OF ITS APPLICABILITY TO TRAINING IN EUS-GUIDED DRAINAGE PROCEDURES.

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INTRODUCTION: There is a growing demand in clinical practice for EUS-guided drainage procedures. EUS-DP are technically challenging and carry morbidity. Porcine models of biliary obstruction by laparoscopic bile duct ligation have been used for training.
AIMS&METHODS: To develop a reproducible and affordable porcine model of biliary obstruction. To assess the potential use of such model for training in therapeutic EUS. After approval, the papilla of 16 swine was clipped using Over-the-scope (OTSC) clips (Ovesco, Tübingen, Germany). Variables used: a) Time to reach and identify the papilla with and without OTSC by the same operator at sequential intubations; b) Success rates at clipping the papilla by two novel & two experienced operators; c) Time to identify papilla Vs Time to place OTSC. Clinical, biochemical and imaging (abdominal ultrasound & laparoscopy) follow-up was performed at 3-4 and 8-10 days to assess efficacy & complications of OTSC placement. The feasibility of EUS-guided bilio-enteric anastomoses after OTSC clipping of the papilla was evaluated using both standard oblique-viewing (n=13) and prototype forward viewing lineal echoendoscopes (n=10) by non-expert (total career experience <25 EUS-DP) endosonographers under experienced operator supervision.
RESULTS: The OTSC clip was successfully deployed on the papilla of 15/16 animals (1 failure). No significant differences were found between time to identify the papilla (460 [158-892] seconds) and time to place OTSC clips (575 seconds). Two animals had post-procedure pain. One died at 48 hours and a gastric perforation was found at necropsy. Another one had a retroduodenal abscess found at necropsy at 10 day follow-up. At immediate follow-up, 14/15 animals had high serum bilirubin (mean value=3.55 mg/dL; mean increase over baseline=2.85 mg/dL). All 4 pigs in which ultrasound or laparoscopy had CBD (>4 mm), gallbladder and cystic duct dilation (but not intrahepatics). At second follow-up 8-10 days post clipping, all surviving animals exhibited at EUS massive CBD dilation (>15 mm). Only 3/14 had intrahepatic dilation. A total of 23 EUS-DP were attempted (16 by novel operators), including hepaticogastrostomy (n=3), choledochoduodenostomy (n=8) or cholecystgastrostomy (n=12). Although EUS-guided access and cholangiography were successful in 23/23, anastomoses were only accomplished in 30.5%

CONCLUSION: OTSC placement on the porcine papilla is a simple, effective model of biliary obstruction which appears to reflect the difficulty of EUS-DP. Its application for training purposes warrants further study.
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Disclosure of Interest: None Declared
Keywords: biliary obstruction, OVER THE SCOPE CLIP

P1306 LEARNING PHASE OF DIRECT PERORAL CHOLANGIOSCOPY USING ULTRA SLIM GASTROSCOPES

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INTRODUCTION: Direct peroral cholangioscopy (POCS) is an emerging technique complementing ERCP. Unless several data demonstrate the clinical relevance of POCS, only few data about the learning process of this technique are available.
AIMS&METHODS: Aim: To investigate the technical success rate and learning process of POCS in a tertiary center.
Methods:
All patients were investigated with standard ERCP and biliary sphincterotomy directly prior to cholangioscopy. After removal of the duodenoscope, an ultra slim gastroscope was directly advanced to the duodenum. The common bile duct was intubated using the balloon anchor technique. All POCS procedures were performed with water irrigation or carbon dioxide indufflation. Histology was taken from suspicious lesions. The investigation times and the success rates were calculated. Special caution was given to the time from oral intubation until visualization of the bile ducts that served as a key technical parameter.
RESULTS: A total of 36 POCS were performed. Intubation was successful in 31/36 (86%). Reasons for failed intubation were small caliber bile ducts, duodenal diverticulum and papillary adenoma. The mean intubation time was 9.2 min (3-23 min). The average intubation time did not change significantly over time (R^2= -0.03). The variance of intubation times changed over time and was 26.5 min in the first half of investigations and 19.2 min in the second half but did not reach significant levels. A minor bleeding caused by the anchor balloon was the only complication that was observed.
CONCLUSION: The technique of direct peroral cholangioscopy using the balloon anchor technique in combination with ultra-slim gastroscopes is technically demanding. Performance is safe after a short learning period at last in a tertiary center. Nevertheless, as POCS is not yet a standard technique, we suggest that POCS may only be performed by experienced endoscopists.
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Keywords: learning curve, peroral cholangioscopy

P1307 OUTCOME AND NATURAL COURSE OF CRITICALLY ILL PATIENTS WITH SCLEROSING CHOLANGITIS

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INTRODUCTION: Sclerosing cholangitis in critically ill patients (SC-CIP) is a severe biliary disease with a poor outcome. The mechanisms leading to this form of bile duct alterations are widely unknown. Data on outcome of a natural course are sparse.
AIMS&METHODS: In a period of 6 years (2005-2011) we includet 57 patients during or after the stay in a ICU in a large bavarian trauma and neurosurgical center from 2/2005 - 9/2009 retrospective and 12/2009 - 11/2011 prospective. All patients showed pathological endoscopic findings by ERCP. Characteristic findings were bile duct stenosis, vanishing bile ducts and biliary casts.
RESULTS: ERCP was performed usually (median) on day 53. 50/58 patients (88%) were followed by routine follow up, readmission, telefone contact or questionnaire with a follow up of 35,5 month. Underlying disorders were intracerebral bleeding (47%), severe poly trauma (29%), severe septic shock (17%), severe burning injuries (6%). Endoscopic therapy with papillotomy, balloon dilatation, cast removal if present was performed in all patients.
27 patients had a favourable (n=8) or stable course (n=19). 3 patients recieved LTX, 5 patients have being listed for LTX. 16 patients died during follow up, 4/16 patients in consequence of the SC-CIP.
CONCLUSION: In contrast to the literature, SC-CIP is not allways a rapidly progressive disease. The letality is 14,5% in a long term outcome of 2,6 years
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Disclosure of Interest: None Declared
Keywords: Biliary cast, Long term outcome, SC-CIP

P1308 ERCP PERFORATIONS IN THE NEW MILLENNIUM - RESULTS FROM 9000 ERCPS/ A LARGE TERTIARY REFERRAL CENTRE EXPERIENC

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INTRODUCTION: Background: Although rare, perforations are one of the most dreaded complications of ERCP. The incidence of perforations during ERCP has been reported to range from 0.3 to 6%. However, this data stems mainly from older studies or retrospective databases. Current data is important, as ERCP has revolutionized to be mainly a therapeutic procedure. Data on outcomes and complications are essential to establish prevalence and incidence rates, standards, quality indicators and risk factors for perforations.
AIMS&METHODS: To assess the incidence of ERCP related perforations and outcomes at a large tertiary referral centre. A review of all patients undergoing ERCP at our institution from January 2003 to November 2012 was performed to assess the ERCP related perforations. All patients are routinely followed-up clinically or via telephone interview within 30 days after the procedure.
RESULTS: Out of a total of 9000 ERCPs that were performed (92% therapeutic interventions), a total of 12 iatrogenic perforations occurred, yielding an incidence of 0,0012%. The mean age of the patients was 58.8 years, range 23 to 79. Most perforations occurr3d in the second portion of duodenum (n = 10, 83%), all of these were related to sphincterotomy. One patient suffered from esophageal perforation and another patient with Billroth II anatomy suffered from a perforation of the afferent limb. Endoscopic closure of the perforation site was not performed in any patients as most of them were either diagnosed after the procedure or were not amenable to endoscopic intervention and needed surgery. Eight out of 12 (67%) patients were managed medically and four surgically. All patients improved and were discharged home. There were no deaths.
CONCLUSION: The perforation rate of ERCP was 0.0013%. Sphincterotomy-related perforations constituted the majority of iatrogenic damage. CT was the best method to detect perforation. Immediate endoscopic closure of the perforation was not done in any patients since most of them were diagnosed after the procedure or were not amenable to endoscopic therapy. Risk factors for perforation included altered surgical anatomy, female sex, sphincter of Oddi dysfunction.
Disclosure of Interest: None Declared
Keywords: ERCP clearance, ERCP complications

P1309 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN ELDERLY PATIENTS.

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INTRODUCTION: Old age is associated with biliary and pancreatic pathology with the consequent need to perform endoscopic retrograde cholangiopancreatography (ERCP). Some studies suggest that ERCP in very old patients is associated with an increasing number of complications and technical failure.
AIMS&METHODS: The aim of this study was to evaluate the clinical effectiveness and associate complications of ERCP in patients older than 85 years.
This was a retrospective review of 48 consecutive patients older than 85 years old, who underwent ERCP, in a 26-month period, in a single center. The data was collected to analyse demographic information, indications, technical and clinical success, ERCP procedures, ERCP diagnosis, complications and length of hospital stay.
RESULTS: Technical success was achieved in 98% of cases in the first attempt and 100% in the second. The median age was 89 years old (range: 86-102) and 68% women. The main indications were: gallbladder and pancreatic cancer (11 cases-23%), suspected choledocholithiasis (18 cases-38%). The main therapies associated with ERCP were: sphincterotomy (n = 36), biliary stent (n = 26); extraction of bile duct stones (n = 22), mechanical lithotripsy (n = 4). Complications occurred in 8% of patients: 2 patients had cholangitis (4%) and 2 pancreatitis (4%). No cases of: 1) need of mechanical ventilation after anesthesia, 2) hemorrhage requiring transfusion, 3) mortality associated with ERCP were recorded. The median length of hospital stay after examination was 2 days (range: 1-103)
CONCLUSION: Diagnostic and therapeutic ERCP is effective and safe in elderly patients who present similar outcomes as younger patients.
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Disclosure of Interest: None Declared
Keywords: elderly patients, Endoscopic retrograde cholangiopancreatography

P1310 ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN CHILDREN AND ADOLESCENTS: A UK SINGLE CENTER EXPERIENCE

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INTRODUCTION: Endoscopic retograde cholangiopancreatography (ERCP) is a specialised endoscopic procedure associated with high risk of complications in adults. ERCP is not commonly performed in children and is mainly indicated for therapeutic interventions, however ERCP can also be a vital diagnostic tool in pancreatobiliary diseases where imaging is non-diagnostic. We report a UK tertiary center experience of ERCP in children and adolescents.
AIMS&METHODS: To prospectively evaluate our ERCP practice in children and adolescents and record technical success and complications. We also assessed correlation of radiological findings pre ERCP to cholangiopancreatography findings at ERCP.

Data was recorded prospectively from children and adolescents who underwent ERCP at University College London hospital between 2005 and 2012. Techincal success at ERCP and complication rates were analysed. We continue to collect data on long term outcomes of these patients.
RESULTS: 36 children underwent 40(n) ERCP procedures using a 11mm duodenoscope.22 patients were males. Median age was 11.5 years (range 3-17). Majority (67%) of ERCPs were performed as daycases. All ERCPs were performed under general anaesthesia by three experienced gastroenterologists. Common indications for ERCP were chronic recurrent pancreatitis needing pancreatic endotherapy (20), choledocholithiasis (10), abnormal liver function test (5), abnormal imaging(4). Majority were cotton grade 2(51%) and grade 3(36%) procedures. Therapeutic procedures performed included biliary sphincterotomy (12),CBD stones removal (10), pancreatic sphincterotomy (3), pancreatic stenting (8) and biliary stenting (2). Intended therapeutic success was achieved in 90% of procedures performed. In 10%of patients ERCP revealed new findings which were not reported on pre ERCP imaging. No major post ERCP complications were seen in our cohort apart from one patient who developed mild post ercp pancreatitis which was managed conservatively. No ERCP related mortality was reported.3 patients (7.5%) needed surgery as ERCP was unsuccessful in achieving intended therapeutic success.
CONCLUSION: ERCP in children and adolescents is safe and effective and can be performed as a daycase. Use of appropriate duodenoscope and accessories are key to success. Complication rates are minimal. ERCP can be a useful diagnostic tool where imaging is inconclusive. ERCP plays an important role in diagnosis and management of pancreatobiliary conditions in children and adolescents and can prevent complex pancreatobiliary surgery in selective cases.
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Disclosure of Interest: None Declared
Keywords: Adolescents, children, ERCP, PANCREATIC ENDOTHERAPY, PANCREATOBILIARY

P1311 WHEN AND TO WHOM SHOULD WE APPLY THE DOUBLE GUIDEWIRE CANNULATION METHOD DURING ENDOSCOPIC BILIARY INTERVENTION? -POST HOC ANALYSIS OF MULTICENTER RANDOMIZED CONTROLLED TRIAL-

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INTRODUCTION: Double guidewire cannulation technique (DGW) is one of the rescue techniques for wire-guided cannulation method (WGC) during ERC. Recent multicenter randomized controlled trial comparing early DGW and repeated WGC at the first unexpected insertion of guidewire into main pancreatic duct (MPD) showed no significant difference in either successful CBD cannulation or development of post ERCP pancreatitis (PEP) between the two groups (reported in DDW 2013). We performed post-hoc analyses to investigate the maximum use of DGW.
AIMS&METHODS: Among 707 consecutive patients with naiive papilla who were to undergo therapeutic biliary intervention with WGC, a total of 274 patients with unintentional insertion of guidewire into MPD on the first cannulation attempt were randomized into Repeated WGC group and Early DGW group. Main outcomes were the success rate of biliary cannulation within 10 attempts and 10 minutes from the randomization and the PEP rate.
RESULTS: Early DGW had a relative rate of successful CBD cannulation of 1.07 (95%CI 0.93-1.24) with a relative risk for PEP of 1.04 (CI 0.93-1.16). Subgroup analysis showed that Early DGW had an advantage in patients with biliary neoplasm (RR 1.36, CI 1.05-1.77) and with intra-/peri-diverticular ampulla (RR 1.24, CI 0.93-1.66). If the cannulation with the randomized way were limited in 5 attempts and 5 minutes, DGW had an increased RRof 1.16 (CI 0.91-1.49) for CBD cannulation with a decreased RR of 0.69 (CI 0.29-1.63) for PEP. Although the risk for PEP was not related to the number of attempts or the time for CBD cannulation in Repeated WGC group, it was significantly increased along with those in Early DGW group (11% in <5 attempts/minutes, 25% in 5-10 attempts/minutes, and 32% in >10 attempts/minutes, p=0.03).
CONCLUSION: In therapeutic ERC using WGC, early DGW neither facilitated CBD cannulation nor reduced PEP compared to repeated WGC. However, DGW might have an advantage in selected patients or by using it within 5 attempts and 5 minutes.
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Disclosure of Interest: None Declared
Keywords: double guide wire technique, post ERCP pancreatitis, Wire guided cannulation

P1312 DISTINGUISHING BENIGN FROM MALIGNANT DOMINANT BILIARY STRICTURES IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS UTILIZING PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY (PCLE): A MULTI-CENTER, EXPERT CONSENSUS REVIEW

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INTRODUCTION: Probe-based confocal laser endomicroscopy (pCLE) enables subepithelial visualization of biliary strictures. Whether fibrosis and inflammation of PSC may alter pCLE interpretation or if expert consensus of findings can be achieved in PSC remains unknown.
AIMS&METHODS: Evaluate pCLE for dominant PSC stenosis by blinded consensus review of image sequences. Methods: 10 pCLE experts from 9 centers (8 US, 1 EU) had a consensus meeting. pCLE video sequences acquired during ERCP using the CholangioFlexTM confocal mini probe (Mauna Kea Tech. Paris, France) passed through a cholangioscope or catheter were reviewed. Investigators were blinded from clinical data. Normal and malignant Miami criteria and inflammatory Paris criteria were assessed. Patients with a minimum two of five malignant Miami criteria were "suspicious", one "reactive"; a normal reticular pattern was "benign". Tissue sampling results at time of ERCP was considered positive if malignant cytohistopathology. ROC curve analysis for pCLE performed. CI calculated.
RESULTS: pCLE sequences from 46 dominant PSC strictures were pooled from five centers. A presumptive diagnosis based on tissue sampling results and clinical follow-up was benign (n=39) and malignant (n=7). Combining pCLE and tissue sampling yielded sensitivity and NPV of 100%. See Table for operating characteristics. ROC of pCLE: AUC =.77 (CI.62-.88; p =0.006).

Operating Characteristics	pCLE	Tissue Sampling	pCLE + Tissue Sampling
Accuracy	80	98	85
Sensitivity	71	86	100
Specificity	82	100	82
NPV	94	98	100

CONCLUSION: The high operating characteristics of tissue sampling in our PSC patient cohort was related to selection bias. The combination of pCLE and tissue sampling in the evaluation of dominant PSC strictures has a high ability to exclude malignancy and may be helpful in determining surveillance intervals in this high-risk population. Operating characteristics of pCLE in the setting of PSC should further improve with increased experience of recognizing inflammatory criteria. A multi-center, international registry of pCLE in PSC patients is ongoing.
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Disclosure of Interest: None Declared
Keywords: cholangiocarcinoma, confocal laser endomicroscopy, ERCP, Primary sclerosing cholangitis

P1313 DOES REALLY DOUBLE BALLOON ENDOSCOPY INCREASES THE ERCP SUCCESS RATE IN PATIENTS HAVE ANATOMICALLY ALTERED GI TRACT?

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INTRODUCTION: Endoscopic retrograde cholangiopancreatography (ERCP) success rate 85- 95% in patients with a normal gastrointestinal anatomy. But its success rate is lower in case of alternated anatomy (60% > 92%).
AIMS&METHODS: We aimed that to evaluate the effect of double balloon endoscope (DBE) on the endoscopic retrograde cholangiopancreatography (ERCP) success rate in patients with a history of Billroth II (BII) gastrectomy or hepaticojejunostomy with Roux-en-Y. The medical records of the patients who underwent ERCP at the Gastroenterology Department of Kocaeli University Medical Faculty Hospital, between December 2008 to September 2012 were examined. ERCP procedure was performed for 2254 patients. Of the 2254 patients, 61 patients (2.7%) have anatomically altered GI tract; 50 patients (26 men and 24 women) with a BII gastrectomy with Roux-en-Y underwent 56 ERCP attempts and 11 patients (6 men and 5 women) have hepaticojejunostomy with Roux-en-Y underwent 11 ERCP attempts before being referred to our center. The mean age of these 61 patients was 63 years (range 35-77 years). In all cases, the ERCP procedures were started using a side-viewing duodenoscope. If intubation of the afferent loop or reaching the papilla failed, we changed to DBE for the ERCP procedure (DBE-ERCP). The DBE-ERCP procedure was

performed using Fujinon EN-450 T5, Japan. We assessed the success rate of afferent loop intubation, reaching the major papilla, selective cannulation, possibility of therapeutic approaches, procedure-related complications, and the overall success rate.
RESULTS: Among the 61 patients have anatomically altered GI tract, the duodenoscope was successfully passed up to the papilla in 30 patients (% 49.2%), and cannulation was successfully performed in 27 patients (44.3%). Thirty-one patients (12 with failure in afferent loop intubation and 19 with failure in reaching the papilla) underwent DBE-ERCP. The DBE reached the papilla or enterobiliary anastamosis in 30 patients (96.8%) and selective canulation of choledocus could be achieved in all except 3 patients (90.3%). 18 patients (58.1%) who had common bile duct stones were successfully treated. In 3 patients with pancreatic head tumor and 2 patient with cholangiocarcinoma biliary stenting was performed. In 4 patients with benign biliary strictures balloon dilatation was performed. We observed perforation in one patient with Whipple, Roux-en-Y for Pancreatic Carsinoma due to procedure. The overall ERCP success rate increased from 44.2% (27/61) to 88.5 % (54/61).
CONCLUSION: The overall ERCP success rate increases with DBE in patients have anatomically altered GI tract.
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Disclosure of Interest: None Declared
Keywords: Anatomically altered anatomy, Billroth II and ERCP, DBE and ERCP, ERCP success rate and DBE, Hepaticojejunostomy and ERCP, R en Y and ERCP

P1314 PREDICTORS OF STENT DYSFUNCTION IN PALLIATIVE ENDOSCOPIC DRAINAGE OF MALIGNANT BILIARY OBSTRUCTION

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INTRODUCTION: The major disadvantage of endoscopic approach for the palliation of malignant biliary obstruction is the stent patency.
AIMS&METHODS: The aim of this study was to identify predictors of stent dysfunction in patients with malignant biliary obstruction caused by unresectable neoplasms. Medical records of consecutive patients who required placement of a biliary stent between August 2009 and August 2012 in a tertiary medical centre were retrospectively reviewed. Stent dysfunction was defined as relevant cholestasis worsening due to stent obstruction or migration, or as symptoms of cholangitis. Demographic data, comorbidity, performance status (ECOG), stricture location, neoplasm characteristics, presence of metastases, laboratory parameters (bilirubin, haemoglobin, albumin, CA 19.9), type of biliary stent, hospitalization time, complications, concomitant chemotherapy and overall survival were compiled. Univariate analysis and multivariate multinomial logistic regression were performed to identify independent predictors associated to stent dysfunction.
RESULTS: 51 of 64 patients with malignant biliary obstruction fulfilled the inclusion criteria and were included (56.9% females, 72.3 ± 13.6 year-old). Pancreatic cancer (49.1%) and cholangiocarcinoma (31.4%) were the most common indications for stent insertion. 17 self-expandable metal stents (15 one-step and 2 elective-exchanged) and 34 plastic stents were endoscopically placed. Twenty (39.2%) patients presented stent dysfunction (11.8% metal vs. 52.9% plastic stents, $p = 0.005$). Placement of metal stent was the only independent factor against dysfunction (OR: 0.045, 95%CI: 0.002-0.96), whereas concomitant chemotherapy (OR: 4.89, 95%CI: 11.16-20.71) was independently associated with the occurrence of stent dysfunction.
CONCLUSION: Concomitant chemotherapy is an independent risk factor for stent dysfunction in malignant biliary obstruction. Self-expandable metal stents must be preferred to plastic stents especially in those patients receiving palliative chemotherapy.
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Disclosure of Interest: None Declared
Keywords: Biliary drainage, Biliary stent, Malignant biliary obstruction

P1315 ENDOSCOPIC PANCREATIC STENTING IN THE TREATMENT OF ACUTE POST-ERCP PANCREATITIS

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INTRODUCTION: The effectiveness of preventive pancreatic stenting for high risk post-ERCP pancreatitis (PEP) is proven, whereas rationality of the main pancreatic duct (MPD) stenting or the treatment of the PEP is disputable.
AIMS&METHODS: to evaluate retrospectively the results of endoscopic stenting of the MPD in the treatment of acute PEP, as a justification for prospective randomized trial.
From 01.01.2009 till 01.01.2013 we carried out 1948 retrograde endoscopic interventions on major duodenal papilla (MDP) and performed preventive pancreatic stenting in 52 (2.7%) cases. Acute PEP originated in 26 (1.33%) other cases (24 f. and 2 m.; mean age 57.9 ± 14.8; range: 34-85 years). The indication for primary endoscopic interventions was jaundice in all cases, caused by stenosis of the MPD and microlithiasis (14), choledocholithiasis (9), polyps of the MDP (2) and restenosis after previously performed EPT (1). Acute pancreatitis developed after failed ERCP in 1 (3.8%) pt.; after balloon papillodilation with extraction of bile stones in 1 (3.8%); after EPT in other 24 (92,4%) pts., including nonselective EPT in 6 cases, additional virsungotomy-in 3, extraction of bile duct stones-in 8.
RESULTS: We tried to perform stenting of the MPD in 21 pts. and succeeded in 19 (90.5%) cases. Pancreatic stents were removed in 5-12 days after their placement. Complications of pancreatic stenting have not been revealed; all patients recovered. The average length of hospitalization was 11.8 ± 3.7 days. Other 7 (26.9%) pts., including 2 pts. with failed attempts of stenting, underwent medical therapy and 2 of them - surgical intervention afterwards. There were 2 (28,6%) lethal outcomes in this subgroup. The average time of hospitalization was 23.8 ± 7.5 days.
CONCLUSION: Endoscopic stenting of the MPD is technically feasible in 90.5% of pts. with acute PEP and act as an effective and safe method of its treatment - after successful stenting there were no complications or progression of disease; all pts. have recovered. At the same time, in the subgroup of pts. where pancreatic stenting was not performed or failed, mortality reached 28.6% and the length of hospitalization was longer more than 2 times. Prospective randomized trial is needed to prove these initial promising results.
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Disclosure of Interest: None Declared
Keywords: preventive pancreatic stenting, endoscopic stenting of the MPD, endoscopic treatment of the PEP, post-ERCP pancreatitis, stenting of main pancreatic duct (MPD), treatment of the PEP

P1316 ERCP IN PATIENTS WITH PRIOR BILLROTH II GASTRECTOMY: REPORT OF A 30- YEAR EXPERIENCE

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INTRODUCTION: ERCP in pts with Billroth II gastrectomy is difficult due to anatomy. Experience of a tertiary referral endoscopy centre is reported.
AIMS&METHODS: From Oct 1982 to Oct 2012, 713 pts with Billroth II reconstruction (567 M, mean age 69yrs) were retrospectively identified from a prospectively collected database. Main indications for ERCP were common bile duct stones (CBDS) (51.2%) and obstructive jaundice (24.3%).
Procedures were always started with a duodenoscope; in case of failure to reach the papilla the duodenoscope was changed with a gastroscope. Endoscopic sphincterotomy (ES) was performed using a long nose sigmoid inverted sphincterotome.
RESULTS: A total of 1050 ERCP were performed in 713 pts [1,47/patient (range 1-33)].
Results of duodenal intubation and bilio-pancreatic cannulation are summarized in ***table 1***.

Table 1. Results of duodenal intubation and bilio-pancreatic cannulation in 713 pts

	N	%
Successful duodenal intubation	**618**	**86.7**
Failed duodenal intubation	**95**	**13.3**
Long and angulated afferent loop	*73*	*76.8*
Jejunal loop perforation	*19*	*20*
Lack of collaboration	*3*	*3.2*
Successful cannulation/opacification	**580/618**	**93.8**
Overall success	**580/713**	**81.3**

In 14/618 pts (2.3%) the papilla was reached by a rendez-vous with a guidewire placed percutaneously.
Biliary and/or pancreatic ES were respectively performed in 490 (84.5%) and 23 pts (4%), including 5 minor papilla ES; 78 pts (13.4%) underwent diagnostic ERCP when MR cholangiography was not yet available; Plastic and metallic stents were inserted in 158 pts (27.2%). Extraction of CBDS and pancreatic stones were respectively performed in 318 (54.8%) and 12 pts (2.1%).
There were 45 complications (4.3%): peritoneal perforation 19 (1.8%); delayed post ES bleeding 11 (1.0%); ERCP related cholangitis 5 (0.5%); mild pancreatitis 5 (0.5%); retroperitoneal perforation 3 (0.3%); respiratory failure 2 (0.2%).
Retroperitoneal perforations were secondary to ES, balloon dilation of the papilla and laceration of a duodenal diverticulum (all managed conservatively). Peritoneal perforation, always required surgery. Two pts died after surgery (overall mortality 0.3%). The other complications resolved by conservative management or endoscopic re-intervention.
CONCLUSION: ERCP in Billroth II pts has comparable morbidity and mortality as in pts with normal anatomy. Main reasons of failure are related to inability to reach the papilla. Peritoneal perforations require prompt surgical approach. The use of a duodenoscope is recommended because it makes bilio-pancreatic cannulation and subsequent endotherapy.
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Disclosure of Interest: None Declared
Keywords: Billroth II, ERCP

P1317 MULTIDISCIPLINARY APPROACH FOR MEDIASTINAL NODAL STAGING OF LUNG CANCER WITH A COMBINED EBUS AND EUS PROCEDURE.

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INTRODUCTION: OBJECTIVE: To assess if the use of Endoscopic Ultrasound-Guided Fine-Needle Aspiration (EUS-FNA) improves mediastinal staging carried out by Endobronchial ultrasound–guided fine-needle aspiration (EBUS-FNA) of patients with lung cancer.
AIMS&METHODS: MATERIAL AND METHODS: We analyze all the punctures performed for mediastinal staging in patients with lung cancer following the criteria of the Spanish Society of Pneumology and Thoracic Surgery (SEPAR) since October 6, 2009 to April 2, 2013. Patients were divided into 2 groups according to the date of introduction of EUS-FNA in the unit: group 1 (G1) who underwent EBUS-FNA (October 2009 to July 2011), and group 2 (G2) in which EBUS-FNA was implemented with EUS-FNA (July 2011 to April 2013). Endoscopic examinations were performed by the same endoscopists: pulmonologist or thoracic surgeon in the case of EBUS-FNA and gastrointestinal endoscopist in EUS-FNA. All procedures were performed under moderate sedation We performed EBUS-FNA first and if it gives a negative result in the in situ histological analysis, EUS-FNA was performed. The presence of lymphocytes or presence of diagnostic cellularity was considered adequate sample. We didńt made histological confirmation in positive samples. Atypia, metaplasia and dysplasia were considered negative. Surgical confirmation (mediastinoscopy or surgery) was performed in all negative punctures. We had cytologist in the room.
RESULTS: We analyzed 150 patients for staging, 64 patients in G1 and 86 patients in G2, and there was no statistically significant difference in age, gender, rate of positive PET or average size of the lymph nodes between groups. The nodal regions punctured were 2R, 4R, 4L, 7, 10R, 11L, 8 and 9, and there was no difference between groups in terms of diagnostic performance. The invalid sample rate in G1 were higher than G2 but not significantly (10.2% vs 4.5%, $p = 0.18$). Comparing the groups (G1 and G2) we find differences with respect to: overall accuracy (93% vs 97%), sensitivity (86% vs 93%) and negative predictive value (88% vs 93%). In both groups, the specificity and PPV were 100%.
CONCLUSION: The combination of EUS-FNA and EBUS-TBNA obtain better results than single EBUS for mediastinal staging in lung cancer.
Disclosure of Interest: None Declared
Keywords: Endoscopic ultrasonography, lung cancer, staging

P1318 SINGLE-TIME COMBINED APPROACH OF TRANSBRONCHIAL ENDOSCOPIC NEEDLE ASPIRATION (TBNA) AND TRANSAESOPHAGEAL ECHOENDOSCOPIC ASPIRATION (EUS FNA) IN THE DIAGNOSIS OF MEDIASTINAL MASSES

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INTRODUCTION: Endoscopic techniques for the diagnosis of mediastinal masses are considered an excellent alternative to mediastinoscopy. TBNA is a safe and efficacy method to obtain tissue from anterior mediastinum. EUS FNA permits to obtain tissue for diagnosis from posterior and lower mediastinum with a good accuracy.
AIMS&METHODS: To evaluate the overall accuracy of TBNA and EUS FBNA performed as a single-time combined approach in the diagnosis of mediastinal masses.
RESULTS: 42 patients with mediastinal masses of uncertain diagnosis were submitted to TBNA and EUS FNA in one time combined approach under deep sedation in order to obtain tissue samples for cytological diagnosis. Cytology examination in ThinPrep was made by an expert pathologist no in site. In case of negativity or insufficient material patients underwent mediastinoscopy.
CONCLUSION: 31 out of 42 patients had a final diagnosis with the combined technique (27 lung cancer, 4 lymph- nodal metastasis by extra -thoracic cancer, 1 mesothelioma). 3 of 11 ''negative'' patients underwent mediastinoscopy that confirmed the absence of malignancy. The accuracy of lung cancer and extrathoracic metastasis diagnosis was respectively 84,8% and 77,7%. Overall accuracy of the combined approach was 83,3%. No complications occurred.
REFERENCES:
1. The combination of TBNA (when Endoscopic Bronchial Ultrasound is not available) and EUS FNA leads to a high rate of accuracy in the diagnosis of mediastinal masses, and the one-time approach has an important clinical impact on the diagnostic process of the disease
Disclosure of Interest: None Declared
Keywords: EUS FNA, Mediastinal masses

P1319 ULTRASONOGRAPHY AND PERIANAL INVOLVEMENT IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: INTRODUCTION: Ano-rectal ultrasonography (AR-EUS) is a simple and well tolerated method with a high diagnostic accuracy in the evaluation of perianal complications in the Inflammatory Bowel Disease (IBD).
AIMS&METHODS: AIM: Characterization of ano-rectal ultrasonography findings in patients with IBD. METHODS: We analyzed 236 patients with IBD with confirmed or suspected perianal involvement who were submitted to a US/EUS-AR in the period between January 2000 and December 2012. Demographic, clinical and ultrasonographic data were collected.
RESULTS: RESULTS: 398 US/EUS-AR were performed to 236 patients with IBD. Baseline characteristics: 220 patients with Crohn Disease (CD) and 16 with ulcerative colitis (UC). Average number of EUS-AR/patient: 1.69 (+-1.2). Female sex: 56%CD, 66%UC. Duration of IBD: 12.65 yrs in CD and 14.32 yrs in UC. Duration of perianal disease: 7.49 yrs in CD, 6.28 yrs in UC. AR-EUS was normal in 7.7% (n=17) patients with CD and in 18% (n=3) with UC. Disease localization of CD (Montreal Classification): L1=27.4%, L2=32.6%, L3=40%. CD Behavior (Montreal Classification): B1 44.5%, B2 31%, B3 24.5%. Previous perianal surgery: n=178. Medical treatment: Antibiotic 87%, Azathioprine/6MP 68%, MTX 11%, Biologic 45%. AR-EUS findings in UC: Intersphincteric fistula: n=7, transphincteric fistula: n=4, suprasphincteric fistula : n=3, anovaginal fistula: n=1, perianal abscesses: n=4, eco-structural changes: n=2. AR-EUS findings in CD: Fistulas: n=270 (Superficial=5, Intersphincteric: n=125,Transsphincteric: n=108, Supraspincteric: n=65, anovaginal: n=12, rectovaginal: n=3, anourethral: n=2), Abscesses: n=84, eco-structural changes: n=82, Internal anal sphincter lacerations: n=50, External anal sphincter lacerations: n=8, Anal fissure: n=24, Anal stenosis: n=3.
CONCLUSION: CONCLUSIONS: Most ultrasonography findings in patients with IBD represent supurative complications, although we have also find a high prevalence of echostructural changes and sphinteric lacerations, most due to prolonged supurative processes and surgical complications. AR-EUS plays a major role in the evaluation of the IBD patient with perianal involvement.
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Disclosure of Interest: None Declared
Keywords: Inflammatory Bowel Diseases, Perianal Fistulas, ultrasonography

P1320 EUS ELASTOGRAPHY STRAIN RATIO IN DIFFERENTIATION OF PANCREATIC MASSES: CROATIAN EXPERIENCE

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INTRODUCTION: EUS elastography has been proven as a promising method in differentiation of pancreatic tumors from the inflammatory masses, reducing the need for fine needle aspiration puncture[1]. Both quantitative elastography methods (strain ratio and histogram) show numeric values of tissue stiffnes. Technical details of the methods are described elsewhere[2,3].
AIMS&METHODS: Aims: to evaluate the diagnostic value of the strain ratio measurement in patients with the focal pancreatic masses, and to determine the cut–off value between inflammmatory focal changes and pancreatic cancer.
Methods: total of 149 patients were examined, 105 with focal pancreatic mases and 44 controls. Patients with history of chronic pancreatitis or presence of pancretic cysts were excluded. Strain values were recorded using Pentax EUS probe FG 38 UX (Pentax, Hamburg, Germany) in combination with hardware and software by Hitachi (Hitachi 8500, Hitachi medical systems). Tissue stifness were measured in the regions of interest before final diagnosis was achieved. Numerically expressed strain ratio between the mass and surrounding pancreatic tissue was automatically calculated by machine software. Finally patients with focal masses were divided in two groups after the diagnosis is established: pancreatic cancer group with positive cytology or histology after surgery (58 patients) and focal pancreatitis group with negative cytology and follow up after 3 and 6 months (47 patients).
RESULTS:

		Pancreatic cancer		
		Yes	No	
Strain ratio	Indicative ≥7.59	True positive 58/58	False positive 5/91	Positive predictive value 92% (87%>92%)
	Non indicative <7.59	False negative 0/58	True negative 86/91	Negative predictive value 100% (96%>100%)
		Sensitivity 100% (94%>100%)	Specificity 95% (91%>95%)	

CONCLUSION: Statistical analysis of our results showed that strain ratio with a cut-off value of 7.59 reaches 100% sensitivity and 95 % specificity in the differentiation of the patients with pancreatic cancer from the patients with the inflammatory pancreatic masses. These data are comparable with the results of other authors[2,4]. Future multicentric studies are needed, including comparison of strain ratio and histogram on the same groups of patients.
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Disclosure of Interest: None Declared
Keywords: elastography, EUS, strain ratio

P1321 THE COMBINATION OF CONVENTIONAL ENDOSCOPIC AND ENDOSCOPIC ULTRASONOGRAPHIC FINDINGS CAN EFFICIENTLY PREDICT INVASION DEPTH OF EARLY GASTRIC CANCER.

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INTRODUCTION: With development of endoscopic intervention for early gastric cancer (EGC), pre-therapeutic diagnosis of the invasion depth (T-staging) has become increasingly important. Recently some studies reported conventional endoscopy (CE) is comparable to endoscopic ultrasonography (EUS) for T-staging of EGC. However, for certain group of EGC, EUS would have additional diagnostic value because it directly provide tomographic image.
AIMS&METHODS: The aim of this study is to establish a diagnostic system for T-staging of EGC by combinating CE and EUS. A total of 233 consecutive EGC patients from April 2007 to March 2012 were included in this study. All patients underwent both CE and EUS for T-staging before treatment at Osaka University Hospital. Using CE, the criteria of massive submucosal invasion was defined as meeting at least one of following findings: 1) irregular surface, 2) submucosal tumor-like marginal prominence, 3) fusion of convergent folds in case of a lesion with fold convergence. Using EUS, massive submucosal invasion was defined as obvious irregular narrowing or budding into the sonographic layer 3. Three experienced endoscopists retrospectively reviewed the endoscopic imaging and made a diagnosis based on the criteria mentioned above. Diagnostic accuracy and inter-observer agreement was compared between CE and EUS.
RESULTS: According to pathological findings, 197 (85%) were mucosal and 36 (15%) were massively invading cancers. Overall accuracy ranged 71 to 79% in CE and 72 to 82% in EUS, respectively. There was no significant difference of diagnostic yield between CE and EUS. CE revealed fair inter-observer agreement ($\kappa = 0.56$ - 0.61). Kappa value of CE was higher than EUS ($\kappa = 0.47$ - 0.53). When diagnosed as mucosal cancer by CE, about 90% was predicted invasion depth accurately. On the other hand, when diagnosed as submucosal cancer by CE, 70% of pathological mucosal cancer was over-estimated invasion depth. EUS salvaged about 60% of these over-diagnosed cancers. Defining mucosal cancer as being diagnosed as mucosal cancer by either CE or EUS, diagnostic accuracy of combination of both modalities was more than 80% and significantly higher than CE alone ($p < 0.0001$, McNemar's test).
CONCLUSION: Using our simple diagnostic criteria, CE accurately picked up mucosal cancer with fair inter-observer agreements. However, CE over-estimates invasion depth of more than half of mucosal cancer, and EUS is useful in salvaging these lesions.
Disclosure of Interest: None Declared
Keywords: Diagnosis, Early gastric cancer, EUS

P1322 ESTIMATION OF THE MALIGNANT POTENTIAL OF GASTROINTESTINAL STROMAL TUMORS: THE VALUE OF CONTRAST-ENHANCED POWER DOPPLER EUS

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INTRODUCTION: The most important issue concerning Gastrointestinal stromal tumor (GIST) is that it is difficult to predict its prognosis. So far, the most important prognostic factors are tumor size, mitotic counts, metastasis to other sites and invasion. However, those factors are not sufficient to predict the malignant potential of such tumors because metastasis to other site sometimes occurs even when the tumor size is less than 5cm or the mitotic count is low. Recently, contrast agents for ultrasonography such as Sonazoid® have been introduced for routine clinical use. The contrast-enhanced power Doppler EUS (CE-PD EUS) with Sonazoid® permits evaluation of the intratumoral vascularity. The purpose of the present study was to evaluate whether vascularity is related to the diagnosis of submucosal tumors (SMTs) and to the malignant grade of the GISTs.
AIMS&METHODS: Eighty-four patients with SMTs were included in the present study. Tumors were observed in a real-time fashion of CE-PD EUS after the injection of Sonazoid® (0.015ml/kg). The vascular patterns were compared with tumor size, histological diagnosis and clinical findings such as metastasis.
RESULTS: The CE-PD EUS images of the SMTs were classified into 3 types according to the blood flow area of the tumors. The image pattern "Abscent" represented no vessels flowing inside of the tumor or only a few vessels around of the tumor, and "Poor" represented vessels flowing only in the peripheral part of the tumor, and "Rich" represented abundant vessels flowing from the periphery to the central part of the tumor. The details of esophagus SMTs were 18 leiomyomas, 2 lipomas and 1cyst. All SMTs were classified as "Abscent" image pattern. The details of stomach SMTs were 31 GISTs, 7 lipomas, 6 cysts, 5 leiomyomas, 1 glomus tumor, 2 schwannomas. GISTs were classified as "Poor" or "Rich" image patterns. In addition, malignant GISTs that diagnosed by histological findings or had metastasis were "Rich" pattern. And benign GIST that diagnosed by histological findings and had no metastasis were "Poor" pattern. The SMTs located in duodenum were 3 GISTs, 6 cysts, 1 lipoma, 1 paraganglioma. GISTs were classified as "Rich" image patterns. According to the CE-PD EUS images, GISTs were classified as "Poor" and the others as "Rich". Based on the final diagnosis, all tumors with "Poor" images were determined to be benign GISTs, and the rest tumors except one with "Rich" images were determined to be malignant GISTs.
CONCLUSION: It was indicated that the malignant GISTs had rich vascularity and the estimation of vascularity by CE-PD EUS offers additional and higher quality information on the malignant potency of GISTs than a histological diagnosis.
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Disclosure of Interest: None Declared
Keywords: EUS, GIST

P1323 SERVE A JUICE PRIOR TO ENDOSCOPIC ULTRASOUND TO REVEAL THE CONCEALED DETAILS OF PANCREAS

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INTRODUCTION: Endoscopic ultrasound is useful to visualize pancreas. Sometimespancreatic ductal details are not fully appreciable during EUS. Secretin issecreted by intestinal epithelial cells and stimulates exocrine pancreas to producepancreatic juice causing temporary dilatation of pancreatic duct. Secretin isexpensive limiting clinical utility. The orange-lemon juice stimulates exocrinepancreas nearly similar to intravenous secretin.
AIMS&METHODS: ***Aim:*** To evaluate usefulness oforange-lemon juice prior to EUS for better visualization of pancreatic ductalchanges.
Methods: Prospective observational study. Patients with pancreaticdiseases including recurrent acute pancreatitis (RAP), chronic pancreatitis (CP)and pancreatic space occupying lesions (SOL's) and controls were enrolled. EUSwas done, pancreatic changes including ductal changes and the diameter ofpancreatic duct at a fixed point was noted. 200 ml of orange- lemon juice wasserved and EUS repeated after1 hour.
RESULTS: ***Results:*** Of 24 cases, 10 were RAP, 6 wereCP, 2 were pancreatic SOL's and 6 were controls. Mean diameter of MPD was2.092±1.912 mm and post juice increased to 3.108±2.29 mm. ($p < 0.001$). Onsub group analysis, the MPD increased from 1.26±0.21 mm to 1.84±0.33 mmin RAP ($p < 0.001$), 4.63±2.48 to 6.53±2.15 in CP ($p=0.002$). Side brancheswere better appreciated in 13/24(54.2%). In a case more number of intraductalstones appreciated. Diagnosis of incomplete divisum was made in a case afterjuice.
CONCLUSION: ***Conclusions:*** Orange- lemon juice facilitated EUS of pancreas increases thepancreatic ductal diameter significantly and is useful in better appreciation ofpancreatic ductal changes.
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Disclosure of Interest: None Declared
Keywords: Endosonography, pancreas

P1324 STUDY OF CHARACTERISTICS OF ESOPHAGEAL STRICTURES ON ENDOSCOPIC ULTRASOUND

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INTRODUCTION: Endosonography helps in delineating the wall pattern of the esophagus. The nature and impact of EUS characteristics of corrosive strictures is not known.
AIMS&METHODS: Aim: To study endoscopic ultrasound features of esophageal strictures of corrosive and non-corrosive etiologies. To study the influence of EUS characteristics on the response to endoscopic dilatation.
Methods: Forty patients of esophageal strictures undergoing endoscopic dilatation were studied. Patients were dilated periodically with 15mm as end point. Need for repeat dilatation after achieving diameter of 15mm was classified as recurrence. All these patients were subjected to EUS(Pentax,Japan) after achieving dilatation to 15mm. On EUS maximal wall thickness, length of stricture, layered pattern of the wall (preserved or lost) was studied. The nature of the EUS characteristics of corrosive and non-corrosive strictures were compared. The role of these characteristics in predicting recurrence was assessed
RESULTS: 40 patients(19males) were analyzed. The etiology of strictures was corrosive in 17 and non-corrosive in 21(peptic(n=9), post radiotherapy (n=8) anastomotic (n=4) or due to drugs (n=2)). Mean age of study group was 48.5 years(36.4 years in corrosive group and 53 years in non-corrosive group). Mean number of dilatations to reach diameter 15mm was 5.5±3.9 in corrosive group and 1.9±0.9 in peptic group ($p=0.051$). The mean length of stricture in peptic group was 3.6+1.9 cm and in the peptic group it was 2.7+1.6cm ($p=0.177$). Differentiation of layered pattern of esophagus was lost in 13(85%)patients in corrosive group and 2(15%)patients in peptic group. Additional findings noted were tuberculous mediastinal lymphadenopathy in one and recurrence of tumor in 2 patients. Recurrence of symptoms occurred in 63% patients. Loss of layered pattern on EUS (85%vs.15%) was associated with higher recurrence($p=0.05$). The mean thickness of the esophagus was unable to predict (5.1+1.3mm vs. 5.2+2.7mm)($p=0.896$).
CONCLUSION: Patients with corrosive strictures had a loss of normal esophageal layered pattern on EUS in contrast to non-corrosive strictures. Loss of layered pattern predicted higher recurrence rates.
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Disclosure of Interest: None Declared
Keywords: endosonography, strictures

P1325 QUANTITATIVE ASSESSMENT OF TUMOUR PERFUSION OF COLORECTAL CANCER PATIENTS BY USING CONTRAST-ENHANCED ENDOSCOPIC ULTRASONOGRAPHY: A FEASIBILITY STUDY

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INTRODUCTION: Contrast enhanced endoscopic ultrasonography (CE-EUS) is a high resolution technique enabling minimally invasive assessment of tumour perfusion. Despite recent technology advancements, the use of CE-EUS in the evaluation of colorectal cancer (CRC) has not been previously reported.
AIMS&METHODS: Therefore the aim of our study was to evaluate tumour vascularity in CRC by using CE-EUS and time intensity curve analysis in correlation with pathology parameters of angiogenesis. We included 35 patients with CRC that were examined by low mechanical index CE-EUS prior to any therapy, using 4.8 ml of Sonovue (*Bracco, Italy*) administered in bolus injection as contrast agent. Time intensity curve (TIC) parameters were determined by offline analysis of recorded video sequences with specific software. Immunohistochemical assessment of tumour vascularisation included microvascular density calculation using CD31 and CD105 specific staining, which was available for 18 of the patients.
RESULTS: Most tumours were well vascularized at CE-EUS examination, demonstrating either homogenous uptake of the contrast agent or inhomogeneous enhancement, with stronger peripheral uptake and avascular areas towards the intestinal lumen. The mean values (± SD) for TIC parameters were: 10.08 ± 3.85 s for arrival time (AT), 24.03 ± 10.94 s for time to peak (TTP), 41.43 ± 19.24 a.u. for peak intensity (PI) and 5477.45 ± 2922.68 a.u.*s for the area under the curve (AUC). An inverse correlation was noted between AT and CD31 MVD, but without reaching statistical significance (*Spearman* $r = -0.55$, $p = 0.1328$) and also between TIC parameters Imax and AUC and lymph nodes involvement ($r = -0.439$, $p = 0.0683$).
CONCLUSION: CE-EUS using low mechanical index examination and TIC analysis is feasible for the assessment of intratumoral perfusion in colorectal cancer. Further studies on larger groups of patients are necessary to improve the examination technique and define its role in the evaluation of CRC patients.
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Disclosure of Interest: None Declared
Keywords: angiogenesis, colorectal cancer, contrast-enhanced endoscopic ultrasonography, immunohistochemistry

P1326 ENDOSCOPIC ULTRASONOGRAPHIC STUDY OF SUBEPITHELIAL TUMORS – WHEN WE ARE SURPRISED WITH SIGNIFICANT PANCREATIC ALTERATIONS

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INTRODUCTION: Pancreatic disease is often misdiagnosed, not only by the nonspecific or scarce symptoms, but also by the difficulty in assessing the gland on routine tests such as abdominal ultrasound. Endoscopic ultrasonography (EUS) allows a detailed evaluation of the pancreas and, even when performed by other information, can be an opportunity to detect pancreatic disease so far unsuspected.
AIMS&METHODS: Objective: To evaluate the frequency of significant pancreatic alterations (SPA) in patients undergoing EUS for the study of subepithelial tumors (SETs) of the upper gastrointestinal tract (UGIT).
Material and Methods: Retrospective analysis of the EUS performed to study UGIT-SETs in our department, between 2009 and 2013. Patients with pancreatic-biliary pathology and neuroendocrine tumors of the gastrointestinal wall were excluded. Demographic, clinical and echoendoscopic (with SETs and SPA characterization) data were collected.
RESULTS: A total of 304 EUS were carried off to study UGIT-SETs. Significant alterations in the pancreas was detected in 3.3% (ten individuals), seven of which men, with a mean age of 63.9 years (47-78). Solid lesions were diagnosed in three individuals, cystic in three and significant changes in the echostructure of the gland in four. We conducted fine needle aspiration (FNA) in three patients, having diagnosed one adenocarcinoma, one neuroendocrine tumor and a mucinous cyst. Both patients with neoplastic disease underwent surgery. Patients with pancreatic echostructural changes were evaluated according to the Rosemont's criteria: two presented aspects suggestive of chronic pancreatitis, one indeterminate for chronic pancreatitis. Patients with small dimension lesions, FNA was not performed, remain under follow-up.
CONCLUSION: This study suggests an important role of endoscopic ultrasound in the early diagnosis of pancreatic lesions. In our sample, significant pancreatic alterations were diagnosed in 3.2% of patients undergoing endoscopic ultrasound to study sub-epithelial tumors of the upper gastrointestinal tract, 0.99% of neoplastic etiology.
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Disclosure of Interest: None Declared
Keywords: EUS, EUS FNA, pancreatic disease, subepithelial tumors

P1327 ENDOSCOPIC ULTRASONOGRAPHY GUIDED PUNCTURE: DIAGNOSTIC VALIDITY IN SOLID PANCREATIC LESIONS

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INTRODUCTION: Fine needle aspiration biopsy guided by endoscopic ultrasound (EE-FNA) in pancreatic lesions overcomes some limitations of traditional puncture methods. However, there is no consensus regarding its usefulness and impact in resectable solid lesions.
AIMS&METHODS: Aim: Evaluation of diagnostic value and safety of EE-FNA in solid pancreatic lesions. Methods:Retrospective study of EE-FNA of solid pancreatic lesions performed between 2007 and 2011. The final diagnosis was obtained by: pathological examination of the surgical specimen, unequivocal cito and/or histology result of EE-FNA and by clinical and/or imaging follow-up. In diagnostic validity calculation, the results were considered suspicious malignant (true or false positives), and the samples insufficient for diagnosis were considered as true or false negatives.
RESULTS: There were 58 EE-PAAF and 53 patients, 27 were male and mean age was 59.6 ± 15.3 (24-81 years). The lesions were located mainly in the pancreatic head (72.5%), performing an average of 1.97 ± 0.95 passages (1-4). The average lesion size was 3.9 ± 1.5 cm. In the anatomo-pathological analysis: 17.2% of samples had no conclusive diagnosis (13.8% insufficient for diagnosis, 3.4% suspicious for malignancy), 60.3% positive for malignancy (including 44.8% ductal adenocarcinoma, 12.1% neuroendocrine tumors, and 3,4% mucinous tumors). It was not possible to get follow-up data of three patients. False negative rate was 9% and false positive rate was 1.8%. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were 87.8%, 92.9%, 97.3%, 72.2% and 89.1%, respectively. Accuracy of repetitive punctures in patients with a first negative result was 66.7%. There were no major complications.
CONCLUSION: EE-FNA has a high diagnostic value in solid pancreatic lesions. The presence of inflammatory perilesional, changes can increase the false positive or negative results.
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Disclosure of Interest: None Declared
Keywords: Endoscopic ultrasonography, solid pancreatic lesions

P1328 ENDOSONOGRAPHY IN THE DIAGNOSIS AND MANAGEMENT OF GISTS IN THE UPPER GASTROINTESTINAL TRACT – PRELIMINARY RESULTS

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INTRODUCTION: Assessing the role of endosonography (EUS) in diagnosis and management of stromal tumors in the upper GI
AIMS&METHODS: For the period November 2011- March 2013 seventeen patients with submucosal lesions of the upper GI tract were evaluated in our centre (seven patients were female (41.2%), 10 patients were male (58.8%) at mean age 58±11). The anatomic sites of the lesions were as follows: esophagus in 4 patients (23.5%), stomach in 9 patients (52.9%) and duodenum in 4 patients (23.5%). All the patients had upper endoscopy findings of submucosal polypoid lesions with medium size of 31.53 ± 13.4 mm, some with surface ulceration. All patients were evaluated by linear endoscopic ultrasonography (EUS).
RESULTS: Endoscopic ultrasound evaluation revealed tumors originating from muscularis propria, and EUS diagnosis of gastrointestinal stromal tumors (GISTs) was assumed in all patients. EUS-FNA (EUS – guided fine needle aspiration) was performed in two of them, but obtained material was not enough for final diagnosis in both cases. Based on EUS features of tumors' malignant potential (size of lesion > 30mm, heterogeneity, cystic regions), tumor location and complications as uncontrolled bleeding, nine patients (53%) were treated in surgery. The rest of the patients (47%) underwent endoscopy treatment (conventional polypectomy, submucosal dissection, biliary stenting in a case with multiple liver metastases). No significant complications were present in both groups. Histology and immunohistochemistry analysis confirmed c-kit: CD 117 positive GIST in 82.4% of patients, correlating with preliminary EUS diagnosis. In 17.6% of cases EUS diagnosis was not confirmed.
CONCLUSION: Endoscopic ultrasonography is a reliable method for evaluation of gastrointestinal stromal tumors. EUS features of the stromal tumors (size, heterogeneity, borders, depth etc.) can predict their malignant potential and define GIST's management.
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Disclosure of Interest: None Declared
Keywords: endosonography, stromal tumors

P1329 DOES FLEXIBLE SPECTRAL IMAGING COLOUR ENHANCEMENT (FICE) COMPARED TO WHITE LIGHT IMPROVE DETECTION OF SMALL BOWEL LESIONS DURING CAPSULE ENDOSCOPY?

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INTRODUCTION: Flexible spectral imaging colour enhancement (FICE) (Fujifilm, Saitama, Japan) reprocesses capsule endoscopic white light (WL) images producing virtual ones at specific optical wavelengths. The aim of this study was to examine the effect of FICE compared to WL on small bowel lesion detection during capsule endoscopy

AIMS&METHODS: Video clips of selected small bowel lesions were organised into 5 categories (angioectasias, ulcers, polyps, bleeding and 'normal') and viewed in 5 modes: WL, FICE-1, 2 and 3 and BM (blue-mode). In total, 25 video clips were examined in randomised order by 13 observers blinded to the content of each clip
RESULTS: There was a significant difference ($p<0.001$) between the 5 modes when all lesions were examined together. Sensitivity was highest for FICE-2 (+17% higher than WL). There was a significant difference in outcome between modes with angioectasias alone ($p<0.001$). FICE-2 had the highest sensitivity (+21% higher than WL). Differences between modes were observed for ulcers. Again, FICE-2 had the highest sensitivity value (+35% higher than WL). The positive predictive value (PPV) between different modes was then compared. There was no overall difference in PPV between the 5 modes when lesions were combined. Differences between modes were observed for angioectasias alone in that FICE-1, 2 & 3 and BM had a significantly lower PPV than WL ($p<0.008$). The number of false positives (NFPs) was significantly higher for FICE-1, 2 & 3 and BM compared to WL when all lesions were combined ($p<0.001$). The highest NFPs was observed for FICE-2 (2.9 times higher than WL). There were significant differences between modes for angioectasias alone ($p<0.001$): NFPs was greatest for FICE-2 (2.2 times higher than WL). A similar picture was observed for bleeding, with higher NFPs for FICE-1 & 2 and BM ($p<0.05$). FICE-3 had the highest NFPs for ulcers (over 3 times higher than WL) ($p<0.001$). For 'normal', FICE-2 had the highest NFPs (almost 5 times higher than WL) ($p<0.001$)
CONCLUSION: Our results suggest that while the sensitivity of specific FICE modes (particularly FICE-2) is higher than WL for SB lesions such as angioectasias and ulcers, FICE is associated with a lower PPV and higher false positive rate due to a tendency to overcall lesions when used in isolation. Applying FICE to interrogate uncertain lesions after WL detection may be a more appropriate use for this technology
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Keywords: capsule endoscopy, FICE, Small Bowel, small bowel lesion

P1330 SEGMENTAL GASTROINTESTINAL TRANSIT TIMES ASSESSED BY AMBULATORY TRACKING OF THREE ELECTRONIC MAGNETIC CAPSULES

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INTRODUCTION: Monitoring of transit abnormalities is important to the management of patients with gastrointestinal (GI) motility disorders. We present a novel ambulatory telemetric capsule system (3D-Transit) designed to evaluate total and segmental GI transit times (GITT) and GI contractile activity.
AIMS&METHODS: The aim of this study was to test the *in vivo* performance of the 3D-Transit (Motilis Medica SA) system. 3D-Transit is consisting of ingestible electronic capsules, an extracorporeal portable detector containing 4 sensors, and visualization software. The electromagnetic field emitted by each capsule is converted into space-time coordinates, relative to the distance and angular orientation of each capsule in relation to the sensors. Changes in position and orientation of the capsules reflect GI contractile activity and dynamic progression. Certain stereotypical movements of the capsule, allied to simultaneous changes in contraction frequencies are used for determining the entry into different gut segments. Twenty healthy volunteers (10 females, median age 32 (range 24-53); median BMI 22.7), with no history or current symptoms of GI disease, ingested three capsules (C1 – C3) at standardised times on consecutive days: C1 and C3 were ingested in the morning of days 1 and 2, and C2 was ingested in the evening on day 1. The subjects also had standardised meals, but were allowed to perform most of their normal daily activities.
RESULTS: The 3D-Transit system was well tolerated and the 3 capsules could be tracked simultaneously. Total and segmental GITT were obtained for all subjects. Median transit times (IQR) for C1 were: Total GITT 29 h (24-34), gastric emptying (GE) 4 h (3-4), small intestinal transit time (SITT) 5 h (4-6) and colorectal transit time (CRTT) 20 h (15-26). However, due to slower transit during the night, all values for C2, aside from CRTT, were longer than for C1: Total GITT 37 h (35-39; P=0.04), GE 7 h (4-8; P= 0.0005), SITT 8 h (5-12; P=0.04), and CRTT 21 h (17-25; P=0.53). Day-to-day variation (difference/mean) between C1 and C3 was 34% for GITT, 45% for GE, 47% for SITT, and 58% for CRTT.
CONCLUSION: The 3D-Transit system provides a safe and comprehensive evaluation of segmental GI transit in ambulatory subjects. Significant diurnal variations in gastric and small intestinal transit times indicate that timing of capsule intake must be standardised. However, day-to-day variation of transit times may be substantial. Nevertheless, the 3D-Transit system holds great promise for the future study of GI function in both health and disease.
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Keywords: Colorectal transit time, Gastric emptying, Gastriontestinal motility, Gastrointestinal transit time, Small Intestinal transit time

P1331 A NOVEL TARGETED (LIMITED RADIATION) CT PROTOCOL PREDICTS SAFE CAPSULE ENDOSCOPY (CE) AFTER RETENTION OF THE AGILE PATENCY DEVICE.

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INTRODUCTION: Capsule endoscopy (CE) is considered safe if the collapsible Agile patency device (Given Imaging Ltd) exits the patients within 30 hrs of ingestion as determined by the absence of a radiofrequency signal from the tag in the device. However, this fails to occur in this timeframe in up to 57%. These patients conventionally undergo plain abdominal X ray (AXR) to localise the device but half are further subjected to fluoroscopy, gastrograffin enemas or CT to clarify whether or not small bowel retention of the device has occurred[1]. This approach is organisationally difficult as it requires at least two further tests requiring expert interpretation including further intervention, irradiation and delays.
AIMS&METHODS: A novel protocol involving a single visit scout film and targeted (limited slice, low radiation exposure) CT to locate the patency device if it had not exited the patient at 30hrs was established, implemented prospectively and outcomes reviewed of consecutive studies between April 2010 – Sept 2012.
RESULTS: Calculated radiation exposures for the scout film, AXR and limited CT (mean of 18x5mm slices) were: 0.16mSv, 0.4mSv and between 0.8-1.4mSv respectively. Of 400 patients (including 102 patients known to have Crohn's disease), an absent radiofrequency signal denoted safe passage of the Agile device in 216 patients (54%). One patient could not swallow the capsule but all 215 remaining patients (100%) underwent CE without retention. Of184 patients with a positive signal undergoing the protocol, 172 (93.5%) were reported as having a patent small bowel (two patients on the basis of a scout film showing no patency device and 170 targeted CT scans identifying it in the colon). CE was performed without retention in 171 (99.4%) of these patients: one patient had a capsule retention after a targeted CT scan was incorrectly interpreted as showing the patency device immediately distal to an ileocolic anastamosis in a patient with Crohn's disease. In 12 patients in whom CT identified the device in the small bowel, further luminal radiology identified strictures in 7 (58%) and none proceeded to CE. Only one of the remaining five patients with normal small bowel radiology underwent CE, which was normal.
CONCLUSION: This is the largest series reporting outcomes of patency capsule small bowel assessment, following which further imaging was needed in as many as 46%. An absent radiofrequency signal predicted safe CE in all patients. Scout film and targeted CT offers a single visit, low radiation method to locate the Agile device and predicted safe CE in 99.4% of patients.
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Disclosure of Interest: None Declared
Keywords: Capsule Endoscopy, Crohn's disease, Small Bowel

P1332 EMERGENCY VIDEO CAPSULE ENDOSCOPY IN PATIENTS WITH ACUTE GASTROINTESTINAL BLEEDING

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INTRODUCTION: Obscure gastrointestinal bleeding is a main indication for video capsule endoscopy. Its use in the emergency setting of acute gastrointestinal bleeding has been rarely analysed yet.
AIMS&METHODS: In this prospective study patients with clinical signs of upper/mid gastrointestinal bleeding (melena, dark or maroon-coloured stool) and hemodynamic instability and/or drop of haemoglobin ≥2g/dl/d and/or need of transfusion ≥2 red blood packed cells/d were included. If gastroscopy did not show the source of bleeding 0.5 l of PEG-solution and the capsule were placed endoscopically into the duodenum followed by drinking of 4l PEG-solution. Capsule recording was stopped after the capsule had reached the colon. The capsule-video was immediately analysed and depending on its result patients received further diagnostics or treatment.
RESULTS: 70 patients have been included in this study yet. In 55/70 patients (79%) gastroscopy showed the source of bleeding. The remaining 15/70 patients (21%) received an emergency video capsule endoscopy. 14/15 of these patients (93%) showed a complete examination of the small bowel. In 11/15 patients (73%) the source of bleeding was detected by capsule endoscopy (9/11 small bowel, 2/11 Caecum). In 2/15 patients the source of bleeding was detected by the subsequent colonoscopy, in 2/15 patients only after repeated gastroscopy.
CONCLUSION: In patients with signs of acute upper/mid gastrointestinal bleeding and negative gastroscopy emergency video capsule endoscopy is useful for the immediate detection of the bleeding site and allows guiding further therapy.
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Disclosure of Interest: None Declared
Keywords: emergency intervention, gastrointestinal bleeding, video capsule

P1333 THE DIAGNOSTIC VALUE IN PAEDIATRIC SMALL BOWEL ASSESSMENT BY WIRELESS CAPSULE ENDOSCOPY: A TERTIARY CENTRE EXPERIENCE

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INTRODUCTION: Wireless capsule endoscopy (WCE) provides a method to assess small bowel pathology by filling the endoscopic gap between push-enteroscopy and ileocolonoscopy. The aim of this study was to assess the diagnostic value, tolerance and safety of WCE in paediatric patients referred to our unit.
AIMS&METHODS: This is a retrospective review of the WCE studies (PillCam SB, Given Imaging) that were performed during a 5.5-year period (May 2007-October 2012). Indications were confirmed/suspected IBD (n=114, 39%), obscure/occult GI bleeding (n=36, 12%), GI polyps syndromes/tumors (Peutz-Jegher's S., angiodysplasias, blue rubber bleb syndrome) (n=16, 5%), protein losing enteropathy(PLE) (n=15, 5%), recurrent abdominal pain (n=26, 9%), eosinophilic gastrointestinal disease (n=19, 7%), non-GI conditions with significant gut manifestations (autoimmune diseases, bone marrow transplantation, immunodeficiencies) (n=15, 5%) and other (coeliac disease, diarrhoea, failure to thrive etc.) (n=47, 16%).
RESULTS: 291 children (140 male, median age 10.8 years (range: 6.5 months to 19.0 years) swallowed 102 capsules(35%), 188 were placed endoscopically into the duodenum under
General anaesthesia using an acorn-like device (n= 179)/"Roth net". 72 patients (25%) were under the age of 8 years. In 220 cases (76%) the WCE was seen in the coecum at end of recording (8 hours). The swallowed capsule did not leave the stomach in 6 patients.2 patients retained the capsule, only one needing surgical removal of TI stricture with a normal contrast study pre WCE. Positive findings were observed in 184 (63%) of the studies of which 101 (34%) were diagnostic in terms of either establishing the diagnosis or altering the therapeutic approach of the patient. The diagnostic yield is highest in PLE (80%), polyposis syndromes/tumors (68%), Crohn's disease (39%) and bleeding (27%).
CONCLUSION: Our experience - which is based on the largest cohort of paediatric patients and the youngest child undergoing WCE - demonstrates that with careful selection of patients, WCE is a useful and safe diagnostic modality in children with suspected small-bowel diseases.
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Keywords: inflamatory bowel disease, intestinal lymphangiectasia, paediatric, polyposis syndrome, wireless capsule endoscopy

P1334 SMALL BOWEL CAPSULE ENDOSCOPY FOR ASSESSING EARLY POSTOPERATIVE RECURRENCE OF CROHN'S DISEASE: CORRELATION WITH THE ENDOSCOPIC SCORE AT 6 AND 12 MONTHS IN A PROSPECTIVE STUDY

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INTRODUCTION: The role of Small Bowel Capsule Endoscopy (SBCE) for assessing early CD recurrence is undefined.
AIMS&METHODS: In a prospective longitudinal study, we aimed to compare the usefulness of SBCE for assessing early postoperative recurrence of CD, when using ileocolonoscopy (IC) as gold standard. We also aimed to assess whether SBCE visualizes the proximal small bowel (SB) lesions not detected by standard techniques and the interobserver agreement. From Febr. 2011 all consecutive patients (pts) undergoing ileo-colonic resection for CD were enrolled. Clinical assessment (CDAI) was performed at 3,6,12 months (mos). Recurrence was assessed by IC within 6mos (T6) and at 12mos (T12)(Rutgeerts' score:recurrence $\geq$1). Small Intestine Contrast Ultrasonography (SICUS) was performed at T6 followed, within 4wks, by SBCE in pts with no stenosis. CD lesions visualized by SBCE were blindly graded by 2 gastroenterologists (score 0-3, recurrence$\geq$1;Buchman AJG 2004). Results were expressed as median and range. Statistical analysis: Student's T test.
RESULTS: A total of 26 pts (17M, age 36, range 19-74) were enrolled. SBCE was not performed in 15 pts, due to strictures (n=3), impact risk (n=3), low compliance to perform SBCE (n=7) or IC (n=2). At T6, among the 11 pts performing all the 3 procedures, 1 showed clinical recurrence (CDAI > 150) and 9 endoscopic recurrence (grades: 1:n=2; 2:n=4; 3:n=3). At T6, findings compatible with recurrence were detected by SICUS in 7 (7TP;2TN;2FN) and by SBCE in 10 pts (both observers: grade 3:n=10; grade 0:n=1; 9TP,1TN,1FP). In 4/11 pts, SBCE showed multiple aphtoid ulcers in the proximal SB not detected by standard imaging. No SBCE retention and a 100% interobserver agreement was observed. At 12mos, 8/11 pts already performed IC, with recurrence graded in 6 (score: 2:n=4; 3:n=1; 0:n=1). When the analysis was restricted to the 6 pts already performing both SBCE and IC at T6 and IC at T12, clinical recurrence was observed in 1 pt at T6 and in 2 pts at T12. The SBCE score at T6 was not correlated with the endoscopic score of recurrence at T6 (p=0.26; r=0.53). Differently, the SBCE score at T6 was significantly correlated with the endoscopic score of recurrence at T12 (p=0.011; r=0.91).
CONCLUSION: Early after surgery for CD, SBCE may visualize superficial lesions of the proximal SB not detected by standard techniques. A significant correlation was observed between the severity of CD lesions assessed by SBCE early after surgery and the endoscopic score of recurrence at 1 year.
Disclosure of Interest: None Declared
Keywords: Clinical recurrence, crohn's disease, Endoscopic recurrence, Postoperative recurrence, small bowel capsule endoscopy

P1335 PROKINETICS IN VIDEO CAPSULE ENDOSCOPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: About 20% of patients undergoing video capsule endoscopy (VCE) fails to complete the examination. This review assessed if prokinetics can result in an improved VCE completion rate, gastric transit time, and small bowel transit time.
AIMS&METHODS: A search of randomized trials until November 2012 was obtained, using MEDLINE and PubMed databases, and the Cochrane Central Register of Controlled Trials. The keywords used were 'video capsule endoscopy' and 'prokinetics'. Randomized controlled trials comparing prokinetics with placebo or no intervention were included. Each study was appraised by two independent reviewers using the Jadad Score. Meta-analysis was performed using the forest plot review. For outcome measures where forest plot was not feasible, a narrative review was done.
RESULTS: Two RCTs on erythromycin and five on metoclopramide involving 485 patients were included in the study. Metoclopramide improves VCE completion rate when compared to control (OR 1.93 [1.22, 3.06], p = 0.005), but not erythromycin (OR 1.13 [0.38, 3.33], p = 0.83). The two studies on erythromycin reported conflicting results with regards to gastric transit time. On the other hand, four out of the five studies on metoclopramide demonstrated significant improvement of gastric transit times among patients given metoclopramide. Metoclopramide and erythromycin were noted to have no effects on small bowel transit time.
CONCLUSION: Metoclopramide may improve VCE completion rate. Such trend was not observed in erythromycin. However, due to moderate heterogeneity, more research is needed to confirm the benefit of giving metoclopramide in VCE.
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Keywords: capsule endoscopy, erythromycin, metoclopramide, Prokinetics

P1336 FINDINGS AND LONG TERM OUTCOMES FOR PATIENTS FOLLOWING VIDEO CAPSULE ENDOSCOPY TO INVESTIGATE IRON DEFICIENCY ANAEMIA

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INTRODUCTION: It is unclear whether there is a benefit in performing capsule endoscopy (CE) in all patients with iron deficiency anaemia (IDA) after negative upper and lower GI endoscopy. British Society of Gastroenterology (BSG) guidelines suggest that CE should be reserved for patients with rapidly recurring anaemia, transfusion dependent anaemia and when there are symptoms to suggest small bowel disease. There is little information about long term outcomes in patients who have undergone CE to investigate IDA.
AIMS&METHODS: This retrospective study analysed findings and long term outcome of 115 patients (median age of 68, 56% female) investigated for IDA by CE after negative upper and lower GI endoscopy between April 2005 and December 2011.
RESULTS: 62 patients (54%) had positive findings on CE. 51 patients (44%) had small bowel pathology: active bleeding (8), angiodysplasia (17), small intestinal erosions and ulcers (21), tumour (3), small bowel mucosal atrophy (2). Six patients had gastric pathology (active bleeding, erosions or gastric antral vascular ectasia). Four patients had colonic pathology (active bleeding or angiodysplasia). There were follow up data for up to six years and the findings at CE resulted in active treatment of the underlying pathology in 16 patients (14% of total cohort). For the remaining 46 patients with positive findings, symptomatic treatment with iron replacement therapy was sufficient. Positive CE findings were detected in 41 of 80 (51%) patients whose anaemia resolved after iron therapy or treatment of underlying pathology versus 21 of 35 (60%) patients with refractory or recurrent anaemia.
For 53 patients with negative CE subsequent follow up revealed a cause in six: Meckel's diverticulum, angiodysplasia, ulcerative colitis, coeliac disease, pernicious anaemia and endometrial cancer. The other patients with negative CE were successfully treated symptomatically with iron replacement therapy.
CONCLUSION: There were relevant findings in over 50% of patients undergoing CE to investigate unexplained IDA and a significant number of these were actively treated. Selection for performing CE based on the presence of recurrent or refractory anaemia did not improve diagnostic outcome.
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Keywords: Anaemia, iron deficiency

P1337 FRENCH MUTICENTRIC EXPERIENCE OF COLON CAPSULE ENDOSCOPY IN REAL PRACTICE : PRIMARY RESULTS OF THE COLON CAPSULE ENDOSCOPY OBSERVATORY "ONECC"

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INTRODUCTION: Most colon capsule endoscopy (CCE) studies are from expert centers following a research protocol. Very few data are available regarding colon capsule performance in usual clinical practice. Colon capsule endoscopy has been implemented in France through a national observatory (ONECC) directed by the French Society of Digestive Endoscopy (SFED) and the French Private Gastroenterology Association (CREGG). The aim of this observatory is to evaluate the feasibility of colon capsule use in general practice and in specific indications.
AIMS&METHODS: Capsule was available for 161 users in 116 centers. Physicians were included in the observatory after accepting a national chart. Indications for capsule were : i) failure or ii) contra-indication to colonoscopy, or iii) well informed refusal of colonoscopy. All users accepted to fill in an e-CRF including indication for colonoscopy and for CCE, preparation (on a 4 level scale : excellent, good, fair, bad), results of CCE, indication for colonoscopy, and one year follow-up including the result of a possible secondary colonoscopy.
RESULTS: Two years after initiation of the observatory, 662 CCE has been registered with 585 e-CRF filled. The indication for CCE was identified in 97.3 % of CRF and corresponded to on third each of the 3 accepted above indications. CCE detected polyps in 253 pts (44 %), with significant polyps in 125 (28.0 %). Significant polyps were detected in 20.4, 23.1 and 14.5 % of patients with an indication for CCE of failure, contraindication, and refusal of colonoscopy respectively. Preparation were performed with classical PEG (4 liters) in 313 pts (50.7 %), with 2 l PEG and sodium ascorbat (PEG/SA) in 133 (21.5 %), with a different preparation in 171 (17.7 %). Preparation results were excellent/good in 79 %, 80 % and 81 % of patients with 4 l PEG, 2 l PEG/SA, and other preparations respectively. Quality of preparation did not impact on the rate of significant polyps (18.5 % of patients with excellent/good versus 22 % of those with fair/bad preparation). The mean colon capsule reading time was of 46 mn. Results of secondary colonoscopy are awaited from the one year follow-up data.
CONCLUSION: Preliminary experience of a national colon capsule endoscopy network and observatory shows the feasibility in real clinical practice, the excellent respect of nationally validated indications for CCE, a 28 % yield of significant polyps, and a satisfying preparation result with different preparation regimens

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Keywords: capsule endoscopy, colon

P1338 IS UPPER AND LOWER ENDOSCOPY TO BE REPETEAD BEFORE PERFORMING CAPSULE ENDOSCOPY IN PATIENTS REFERRED TO TERTIALY CENTER FOR OBSCURE GASTROINTESTINAL BLEEDING ?

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INTRODUCTION: CE rapidly became in the last ten years first line examination after negative upper and lower GI endoscopy for obscure gastrointestinal bleeding. Approximately two thirds of patients undergoing capsule endoscopy (CE) for obscure GI bleeding (OGIB) will have an abnormality found in the small bowel. Despite this, many other patients that underwent CE for OGIB, had the source of their blood loss only in the stomach or the colon
AIMS&METHODS: To evaluate the indication to repeat a new complete endoscopic work-up in subjects related to a tertiary center for obscure bleeding before CE.
A review was made of a prospective database of 637 out of 1008 consecutive patients undergoing capsule endoscopy for obscure GI bleeding at our tertiary center.
RESULTS: One hundred seventy nine patients out of 637 (28.1%) had lesions in the upper or lower digestive tract (stomach, duodenum or proximal colon) without small bowel lesions. Specifically, 138 out of 637 (21.6%) patients had lesions in the upper digestive tract as the probable cause of the bleeding missed by esophagogastroduodenoscopy: 11 gastric angiodysplasias; 13 gastric antral vascular ectasia (GAVE), 1 gastric cancer, 1 gastric peri-anastomotic cancer in B-II gastric resection, 3 gastric ulcers and 3 cases of multiple gastroduodenal erosions. Forty one out of 637 (9.5%) patients had lesions in lower gastrointestinal tract missed at previous colonoscopies. In particular, 24 angiodysplasias, 8 ulcers/erosions, 8 active bleeding without a clear source, 2 cecal carcinoma, 1 diverticular disease and 3 cases of erosive colitis. The identification of these lesions was aided by the suspected blood indicator. All patients underwent endoscopic therapy or surgery for their non-small-bowel lesions.
CONCLUSION: About 30% of patients submitted to CE for obscure bleeding had missed lesions in upper or lower GI tract. The reasons why these lesions have been missed are unclear. In this setting a cost analysis evaluation could be warranted in order to understand if it could be "economically" more appropriate to repeat a conventional endoscopic work up before CE.

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P1339 DOES BOWEL PREPARATION IMPROVE SMALL BOWEL IMAGE QUALITY AND READER CONFIDENCE LEVELS WHEN EXCLUDING SIGNIFICANT FINDINGS AT CAPSULE ENDOSCOPY?

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INTRODUCTION: Capsule endoscopy (CE) is the first line of investigation for examining the small bowel (SB) mucosa. While standard preparation (SP) is more convenient for patients, mucosal visibility may deteriorate within the distal SB. Recent meta-analyses suggest that bowel-cleansing agents (BCA) can improve small bowel image quality (IQ). The influence of BCA compared to SP on reader confidence levels (RCL) when excluding clinically significant findings (CSF) has not been examined.
AIMS&METHODS: To compare RCL when excluding CSF and assessing IQ during reading following SP or BCA prior to CE.
We performed a retrospective analysis of SB capsule images of 100 consecutive patients who underwent a complete CE examination at our institution from Oct 2012 - Mar 2013. Patients had SP (intake of clear liquids for 18 hours & 12 hour fasting prior to the procedure without BCA) or BCA (2l of polyethylene glycol (PEG) or magnesium citrate (MC) in addition to SP). The participants' demographic and clinical data were collected and SB transit time (SBTT) calculated. A four-point scale was used to assess IQ (grade 1 = $<80\%$ of mucosa visible $\pm$ excessive debris $\pm$ severely reduced brightness to grade 4 = $\geq$ 90% of mucosa visible $\pm$ mild debris$\pm$ mildly reduced brightness). The SBTT was divided into quartiles (Q1-Q4) by time and the IQ score, RCL and number of CSF for each quartile were determined by a gastroenterologist experienced in CE, blinded to the preparation. Procedures were examined in randomised order.
RESULTS: 49 (49%) patients had SP (group A) while 51 (51%) had one of the BCA (39% had PEG and 61% had MC, group B). There was no significant difference in age (p=0.87), sex (p=0.57), indication (p=0.25) and SBTT (group A: 264±112 mins vs. group B: 233±100mins, p=0.14) between groups. For each quartile, IQ scores were significantly higher for group B than A except in Q1 (Q1: 3.7±0.7 vs 3.5±0.6, p=0.06; Q2: 3.6±0.5 vs 3.1±0.6, $p<0.0001$; Q3: 3.2±0.6 vs 2.3±0.7, $p<0.0001$; Q4: 2.8±0.5 vs 1.9±0.8, $p<0.0001$). There was no difference in detection of CSF between group A and B (41% vs 51%, p=0.33, respectively). For each quartile, RCL for excluding significant findings were significantly higher for group B than A except in Q1 (Q1: 100% vs 96%, p=0.06; Q2: 96% vs 73%, $p<0.0001$; Q3: 88% vs 33%, $p<0.0001$; Q4: 77% vs 20%, $p<0.0001$). There was no significant difference in IQ or RCL between PEG or MC. 3 procedures (all SP) were considered unsatisfactory for IQ with recommendation to repeat after BCA.
CONCLUSION: BCA pre-CE significantly improve small bowel IQ and RCL when excluding CSF. BCA appear to be an important parameter for optimising the qualitive aspects of CE reading.

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Disclosure of Interest: None Declared
Keywords: Bowel cleansing agents, Capsule Endoscopy, Image quality, Reader confidence

P1340 HOW USEFUL IS SMALL BOWEL CAPSULE ENDOSCOPY FOR THE INVESTIGATION OF IRON DEFICIENCY ANAEMIA AND CAN CLINICAL PHENOTYPE PREDICTS FINDINGS?

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INTRODUCTION: Small bowel capsule endoscopy (SBCE) is a useful diagnostic tool for the evaluation of small bowel (SB) disorders. Iron deficiency anaemia (IDA) is one of the most common indications for SBCE.
AIMS&METHODS: Our aim was to evaluate the presence or absence of influencing factors that predispose to a positive or negative SBCE in an IDA setting. We carried out a retrospective review of our tertiary referral centre's SBCE procedures performed between Oct 2011-Mar 2013. All non-vegan patients with a history of IDA with complete SB examinations were included. Demographic and clinical data were collected and SBCE reports evaluated.
RESULTS: A total of 250 patients had SBCE for IDA (56% females, mean age 61yrs). Clinically significant SB findings (CSFs) were found in 32% (79/250) of patients, including vascular lesions (33%), inflammatory lesions (33%), coeliac (13%), active bleeding/altered blood (15%) and others (5%). 193 (77%) patients presented with IDA alone (Group A), while the remaining patients had an additional history of overt GI bleeding (OGB) (Group B). No significant difference for CSFs between groups was identified (30% vs. 37% for Group A and B, respectively, p=0.34). 112 (45%) patients had a history of usage of pro-haemorrhagic medication (aspirin, clopidogrel, NSAIDS or warfarin). CSFs were significantly higher in patients who had taken these medications than those who had not (42% vs. 22%, p=0.0017). The difference was even more significant when considering OGB as an additional risk factor (40% vs. 20% respectively, p=0.0009). In order to identify a CSF for patients without a history of pro-

haemorrhagic medication use or OGB, an additional 8 SBCE's were needed (number needed to treat = 9). 120 patients (48%) had no GI cause for IDA found (negative gastroscopy, colonoscopy and SBCE). 56 patients had a SB radiological investigation (RI) (CT enterography/MR enterography/barium follow through) prior to SBCE. CSFs were found in 9% and 95% of patients, respectively, who had an RI vs. SBCE ($p < 0.0001$).

CONCLUSION: SBCE is a useful diagnostic tool for the investigation of IDA when a history of OGB, antiplatelet therapy, NSAIDs or warfarin usage is present, since the likelihood of CSFs is significantly increased. The benefit of SBCE in IDA when these factors are absent is potentially debatable. Almost half of patients with IDA have a normal GI tract, indicating that non-GI causes need to be considered, while RI is of low value for the investigation of IDA.

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Disclosure of Interest: None Declared

Keywords: Capsule endoscopy, Iron Deficiency Anaemia, Overt bleeding

P1341 COMPARISON OF VIDEO CAPSULE ENDOSCOPY AND FAECAL CALPROTECTIN AS DIAGNOSTIC TOOLS IN PATIENTS WITH ABDOMINAL SYMPTOMS SUGGESTIVE OF SMALL BOWEL CROHN'S DISEASE

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INTRODUCTION: Faecal calprotectin (FC) is a widely agreed non-invasive marker of gastrointestinal (GI) inflammation. There is a dearth of evidence comparing FC levels to findings of video capsule endoscopy (VCE). Particularly, there is a scarcity of data investigating the suitability of FC as a screening tool to select individuals requiring VCE in the investigation of patients with abdominal symptoms suggestive of small bowel Crohn's Disease (CD). We studied the correlation between FC levels and VCE findings and analysed their combined utility in detecting small bowel CD.

AIMS&METHODS: We retrospectively compared VCE findings and FC levels in adult patients referred with GI symptoms (abdominal pain, diarrhoea, weight loss, anaemia and bloating). Where multiple FC were measured, the value closest to the date of VCE was used. History of non-steroidal anti-inflammatory drugs, aspirin, clopidogrel and prednisolone use in the six weeks prior to VCE were identified. Findings of relevant investigations (GI endoscopy, MRI, CT, coeliac serology, histology, haemoglobin, C-reactive protein and platelet count) were also reviewed. FC and VCE findings were analysed against final diagnosis.

RESULTS: 62 patients were studied (21 males, mean age 41). One study was excluded due to capsule retention in the stomach. The median time between FC and VCE was 92 days. 29 had a normal FC ($\leq$60mg/g, mean 18mg/g) of whom 5 had abnormal VCE findings (17.2%). 32 had a raised FC ($>$60mg/g, mean 263mg/g) of whom 7 had abnormal VCE findings (21.9%). Two-tailed Fisher's exact test revealed that the difference between the two groups was not statistically significant ($p=0.75$).

In the normal FC/abnormal VCE group 3 out of 5 patients were diagnosed with CD (one had CD confirmed on colonoscopy). One case had mild patchy terminal ileal (TI) erythema. Another had non-specific TI aphthous ulcers. In the raised FC/abnormal VCE group 3 out of 7 patients were diagnosed with CD (all 3 had active CD on colonoscopy). Two cases had jejunal apthous ulcers, and there was one case each of mild patchy TI erythema and TI apthous ulcers. Two-tailed Fisher's exact test revealed that the difference between these two groups was also not statistically significant ($p=1$).

CONCLUSION: The utility of FC to diagnose small bowel CD remains debatable, with previous studies showing differing outcomes.[1,2] In our cohort, FC levels did not reliably correlate with VCE findings. The correlation of FC level with the diagnosis of small bowel CD by VCE was also not statistically significant. Based on our findings, the decision to proceed to VCE should be based on clinical symptoms, and not on abnormal FC levels.

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Keywords: capsule endoscopy, crohn's disease, Faecal Calprotectin (FC), video capsule

P1342 THE EFFICIENCY OF COLONIC CAPSULE ENDOSCOPY IN DETECTION OF COLORECTAL POLYPS AND CANCERS COMPARING TO COLONOSCOPY: MULTICENTER, PROSPECTIVE CROSSES OVER STUDY

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INTRODUCTION: To assess the feasibility, accuracy, and safety of second-generation of colon capsule (CCE-2) in screening population in a head-to-head comparison with colonoscopy. The interim analysis of results is presented.

AIMS&METHODS: In this multicentre (four centers) feasibility study, second generation of colon capsule endoscopy has been prospectively compared with conventional colonoscopy (standard method) in a cohort of colorectal neoplasia low risk patients (screening population). The efficiency in detection of colorectal polyps ($\geq$ 6 mm and $\geq$ 10 mm) and cancers has been assessed. Colonoscopy was independently performed within 10 hours after capsule ingestion. Capsule-positive but colonoscopy-negative cases were counted as false positive. Level of bowel preparation, rate of adverse events and patient preferences were assessed.

RESULTS: From January 2011 until April 2013, 139 patients (mean age 60 years) has been enrolled; data from 119 patients has been analyzed. The capsule has been excreted within 10 hours after ingestion and before the end of the battery lifetime in 85% of patients. Patient rate for polyps of any size was 50%; in 49% of these patients adenomas have been found. The capsule sensitivity for detection of patients with polyps of size $\geq$ 6mmas 67 % and for those with polyps $\geq$ 10mm it was also 67 %, with specificities of 64 % and 93 %, respectively. One invasive carcinoma has been detected by CCE-2 and colonoscopy. For all lesions, the sensitivity of capsule endoscopy was higher in patients with good or excellent bowel preparation (on four grade scale). Overall colon cleanliness for capsule endoscopy has been adequate in 81% of patients. Four mild adverse events related to both procedures have been reported. 56% of patients would prefer CCE-2 as a primary screening method.

CONCLUSION: Second generation of colon capsule has appeared to have a high sensitivity for the detection of clinically relevant colorectal neoplasia in screening population. This method might be considered as an adequate tool for colorectal cancer screening.

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Disclosure of Interest: None Declared

Keywords: colon cancer screening, colon capsule endoscopy, colonoscopy

P1343 EFFICACY OF DOUBLE PIGTAIL STENT AS CONSERVATIVE TREATMENT OF GRADE B PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY WITH PANCREATOGASTRIC ANASTOMOSIS.

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INTRODUCTION: Despite improvements in surgical techniques and immediate postoperative care, the morbidity rate associated with pancreatoduodenectomy (PD) is still high - notably due to a pancreatic fistula (PF) rate of between 2% and 30%. Pancreatic fistula is diagnosed when the amylase level in abdominal drain fluid on postoperative day 3 is three times higher than the normal serum amylase level. Grade B PF is defined as a symptomatic pancreatic fistula and requires a specific combination of radiologically guided external drainage, drug treatment and nutritional support. This treatment is effective but requires prolonged hospitalization and the maintenance of external drainage. The objective of the present study was to evaluate the feasibility and efficacy of endoscopically guided internal drainage (with a double-pigtail stent (DPS)) of grade B PF after PD with pancreatogastric anastomosis.

AIMS&METHODS: Between January 2008 and October 2011, all patients presenting grade B PF after endoscopic PD (n=6) were included in the study. The PF was diagnosed according to the International Study Group on Pancreatic Fistula's criteria. Endoscopic treatment was standardized with a DPS and a nasocystic drain. The primary efficacy endpoint was the feasibility and efficacy of DPS placement. Secondary endpoints included data on the PF, the DPS placement procedure and the long-term outcome.

RESULTS: Endoscopic DPS placement was achieved in all patients and there were no complications. The median (range) time to onset of PF after PD was 14 days (3–18). The median time to DPS placement after discovery of the PF was 6 days (0–37). Closure of the external PF was obtained 7 days (median) after implementation of DPS (range: 7–26). The median time to external drain removal was 7 days (7–27) after DPS placement. Median time to oral refeeding was achieved 7 days after the DPS placement for all patients. The median time to DPS removal was 60 days (49–120). The median length of hospital stay after DPS placement was 10 days (7–28). During a median follow-up period of 21 months (16-49), there was no recurrence of peri-anastomotic collection after removal of the DPS.

CONCLUSION: Endoscopic treatment of grade B PF after PD appears to be effective and safe and is associated with shorter hospitalization. These encouraging results need to be confirmed in a larger series.

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Disclosure of Interest: None Declared

Keywords: double-pigtail stent, endoscopically guided drainage, pancreatic fistula, pancreatoduodenectomy, pancreatogastric anastomosis.

P1344 STENT AND VENT: DUAL TRANSGASTRIC AND TRANSPAPILLARY APPROACH FOR THE MANAGEMENT OF PANCREATIC PSEUDOCYSTS WITH PANCREATIC DUCT DISRUPTION

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INTRODUCTION: Management of pancreatic pseudocysts remains controversial and complex with few studies describing a multimodality approach. With increasing experience with endoscopic techniques, surgical intervention is reducing. We review outcomes of single-operator management of symptomatic pseudocysts within a single centre with an interest in pancreatic endotherapy.

AIMS&METHODS: Retrospective analysis of patients with symptomatic pseudocysts between 2002-2012 was performed. All patients underwent ERCP,

sphincterotomy and bile duct trawl. Where possible, pancreatic duct stenting with papillotomy was performed, bridging any rupture or stricture with a 7 or 10Fr straight Teflon stent. All patients underwent curvilinear endoscopic ultrasound (EUS)-guided drainage of the pseudocyst if the cyst wall bordered the gastric wall. The cyst was punctured with a 19G needle, followed by diathermy or balloon dilatation of the tract using a 10F cystotome (Wilson-Cook, Ireland) or Hurricane RX biliary dilatation balloon catheter (Boston Scientific, Ireland). A 10F double pigtail Teflon stent was then inserted. Where not possible, alternative methods of drainage were explored. Pancreatic stents were retrieved within 8 weeks. Cystgastrostomy stents were removed once patients were convalescent and resolution of cyst confirmed. Successful therapy was defined as resolution of pseudocyst.

RESULTS: 24 patients were referred (17 male) with a median age of 44yrs (21-81). Notes were available for 22. 1 was lost to follow up and 2 (8%) did not survive due to multiorgan failure. Of the remaining 19, 18 (95%) demonstrated resolution of pseudocyst. At ERCP, 20 (91%) had successful pancreatic duct cannulation and transpapillary stenting and 19 of these (95%) demonstrated complete healing of pancreatic duct disruption. Complications included stent migration (2), fracture (1). At EUS, 16 pseudocysts (73%) were amenable to drainage. The remainder underwent percutaneous drainage (2), surgery (1), or resolved spontaneously (3). Of those drained via cystgastrostomy, 1 patient died and 1 was lost to follow up. 12 (86%) of the remaining cysts resolved. 1 required surgical drainage due to early migration of stent and 1 has persistent small pseudocyst. Complications included bleeding (1), stent migration (2), gastric perforation (1). Cystgastrostomy stents were retrieved at a median of 9.5 months (2-36).

CONCLUSION: Dual transgastric and transpapillary management of symptomatic pancreatic pseudocysts with pancreatic duct disruption is safe and effective. Our data suggests that this approach can limit surgical intervention, potentially reducing associated morbidity and mortality.

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Disclosure of Interest: None Declared

Keywords: cystgastrostomy, pancreas, pseudocyst, stenting of main pancreatic duct (MPD)

P1345 DIFFICULTIES ENCOUNTERED FOR REMOVING FULLY COVERED SELF-EXPANDING METAL STENTS INSERTED IN BENIGN BILIARY CONDITIONS

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INTRODUCTION: Use of fully-covered self expanding metal stents (FCSEMSs) for benign biliary conditions is increasing. They have been used to manage benign biliary strictures, refractory leaks, to tamponade biliary sphincterotomy bleeding, to close biliary sphincterotomy perforations, to remove uncovered SEMS with a stent-in-stent technique and even for complex and difficult common bile duct stones. Apart from the larger diameter they offered compared with a single plastic stent, easy extraction is of major importance when they are used in such benign conditions. Metal materials, although fully covered with different coating membranes, appear to produce always some tissue hyperplasia that can lead to bury the FCSEMSs duodenal end, without excluding some inward migration.

AIMS&METHODS: Retrospective, single centre study of problems found at FCSEMSs removal when the duodenal stent part was buried in the papillary area.

RESULTS: Extraction of biliary Wallflex FCSEMSs (Boston Scientific, Natick, USA) inserted for bening biliary conditions was attempted in 49 ocassions. The duodenal stent part was found buried in nine (9/49 or 18.4%). In three occasions, a guidewire was passed beyond the stent and a 15 mm dilation balloon inflated inside the stent followed by pulling manoeuvres. All FCSEMSs were removed but in one circumstance the duodenoscope slipped back and perforated the duodenum. This patient was operated but unfortunally died postoperatively. The technique was abandoned and replaced in the remaining six occasions for pulling from inside the stent with a 15 mm common bile duct stones extraction balloon. ERCPs were time-consuming but successful. All FCSEMSs could be removed. Nine buried stents had remained for a mean of 301 days (range 240-360) whereas 40 visible stents in the papillary area and easily extracted with a foreign bodies forceps, were in place for a mean of 145.6 days (range 30-273) ($p < 0.05$).

CONCLUSION: In this single centre and relatively small series, all FCSEMSs inserted for benign conditions could be removed. Brusque manoeuvres have to be avoided. In our opinion and in a certain subjective figure, FCSEMSs should not remain in place for more than six months if an easy extraction wants to be anticipated.

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Disclosure of Interest: None Declared

Keywords: benign biliary conditions, fully covered self-expandable metal stent

P1346 EFFICACY AND LIMITATION OF PANCREATIC STENTING FOR PATIENTS WITH CHRONIC PANCREATITIS

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INTRODUCTION: To evaluate the efficacy of pancreatic stenting in patients with chronic pancreatitis with intraductal stones as short-term stenting, and inserting ENPD at the time of stent removal.

AIMS&METHODS: From 1998 to 2013, 98 patients of chronic pancreatitis with intraductal stones were performed lithotripsy. The population consisted of 87 males and 11 females with mean age 54.8. The etiology of chronic pancreatitis was alcohol abuse in 70, idiopathic in 21, and pancreas divisum in seven. 76 patients succeeded in lithotripsy, and 67 of them remained upstream ductal dilation after lithotripsy. In the 67, we performed pancreatic stenting. 52 patients were performed through the major papilla, and 15 through the minor papilla. As short-term stenting, we inserted 10-Fr stent and removed it within 6 weeks. We also inserted 5Fr ENPD at the time of 10-Fr stent removal, and removed it in one or two days after.

RESULTS: We succeeded stenting in 79.1% (53 patients, 231 stents). Stents were advanced across the stricture of the MPD through the major papilla (39 patients, 191 stents) or minor papilla (14 patients, 40 stents). Over 6 months after stent removal, we could follow 49 patients (major papilla 36 patients, minor papilla 13) who were able to abstain from drinking alcohol. 26 patients (53.1%) presented with recurrence of intraductal stones. The patients of whom the diameter of the upstream MPD after 10-Fr stent removal was less than 7mm, were named the dilation improved group. Their recurrence rate was 41.2% (14/34 patients)(major papilla 37.0%, minor papilla 57.1%). The recurrence rate of the dilation non-improved group; the diameter of the upstream MPD 7mm and above; was 80.0% (12/15 patients) (major papilla 66.7%, minor papilla 100%). The non-improved group had a significantly higher recurrence rate. Median time to recurrence of the dilation improved group was 380 days, and significantly longer than of the non-improved group 266 days. Inserting 5Fr ENPD at the time of 10-Fr stent removal had no effect on recurrence rate of intraductal stones, but could prolong the time to recurrence on the dilation non-improved group. Median time to recurrence of the non-improved group was 199 days when we didn't insert ENPD, but 510 days when we inserted.

CONCLUSION: On the dilation improved group, we confirmed the efficacy of pancreatic stenting. And on the dilation non-improved group, inserting ENPD might prolong the time to recurrence.

Disclosure of Interest: None Declared

Keywords: chronic pancreatitis, ductal dilation proximal to a stricture of the main pancreatic duct, endoscopic pancreatic stenting, pancreatic intraductal stones

P1347 LONG TERM MANAGEMENT OF IRRETRACTABLE COMMON BILE DUCT STONES: ELECTIVE STENT EXCHANGES OR EXPECTANT APPROACH? A TERTIARY CENTRE EXPERIENCE OF 6 YEAR FOLLOW UP.

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INTRODUCTION: Long term management of difficult Common bile duct stones (CBDS) is either 'elective stent exchange' (ESE) 6-12 monthly or 'permanent stent insertion' (PSI) in selected cases with biliary stenting as sole management option.

AIMS&METHODS: The aim of our study was to evaluate the clinical outcomes of ESE and PSI for irretractable CBDS in our centre.

A retrospective review of all patients who underwent plastic stent insertion for biliary access in difficult CBDS from January 2006 to December 2011. Electronic patient records were used to gather data. Patients who had plastic stents inserted for irretractable CBDS were included in the study. Patients with biliary strictures/leak, hepato-biliary cancer and those who had metallic stents inserted during their follow up period were excluded. Patients in ESE group underwent planned exchange of biliary stents every 12 months whereas in PSI group patients had biliary stents inserted with an intention to replace only if blocked or if patients represented with biliary complications. The decision as to which group patients were in was based on individual clinician and patient preferences.

RESULTS: 674 patients underwent 1769 stent related procedures in the study period. 165 patients met the inclusion criteria among which 119 patients had temporary plastic stent insertions and subsequent duct clearance. 18 patients were identified as in PSI group and 28 in ESE group. Mean age of patients in each group was similar (ESE-Mean 84.6, range 70-95, PSI- Mean 83.1, range 57-95) but patients in PSI group had multiple co-morbidities represented by high American Society of Anaesthesiologists (ASA) score (PSI-3.0, ESE-2.7). Although number of procedures performed in PSI group were lesser than ESE group but biliary complications were significantly higher. Characteristics of each group are given in Table 1.

	ESE group	PSI group
Total number of procedures	45 (mean 1.95)	9 (Mean: 0.52)
Blocked stent	1/28 (3.5%)	9/18 (50%)
Procedure related complications	2 Minor bleeds 2 Desaturations	3 Minor bleeds 2 Desaturations 1 Bradycardia 1 pancreatitis
Ducts cleared	4 (14%)	1 (5%)
Follow up	736 months (mean 27.25 months)	603 months (mean 33.5)
Deaths (within 30 days of procedure)	2 (non-biliary)	2 (1 biliary sepsis, 1 non-biliary)

CONCLUSION: In our series, patients selected for expectant management (PSI) had higher comorbidity; 50% re-presented acutely with stent blockage. Whilst this is not a randomised comparison, it suggests that expectant management option may be suitable only for patients with limited life expectancy.
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Disclosure of Interest: None Declared
Keywords: Biliary stent, CBD stones

P1348 THE PREDICTORS OF COMPLICATIONS AND LONG-TERM OUTCOME AFTER ENDOSCOPIC TREATMENT IN PATIENTS WITH PANCREATIC PSEUDOCYSTS

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INTRODUCTION: To estimate the pancreatic pseudocysts (PP) features and technique of endoscopic drainage (ED) as potential predictors of complications and late recurrence rate (RR).
AIMS&METHODS: 94 patients with PP have been evaluated, included 20 (21.3%) after acute pancreatitis and 74 (78.7%) with chronic pancreatitis. In 83 from them (88,0%) diagnosed communication with main pancreatic duct. Multiple cysts (not more than 3 in one patient) were determined in 8 (9.0%) and septaited in 2 (2.2%) patients. Among these 20 patients underwent transpapillary ED. In 74 patients was performed transmural ED, included 30 cases with endosonography assistance. Combination of methods was used in 13 (13.8%) patients.
RESULTS: minor complications occurred in 15 (15.95%) patients. 3 (3.3%) during the procedure and 12 (13.5%) in early postoperative period): cyst leakage, stent dislocation, secondary infection and hemorrhage. All of them but two were treated endoscopically. One patient died (1.06%) from cause, not related to ED procedure.
Higher level of septic complication after ED of ''younger'' PP (8-12 weeks) was found ($p=0.089$). CR was higher after introduction of straight stents ($p=0.037$). EUS-guided drainages completely prevented bleeding.
Remote surveillance was performed in 71 patients. Cyst recurrence revealed in 8 (11.3%) cases. ''Free of relapse survival'' analysis showed better prognosis in alcohol PP vs. biliary ($p=0.01$ Cox's F-test), cystostomy balloon dilation ($p<0.001$), stents *in situ* more than 3 months. There were no recurrence in pancreatic body cysts, but 17.9% in head and 21.4% in tail cysts ($p=0.02$ and $p=0.03$). Better results were in patients with more than 2 stents (0 vs 13%) and with pseudocyst without PD communication (0 vs 11,3%).
CONCLUSION: The prevention of stent dislocation for the decreasing of CR and prophylaxis of recurrence is important. Pig-tail stent fits the best for these purposes. Balloon dilation and setting of more than 2 stents is necessary for diminishing of RR especially of pancreatic head and tail cysts in biliary pancreatitis.
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Disclosure of Interest: None Declared
Keywords: endoscopic drainage, pancreatic pseudocyst

P1349 PERCUTANEOUS AND ENDOSCOPIC TREATMENT OF BILIARY STRICTURES AFTER LIVER TRANSPLANTATION IN CHILDREN – MANAGEMENT, OUTCOME AND RISK FACTORS

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INTRODUCTION: Biliary stricutres (BS) are common complication in paediatric liver transplantation and in spite of the overall progress they remain a significant cause of graft loses.
AIMS&METHODS: We performed the retrospective chart review of 50 liver transplantations (48 patients: 29 male/19 female and 34 cadaveric/16 living - related) presenting with biliary strictures. In regard to biliary anastomosis, patients were referred to endoscopic retrograde cholangiopancreatography (ERCP) or percutaneous transhepatic biliary drainage (PTBD) with balloon dilatation and biliary stent or catheter interposition. The aim of the study was to analyze our experience in the treatment of BS after liver transplantation.
RESULTS: Anastomotic BS were diagnosed in 37 (74%) cases and multilevel in 13 (26%). Most BS developed in the first year after LTx – 32 (64%). At the moment of first non-surgical intervention 29 patients had hepaticojejunal anastomosis and 21 had choledochocholedochal anastomosis. Sixty-two ERCP procedures were performed in 21 patients (mean 2,9 per patient). They were successful in 15 (71,4%). The total median duration of ERCP treatment was 1,23 (0,72-2,43). In 34 patients 86 PTC procedures were performed (mean 2,5 per patient). PTBD was successful in 22 patients (64,7%). The interventions were complicated in 19% (ERCP) and 10% (PTBD). 8 patients underwent surgery after failed PTBD, successful in 4 cases. 9 patients were either re-transplanted or listed for ReLTx (19%). The overall good outcome of treatment without need for ReLTx was achieved in 41 (82%) patients. Non-surgical interventions were successful in 37 (74%). Median age at first percutaneous or endoscopic intervention was 13.5 years (0,9-1,9) and time from LTx to first ERCP or PTC 0,68 years (0,08-11,4). Total median follow up after transplantation was 5,6 years (1,13-16,1) and after last biliary intervention 3,72(0,6-8,3) years. The only risk factors of poor outcome were presence of multilevel BS and period of treatment before 2008.
CONCLUSION: Non-surgical approach is effective and safe in biliary strictures after liver transplantation. The majority of patients require repeatedly performed interventions. Surgical approach should be considered in selected cases with poor response to primary treatment.
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Disclosure of Interest: None Declared
Keywords: biliary commplications, ERCP, pediatrics, liver transplantation, reduced liver

P1350 ENDOSCOPIC TREATMENT OF PANCREATIC PSEUDOCYST BY USING DIABOLO STENT IN 16 PATIENTS

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INTRODUCTION: Diabolo stent, because of its wide diameter (10 or 16mm), permits either an adequate drainage of pancreatic cystic liquids towards the digestive tube or endoscopic access to the cystic cavity.
AIMS&METHODS: Between September 2011 and September 2012 we placed 24 Diabolo stents (Cousin Endosurg; Taewong medical) in 16 patients of symptomatic or complicated pancreatic pseudocysts (9 males, 7 females aged 32 to 84). Among these 16 patients, 10 patients had pancreatic pseudocysts (6 to 17cm) with clear or colored liquid. The duration of stenting was for one month in our first patient and then it was from 4 to 6 months for the rest of our group. In the second group there were 6 patients with necrotic and infected pancreatic pseudocysts after an acute pancreatitis. In this group we performed N. O.T.E.S (Natural Orifice Transluminal Endoscopic Surgery).
RESULTS: No major per procedure complications occured. Early response (<1month) in our first group of 10 patients with clear liquid pseudocysts shows significant decrease in the cyst size in 2 patients, disappearance of cyst in 7 patients and removal of the stent in 1 patient on day 18 because of direct contact of the stent with splenic vein. Intermediate response (6 months) shows spontaneous migration of the stent without cystic recurrence in 1 patient, stent in place without cystic recurrence in 5 patients and backward movement of stent without cystic recurrence in 3 patients. In our second group with infected and necrotic pseudocysts, we placed from 1 to 3 stents for each patient with early removal to perform the N.O.T.E.S for necrosectomy. In this group the early and intermediate term response was favorable in 3 patients by regression of the pseudocyst size and disappearance of the symptoms, 3 patients had to be operated on, one preciously because of rupture the pseudocyst after opacification, 2 because of inadequate endoscopic drainage with early favorable response and one unfavorable response because of sepsis and multiple organ failure.
CONCLUSION: Endoscopic treatment of pancreatic pseudocysts by placing Diabolo Stent is not a complicated procedure; in case of pseudocyst with clear liquids there is a favorable clinical and radiological early and intermediate term response. We will know about the long-term response by our patients' follow up. As to the infected and necrotic pseudocyst the Diabolo stent is theoretically interesting, easy to place and has a very low complication rate of this procedure, though the efficiency has to be determined.
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Disclosure of Interest: None Declared
Keywords: diabolo stent, pancrease, pseudocyst

P1351 A PROSPECTIVE MULTICENTER STUDY OF A FULLY-COVERED METAL STENT IN PATIENTS WITH DISTAL MALIGNANT BILIARY OBSTRUCTION: WATCH-2 STUDY.

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INTRODUCTION: We previously reported a longer time to recurrent biliary obstruction with less stent migration using a partially-covered nitinol self-expandable metallic stent (Wallflex™ Biliary RX Partially Covered Stent; Boston Scientific Corp, Natick, Mass) in a multicenter prospective study: WATCH study (Gastrointest Endosc. 2012;76:84-92). A fully-covered type of this SEMS (Wallflex™ FCSEMS) is commercially available but there is a concern about the increased risk of stent migration in FCSEMS.
AIMS&METHODS: The aim of this study is to evaluate the safety and efficacy of a new, commercially available FCSEMS. Between September 2011 and July 2012, 156 patients (64 males, a median age of 75 years old, and median survival time of 198 days) with unresectable distal malignant biliary obstruction underwent FCSEMS placement in sixteen Japanese referral centers. Data on baseline characteristics, survival, stent patency, stent-

related complications and removability were prospectively collected. Primary endpoint was recurrent biliary obstruction (RBO) and secondary endpoints were technical success rate, stent-related complications and stent removal.
RESULTS: Stent placement was technically successful in all patients. The rate of RBO was 29% (stent occlusion, 15% and stent migration, 14%). The cause of stent occlusion was biliary sludge (6%), food impaction (3%), tumor overgrowth (2%) and others (5%). Tumor ingrowth was not observed. Median cumulative time to RBO was 318 (interquartile range: 157-NA) days. Other stent-related complications included pancreatitis (6%; mild in 5% and moderate in 1%), cholecystitis (4% of 150 patients with gallbladder in situ) and cholangitis without stent occlusion (4%). Stent removal was successful without complications in all 25 attempted cases (100%) after a median of 120 (range, 3-471) days from stent placement.
CONCLUSION: Wallflex™ FCSEMS appeared comparable to PCSEMS in terms of RBO, but stent migration rate was relatively high. Endoscopic removal is easily and safely accomplished in all 25 attempted cases. (Clinical trial registration number: UMIN000007131)
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Disclosure of Interest: None Declared
Keywords: distal malignant biliary obstruction, Metal stent

P1352 RISK FACTORS FOR PANCREATITIS FOLLOWING METAL STENT PLACEMENT FOR UNRESECTABLE MALIGNANT MIDDLE-, LOWER- COMMON BILE DUCT OBSTRUCTION

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INTRODUCTION: Transpapillary metal stent (MS) placement is a useful strategy for patients with malignant biliary obstruction (MBO) but can be associated with post-procedure pancreatitis.
AIMS&METHODS: The objective of the present study was to identify risk factors for the occurrence of pancreatitis following this procedure. Eighty consecutive patients who underwent MS placement were studied. The rate of pancreatitis after MS placement and risk factors for pancreatitis were investigated. The following variables were assessed: gender; sex; etiology of MBO (pancreatic cancer vs. non-pancreatic cancer); timing of MS placement (one-step vs. two-steps or more); type of stent (covered vs. uncovered); EST; pancreatic duct injection; diameter of pancreatic body; and pancreatic duct diameter at the pancreatic body.
RESULTS: Pancreatitis after MS placement was identified in 10 of 80 patients (12.5%). In univariate analysis, the frequency of pancreatitis was significantly higher (p=0.001) in patients with non-pancreatic cancer (32.0%, 8/25) than in those with pancreatic cancer (3.6%, 2/55). Pancreatitis occurred more frequently (p=0.031) in patients whose pancreatic duct diameter at the pancreatic body was $<$3 mm (25.0%, 7/28) when compared with patients whose pancreatic duct diameter was $>$3 mm (6.1%, 3/49). Multivariate logistic regression analysis showed that the etiology of MBO (non-pancreatic cancer) was the only strong risk factor for pancreatitis (adjusted OR, 19.52; 95% CI, 2.07-184.03; p=0.009).
CONCLUSION: Non-pancreatic cancer was the only strong risk factor for pancreatitis after MS placement for MBO.
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Disclosure of Interest: None Declared
Keywords: biliary metal stent, malignant biliary obstruction, pancreatitis

P1353 INTERIM ANALYSIS OF A PILOT STUDY OF NEW COVERED METALLIC STENTS WITH A LARGE BORE SIZE (NITI-S SUPREMO-12 STENT) FOR UNRESECTABLE DISTAL BILIARY MALIGNANCIES

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INTRODUCTION: Self-expandable metallic stents (SEMSs) have a significantly longer patency than plastic tube stents because of their larger dimensions. Moreover, covered SEMSs might have longer patency than uncovered SEMSs because they can prevent tumor ingrowth through the stent mesh. However, a new concern regarding covered SEMSs is an increased risk of stent migration. Theoretically, SEMS with larger dimensions might increase patency and reduce the risk of migration. Therefore, we have invented a novel, fully covered SEMS (FCSEMS), Niti-S SUPREMO-12 (SUPREMO-12), with a diameter of 12 mm. In addition to its larger bore, its flared ends prevent migration, and the knitting structure comprises large and small cells that alternately increase and decrease the amount of radial force, such that the stent fits into the bile duct.
AIMS&METHODS: To investigate the clinical safety, efficacy, and complication rates associated with Niti-S SUPREMO-12 stent for malignant distal biliary obstructions (Clinical trial registration number: UMIN000007061). Outcome Measurements: The primary outcomes were (1) stent occlusion and dysfunction rates at 180 days after stent placement, (2) stent patency duration, (3) time to recurrent biliary obstruction (TRBO), and (4) overall stent patency and function rates; secondary outcomes included (1) the median survival time, and (2) the stent-related complication rate.
RESULTS: Thirty-eight consecutive patients were enrolled into this prospective pilot study between June 2011 and November 2012. The median observation period was 238 days (range, 13–680 days). Among the 38 patients, 12 (32%) survived. Stent dysfunction was observed in 9 patients (24%). Stent occlusion, because of food impaction, was observed in 3 patients and tumor ingrowth was observed in 2 patients; stent migration was observed in 3 patients (1 proximal and 2 distal migration). Furthermore, mild cholecystitis and mild pancreatitis developed in 1 patient. Stent patency rate and the TRBO at 6 months were 89% and 82%, respectively. Mean stent patency and TRBO were 270 ± 13 and 264 ± 16 days, respectively. Stent removal was attempted in 6 patients and was successful in all of them.
CONCLUSION: The preliminary results suggest that this stent may be safe to use, with acceptable complication rates. Randomized controlled trials with conventional FCSEMSs will be necessary for evaluating the usefulness of this stent.
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Disclosure of Interest: None Declared
Keywords: 12mm diameter, covered metallic stent, large bore size, unresectable malignant distal biliary obstructions

P1354 LONGER LENGTH TO THE STRICTURE FROM THE PAPILLA WAS RISK FACTOR FOR DYSFUNCTION OF COVERED METAL STENT IN PATIENTS WITH DISTAL MALIGNANT BILIARY OBSTRUCTION.

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INTRODUCTION: Placement of covered self-expandable metal stent (CSEMS) has been reported to be effective for palliation of distal malignant biliary obstruction. However, the risk factors for their dysfunction remained unclear.
AIMS&METHODS: The aim of this study was to identify the risk factors for dysfunction of CSEMS. One hundred forty patients (median age 66, male/female 84/56, pancreatic carcinoma/cholangiocarcinoma/others 105/17/18) who underwent CSEMS placement for distal malignant obstruction between October 2005 to April 2013 in a tertiary care center were included. Distal end of CSEMS was located in the duodenum. The median length to the stricture from the papilla was 30.8mm. Wallstent and ComVi stent were classified as the previous CSEMS group (n=35), while Wallflex and Supremo stent were the latest CSEMS group (n=105). We retrospectively examine the stent patency by using Cox proportional hazard analysis.
RESULTS: Stent dysfunction was observed in 26 (18.5%) patients. The rate of dysfunction was 42.9 and 10.8% in patients with the previous CSEMS group and the latest CSEMS group respectively. The cause of dysfunction was as follows; food impaction in 8, tumor overgrowth in 8, biliary sludge in 4, nonocclusion cholangitis in 3, and stent migration in 3. The median time to stent dysfunction was 535 days. Multivariate analysis by Cox proportional hazard model revealed that patients in the previous CSEMS group (Hazard ratio 3.36 [95%CI: 1.53-7.58], p=0.003) and with longer length to the stricture from the papilla (2.30 [1.02-5.51] p=0.045) were significant risk factors for stent dysfunction.
CONCLUSION: The latest CSEMS had longer stent patency than the previous CSEMS. The longer length to the stricture from the papilla was the significant risk factor for dysfunction of CSEMS in patients with malignant distal biliary obstruction.
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Disclosure of Interest: None Declared
Keywords: biliary strictures, COVERED SELF EXPANDING METAL STENT, distal malignant biliary obstruction

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00
SURGERY III – Poster Area

P1355 PANCREATIC CYSTIC LESIONS: COULD DIAGNOSTIC STRATEGY BE OPTIMIZED?

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INTRODUCTION: Pancreatic cystic lesions (PCL) are relatively common in our clinical practice but its diagnostic approach is complex. A correct diagnosis of the type of cystic lesion is essential to avoid unnecessary surgeries.
AIMS&METHODS: To establish diagnostic accuracy of preoperative laboratory and imaging methods when compared with gold-standard – definitive histological diagnosis following surgical resection. This was a retrospective study that included all patients submitted to surgical excision of PCL between 1998 and 2012. Clinical parameters and pre-operative diagnostic procedures were analyzed and compared with definitive histological diagnosis. Statistical analysis performed with SPSS v20.0.
RESULTS: The study included 38 patients (female–22; mean age–55.7±15.3 years). *Clinical presentation*: abdominal pain–65.8%; nausea/vomiting–36.8%; jaundice–18.4 %; diarrhea/steatorrhea–15.8%, abdominal mass–5.3%; 5 patients (13.2%) were asymptomatic. *Elevated serum tumour markers*: CA19.9–23.7%; CA125–7.8%; CA72.4–2.6%; CEA–2.6%. *Imaging methods used in the diagnosis*: abdominal ultrasound–81.6%; abdominal CT–97.4%; abdominal MRI–39.5%. *Imaging characteristics of the lesions*: average size–51±27mm; location in the head of pancreas–55.3%; 3 patients had multiple lesions. *Radiological diagnosis*: Mucinous Cystic Neoplasm (MCN)–13.2%; Intraductal Papillary Mucinous Neoplasm (IPMN)–10.5%; Pseudocyst–5.3%; Neuroendocrine tumor–2.6%; Cystadenocarcinoma–2.6%; Solid pseudopapillary neoplasm (SPN)–2.6%; Indefinite–63.2%. Endoscopic ultrasonography (EUS) evaluation was made in 14 patients, and it was complemented with fine needle aspiration (EUS-FNA) in 12. The liquid CEA was $>$192ng/ml in 3 of the 5 patients in which it was determined. *Diagnosis made by EUS* (14 patients): MCN–28.6%;

Adenocarcinoma–7.1%; Indefinite–64.3%. *Diagnosis made by EUS-FNA* (12 patients): MCN–41.7%; Cystadenocarcinoma–25%; Pseudocyst–16.7%; Serous Cystadenoma–8.3%; IPMN–8.3%. *Definitive histological diagnosis*: Serous Cystadenoma–31.6%; IPMN–23.7%; MCN–21.1%; Pseudocyst–13.2%, MCN with associated carcinoma–5.3%; SPN–2.6%; Lymphoepithelial Cyst–2.6%. *Preoperative diagnostic accuracy*: Radiological methods – 5/38 patients (13.2%); EUS – 3/14 (21.4%); EUS-FNA – 7/12 (58.3%). The false negatives of EUS-FNA were associated with the cytology and not with the determination of CEA.

CONCLUSION: Radiological methods and EUS have limited diagnostic accuracy to correctly identify the type of PCL. EUS-FNA, particularly with CEA determination, is the technique with greater sensitivity and should play a greater role in the diagnostic strategy of PCL.

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Disclosure of Interest: None Declared

Keywords: Endoscopic ultrasonography, Imaging, Pancreatic cyst

P1356 LAPAROSCOPIC RESECTION OF BENIGN LIVER CYSTS HAS A HIGH SUCCES RATE

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INTRODUCTION: Large benign liver cysts often tend to be symptomatic with the most common symptoms being pain, abdominal discomfort or nausea.

AIMS&METHODS: The aim of this study was to evaluate the outcome of laparoscopic resection of benign liver cysts.

We did a retrospective study of the records of patients who had surgery for liver cysts between December 2007 and December 2012 at our institution. In addition, patients were contacted by telephone in March 2013 with a questionnaire regarding present symptoms.

RESULTS: 31 patients underwent laparoscopic surgery for benign liver cysts (27 women, 4 men). Median age was 61 years (range 27 to 81 years). Main indication for surgery was upper abdominal pain (n= 27 (87%)) followed by abdominal discomfort (n= 11 (35%)). In 19 patients (59 %) the indication for surgery was based on the findings at CT, in 15 patients (48%) on the findings at ultrasonography, and in 4 patients (13%) both procedures were performed preoperatively. In one case (3%) MRI was the only preoperative diagnostic imaging procedure performed. The laparoscopic approach was successful in 29 patients (94%). Thus, two conversions (6%) to open surgery were necessary due to intraperitoneal adherences from previous surgery and cyst puncture(s). Mean postoperative hospital stay was one day (range 1 to 14 days). Histological evaluation revealed 29 non-neoplastic cysts (94%) and two cyst adenomas (6%). Two minor postoperative complications occurred: one patient suffered minor bleeding into the cyst cavity and one patient had bile leakage into the cyst cavity. None of these had however had need for re-operation. There was no 30-day mortality. Mean follow-up time was 28 months (range 1 to 60 months). At follow up, nine patients (28%) have had reoccurrence of cysts that had been verified by imaging procedures. In five patients (16%) the reoccurring cysts gave symptoms (i.e. pain) and all these patients were offered re-operation. However, only three had wanted this and undergone new laparoscopic operation. Three patients (10%) have had ultrasonically guided cyst puncture during follow-up, and one patient have had both surgery and external cyst puncture. Two patients were lost to follow up.

CONCLUSION: Laparoscopic resection of benign liver cysts has a high success rate in terms of pain relief and it is a safe procedure with a short postoperative hospital stay. However, some patients suffer from recurrent symptoms and need re-therapy. It is not known whether this re-occurrence of symptoms is because of recurrence of the cyst or because of development of a new one.

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Disclosure of Interest: None Declared

Keywords: Laparoscopy, liver cyst

P1357 CORRELATION BETWEEN FECAL ELASTASE-1 AND PANCREATIC VOLUME IN PATIENTS WITH PANCREATIC DISORDERS OR AFTER PANCREATIC RESECTION

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INTRODUCTION: Ideally, pancreatic function tests should allow a quantification of the amount of functioning pancreatic parenchyma. This assumption is widely accepted when considering duodenal output of pancreatic enzymes after maximal hormonal stimulation. No data are available to confirm this assumption considering the concentration of an enzyme, elastase-1 (FE-1), on a spot fecal sample, after physiologic stimulation by meals.

AIMS&METHODS: Aim of our study was to confirm the efficacy of FE-1 in the evaluation of pancreatic volume.

FE-1 and pancreatic volume were studied in patients with three different pancreatic disorders: asymptomatic chronic hyperenzymemia (CH; our control group); previous duodeno-cefalo-pancreatectomy (DCP); chronic pancreatitis (CP). These patients were studied over the last five years by both magnetic resonance and FE-1 tests, with a maximum time interval of 6 months between each other. Mean ±1 SEM are reported. ANOVA, Student's t test and the linear Pearson's test were used for statistical analysis. $P<0.05$ was accepted as the limit for significance. FE-1 was measured by an ELISA test on a spot fecal sample. Pancreatic volume was obtained using VIBE T1-depending sequences after contrast-enhanced MR.

RESULTS: We studied 154 patients (64 CH; 32 DCP; 58 CP). A significant difference was found among the three groups both for FE-1 (CH 468.6± 11.0 μg/g; DCP 83.8± 19.4; CP 285±23.6) both for pancreatic volume (CH 112.4±3.7 ml; DCP 30.5±2.7; CP 53.0±3.6) ($p<0.001$, ANOVA; $p<0.001$, Student's t test, for all contrasts). All CH had a volume >50 ml and FE-1 >200. A significant linear correlation was found between FE-1 and pancreatic volume for all patients ($r=0.655$, $p<0.001$). A correlation was confirmed considering separately DCP ($r=0.58$, $p<0.001$) and CP patients ($r= 0.34$, $p=0.009$) but not CH ($r=-0.03$; NS).

CONCLUSION: Fecal elastase-1 is well correlated with pancreatic volume, measured by magnetic resonance. The correlation is found only in patients with a reduction in residual pancreatic parenchyma, either due to chronic pancreatitis or to pancreatic resection. In patients with benign asymptomatic hyperenzymemia (our control group) no correlation could be demonstrated. The dispersion of data might be due to the spot fecal collection (rather than to total output) and to a submassimal pancreatic stimulation provided by meals.

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Disclosure of Interest: None Declared

Keywords: duodenopancreatectomy, fecal elastase, magnetic resonance imaging, pancreatic function tests, pancreatic hyperenzymemia

P1358 SIGNIFICANCE OF EN BLOC RESECTION WITH THE ANTERIOR RENAL FASCIA FOR ADENOCARCINOMA OF THE LEFT PANCREAS

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INTRODUCTION: The radical antegrade modular pancreatosplenectomy (RAMPS) has logically advantage for curative resection of the adenocarcinoma of the left pancreas. The anterior renal fascia is a key structure and resection planes should set behind this fascia. But it is difficult to find out this fascia and set appropriate plane accurately. We developed a modified technique to set the dissection plane easy and accurately.

AIMS&METHODS: Excision of the anterior surface of the IVC at the level of the 3rd portion of the duodenum is a first step to approach the posterior dissection plane behind the anterior renal fascia after clamping the splenic artery. This dissection plane proceeds along the left renal vein toward the hilum of the kidney. After that this plane proceeds cranial to the upper edge of the pancreas.

RESULTS: Between July 2007 and December 2012, 25 patients with pancreatic adenocarcinoma underwent the modified RAMPS. The mean age was 67 years, the mean tumor diameter was 35 mm, mean operating time was 385 minutes, and mean blood loss was 349 ml. No postoperative deaths occurred. Invasion to the retropancreatic tissues and lymph node metastases were detected in 17 and 13 cases, respectively. The surgical margins were histologically clear (R0 resection) in 21 patients (84%). Median survival was 29 months and 5-year overall survival rate was 45%. There are 5 patients who live over 5 years without recurrence.

CONCLUSION: This modified RAMPS has advantage for en bloc resection including the anterior renal fascia and contribute to improve the survival of the distal pancreatic carcinoma.

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Disclosure of Interest: None Declared

Keywords: anterior renal fascia, en bloc resection, modified RAMPS, pancreatic carcinoma

P1359 MAJOR HEPATIC RESECTION IN HEPATIC HYDATIDOSIS,MAJOR HEPATIC RESECTION IN HEPATIC HYDATIDOSIS

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INTRODUCTION: Ecchinococcal disease is still a serious problem in certain parts of the world, with liver as the most affected organ. Surgery remains the mainstay of treatment of hydatidosis, but the optimal surgical procedure remains unsettled

AIMS&METHODS: Objective: Safety and efficacy of major hepatic resection in multiple and giant hepatic hydatidosis.

Patients& Methods: 63 patients had hepatic hydatidosis associated with spleen, lung, and suprarenal hydatidosis were managed by major hepatic resection between April 2005 to April 2011. 43 (68%) males and 20(32%) females, age range 8-56 years. Cysts were found in the liver only in 51 (81%) patients, liver with spleen in 5 (8%), liver, spleen with lung in 2 (3.1%), liver and lung in 4 (6.3%), liver and suprarenal in one patient (1.6%).

RESULTS: Multiple cysts were found in 38 (60%) and solitary cyst in 25 (40%) with Cysts diameter ≤ 5 cm in 22 (35%), 5-10 cm in 16 (25%), and 10-38 in 25 (40%). Right hepatectomy in 24 (38%),Right trisectionectomy in 2(3.2%), right hepatectomy with Segment III in 4 (6.3%), right hepatectomy with Segment I in 2 (3.2%), left hepatectomy in 12 (19%), left lateral Sectionectomy in 6 (9.5%), left hepatectomy with Segment VI in 3 (4.8%), left lateral sectionectomy with Right posterior sectionectomy in 2 (3.2%), right hepatectomy with splenectomy in 7 (11%) and right hepatectomy with right suprarenal in one (1.6%) patient were performed. Hospital stay was 4.2 (3-13 days) There was one mortality and 12(19%) morbidities. No recurrence on follow up period (8-60 months) was observed.

CONCLUSION: : Radical procedure is safe and effective option for hepatic hydatidosis and should be performed when the entire lobe is diffusely involved by huge or multiple hydatidosis with little healthy liver tissue.

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Disclosure of Interest: None Declared

Keywords: Ecchinococcosis, Hepatic hydatidosis, Hepatic resection, Mortality, morbidity., Ecchinococcosis, Hepatic hydatidosis, Hepatic resection, Mortality, morbidity.

P1360 IS PANCREATICODUODENECTOMY FOR CANCER IN CIRRHOTIC PATIENTS REASONABLE: A CASE-CONTROL STUDY FROM THE SURGICAL FRENCH ASSOCIATION REPORT FOR PANCREATIC SURGERY 2010.

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INTRODUCTION: The pancreaticoduodenectomy (PD) is the efficient treatment to obtain long-term survival for adenocarcinoma of the pancreatic head (APH). The presence of cirrhosis is usually considered as a contraindication for surgery based on old data. The objective of this study was to evaluate the results of PD for APH in cirrhotic patients compared to non-cirrhotic

AIMS&METHODS: This was a French retrospective multicenter study in patients with APH with cirrhosis between January 2004 to March 2012. A matching in 2: 1 with patients with APH but non-cirrhotic from the Surgical French Association report 2010 was conducted among a selection of 1886 patients. The matching was performed on demographic criteria and operative data. The primary endpoint of the study was the morbidity and mortality of the PD for APH in cirrhotic patients. Secondary endpoints were operative data, morbidity specific to pancreatic surgery and cirrhosis and follow-up data

RESULTS: 32 patients were matched with 64 non-cirrhotic patients. There was 27 male (84%) with a mean age of 62.1 years. The mean percentage of weight loss was 6.5%. 68% of cirrhotic patients were Child A while the other were Child B. 35% had portal hypertension. Alcohol was the cause of cirrhosis in 60%. The overall complication rate was 84.3% vs. 40.6% ($p \leq 0.05$) with 50% vs. 22% major complication ($p \leq 0.05$). Pancreatic fistula rate was 12.5% vs. 6.2% (NS). Post-operative mortality rate was 15% vs. 4.7% (NS). In the cirrhosis group, 46.8% had post-operative ascites and 15.6% had liver failure. There was no difference in tumoral, lymph node staging and R1 resection between the two groups. Major complication rate in Child A group was 33%, with 9% of pancreatic fistula and 4.5% of post-operative mortality. Post-operative mortality of Child B cirrhosis was 40%. Access to adjuvant therapy rate was 57% in Child A, 25% in Child B and 65% in control group. Recurrence rate was 43.5% in Child A vs. 51.5% in control group. Mean overall survival was 24 months in cirrhosis group vs. 23 months in control group

CONCLUSION: The PD for adenocarcinoma of the pancreatic head in cirrhotic patients is feasible, but with an increased risk of complications not specific to pancreatic surgery, but to cirrhosis. Presence of Child B cirrhosis must consindicate surgery.

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Disclosure of Interest: None Declared
Keywords: adenocarcinoma of the pancreatic head, ascites, cirrhosis, pancreatic fistula, pancreatoduodenectomy

P1361 IMPACT OF TECHNICAL MODIFICATION OF EUS-GUIDED ENDOSCOPIC PAPILLECTOMY FOR AMPULLARY NEOPLASM ON THE RATE OF POST-RESECTION ACUTE PANCREATITIS

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INTRODUCTION: The insertion of a temporary pancreatic duct (PD) stent seems to prevent acute pancreatitis (AP) after endoscopic papillectomy (EP).
AIMS&METHODS: The aim of this study was evaluate the usefulness of a modified technique of endoscopic papillectomy (EP) is decreasing the rate of AP. Indications for EP: tumor confined to the papilla (T1) without tumor spread into the bile/pancreatic duct. EUS tumor staging was done to determine main PD (MPD) diameter before EP in all patients. After staging 14/41 patients underwent endoscopic snare papillectomy with the echoendoscope. A PD stent was placed in patients without MPD dilatation (30 and 35 mm) determined by EUS measure. 25 (group A [GA]) underwent EP without insertion of a PD stent. 16 (B-Control [GB]) underwent EP with insertion of a PD stent. The occurrence of adverse events (AEs) was compared between the groups in relation to the MPD diameter as determined by EUS.
RESULTS: 18 patients had adenomas, 12 adenocarcinomas, 4 hyperplastic lesion, 3 neuroendocrine tumor, 2 lipoma, 1 gastrointestinal stromal tumor and one hamartoma. The average size of the lesion removed in Group A and B was 18 mm (10-43) and 13 mm (5-16), respectively (p=0.04). The average MPD diameter in GA was 45 + sd (0.09) and GB 36 mm + sd (0.1) with p=0.11. AEs occurred in 43.9% (AP (10), bleeding (6), cholangitis (1) and cholecystitis (1)). There was a difference between groups A and B (36% vs. 56.2%, odds ratio [OR] 0.44, 95% [CI], 0.12 to 1.58). The frequency of early AEs in GA was lower than in GB (28% vs. 50% [OR] 0.37, 95% [CI], 0.10 – 1.34). AP occurred in 24.3%. There was significant difference between GA and GB (8% vs 50%; $p<0.001$). Late AEs occurred in 7.3%. There was no significant difference between groups (8% vs 6.2% [OR] 1.3, 95% [CI] 0.11 to 15.7). Local recurrence occurred in 9.7%.
CONCLUSION: The use of EUS before endoscopic papillectomy allows proper staging (T1) and MPD measurement. With a MPD > 36 mm and wide excision during EP obviate the need for MPD stent placement. In expert hands, complications are infrequent and can't be avoided by routine placement of a pancreatic duct stent. Further studies are needed to confirm these findings.
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Disclosure of Interest: None Declared
Keywords: Adenocarcinoma, ampullary tumor, benign biliary conditions, endosonography, PAPILECTOMY, staging

P1362 PROGRAMED EUS-GUIDED NECROSECTOMY (EUS-N) VERSUS OPEN SURGICAL TREATMENT (SUR-N) OF INFECTED WALLED OFF PANCREATIC NECROSIS (WOPN)

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INTRODUCTION: The surgical approach in patients with infected WOPN there is a significant risk of complications and mortality. This approach consists in open surgical necrosectomy (SUR-N) or video-assisted retroperitoneal debridement. An alternative treatment is an endoscopic or EUS-guided step-up approach consisting of endoscopic transluminal necrosectomy.
AIMS&METHODS: The primary endpoint of this study is to compare the results of SUR-N versus programmed EUS-N in relation to adverse events, clinical and technical success, morbidity and mortality. In this study, we assigned 52 patients with necrotizing pancreatitis and suspected or confirmed infected necrotic tissue to undergo primary open SUR-N or a programmed EUS-N with a step-up approach to treatment. The step-up approach consisted of programmed EUS-N every 7 days followed, if necessary, by open necrosectomy in case of severe adverse events.
RESULTS: The primary end point occurred in 35 of 52 (67%) assigned to open necrosectomy and in 17 of 52 patients (33%) assigned to the EUS-N step-up approach. The average hospital stay for patients undergoing EUS-N [20 (6-48d)] and SUR-N [16 (3-105d)]. The clinical insuccess rate was 11.8% vs. 37.2% (p = 0.254) for patients undergoing EUS-N and SUR-N, respectively. New-onset adverse events occurred less often in patients assigned to the EUS-N than in those assigned to SUR-N (23% vs. 54%, P=0.279). The rate of death did not differ significantly between groups (12% vs. 0%, P=0,119). Patients assigned to the EUS-N had a lower rate of new-onset diabetes (5.8% vs. 17.1%, P=0.422).
CONCLUSION: A EUS-N, as compared with open necrosectomy, reduced the rate of the adverse events composite end point of major complications among patients with necrotizing pancreatitis and infected necrotic tissue.
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Disclosure of Interest: None Declared
Keywords: Acute Pancreatitis, Debridement, Drainage, endosonography, surgery, Walled off pancreatic necrosis

P1363 PATIENT-SPECIFIC 3D ORGAN MANUFACTURING BY MULTI-MATERIAL 3D PRINTER FOR SURGICAL SIMULATION OF LIVER TRANSPLANTATION AND HEPATECTOMY

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INTRODUCTION: Our new technology of Bio-Texture Modeling by multi-material 3D printing system enabled manufacturing patient-specific 3D organ models by simultaneous jetting of different types of model materials and compounding the PVA, which is a water-soluble synthetic resin. We have used 3D personalized models of patients' organs for surgical simulation and navigation purposes. We evaluated its feasibility for liver transplantation and hepatectomy in five clinical cases.
AIMS&METHODS: Based on MDCT data, after generating its surface polygons using OsiriX application, the inkjet 3D printer created 3D liver and abdominal cavity models. This system enabled the simultaneous use of two different materials to shape and color the models in different ways, such as transparent colors or changing their firmness, textures and structures. We created life-size copies of the liver and abdomen of patients using two different kinds of plastics injected in layers, with each layer measuring 0.016 millimeters in thickness. We programed a printer to create clear models made from acrylic resins that allowed them to visualize and understand the liver's complex internal structures, such as bile duct and blood vessels or the exact location of a tumor.
Then, we printed liver models in part from polyvinyl alcohol to mimic the wetness and texture of a human liver, and to make the model a realistic stand-in for surgical practice.
RESULTS: Before a liver transplant surgery begins, we have used 3D replicas of a child's abdominal cavity and an adult-sized donor's graft liver to determine where and how to best trim. We took a knife to a 3D donor's liver replica, the models helped us figure out where to carve it. So that it would fit into the smaller space while preserving the organ's key functions, leading to a successful living-related liver transplant. For the liver cancer surgeries, the actual size transparent liver model with vessels and tumor could be manufactured and be handled. All hepatic cancers were successfully resected including multiple liver metastases. The elastic liver models were useful for surgical simulation and educational aspects.
CONCLUSION: Surgeons usually faced a dilemma before transplanting a parent's liver into a child: How exactly to trim the organ to fit the space in the child's smaller cavity while preserving its functions. We believe that the technology could help younger, less experienced surgeons practice with accurate copies before surgery.
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Disclosure of Interest: None Declared
Keywords: 3D PRINTER, liver transplantation, hepatectomy, HCC, surgical imaging, SURGICAL NAVIGTION

P1364 DISORDERS OF CARBOHYDRATE METABOLISM IN PATIENTS WITH CHRONIC PANCREATITIS BEFORE SURGERY

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INTRODUCTION: Violation of endocrine pancreatic function occurs in 30-83% of patients with chronic pancreatitis [2]. The progressive pancreas parenchyma fibrosis with inflammatory and degenerative changes leading to reduction in β-cells of islets of Langerhans and decreased insulin secretion [1]. Violation of insulin secretion may run, in the form of glucose intolerance and pancreatic diabetes [2]. According to the literature, the incidence of pancreatic diabetes is extremely difficult to establish because of the difficulty of diagnosis of chronic pancreatitis and high compensatory potential endocrine organ function [3]. Few data on the role of C-peptide in the early diagnosis of disorders endocrine pathology software tool [4].
AIMS&METHODS: Aim – examine the nature of software changes endocrine function in patients with Chronic Pancreatitis in the preoperative period.
The study is based on the analysis of patients with Chronic Pancreatitis, operated in the surgical department of the Ivano-Frankivsk Regional Clinical Hospital from 2006 to 2011. Inclusion criteria: Patients with Chronic Pancreatitis diagnosed according to the Shalimov's classification (1997), which performed surgery on the pancreas. Condition endocrine functions investigated by determination of plasma glucose, glucose tolerance and C-peptide by ELISA (normal 0.5-3.2 ng/ml).
RESULTS: Analyzed 90 patients: 72 (80%) – the operation carbohydrate metabolism was not in the 10 – (11.1%) was observed glucose intolerance, diabetes mellitus was found in 8 (8.9%) patients. In 30 пациентс investigated C-peptide. Level was normal in 21 (70%) patients, 9 (30%) – reduced, including in 4 (13.3%)

cases of diabetes occurred in 2 (6.7%) – was marked glucose intolerance and in 3 (10%) is observed violations. Attention is drawn to the general downward trend in C-peptide in the group with no carbohydrate metabolism, indicating a gradual depletion of insular apparatus of the pancreas and the possible risk of diabetes, indicating lack informative determine the glucose levels in the early diagnosis of disorders endocrine function of pancreas.

CONCLUSION: C-peptide can be considered a marker of early changes endocrine pancreas functions in Chronic Pancreatitis in conjunction with the study of glycemic profile.

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Keywords: Chronic Pancreatitis, C-peptide, endocrine pancreas functions

P1365 A PROSPECTIVE SINGLE CENTER RANDOMIZED DOUBLE-BLIND PARALLEL GROUP COMPARATIVE TRIAL TO DETERMINE THE EFFICACY OF PROPHYLACTIC SINGLE DOSE CEFAZOLIN VERSUS PLACEBO REDUCING SURGICAL SITE INFECTION IN GENERAL LAPAROSCOPIC CHOLECYSTECTOMY PATIENTS

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INTRODUCTION: Laparoscopic cholecystectomy (LC) is the safest procedure for patients who have gallbladder disease, especially gallstones(1). The average rate of surgical site infection (SSI) of LC is occured between 0.4% and 3.8%(2-6) especially in high risk patients. The prophylactic antibiotic for LC has been questioned, however, as recent meta-analyses have concluded that prophylactic antibiotics for elective laparoscopic cholecystectomies in low risk patients is not useful(7-9). Given this current controversy concerning the efficacy of prophylactic antibiotics in LC.

AIMS&METHODS: The aim of this study was to determine whether the use of prophylactic antibiotics was associated with a lower rate of surgical site infection in elective laparoscopic cholecystectomy in patients with low and high risk factors of surgical infection.

Patients who met the inclusion criteria were randomized into two double-blinded groups, one of which received an isotonic sodium chloride solution of 10 mL (group A=placebo) and the other of which was given cefazolin 1 g (group B=study drug) via slow intravenous injection 30-60 minutes before the initial skin incision. The 4-port laparoscopic cholecystectomy technique was used in all procedures. The patient risk of infections was recorded and patients were monitored at least 30 days postoperatively for development of surgical site infections.

RESULTS: A Total of 299 cholecystectomy patients were randomized (149 in group A and 150 in group B). Surgical site infection occurred in seven patients (2.34%), 5 patients (1.67%) in the placebo group and 2 patients (0.67%) in the cefazolin group, which was not a statistically significant difference (p-value=0.248). No specific risk factors for surgical site infection such as diabetes mellitus, bupivacaine injection at surgical wound, postoperative intra-abdominal drainage, American Society of Anesthesiologists class 3, age more than 60 years, liver cirrhosis, continuous prednisolone use, obesity and conversion to open cholecystectomy were identified.

CONCLUSION: A single dose of preoperative prophylactic cefazolin had no benefit in reducing the incidence of surgical site infection in laparoscopic cholecystectomy, in patients with either low risk or high risk of infections.

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Disclosure of Interest: None Declared

Keywords: Cefazolin, Laparoscopic cholecystectomy, Prophylactic antibiotics, Surgical site infection

P1366 DOES DISTAL PANCREATECTOMY WITH CELIAC AXIS RESECTION REALLY IMPROVE THE SURVIVAL OF PATIENTS WITH PANCREATIC BODY CANCER?

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INTRODUCTION: The survival impact of the distal pancreatectomy with en-bloc celiac axis resection for locally advanced pancreatic body cancer remains controversial. The aim of this study was to analyze the role of distal pancreatectomy with celiac axis resection (DP-CAR) for carcinoma of body of the pancreas.

AIMS&METHODS: Between 2002 and 2012, a total of 14 patients underwent DP-CAR, whereas 52 underwent standard distal pancreatectomy (DP). The indication of DP-CAR is a) tumor invasion of either celiac axis or common hepatic artery or both (CA/CHA (+)), b) tumor invasion of the root of splenic artery which is difficult to dissect without secure the enough surgical margin (CA/CHA (-)). Among the patients with DP-CAR, CA/CHA (-) and CA/CHA (+) were detected in seven patients each. The short and long-term surgical results were compared between DP and DP-CAR, and CA/CHA (-) and CA/CHA (+).

RESULTS: DP-CAR was associated with significantly longer operation time compared to DP (334min vs 257 min, p=0.001), greater blood loss (941ml vs 498ml, p=0.013), and higher incidence of positive surgical margin (43% vs 15%, p=0.014). Combined portal vein resection and reconstruction tended to be performed more frequently in DP-CAR compared to DP (29% vs 10%, p=0.087). However, morbidity was almost identical (86% vs 69%, p=0.318). There was no hospital death in both groups. The median disease-free survival time was 15.1 months in DP and 8.2 months in DP-CAR (p=0.022). The median overall survival time was 28.3 months in DP and 26.2 months in DP-CAR (p=0.347). In patients who underwent DP-CAR, there was no significant difference regarding the short-term results between CA/CHA (-) and CA/CHA (+) groups. The R1 resection rate of CA/CHA (+) was twice compared to that of CA/CHA (-) (57% vs 28%, p=0.592). The median disease-free survival was 14.3 months in CA/CHA (-) and 3.8 months in CA/CHA (+) (p=0.013). All patients with CA/CHA (+) had recurrence within 12 months after resection. The median overall survival time was 31.2 months in CA/CHA (-) and 13.3 months in CA/CHA (+) (p=0.002).

CONCLUSION: The indication of DP-CAR were classified into two; CA/CHA (-) and CA/CHA (+) according to postoperative survival. Patients with CA/CHA (-) are good candidates of DP-CAR. However, DP-CAR does not improve the survival of patients with CA/CHA (+), therefore these patients might be considered as having borderline resectable cancer.

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Disclosure of Interest: None Declared

Keywords: distal pancreatectomy, Pancreatic Cancer

P1367 PATENCY OF THE MAIN PANCREATIC DUCT AFTER PANCREATICODUODENECTOMY WITH INVAGINATION ANASTOMOSIS.

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INTRODUCTION: Invagination technique is one of the most widely used methods to accomplish a pancreaticojejunostomy (PJ) after pancreaticoduodenectomy.
However, patency of the main pancreatic duct after pancreatoduodenectomy with invagination anastomosis is unclear.
AIMS&METHODS: The purpose of this study was to determine whether patency of the main pancreatic duct after pancreatoduodenectomy with invagination PJ is lower than duct to mucosa PJ.
Thirty patients underwent pancreatoduodenectomy in Aichi Cancer Center between January 2011 and December 2011. Their medical records were reviewed to evaluate the patency of the main pancreatic duct after surgery. Invagination anastomosis was performed in 18 patients, while duct to mucosa anastomosis was performed in 12 patients.
The diameter of main pancreatic duct, the thickness of pancreas and the fatty liver which are evaluated by CT after pancreatoduodenectomy are compared between invagination PJ group (IV) and duct to mucosa group (DM).
RESULTS: Patients with soft pancreatic texture were 20 (67%), narrow main pancreatic duct were 17 (57%). The overall pancreatic fistula rate was 33.3%.
The median observation period was 369.5 days (121-675) and there were no significant differences between two groups.
The number of patients with soft pancreas texture were significantly higher in IV group (p=0.045).
There were no significant differences between two groups in both preoperative (DM=3.5±1.7mm versus IV=2.4±1.0mm) and postoperative (DM=1.1±0.3mm versus IV=1.1±0.2mm) diameter of the main pancreatic ducts.
There were no significant differences in the pancreas texture (DM=9.5±1.4mm versus IV=10.3±1.0mm).
There were no significant differences in CT value of the liver between two groups both before and after surgery (DM=60.7±3.6HU versus IV=60.5±2.7HU).
Postoperative CT value of the liver was lower than preoperative CT value in both groups, but the difference of CT value between before and after surgery did not reveal significant differences.
CONCLUSION: There was no evidence of lower patency of the main pancreatic duct after pancreatoduodenectomy with invagination anastomosis.
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Disclosure of Interest: None Declared
Keywords: invagination anastomosis, pancreatoduodenectomy

P1368 LAPARO-ENDOSCOPIC MANAGEMENT FOR CHOLELITHIASIS AND COMMON BILE DUCT STONES

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INTRODUCTION: The ideal management of cholelithiasis and common bile duct stones (CBDS) is still a matter of debate. A single stage option based on laparoscopic cholecystectomy (LC) followed by an intraoperative endoscopic retrograde cholangio-pancreatography (ERCP) seems to offer some advantages. The aims of the study is to investigate the feasibility, results and procedure-related complications.
AIMS&METHODS: A retrospective chart review was done from all consecutive patients undergone to LC and ERCP between 2003 and 2012 at our surgical unit. We reviewed patients' characteristics, indication for surgery, conversion rate to open procedure, post-operative complications and hospital stay
RESULTS: During the study period, 184 patients (male 76; female 108) were identified with a median age of 69 years (IQR 55.5-77.5). 159 patients underwent an urgent procedure (86.5%), while 25 patients were operated electively. Laparoscopic procedure was attempted in all patients and a conversion to open procedure was necessary in 9 (4.9%). The endoscopic cannulation technique was successful in all patients. The primary stone clearance rate was 98.4% (181/184). There was no mortality. A complication was recorded in 12 patients (6.5%): pancreatitis in eight, small bleeding in two, cholangitis in one, bile leakage from the cystic duct in one. The median hospital stay was 7 days (IQR 10-15).
CONCLUSION: Laparo-endoscopic management of CBDS is feasible, safe and has a high stone clearance rate. Obviously, the technique requires logistics to perform LC and ERCP in the operating room, but is a single stage option that may reduce the hospital charges.
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Disclosure of Interest: None Declared
Keywords: bile duct stones, cholelithiasis, Laparoscopic cholecystectomy

P1369 SHOULD LAPAROSCOPIC CHOLECYSTECTOMY BE PERFORMED REGARDLESS OF AGE?

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INTRODUCTION: Since elderly patients become a growing part of the population and advanced age is associated with an increase in post-operative complications, this study was conducted to evaluate the outcomes of laparoscopic cholecystectomy (LC) in patients aged 80 years or older.
AIMS&METHODS: A retrospective chart review was done of LC performed in a consecutive series of elderly patients between 2003 and 2012 at our surgical unit. We reviewed patient' characteristics, indication for surgery, comorbid conditions, conversion to open procedure, postoperative complications and hospital stay.
RESULTS: During the study period, 102 patients (male 39; female 63) underwent LC with a median age of 83 years (IQR 80.5-86). Of these, a comorbid condition was present in 45 patients (44%). Seventy patients (68.5%) underwent an urgent procedure, while 32 patients (33%) were operated electively. A conversion to open procedure was necessary in 5 (4.9%). An intraoperative endoscopic retrograde cholangio-pancreatography was necessary in 23 patients (22.5%) for associated common bile duct stone presence. Mortality was nihil and morbidity rate was 18.6%. No bile duct injury occurred. The median hospital stay was 9 days (IQR 7-14).
CONCLUSION: LC in extremely elderly is feasible and well tolerated, that can be accomplished with acceptable low morbidity even as an emergency procedure.
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Disclosure of Interest: None Declared
Keywords: elderly patients, Laparoscopic cholecystectomy

P1370 FEASIBILITY AND SAFETY OF TOTALLY LAPAROSCOPIC RESTORATIVE PROCTOCOLECTOMY FOR ULCERATIVE COLITIS IN THE ELDERLY. A PROSPECTIVE COHORT STUDY.

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INTRODUCTION: Since its introduction in the early 1980s, very few data are available on the ileo-pouch-anal anastomosis (IPAA) performed in elderly patients. Laparoscopy seems to reduce morbidity in many surgical fields. Aim of the present study is to prospectively evaluate the feasibility and safety of laparoscopic IPAA for Ulcerative Colitis (UC) in patients over 65 years of age.
AIMS&METHODS: Starting from January 2007, all the consecutive, unselected patients with UC admitted in our Department and treated with a restorative proctocolectomy procedure were inserted in a prospective database. All surgical procedures, both proctocolectomy and abdominal colectomy followed by proctectomy and IPAA (staged surgery), were performed videolaparoscopically. Patients >65 years were compared to younger patients in terms of clinical characteristics, surgical procedure, and perioperative outcome. Analysis of data was performed using Student's t test, Fisher exact test, and Chi-square where appropriate.
RESULTS: From January 2007 to June 2012, 99 patients entered the study. 77 completed all the surgical steps up to the ileostomy closure. Of these, sixty-three (39 males) patients were <65 yrs and 14 (9 males) >65 yrs. The elderly group had a mean age of 69 yrs (compared to 45 yrs), duration of disease of 13 yrs (compared to 11 yrs; p = 0.04), higher ASA score (p = 0.002), dysplasia or cancer rate of 29% (compared to 18%, ns), emergency setting of 28% (compared to 26%, ns), conversion rate of 7% (compared to nil, ns), a one or two versus three steps procedure of 71% (compared to 52%, ns), stapled IPAA of 93% (compared to 89%, ns), overall major and minor complication rate of 28% and 7% (compared to 19% and 28%, ns), overall readmission and reoperation rate of 7% and 14% (compared to 28% and 17%, ns). No significant differences were found in preoperative medication with steroids, immunomodulators (thiopurine, cyclosporine and anti-TNF) or combined therapy. Operative data were similar for both groups.
CONCLUSION: Totally laparoscopic proctocolectomy with IPAA for UC in elderly patients over 65 yrs of age is a safe and effective procedure. Minimally invasive approach seems to maintain its advantages in older patients, reducing the surgical impact in patients with high comorbid conditions. Age and comorbidities do not seem to be a contraindication to totally laparoscopic IPAA surgery.
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Disclosure of Interest: None Declared
Keywords: Elderly, laparoscopic surgery, Ulcerative Colitis

P1371 LAPAROSCOPIC LAVAGE IN HINCHEY III ACUTE SIGMOID DIVERTICULITIS (ASD)

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INTRODUCTION: Hartman's procedure is conventionally considered the gold standard for patients with generalized peritonitis (Hinchey III, IV). Colectomy is an effective means of controlling peritonitis, yet it carries considerable risks of short-term and long-term morbidity and mortality. Therefore there has recently been a trend toward a more conservative approach, i.e. laparascopic lavage without colonic resection.
AIMS&METHODS: Retrospectively we analyzed patients, treated for acute sigmoid diverticulitis at our institution (two departments) between 2008 and 2012.
In our secondary surgical centre 70 patients were treated every year for ASD. Average age and average time of hospitalization were 64 years and 6 days, respectively. In our tertiary surgical centre 12 patients on average were treated every year. Average age and average time of hospitalization were 63 years and 13 days, respectively. Hinchey stage, type of operation and the rate of postoperative morbidity and mortality were analyzed retrospectively for both departments.
RESULTS: Secondary surgical centre: 82% of patients had Hinchey I ASD, 5% Hinchey II, 5% Hinchey III and 3% Hinchey IV. 13% of patients were operated on. In 2/3 of patients a colectomy was made (2/3 with anastomosis, 1/3 Hartman's procedure), in 1/3 a laparoscopic lavage only was done. The rate of postoperative morbidity and mortality were 20% and 10%, respectively.

Tertiary surgical centre: 30% of patients had Hinchey I ASD, 46% Hinchey II, 12% Hinchey III and 12% Hinchey IV. 67% of patients were operated on and in 85% a colectomy was made (½ Hartman's procedure, ½ anastomosis). In 15% a laparoscopic lavage only was done. The rate of postoperative morbidity and mortality were 18% and 11%, respectively.
CONCLUSION: Prospective, randomised, well prepared studies with adequate follow up are needed to further our understanding of the (potential) role of laparoscopic lavage in the treatment of ASD. Currently, 4 European groups are conducting such trials. The results are eagerly awaited.
Disclosure of Interest: None Declared
Keywords: Colectomy, Diverticulitis, Hinchey, Laparoscopic lavage

P1372 SUCCESSFUL TREATMENT OF SUPERFICIAL DUODENUL NEOPLASMS BY LAPAROSCOPIC WEDGE DUODENECTOMY WITH ENDOSCOPIC TRANSMURAL MARGINATION: A SINGLE-CENTER STUDY

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INTRODUCTION: Superficial duodenal neoplasm (SDN) is a rare disease for which there is no established treatment method. Endoscopic resection is technically difficult, surgical approach is difficult to decide the borderline of the lesion precisely. We invent the new approach to remove SDN that involves a combination of endoscopic and laparascopic technics: laparoscopic wedge duodenectomy with endoscopic transmural margination (LWDETM).
AIMS&METHODS: The aim of this study was to investigate the results of a single center experience and assess the validity of LWDETM for SDN. Between January 2011 and April 2013, 35 patients with SDN (a total of 38 lesions) underwent LWDETM. All cases were assessed for their age, sex, location, en-bloc resection rate, R0 resection rate, lesion size, sample size, procedure time, length of hospital stay after LWDETM, complication, and histpathological report. LWDETM procedure: Under general anesthesia, the duodenum was first mobilized laparoscopically. Then the tumor location was confirmed by endoscopy. The peripheral margin was marked around the tumor endoscopically and each marking was perforated intentionally using a needle knife in the coagulation mode under laparoscopic observation. Subsequently, the seromuscular layer was laparoscopically dissected along the marking circumferentially using an ultrasonically activated device. After sero-muscular layer incision, submucosa-mucosal layer was dissected along sero-muscular layer incision with ultrasonically activated device. The closure of the defect in the duodenal wall was performed by the laparoscopic hand-suturing technique.
RESULTS: 35 patients (27 males and 8 females, mean age 63.3) were treated by LWDETM. In 3 patients, because 2 lesions were located quite closely, we resected them at the same time. 24 lesions were located at the second portion, 12 at the bulb and 2 at the third portion of the duodenum. En-bloc and R0 resection was achieved for 97.4 % (37/38), too. The mean resected lesion size was 11.6 mm, and the mean resected specimen size was 26.1 mm. The mean procedure time was 128 minutes. The mean length of hospital stay after LWDETM was 12.6 days. There were no severe complications. Histopathological examination confirmed that 19 were adenomas, 8 adenocarcinomas 6 neuroendcrine tumors and 5 hyperplastic polyps.
CONCLUSION: In our experience of LWDETM for SDN, successful en-bloc and R0 resection was achieved without severe complications. We believe that in treatment of SDN this method will be considered as one of the powerful options.
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Disclosure of Interest: None Declared
Keywords: endoscopic resection, laparoscopic duodenectomy, laparoscopic surgery, superficial duodenal neoplasm

P1373 BASIC LAPAROSCOPIC SKILLS ACQUIRED IN INTENSIVE VIRTUAL REALITY TRAINING MODULE IN PRE-GRADUATE EDUCATION - ARE THEY TRANSFERABLE INTO REALISTIC ENVIRONMENT? PROSPECTIVE EXPERIMENTAL STUDY

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INTRODUCTION: Although virtual reality simulation has been suggested to be an effective tool in basic laparoscopic skills training, limited data is available concerning the structure of effective training modules and their application in pre-graduate education.
AIMS&METHODS: Aim of the study was to assess transferability of basic laparoscopic skills acquired during intensive virtual reality training module in pre-graduate education into realistic environment. Medical students included in this prospective experimental study practiced well defined simple complex task (peg transfer) on virtual reality trainer (15 repetitions). Identical task was performed prior and after virtual reality training in realistic conditions (box trainer) with time to complete task recorded. Results achieved were tested for statistically significant differences.
RESULTS: 100 trainees participated in the study (65 males, 35 females; mean age 24.05±1.39 years). Mean duration of training module was 122.5±13.5 minutes. Time needed to perform task on box trainer prior virtual reality training was 420.2±143.8 seconds. Performance time after virtual reality training was shortened by 31.4±12.5 % to 278.9±81.6 seconds. This difference was proven to be statistically significant ($p < 0.001$).
CONCLUSION: Basic laparoscopic skills acquired during pre-graduate virtual reality training on the level of simple complex tasks in intensive training module appear to be transferable into realistic environment. As a result, virtual reality training carries potential for utilization not only in post-graduate but also in pre-graduate education and training. Retention of such skills should be further investigated to allow for optimal timing in pre-graduate curriculum.
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Disclosure of Interest: None Declared
Keywords: education, laparoscopic surgery, skills, training, virtual reality

P1374 COMPLEXITY OF LAPAROSCOPIC PROCEDURES AND FREQUENCY OF ELECTRIC EQUIPMENT FAILURE - PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION: Although electric equipment extensively used in laparoscopic surgery is supposed to be reliable and safe, several studies reported relatively high incidence of its failure. Nevertheless, the influence of complexity of surgery on frequency of failures was not described yet.
AIMS&METHODS: Prospective observational study was carried out in a single university centre setting with cart based operating room setup. Laparoscopic procedures observed were categorized according to their complexity: basic (laparoscopic cholecystectomy, TAPP hernioplasty, laparoscopic appendectomy) and advanced (laparoscopic Nissen fundoplication, splenectomy, adrenalectomy, colorectal resections, bariatric procedures). Electric equipment failure was defined as a situation when it was not functioning at all or had impaired function at the time it was needed. To detect and assess failures, laparoscopic procedures were observed by an independent researcher.
RESULTS: 153 consecutive basic procedures (group I.) were compared to 78 advanced ones (group II.). Overall, 133 (57.6 %) surgeries were disturbed by troubles with electric equipment – 218 incidents were recorded, ranging from 0 to 4 per procedure, with mode value 1 failure per surgery. No clinically relevant adverse consequences were noticed. 128 failures (58.7 %) were due to malposition (equipment missing or missplaced) and 90 (41.3 %) due to malfunction. In case of malfunction, defect was a cause only in 4 cases (1.8 %) and reason remained unclear 15 times (6.9 %), while remaining failures (91.3 %) were related to faulty connection or improper equipment setup. Mean time to solve the problem was 1.88 minutes with range from 0.5 to 10 minutes. No statistically significant difference was detected between groups concerning number of procedures disturbed by failure, number of incidents, type and reason of failures and time to repair (p=ns). Operating time was significantly prolonged in advanced procedures group (group I. 59.18±21.26 min, group II. 163.27±36.11 min) ($p < 0.001$).
CONCLUSION: Although electric equipment is used significantly longer during advanced laparoscopic procedures due to prolonged operating time, increased complexity of surgery does not seem to influence number of failures. This result can be explained by observation that majority of incidents is related to equipment positioning and setting. Even though these failures rarely achieve clinical significance, any incident prolongs operating time, disturbs surgical team and carries potential risk for adverse event. As more than 90% of incidents are easily preventable by definition, every effort should be made to prevent them.
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Disclosure of Interest: None Declared
Keywords: equipment failure, laparoscopic surgery, risk assessment, Safety

P1375 FORCED ARGON PLASMA COAGULATION IS A SAFE AND FEASIBLE TECHNIQUE FOR ENDOSCOPIC HEMOSTASIS OF BLEEDING OF LIVER AND SPLEEN DURING NOTES PROCEDURES – A RANDOMIZED CONTROLLED ANIMAL STUDY.

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INTRODUCTION: In many natural orifice transluminal endoscopic surgery (NOTES) interventions the peritoneal cavity is accessed through the gastrointestinal wall. Thus, severe bleeding from intraabdominal vessels or accidentally damaged organs is a likely complication. Successfull termination of intraabdominal hemorrhage by endoscopic means is an important issue. Several techniques are established, but there are no data available that directly compare the suitability and complication rate of the different methods.
AIMS&METHODS: Aim: To prospectively examine the efficacy and safety of 3 endoscopic prototype devices for the treatment of acute bleeding of lacerations in liver and spleen.
Method: 12 pigs (30-37kg) were randomised for transgastric (TGA, n=6) and transvaginal (TVA) access. After gastric or vaginal full-thickness wall incision the endoscope was introduced into the peritoneal cavity. Three lacerations of liver and spleen of approximately 2.5cm were created laparoscopically in each animal. After randomisation 3 haemostatic techniques were used: i) endoscopic suturing with t-bars (EST); ii) prototype monopolar forceps (MF); iii) experimental Forced Argon Plasma Coagulation (FAPC). Intraabdominal pressure and pulmonary arterial pressure (PAP) were monitored continuously during the procedures. Autopsy and histology were carried out 6 weeks after the procedure.
RESULTS: In liver and spleen hemorrhage EST failed to control the bleeding quickly enough before vision was inhibited. MF achieved liver hemostasis in 50% of cases after a mean time of 40.0±4.1min. Using FAPC it took 21.4±2.9min to entirely control liver hemorrhage ($p < 0.0001$ compared to MF). Splenic hemorrhage could neither be controlled nor stopped in any of the cases using the MF device. FAPC achieved control of the splenic bleeding in 100% of cases in

30.6±3.1min. Intraabdominal pressure was limited to 12 mmHg in all cases (mean 9.6±0.6mmHg). PAP was 21.6±0.9mmHg before the procedure and 21.8±1.1mmHg after the procedure ($p > 0.05$). There was no difference in PAP between MF and FAPC ($p > 0.05$).

CONCLUSION: FAPC is a valuable technique to control severe bleeding from liver and spleen even when other techniques fail. FAPC can be safely applied when the intraabdominal pressure is limited to 12mmHg without an increase in PAP excluding pulmonary embolism. Further studies in humans are needed to prove these data.

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Disclosure of Interest: None Declared

Keywords: Argon plasma coagulation, bleeding, Complication

P1376 MUCOSAL VS. SEROSAL OTSC CLOSURE IN NOTES: A RANDOMIZED CONTROLLED STUDY

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INTRODUCTION: Efficient and safe closure is critical for clinical application of natural orifice transluminal endoscopic sugery (NOTES). Over the scope clip (OTSC) has become a widely accepted technique of transluminal closure. However, the usual clip application is based on mucosa approximation and does not fulfill the surgical principle of serosa-to-serosa approximation in hollow organ closures.

AIMS&METHODS: The aim of the study was to evaluate the feasibility, safety and efficiency of serosal OTSC closure in comparison to the standard mucosal OTSC closure in a porcine survival model.

After performing a gastric incision with a needle knife followed by 18 mm balloon dilation, twenty female pigs (25-45kg) were randomized to receive either mucosal (10 animals) or serosal (10 animals) OTSC closure. In mucosal closure, the mucosal portions of the incision edges were approximated by a double grasper and pulled into the clip's cap, whereas in serosal closure, the serosal portions of the incision edge were grasped, approximated and pulled into the cap. Laparoscopic assistance with a 5mm camera was used to ensure serosal approximation. Immediate air leak tests were performed and the animals were closely observed for a period of two weeks when they were sacrificed for postmortem examination.

RESULTS: All OTSCs were applied successfully in a mean time of 5.3 min (range 2-7 min) in the mucosal group and in a mean time of 8.8 min (range 4-12 min) in the serosal group ($p=0.001$). Air leak tests were negative in all closures. All animals survived without complications. The clip was in place at 14 days in 6 animals in the mucosal group and in 7 animals in the serosal group, respectively ($p > 0.01$). Minor adhesions were present in half of the animals in both groups. Necropsy demonstrated patent full-thickness gastric closure with no macroscopic signs of infection in all animals. However, 4 animals in the mucosal group and 5 animals in the serosal group had microscopic signs of mucosal inflammation, which was in 2 animals in the mucosal group and 3 animals in the serosal group positive for Gram staining ($p > 0.01$). Histologically, the mucosal closure was characterized by an end to end apposition of the gastric wall layers, whereas the serosal closure was characterized by a side to side apposition of the layers.

CONCLUSION: Serosal OTSC closure was feasible, safe and efficient. It required a longer time to perform due to increased technical difficulty. Serosal OTSC closure does not seem to add any benefit to the standard mucosal OTSC closure.

Disclosure of Interest: None Declared

Keywords: closure, endoscopy, NOTES

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00

IBD III – Poster Area

P1377 THE FAECAL FLORA DOES NOT REFLECT THE COLONIC MUCOSAL FLORA, A 454 PYROSEQUENCING STUDY OF A POPULATION-BASED COHORT OF HEALTHY INDIVIDUALS

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INTRODUCTION: The introduction of non-cultured based methods has revolutionized our understanding of microbiota. Yet, there are still surprising gaps in the characterization of this ecosystem and data on the microbial composition in Crohn's disease are inconsistent. Due to its simplicity in collection, faecal samples are often used for characterization and comparisons of gut microbiota. However, the degree to which faecal microbiota reflects the mucosal flora remains uncertain and previous data are contradictory.

AIMS&METHODS: We aimed to characterize the agreement in diversity in faecal flora and colonic mucosal flora in a population-based cohort of healthy individuals, using culture-independent high-throughput 454 pyrosequencing of the 16S rRNA gene.

Faecal samples and biopsies were selected randomly from 33 individuals, who were not treated with antibiotics within the last three months, within the population-based randomised colonoscopy (Popcol) study.(1) Biopsies were collected from the caecal region of colon during endoscopy, after standard bowel cleansing (Phosphoral, CCS Healthcare). Faecal samples were posted by mail and collection of faecal samples within two days before colonoscopy was an inclusion criteria. The microbiotic composition was analyzed by 454- pyrosequencing according to previous described methods.(2) Shannon index of diversity was used to assess the diversity of the microbial community. Differences in continuous data were analysed by paired t-test.

RESULTS: In 32/33 subjects, fecal samples and biopsies meeting the inclusion criteria were available. The median age of enrolled subjects was 46 (24-70) years. Analysis of OTUs showed a trend towards higher overall diversity in biopsies compared with faecal samples ($p=0.06$).

CONCLUSION: Our data suggest that the microbiotic profile in faeces does not mirror the mucosal bacterial composition in the proximal colon accurately. Further studies are needed to characterize the possible differences in faecal- and mucosal flora in more detail.

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Disclosure of Interest: None Declared

Keywords: Inflammatory bowel disease (IBD), microbiota

P1378 BIOGEOGRAPHY OF THE COLONIC MICROBIOTA DEMONSTRATES CONSERVED STRUCTURE IN HEALTH WITH ALTERATIONS IN INFLAMMATION

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INTRODUCTION: Large sequencing projects based on stool sampling have related diet, host phenotype, geography and age in the search for functional and phylogenetic cores which may explain the complexity and interindividual variability characteristic of the human lower gastrointestinal tract microbiota. While the Human Microbiome Project has sought to incorporate spatial structuring of community assembly through biogeographic characterisation of multiple body sites, more subtle ecological landscapes may be apparent within host niches in the human colon.

AIMS&METHODS: Protected specimen brush (PSB) sampling was used in conjunction with biopsy sampling and laser capture microdissection to sample across four regions of the colon in four healthy volunteers undergoing colonoscopy and two patients with ulcerative colitis undergoing colonic resection. The regional microbiota was extensively sequenced in these individuals using amplicon pyrosequencing comparing whole mucosal biopsy with luminal brush samples and laser capture microdissection-retrieved samples from the mucus gel layer.

RESULTS: There was a statistically significant reduction in the proportion of Bacteroidetes in samples of adherent mucous when compared to both whole mucosal biopsies and luminal brush samples. There was a corresponding increase in the proportion of Firmicutes and Actinobacteria in the mucosa-associated mucous gel compared to both whole biopsies and luminal samples. Within individuals, samples separated according to luminal or mucus-gel layer origin by unweighted UniFrac. When two patients with ulcerative colitis were added, increased mucosa-associated levels of Clostridiaceae and Peptostreptococcaceae were noted as well as a breakdown in the luminal and mucosal segregation in areas of severe inflammation.

CONCLUSION: Within the context of inter-individual variability in the colonic microbiota, certain patterns of spatial organisation are apparent. As glycan foraging is an important mechanism for endurance of bacterial species within the gut microbiota, it is possible that the mucus gel layer provides a platform for the stable preservation of key microbial lineages in health, while luminal communities are more closely involved in the commerce of dietary metabolism. The breakdown of such a structure and the expansion and perseverance of certain OTUs in inflammation may contribute to chronicity in inflammatory bowel disease.

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Disclosure of Interest: None Declared

Keywords: Biogeography, Microbiota, ulcerative colitis

P1379 APPENDICEAL DENDRITIC CELLS ARE PRO-INFLAMMATORY, DRIVE GUT-SPECIFIC T-CELL RESPONSES AND ARE ALTERED IN ULCERATIVE COLITIS

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INTRODUCTION: Appendicectomy is associated with reduced risk of developing ulcerative colitis (UC). UC develops from a disruption of intestinal immune homeostasis and inflammatory T-cell infiltrates. It is unclear whether the appendix is an immunologically active organ. Gut dendritic cells (DC) determine mucosal immune homeostasis, governed by their ability to drive effector T-cell responses, and determine whether T-cell responses generated are immunogenic

or tolerogenic. However, gut DC are poorly characterised in humans and *bona fide* DC from the human appendix had previously not been characterised.
AIMS&METHODS: We aimed to identify DC from the human appendix from UC patients and non-inflammatory controls. The appendix, with caecal/ileal samples were removed from surgical resection specimens from patients with active UC or familial adenomatous polyposis patients (pre-malignancy; control samples) undergoing colectomy. DC were identified by flow cytometry and used for *in vitro* T-cell stimulation assays.
RESULTS: Human appendiceal DC were identified; the majority expressed lymph-node homing marker CCR7. Appendiceal DC exhibited an activated/inflammatory profile compared to their caecal/ileal counterparts with enhanced expression of DC activation marker CD40 and enhanced production of pro-inflammatory cytokines IL-1β and IL-23. T-cells from the appendix expressed gut-homing marker β7 integrin; furthermore, appendiceal DC generated dose-dependent stimulation of T-cells expressing β7. However, despite appendiceal ability to drive gut-specific T-cell responses, their stimulatory capacity was lower than caecal or ileal DC. In UC, appendiceal DC exhibited similar changes to those found in colonic DC i.e. restricted expression of DC activation marker CD40 and an enhanced proportion of non-myeloid ($CD11c^-$) DC compared to control DC.
CONCLUSION: The appendix is immunologically active. The lymph-node homing potential of appendiceal DC, taken with their ability to drive gut-specific T-cell responses strongly suggests a role for the appendix in mucosal immune homeostasis. These data provide a mechanism for appendiceal DC involvement in generating immune responses affecting the rest of the GI tract. The antigen-sampling role of DC and the inflammatory profile of appendiceal DC may be indicative of a separate reservoir of enteric bacteria within the appendix. The loss of DC function observed in colonic DC in UC also applies to DC within the appendix and provides an explanation for appendicectomy being associated with reduced risk of UC.
Disclosure of Interest: None Declared
Keywords: Appendicectomy, dendritic cells, ulcerative colitis

P1380 TNBS-INDUCED CHRONIC COLITIS IS ASSOCIATED WITH FIBROSIS AND MODULATES TGF-B1 AND AKT SIGNALING IN RATS.

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INTRODUCTION: Fibrosis is a major complication in Crohn's disease and no specific treatment except surgery is available. To better understand mechanisms underlying intestinal fibrosis, a chronic model of intestinal inflammation has been developed.
AIMS&METHODS: We aimed to explore signaling pathways involved in fibrosis, including TGF-β pathway during chronic experimental colitis. As proteasome inhibition by bortezomib exhibits antifibrotic properties in other organs, we tested its potential antifibrotic effect in this model.
Chronic colitis was induced at D0 in male Sprague-Dawley rats by weekly intrarectal injection of increasing doses of 2,4,6 trinitrobenzene sulfonic acid (TNBS, n=8) for 6 weeks while the control received the vehicle (Control, n=10). To test the effect of bortezomib, rats received intraperitoneal injections of bortezomib ($25mg.kg^{-1}.d^{-1}$ twice a week, TNBS+BTZ, n=8) from D37 to D44 or vehicle. Fibrosis and inflammation were assessed macroscopically and histologically. We studied TGF-β production by ELISA and TGF-β signaling pathway, i.e. phospho-SMAD2/3, phospho-ERK2/ERK2, phospho-p38/p38, and Akt by western blot. Proteasome inhibition was assessed by chymotrypsin-like activity measurement.
RESULTS: TNBS rats had a colon higher inflammatory and fibrosis score than controls (2 versus 0, $p<0.01$; 2 versus 0, $p<0.01$) and tended to have a higher production of colon TGFβ (5500 versus 3700 $pg.mg^{-1}$, p=0.06). TNBS rats had a higher expression of TGF-β-related proteins such as phospho-SMAD2/3, phospho-ERK2/ERK2, phospho-p38/p38, and Akt (1.97 versus 1.12, $p<0.05$; 0.79 versus 0.264, $p<0.05$; 2.79 versus 0.06, $p<0.05$; 1.17 versus 0.05, $p<0.001$ respectively). While bortezomib significantly decreased, as expected, chymotrypsin-like activity (20357 versus 6912, $p<0,05$), bortezomib had no statistically significant effect on fibrosis score and fibrosis related proteins.
CONCLUSION: Rats with TNBS-induced chronic colitis exhibited colon fibrosis associated with high expression of TGFβ signaling especially in the Akt pathway. Proteasome inhibition by bortezomib had no effect on fibrosis in our experimental conditions. As Akt seems to be involved in this model, targeting this pathway may be considered in intestinal models of fibrosis.
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Disclosure of Interest: None Declared
Keywords: bortezomib, chronic colitis, Fibrosis, TGF-beta1, tnbs

P1381 IMPACT OF DIAGNOSTIC DELAY ON CLINICAL OUTCOME OF CROHN'S DISEASE

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INTRODUCTION: The diagnosis of Crohn's disease (CD) may be difficult due to unspecific symptoms and limited test accuracies and is frequently associated with a variable diagnostic delay. The impact of delay in diagnosis on outcome of CD patients is still unknown. This study aimed at determining if the diagnostic delay affects the clinical outcome of CD patients.
AIMS&METHODS: This is a retrospective cohort study including a 250 consecutive patients (Mean age: 49,6 yrs; male: 146 pts) regularly followed at IBD unit of our Hospital. For each patient the following data, directly obtained by a patient questionnaire and checked in the clinical charts, were recruited: sex, age, time of onset of the symptoms, exact date of definitive diagnosis of Crohn's disease, smoking habit, active perianal disease, current or past medical therapy for CD, including the use of immunosuppressants, biological and steroid therapy, history of perianal and abdominal conservative or resective surgery for CD. The need of surgery, immunosuppressive or biological therapy was considered as clinical variable of bad outcome of CD. Influence of diagnostic delay and other possible predictors on outcome of CD was evaluated by univariate and multivariate binary logistic regression analysis.
RESULTS: Diagnostic delay in CD patients varied from 0 to 298.30 months (mean: 27.22 mths). 68 patients were treated with immunosuppressants and biological therapy and 80 patients underwent surgery for perianal (n=7) or abdominal complications of CD (n=73) and 34 patients in immunosuppressant therapy underwent resective surgery. The delay of diagnosis was significantly associated with need resective surgery (p 0.043) but not with other clinical variables such as the use of biologics, steroids and immunosuppressants. With univariate regression analysis we found a significant association between longer diagnostic delay and resective surgery (OR 1.005; 95% CI 1.00-1.012; p 0.043) and period of diagnosis (OR 3.0; 95%CI 1.5-6.3). Diagnostic delay and period of diagnosis were independent predictors of increased risk of surgery. No parameters were associated to increased need of conservative surgery and perianal surgery.
CONCLUSION: Diagnostic delay and period of diagnosis of CD are independent predictors of increased need for resective surgery. The conformation of this preliminary finding in a wider series of patients may have significant impact on the work up of patients with suspected CD.
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Disclosure of Interest: None Declared
Keywords: Crohn disease, Diagnostic delay, Outcome

P1382 ENTEROCOCCUS FAECALIS LIPOPROTEINS CONTRIBUTE TO VIRULENCE BOTH IN CHRONIC INFLAMMATION AND IN INFECTION MODELS

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INTRODUCTION: *Enterococcus faecalis* is an ubiquitous bacterium occurring both as member of the core microbiota and as nosocomial pathogen and it has been shown that IL10-/- mice are susceptible to *Enterococcus faecalis*, developing chronic colitis after monocolonization with this microorganism (1).
AIMS&METHODS: We investigated the role of *Enterococcus faecalis* lipoproteins (highly conserved bacterial structures recognized by Toll-like receptor 2 (TLR2)) by deleting the *lgt* gene encoding a prolipoprotein diacylglyceryl transferase involved in bacterial lipoproteins synthesis (2). Wild type and mutant bacteria (Δlgt) were compared regarding development of colitis in IL10-/- mice and virulence in two invertebrate models - *Galleria mellonella* and *Caenorhabditis elegans*. Additionally, the impact of *lgt* deletion on the innate immune response was investigated *in vitro* using bone marrow-derived dendritic cells and mouse embryonic fibroblasts stimulated with bacterial lysates of the two bacterial strains.
RESULTS: Monoassociation of germ-free IL10-/- mice with Δlgt mutant resulted in significant reduction of inflammation in the distal colon, which was associated with decreased spleens and mesenteric lymph nodes weights. Additionally, increased infiltration of CD3-positive cells could be observed by immunofluorescence in the mice monoassociated with the wild type bacteria. These effects were not due to differences in bacterial colonization, as both wild type and the mutant bacteria were recovered in similar numbers from the cecum of the monoassociated mice. Deletion of *lgt* gene resulted in decreased dendritic cells maturation and significantly lower capability to induce secretion of interleukin-6 and TNF in bone marrow-derived dendritic cells and in mouse embryonic fibroblasts after stimulation with bacterial lysates. Using bone marrow-derived dendritic cells isolated from mice lacking TLR2, secretion of the above-mentioned pro-inflammatory cytokines was highly reduced, independently from the bacterial strain used to stimulate the cells. These effects confirm the role of lipoproteins as ligands for TLR2. Both in an insect (*Galleria mellonella*) and a nematode (*Caenorhabditis elegans*) model of infection, *lgt* deletion resulted in attenuated invertebrate mortality.
CONCLUSION: *Enterococcus faecalis* lipoproteins are involved in innate immune recognition and are relevant structures both in infections and in chronic inflammation models.
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Disclosure of Interest: None Declared
Keywords: colitis, IL-10 KO mice, microbiota

P1383 PERI-ANAL DISEASE AS A PREDICTIVE FACTOR OF DISABLING CROHN'S DISEASE

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INTRODUCTION: Peri-anal disease is considered a predictive factor for disabling Crohn's disease. However, its real impact in the global prognosis is not well known.
AIMS&METHODS: Evaluate peri-anal disease as a prognostic factor for intra-abdominal Crohn's disease, in a cross-sectional study in patients with Crohn's Disease followed in our Inflammatory Bowel Disease outpatient clinic.
RESULTS: Six hundred and eighty three patients were identified, 49.9% females, with mean age of 41±14 years. Mean age at diagnosis was 29±12 years, with a mean duration of the disease of 146±99 months. Forty-six percent had ileal, 39% ileo-colic and 15% colic disease, with upper digestive tract involvement in 11%. Twenty-eight percent had peri-anal disease. No differences between patients with or without peri-anal disease were found regarding steroids the need to use steroids (p=0,724) or hospitalization (p=0.180) at diagnosis, as regarding the mean number of intra-abdominal surgeries (0.48 vs 0.40, p=0.153), or time to anti-TNF therapy (93 vs 87 months, p=0,732). Peri-anal disease was not a risk factor for intra-abdominal surgery (RR=1.277, CI 95% 0.877-1.861), and patients without peri-anal disease had the first abdominal surgery earlier (33 vs 54 meses, p=0.011). In the other hand, patients with peri-anal disease needed more cycles of steroids (2.95 vs 2.23, p<0,001), more number of hospitalizations (2.48 vs 1.33, p<0,001) and immunosuppression with azathioprine earlier (58 vs 43 months, p=0,042). All the results showing no statistical significant differences had a statistical power greater than 99%.
CONCLUSION: Patients with peri-anal disease did not have worse prognosis in terms of intra-abdominal disease. However, they needed more hospitalizations, more steroids and earlier immunosuppression.
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Disclosure of Interest: None Declared
Keywords: Disability criteria in Crohn's disease, Peri-anal disease

P1384 THE ROLE OF HUMAN NEUTROPHIL ELASTASE AND ITS INHIBITOR ELAFIN IN ULCERATIVE COLITIS

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INTRODUCTION: Mucosal inflammation in ulcerative colitis (UC) is characterised by an influx of neutrophils which secrete large amounts of human neutrophil elastase (HNE), causing matrix degradation. They also produce the elastase-specific inhibitor, elafin.
AIMS&METHODS: The aim of this study is to evaluate the relative production of elastase and elafin in active UC, and to investigate the modulatory effect of elafin on mucosal proteolytic activity *ex vivo*.
We utilised intestinal biopsies from 18 patients with active UC and 12 non-UC healthy controls. Biopsies were homogenised and lysed to extract mucosal proteins. Proteolytic activity, using elastin as a substrate, was determined. Concentrations of elafin were measured using ELISA. The effect of protease inhibitors on proteolytic activity were determined *in vitro* using elafin, marimastat (matrix metalloproteinase inhibitor) and the synthetic elastase inhibitor, AAPV [N-(Methoxysuccinyl)-Ala-Ala-Pro-Val Chloromethyl Ketone]. The effect of elafin on proteolytic activity *ex vivo* was assessed by 24 hour organ culture in the presence and absence of elafin.
RESULTS: Mucosal protein homogenates from patients with active UC displayed higher proteolytic activity in comparison to healthy controls (p=0.002). Elafin levels were increased in mucosal homogenates from active UC (p=0.007). The addition of elafin, marimastat or AAPV, *in vitro*, each diminished proteolytic activity. Organ culture of UC biopsies in the presence of elafin reduces the proteolytic activity of active UC *ex vivo*.
CONCLUSION: Colonic mucosal tissue from UC patients displays significantly higher elastinolytic activity in comparison to healthy controls. The addition of elafin has a restorative effect on the elastinolytic activity of UC mucosal homogenates, with the most notable effect in those tissues that had highest proteolytic activity. This occurs in the presence of significantly higher quantities of elafin in active UC mucosa. These data also show a beneficial modulatory effect of elafin on human gut tissue, suggesting a possible role for supplementary elafin in the treatment of UC.
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Disclosure of Interest: None Declared
Keywords: elafin, human neutrophil elastase, ulcerative colitis

P1385 THE NEUROTROPHIC AGENT SR 57746A PROMOTES MUCOSAL HEALING AND PREVENTS MUCOSAL INJURY IN THE INTESTINE

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INTRODUCTION: Neurotrophic growth factors are likely to play a major role in maintaining the integrity of the gut epithelium by promoting mucosal healing and thereby stabilizing the intestinal barrier. At the molecular level these compounds prevent apoptosis of enterocytes that otherwise leads to increased mucosal permeability. SR 57746A is a selective agonist at 5-HT1A receptors which has neurotrophic and neuroprotective properties.
AIMS&METHODS: The aim of this study was to evaluate if SR 57746A could have therapeutic potential in model systems of experimental colitis and could hence qualify as a novel therapeutic strategy for IBD patients.
Cell proliferation, apoptosis and migratory capacity were assessed in transformed and non-transformed colonic epithelial cells along with the apoptotic response in primary rat enteric glial cells upon treatment with SR 57746A. Furthermore, enema application of SR 57746A and i.p. infliximab were investigated in a therapeutic as well as a prophylactic setting in the DSS- and CD4-transfer colitis models. The effect of both agents was determined by endoscopy and immunohistochemistry.
RESULTS: SR 57746A potently prevented Apo-1- or TRAIL-induced apoptosis by an ERK- and AKT- dependent mechanism without inducing proliferation or migration in intestinal epithelial cells. In addition, SR 57746A prevented cytokine-induced apoptosis of enteric glial cells. *In vivo* SR 57746A treatment promoted mucosal healing by both, clinical and histological assessment in the experimental colitis models. Interestingly, SR 57746A also prevented mucosal injury in a prophylactic setting. Surprisingly, topical application of SR 57746A was as efficient as i.p. application of infliximab in both settings.
CONCLUSION: SR 57746A prevents colonic epithelial and enteric glial cells from apoptosis by a ERK-/AKT- signalling dependent mechanism. Enema application of SR 57746A showed promising results in two independent mouse models of experimental colitis in the therapeutic and prophylactic setting. Clinical trials are now warranted to test the efficacy of this strategy in patients.
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Disclosure of Interest: None Declared
Keywords: apoptosis, enteric glia, inflammatory bowel disease, neurotrophic factor, SR 57746A

P1386 IL-9 AND IL-9R ARE OVEREXPRESSED BY ULCERATIVE COLITIS PERIPHERAL BLOOD CELLS

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INTRODUCTION: Many of the functions that have been historically linked to the Th1/Th2 paradigm are increasingly becoming associated with Th17- and more recently with Th9-type responses. Whereas the contribution of Th17 cells has been extensively explored, the role of IL-9 and its receptor in ulcerative colitis, a disease characterized by dense neutrophilic infiltration of the gut resulting in crypt abscess, has not been addressed so far.
AIMS&METHODS: We investigated the role of leukocyte-expressed IL-9 and its receptor in ulcerative colitis. Whole blood or fractionated leukocyte populations were investigated for the presence of the IL-9 receptor using western blot, immunofluorescence and flow cytometry. Interleukin production by peripheral blood mononuclear cells was assessed under anti-CD3/anti-CD28 and/or PMA-ionomycin stimulation using sandwich ELISA and flow cytometry. IL-9-dependent modulation of neutrophils' life-span was addressed by flow cytometry with Annexin V and 7-AAD. Additionally, the presence of the IL-9 receptor in gut biopsies was investigated by double immunofluorescence stainings using confocal microscopy.
RESULTS: Peripheral blood mononuclear cells from ulcerative colitis patients produced significantly more IL-9 compared to cells from healthy controls whereas non-stimulated cells produced solely negligible levels of IL-9. There was a high degree of correlation between IL-9 levels and the general inflammatory status of patients as measured by the C reactive protein values. Neutrophils from ulcerative colitis patients expressed significantly more IL-9 receptor compared to control cells. Functionally, IL-9 on its own had little influence on the cultured neutrophils but significantly prolonged the life-span of GM-CSF-stimulated granulocytes from ulcerative colitis patients. Additionally, neutrophils found in biopsies form ulcerative colitis patients also stained positive for the IL-9 receptor indicating their possible *in situ* implication in the pathogenesis of ulcerative colitis.
CONCLUSION: Our present study provides the first data on the implication of leukocyte-expressed IL-9 and IL-9 receptor in the pathogenesis of ulcerative colitis. By producing more IL-9 and/or better responding to its pro-inflammatory actions, leukocytes from ulcerative colitis patients may be critically involved in the outcome of disease. Furthermore, the study suggests that IL-9 and its receptor could become useful disease markers or targets for specific therapies.
Disclosure of Interest: None Declared
Keywords: IL-9, inflammatory bowel disease, neutrophil, ulcerative colitis

P1387 ANTIBIOTIC-INDUCED ALTERATION OF THE GUT MICROBIOTA PROTECTS TNFDELTAARE MICE FROM CROHN'S DISEASE-LIKE ILEITIS

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INTRODUCTION: Crohn's disease is associated with dysbiosis of the gut microbiota. To test the causative role of intestinal microorganisms in the development of genetically-driven chronic inflammation and to identify bacterial taxa

associated with disease, we used the TNF^{deltaARE} mouse model of Crohńs disease-like ileitis.
AIMS&METHODS: To modify the intestinal microbial composition, two antibiotics (Van/Met: vancomycin (0.25 g/l), and metronidazole (1 g/l)) were administered to TNF^{deltaARE} and wild-type mice (each n = 6) in drinking water for 4 weeks. Inflammation was scored by microscopic observation of distal ileal, caecum tip and proximal colon sections directly after antibiotic therapy or after a recurrence phase of two, four, or six weeks. Bacterial composition was analyzed by high-throughput 16S rRNA gene sequencing and bacterial spatial distribution was shown by Fluorescence *in situ* hybridization. Metabolomic analysis of caecal content via FT-ICR/MS allowed mapping of gut metabolic networks associated with inflammation.
RESULTS: Antibiotics substantially reduced ileitis in TNF^{deltaARE} mice (histopathology of 1.6 ± 1.2 *vs*. 4.9 ± 0.8 in the antibiotic *vs*. control group; n = 5-6; p < 0.001), but had no effect on tissue pathology in the caecum and proximal colon. Four weeks after antibiotic treatment, recurrence of ileitis was observed (score of 4.1 ± 1.5). 16S rRNA gene sequencing showed marked changes in bacterial diversity and composition in the caecal lumen and the ileal mucosa. Total bacterial counts were not affected. In control mice, *Firmicutes* and *Bacteroidetes* were the dominant phyla (> 82 % total sequences). Antibiotics increased the occurrence of lactobacilli in the ileal mucosa (19.6 ± 27.6% *vs*. 76.3 ± 19.8%), whereas the proportion of *Bacteroidetes* was reduced (7.2 ± 10% *vs*. 15.0 ± 6.0%). Fluorescence *in situ* hybridization (EUB-338 probe) showed changes in the spatial distribution of ileal bacteria in TNF^{deltaARE} mice, relative to the epithelial layer. Metabolite profiling of caecal content by FT/ICR-MS indicated changes in bile acid and carnitine metabolism. Mono-association and caecal microbiota transplant experiments are currently underway to address the causative role of gut bacteria in experimental ileitis.
CONCLUSION: Our findings indicate an essential role of intestinal bacteria in the development of Crohn's disease-like ileitis.
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Disclosure of Interest: None Declared
Keywords: caecal microbiota transplant, ileitis, intestinal microbiota, TNFdeltaARE mice

P1388 TOLL-LIKE RECEPTORS 2 AND 4 ARE EXPRESSED ON DENDRITIC CELLS IN CROHN'S AND IDIOPATHIC PERIANAL FISTULAE.

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INTRODUCTION: Genetic, microbiological and immunological factors play a role in the aetiology of Crohn's disease (CD). However, the aetiology of fistulating perianal Crohn's disease remains unclear and the disease a challenge to treat due to poor healing and high recurrence rates. Dendritic cells play major roles in the pathogenesis of Crohn's disease and express Toll-Like receptors (TLR) which are pattern recognition receptors that are activated by bacterial ligands. Previous studies have shown increased expression of TLR 2 and 4 in colonic Crohn's biopsies as compared to normal. Data on the characterisation of dendritic cells from perianal Crohn's and idiopathic fistulae are sparse.
AIMS&METHODS: We aimed to determine alterations in TLR 2 and 4 expression on dendritic cells from Crohn's and idiopathic perianal fistulae.
Biopsies were taken from anal fistula tracts of 20 Crohn's and 20 idiopathic patients. Samples were incubated in complete medium overnight and 'Walk out' cells isolated from the cell culture supernatant. Dendritic cells were identified and characterized by flow cytometry as HLA-DR positive and lineage (CD3, CD14, CD16, CD19, CD34 and CD56) negative. The expression of TLR 2 and 4 was determined. Unpaired student t-test was used for comparisons and $p < 0.05$ was considered as significant.
RESULTS: TLR 2 and 4 were expressed on dendritic cells from both Crohn's and idiopathic perianal fistulae. There was no significant difference in the expression of TLR 2 between Crohn's and idiopathic fistulae (p=0.27). TLR 4 expression was equally expressed on dendritic cells from both Crohn's and idiopathic fistulae (p=0.45)
CONCLUSION: Toll-like receptors 2 and 4 are expressed on dendritic cells from Crohn's and Idiopathic perianal fistulae. Although a direct comparison can not be made, it is interesting to note that the expression of TLR 2 and 4 in luminal disease (Hart et al 2005) differs to that in perianal fistulae. Similar levels of expression of TLR 2 and 4 have been noted in Crohn's disease in contrast to perianal Crohn's where the upregulation of TLR 4 seems to be more marked than TLR 2. This may suggest the important role that bacterial products play in the immunopathogenisis of both Crohn's and idiopathic perianal fistula disease
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Disclosure of Interest: None Declared
Keywords: Dendritic cell, Perianal Fistulas, Toll like receptor

P1389 THE ROLE OF THE GUT HOMING MARKER (B7) IN THE IMMUNOPATHOGENISIS OF PERIANAL CROHN'S FISTULAE – INCREASED EXPRESSION ON DENDRITIC CELLS

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INTRODUCTION: The aetiology of fistulating perianal Crohn's disease remains unclear and the disease a challenge to treat due to poor healing and high recurrence rates. Dendritic cells play major roles in the pathogenesis of Crohn's disease and express tissue-specific homing markers. Data on the characterisation of dendritic cells from perianal Crohn's and idiopathic fistulae are sparse. We aimed to determine alterations in homing marker expression on dendritic cells from Crohn's and idiopathic perianal fistulae.
AIMS&METHODS: Biopsies were taken from anal fistula tracts of 23 Crohn's and 21 idiopathic patients. Dendritic cells were identified as HLA-DR positive and lineage (CD3, CD14, CD16, CD19, CD34 and CD56) negative, and were characterized by flow cytometry. The expression of the skin-homing marker CLA, and the gut-homing marker $\beta7$ was determined. Unpaired student t-test was used for comparisons and $p < 0.05$ was considered as significant.
RESULTS: Percentage expression of b7 on dendritic cells was significantly higher in Crohn's compared with idiopathic perianal fistulae (p=0.017). There was no significant difference in CLA expression, which was low in both groups. When comparing the proportion of Dendritic cells that are double positive for both $\beta7$ and CLA between the Crohn's and idiopathic groups, we found that these cells are significantly lower in Crohn's (p=0.002).
CONCLUSION: Increased expression of $\beta7$ on dendritic cells of Crohn's perianal fistulae may lead to increased gut dendritic cells infiltrates contributing to impairment in healing. Anti-$\beta7$ therapies may aid healing when applied to perianal Crohn's fistulae.
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Disclosure of Interest: None Declared
Keywords: dendritic cells, fistula, Perianal Crohńs Disease

P1390 THE PRESENCE OF ENDOTOXINS IN CROHN'S AND IDIOPATHIC PERIANAL FISTULA TRACKS

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INTRODUCTION: Theories on the aetiology of idiopathic perianal fistulae suggest that fistulas occur following a cryptoglandular infection. It has been suggested that persistence of an infective agent or the type and virulence of the infective agent may be involved in pathogenesis. However, studies assessing microbiological changes in Crohn's fistulas are sparse. Recent studies in our laboratory did not identify any live bacteria in fistula tracks of both idiopathic and Crohn's fistulae. In case that bacteria have a role in the pathogenesis of perianal fistulae, it is possible that bacterial products may be responsible for the inflammation and not live bacteria. Endotoxins are bacterial products which are not secreted but released when cells are disrupted. They are heat-stable toxins which are associated with the outer membranes of gram-negative bacteria. There is currently no published literature regarding the presence of endotoxins in perianal fistula tracks.
AIMS&METHODS: We aimed to assess for the presence of endotoxins in samples taken from Crohn's and idiopathic perianal fistula tracks.
Biopsy samples were taken from anal fistula tracks of 20 Crohn's and 23 idiopathic patients. Samples were taken from the top of the track (as close to the internal opening as possible), the middle of the track and the bottom of the track (as close to the external opening as possible). Samples were incubated separately in medium overnight. After centrifugation, the supernatant was recovered and frozen at -80°C and stored for bulk analyses. The Limulus Amebocyte Lysate (LAL) test kit was used for endotoxin (lipopolysaccharide) analysis.
RESULTS: Endotoxins were found to be present in some of the samples but not in all. This displays both an intra- and inter-individual variability. However, when the differences between the different parts of the fistula track were analysed, there was no statistically significant difference between the percentage positive expression of endotoxins at the top of the fistula track (p=0.45), the middle of the fistula track (p=0.73) and the bottom of the fistula track (p=0.74).
CONCLUSION: Endotoxins are present in both idiopathic and crohn's perianal fistula tracks. A non-statistically significant trend has been observed in percentage positive expression of endotoxins at the top of the fistula track as compared with the middle and the bottom. These results improve our understanding of the aetiology of perianal fistulae and may provide a therapeutic target in the future.
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Disclosure of Interest: None Declared
Keywords: Lipopolysaccharide, Perianal fistula

P1391 INTRACELLULAR KILLING OF BACTERIA IS NOT IMPAIRED IN CROHN'S DISEASE MONOCYTE-DERIVED MACROPHAGES

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INTRODUCTION: Patients with Crohn's disease exhibit an attenuated inflammatory response after trauma or *Escherichia coli* infection and have delayed clearance of subcutaneous bacteria compared to healthy controls. Adherent, invasive *E. coli*, increased in Crohn's disease, replicate within macrophages and may have a primary pathogenic role. Crohn's disease patients' macrophages may have a primary defect in bacterial killing, allowing survival of AIEC
AIMS&METHODS: We aimed to assess the relative ability of monocyte-derived macrophages from Crohn's patients to kill intracellular *E. coli* and *Staphylococcus aureus* compared to healthy controls. Peripheral blood monocytes were obtained from consenting adults by centrifugation over Lymphoprep™ followed by 2h adherence to plastic NuncÒ tissue culture dishes and subsequent differentiation into macrophages by 5d culture (as per Smith *et al*, J.Exp.Med. 2009, 206: 1883-97). Macrophages were infected with an adherent, invasive *E. coli*

HM605, *E. coli* K12 or *Staph. aureus* Oxford strain. Intramacrophage killing was assessed using the gentamicin protection assay. Cytokine release to the culture medium was also determined by sandwich ELISA. Macrophage-mediated chemotaxis of human neutrophils, obtained from healthy controls by centrifugation over Polymorphoprep™, was quantified in Boyden chambers
RESULTS: No significant difference in the relative killing of *E.coli* K12 (-14±11% vs -45±9%) and *Staph. aureus* (-52±4% vs -63±5%) nor in the relative survival of AIEC HM605 (+50±26% vs +8±22%) within monocyte-derived macrophages was seen (healthy controls vs Crohn's disease respectively; n=10 each group, ANOVA). TNFα, IL-6 and IL-8 production were not significantly different between the two groups and neutrophil chemotaxis was equivalent. Smoking status did not affect bacterial survival, with no differences observed in killing between current smokers, ex-smokers and non-smokers
CONCLUSION: Macrophages from patients with Crohn's disease do not appear to have an inherent defect in killing and exhibit normal pro-inflammatory responses. We postulate that local environmental factors may inhibit macrophage function *in vivo*. AIEC evade killing and possess the ability to replicate within macrophages from both healthy controls and Crohn's disease patients
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Disclosure of Interest: P. Flanagan Financial support for research from: Awarded a Shire innovation fund for SpRs, B. Campbell: None Declared, S. Subramanian: None Declared, J. Rhodes Lecture fee(s) from: has received speaking honoraria from Abbott, Falk, Ferring, Glaxo Smith Kline, Procter and Gamble, Schering Plough, Shire and Wyeth, Consultancy for: a member of advisory boards for Atlantic, Procter and Gamble and Falk, Other: with the University of Liverpool and Provexis UK, holds a patent for use of a soluble fibre preparation as maintenance therapy for Crohn's disease plus a patent pending for its use in antibiotic-associated diarrhoea
Keywords: Crohn's disease, Escherichia coli, macrophage

P1392 DIFFERENTIAL EXPRESSION OF AQUAPORINS IN HUMAN INTESTINAL MUCOSA DURING EARLY STAGE INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Aquaporins (AQPs) are a family of pore-forming proteins that efficiently and selectively mediate transport of water and small solutes across biological membranes. AQPs belong to a distinct family of membrane transport proteins that are selective for water molecules. Studies of AQPs have provided important insight into mechanisms that mediate water homeostasis and their role in human health and disease.
AIMS&METHODS: Here, we characterize the tissue-specific expression of selected AQPs using biopsies from the terminal ileum and colon of patients with newly diagnosed Crohn's disease (CD) or ulcerative colitis (UC). The goal was to investigate the relationship between AQP expression and the pathological features of inflammatory bowel disease (IBD) in humans. AQP1, 3, 4, 5, 7, 8 and 9 gene expression was quantified in biopsies from distal ileum and proximal and distal colon by quantitative real-time polymerase chain reaction (qRT-PCR). Protein expression of selected AQPs was also assessed by confocal microscopy with immunofluorescence (IF). Through multiple alignments of the deduced amino acid sequences, the putative 3D structure of AQP1, 3, 7, and 8 were modelled.
RESULTS: The qRT-PCR data indicated that AQP1, 3, 7 and 8 genes are expressed in all parts of the intestinal mucosa examined in this study. Notably, expression of AQP1 and AQP3 was downregulated in the ileum of CD patients and expression of AQP7 and AQP8 was downregulated in the ileum and the colon of UC patients. The findings were confirmed by confocal IF which also indicated a loss of apical immunolabeling for AQP3 and AQP8 in colonic surface epithelium and crypts of the IBD samples.
CONCLUSION: AQPs 1 and 8 and the aquaglyceroproteins 3 and 7 are the predominant aquaporins expressed in the human lower intestinal tract, their expression is significantly reduced in patients with IBD and they are differentially expressed in specific bowel segments in patients with CD and UC. These data represent a new link between gut inflammation and water/solute homeostasis and suggest that AQPs may play an important role in IBD pathophysiology.
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Disclosure of Interest: None Declared
Keywords: aquaporin, crohn disease, Intestinal epithelial barrier, ulcerative colitis

P1393 NEUTRALIZING ANTIBODIES AGAINST PLACENTAL GROWTH AS A NOVEL TREATMENT MODALITY IN EXPERIMENTAL CROHN'S DISEASE.

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INTRODUCTION: In contrast to vascular endothelial growth factor-A (VEGF-A), placental growth factor (PlGF) is exclusively involved in pathological angiogenesis. Therefore, PlGF is an attractive target for the treatment of diseases associated with increased angiogenesis, like inflammatory bowel disease (IBD).
AIMS&METHODS: The aim of this study was to analyze the potential of neutralizing PlGF antibodies in a mouse model of Crohn's disease (CD).
Intestinal mucosal VEGF-A and PlGF levels were assessed by ELISA during the course of chronic ileitis in the murine TNFDARE model of Crohn's disease. To analyze the effect of PlGF inhibition in this model, mice were treated with neutralizing anti-PLGF antibodies (50mg/kg, 2x/week intraperitoneally, N=8) or an equal dose of the corresponding control IgG (N=8), starting at an advanced stage of disease (week 9). The mice were clinically monitored and finally sacrificed for histological analysis and quantification of myeloperoxidase levels, inflammatory cytokines and leukocyte adhesion molecules. A subgroup of the mice was scanned with deoxy-2-[18F]fluoro-d-glucose (FDG) micro-positron emission tomography (μPET)/computed tomography (CT) before sacrification.
RESULTS: In contrast to VEGF-A, intestinal PlGF levels showed a linear increase with the progression of experimental chronic ileitis. Anti-PLGF reduced PlGF activity in the terminal ileum without affecting the VEGF-A levels. PlGF inhibition resulted in progressive weight gain of diseased TNFDARE mice ($P<0.01$ versus IgG-treated mice). Compared to IgG-treated mice, anti-PLGF-treated mice showed less histological inflammation, reduced levels of MPO and inflammatory cytokines ($P<0.05$ for all parameters) and lowered inflammation-induced terminal ileal FDG-uptake on μPET-CT after three weeks of treatment.
CONCLUSION: Placental growth factor is highly involved in chronic intestinal inflammation and its suppression with neutralizing monoclonal antibodies dampens the inflammatory process in a mouse model of CD-like chronic terminal ileitis. These results warrant a clinical trial with anti-PLGF in human CD.
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Disclosure of Interest: None Declared
Keywords: antibodies to placental growth factor, Crohn's disease

P1394 ENTERIC GLIAL CELLS FROM CROHN'S DISEASE PATIENTS HAVE ALTERED FUNCTION ON INTESTINAL EPITHELIAL BARRIER: TOWARD THE IDENTIFICATION OF NOVEL ESSENTIAL LIPIDIC GLIOMEDIATORS.

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INTRODUCTION: Evidence have identified enteric glial cells (EGC), the major constituent of the enteric nervous system, as key regulators of intestinal epithelial barrier (IEB) functions. Under physiological conditions, EGC enhance IEB repair, reduce its permeability, and increase its resistance to pathogens. These mechanisms are altered during inflammatory bowel disease (IBD) such as Crohn's Disease (CD) and Ulcerative Colitis (UC). EGC lesions have also been observed in IBD, but there is a lack of information about pathophysiological processes that could link IBD EGC to IEB dysfunctions.
AIMS&METHODS: To address this question, we have characterised EGC isolated from CD, UC, and cancer patients (considered as control EGC). We have compared their phenotype by measuring glial marker expression (GFAP, S100beta, Sox10) and have analysed their production for EGC-derived soluble factors (IL6, TGFbeta, proEGF, GSNO) but also for 31 lipidic mediators. In parallel we have studied EGC functional impact on IEB in a co-culture model using the human intestinal epithelial cells (IEC; Caco-2). In this model we have measured IEB transepithelial resistance (EVOM) and paracellular permeability (sulfonic acid-FITC flux). We have also analysed Caco-2 spreading (ZO1 immunostaining and cell area measurement), and proliferation (Ki67 immunostaining).
RESULTS: EGC from CD, UC or control patients expressed the same level of GFAP, Sox10, S100beta and did not present significant variations in their proliferation rate. In the same manner, their expression/production of IL6 and TGFbeta mediators and their impact on IEB permeability were comparable. But whereas control EGC increased significantly IEC transepithelial resistance and spreading, CD EGC had no effect. Analysis of the lipid profile of EGC supernatants revealed that CD EGC produced significantly less 5- and 15-HETE compared to control or UC EGC.
CONCLUSION: All together, these results show that human EGC from CD patients have lost their protective property on IEB that are IEC spreading and IEB resistance. These defects could be due to a lack of lipidic mediator production by CD EGC.
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Disclosure of Interest: None Declared
Keywords: crohn disease, enteric glial cells, enteric nervous system, Intestinal epithelial barrier

P1395 PPARGAMMA IMPROVES INTESTINAL FIBROSIS BY TARGETING THE EMT-ACTIVATOR ZEB1

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INTRODUCTION: Intestinal fibrosis is a common consequence of Inflammatory Bowel Disease (IBD), in which excessive extracellular matrix (ECM) components deposition causes obstruction and loss of function. Our previous data show inhibition of TGF-β1/Smad pathway mediated by a new transrepressive PPARγ modulator, GED-0507-34 Levo, and relative improvement of fibrotic disease in a DSS model of chronic colitis. TGF-β1/Smad is

the prototypical pathway regulating epithelial to mesenchymal transition (EMT) in fibrosis. PPARγ is highly expressed in intestinal epithelial cells (IEC) and its GED-mediated activation may inhibit TGF-β induced phenotypic EMT and in particular the over-expression of Zinc finger E-box-binding homeobox 1 (ZEB1), a pivotal epithelial markers transcriptional repressor.

AIMS&METHODS: Aim: To evaluate the role of GED-induced PPARγ activation to reverse the progression of TGF-β induced EMT, and to determine its ability to downregulate ZEB1 expression in intestinal epithelial cells.

Methods: Intestinal epithelial cells (HT29) differentiated by a 4 day treatment with TGF-β1 (10 ng/ml) were stimulated with GED 1mM. A PPARγ knockdown HT29 (ShPPARγ HT29) cell line was included in the study to confirm the PPARγ-dependence of GED effect. After 4 day of combined treatments EMT was determined by quantitative real-time PCR analysis of A33 and Cytokeratin 20 (two specific intestinal epithelial markers) aSMA, Collagen, Fibronectin and ZEB1. Collagen deposition was evaluated by Picrosirius red staining.

RESULTS: TGF-β1 induced phenotypic EMT in cultured HT29 and ShPPARg HT29 cell line via significantly reduced A33 and Cytokeratin 20 expression ($p<0.05$) and significantly increased expression of mesenchymal differentiation markers, α-SMA and Fibronectin ($p<0.01$) in association with the loss of epithelial morphology. GED reduced αSMA and Fibronectin mRNA expression (1.2 fold and 2.5 fold vs TGF-β, respectively. $p<0.05$) and restored specific IECs markers. GED determined a 65% reduction of TGFβ-induced collagen deposition ($p<0.05$). ZEB1 mRNA expression was downregulated by GED in TGF-b treated IEC by 2.2 fold ($p<0.05$) compared to TGF-β treated cells. Significant effects of GED treatment were not observed in ShPPARγ HT29.

CONCLUSION: GED reversed all EMT markers in a PPARγ-dependent manner. The present study could represent a useful start point to better highlight the action spectrum of PPARg in prevention and care of intestinal fibrosis and to identify new specific molecular target to develop efficient therapeutic strategies.

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Keywords: Epithelial-mesenchymal transition, IBD, Intestinal Fibrosis, PPAR-γ, TGF-beta1, ZEB1

P1396 ENTEROCOCCAL POLYSACCHARIDE ANTIGEN (EPA)-MEDIATED ADHESION CONTRIBUTES TO VIRULENCE OF PATHOBIONTS IN INFECTION AND CHRONIC INFLAMMATION MODELS

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INTRODUCTION: *Enterococcus faecalis* – a commensal of the human intestinal microbiota - was shown to induce intestinal inflammation in the IL-10-/- mouse model of experimental colitis making this an exemplary model to analyze structure-function relationships for microbe-host interactions. The enterococcal polysaccharide antigen (Epa) was previously described to affect *E. faecalis* virulence.

AIMS&METHODS: In this study, we characterized enterococcal virulence using a newly generated epaB deletion mutant (TX5692).

RESULTS: *E. faecalis* Δ*epaB* mutant showed reduced virulence in *Galleria mellonella* and *Caenorhabditis elegans* infection models. A deletion of epaB resulted in diminished biofilm generation including attenuated formation of microcolonies and impaired adhesion to epithelial cells *in vitro*. To further analyze microbe-host interaction, germ-free *Manduca sexta* larvae, a natural host to *E. faecalis*, were mono-associated with *E. faecalis* mutant and wild-type strains. Compared to wild-type OG1RF, the Δ*epaB* mutant showed impaired midgut colonization and altered adhesion to larval intestinal epithelium. In a mono-association experiment, IL-10-/- mice associated with Δ*epaB* mutant strain showed significantly diminished intestinal pathology and reduced chronic inflammation markers, such as lower spleen weight and less increased colon length, compared to OG1RF-associated mice.

CONCLUSION: Our experiments show an impact of epaB on *E. faecalis* virulence and intestinal pathogenesis in a colitis mouse model. This indicates to mechanisms related to altered adhesion of *E. faecalis* to mucosal surfaces and may unravel a track of how epaB-mediated adhesion contributes to *E. faecalis*-host interaction.

Disclosure of Interest: None Declared

Keywords: commensal bacteria, Inflammatory bowel disease (IBD)

P1397 SERUM METABOLOME IN MILD-MODERATE ACTIVE ULCERATIVE COLITIS AND CELIAC DISEASE

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INTRODUCTION: Ulcerative colitis (UC) is a chronic autoimmune inflammatory bowel disease whose pathogenesis is not fully understood. Celiac disease (CD) is a disorder that caused by an abnormal immune reaction to the dietary gluten and primarily affects the small intestine. Gas chromatography-mass spectrometry (GC-MS) of serum generates comprehensive metabolic profiles, reflecting integrated human (systemic) and gut microbial metabolism which may be altered in disease states.

AIMS&METHODS: The aim of this study was to investigate GC-MS-based serum metabolomic profiles in UC patients, CD patients and healthy controls, potentially to provide insights into disordered integrated metabolism and underlying mechanisms.

Serum metabolic profiles and fecal samples were collected from 75 individuals (20 patients with mild-moderate active UC, 35 CD patients, and 20 healthy controls). The multivariate analysis techniques such as principal components analysis (PCA) and other methods were used to assess differences between groups.

RESULTS: We characterized 84 serum metabolites by use GC-MS and multivariate analysis to differentiate between diseased and non-diseased individuals, as well as between the UC and CD cohorts. 18 metabolites at least have a combined (human + microbial) origin. In serum of UC patients, phenylacetic acid (PAA), 4-hydroxyphenylacetic acid (4-HPAA), 3-indolylacetic acid (IAA), succinic acid (SA) and fumaric acid (FA) were the metabolites most prominently increased, whereas 3-phenylpropionic acid (PPA) was significantly decreased. Serum of CD patients showed significant increases in IAA, 3-indolepropionic acid (IPA), SA and FA. Differences in serum metabolite levels of UC patients, CD patients and controls may indicate the difference in the metabolic activity of gut microbiota (some *Clostridia* and *Bacteroides* spp.) involved in phenylalanine and tyrosine metabolism. Increased serum levels of succinic acid, produced abundantly by some *Bacteroides* spp., suggest its possible damaging effect on intestinal mucosa especially in ulcerative colitis. Orally administered butyrate + inulin (Zacofalk NMX, Dr. Falk Pharma GmbH, 3 tablets per day for 4 weeks) as supplement to mesalazine in UC or gluten free diet (GFD) in CD was effective in reducing disease activity, with a marked improvement of gut microbiota and serum metabolic profiles in both diseases.

CONCLUSION: Quantitative metabolomic profiling of serum using GC-MS discriminates between UC patients, CD patients and healthy controls. Metabiotic consisting of butyric acid and inulin can be effectively used in UC, as well as in CD, improving symptoms and metabolic profiles.

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Disclosure of Interest: None Declared

Keywords: butyrate, celiac disease, inulin, metabolomics, ulcerative colitis

P1398 DIRECT ROLE OF IFX ON INTESTINAL MUCOSA SUSTAINS MUCOSAL HEALING: EXPLORING NEW MECHANISMS OF ACTION

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INTRODUCTION: Infliximab (IFX), the first born chimeric antibody anti-TNF-a in IBD, is effective in IBD through several mechanisms of actions, including an action on both immune and no immune intestinal cells. Although clinical studies demonstrated clear efficacy of IFX in inducing and maintaining IBD remission, it is still not clear whether IFX really acts at mucosal levels.

AIMS&METHODS: Aim of this study is to verify mechanisms of action of IFX at intestinal mucosal level and whether these pathways contribute in mucosal healing. The direct effect of IFX was assessed on human colonic mucosa biopsies, taken from IFX naïve patients in active state of disease. Biopsies were washed, weighted and incubated for 12 hours in 24-well plate, with or without IFX (50 µg/ml). Supernatants were assessed for multiplex cytokines evaluation (Bio-Plex®, BIO-RAD). Moreover, cultured biopsies were included for histological evaluation and then stained to evaluate CD68, CD3, E-cadherin expression and apoptosis by the terminal deoxynucleotidyl transferase (dUTP) nick end labeling assay.

RESULTS: IFX- treated biopsies displayed reduced inflammatory infiltrate with a reduction in total counts of CD68 and, particularly, for CD3 positive cells when compared to untreated biopsies, with an increase of E-cadherin expression and apoptosis at Tunel assay. Cytokines evaluation on supernatants of biopsies treated with IFX showed lower TNF-α, IL-17, IL-6 and IL-8 concentration, with an increase in INF-γ, FGF and IL-1β. Biopsies from active IBD patients exposed to a direct incubation with IFX for 12 hour showed a better and more conserved histology aspect then that of IFX-untreated biopsies.

CONCLUSION: These data suggest that IFX acts directly on intestinal mucosal level and that it could contribute to slower loss of glandular epithelium, probably because of the decrease in the pro-inflammatory cytokines activity and an increase in genes involved in repair function, like basic FGF.

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Disclosure of Interest: None Declared

Keywords: IBD, infliximab, mechanism of action, mucosal healing

P1399 IN VITRO EVIDENCE ON POTENTIATION IMMUNE REGULATORY PROPERTIES OF A UNIQUE SUBPOPULATION OF HUMAN MSC

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INTRODUCTION: MSCs have been found to have significant immunosuppressive capacities which make it as a potential treatment for various immune disorders including IBD. MSCs pretreated by proinflammatory cytokines such as INFr and TNFa obtain intensive immunoregulatory effect, thus far the qualification of activated MSCs is still unclear, especially for human cell as the effect molecule seems different between the cell of human and mice.
AIMS&METHODS: The hMSChireg, a subpopulation of human mesenchymal stem cells with character of CD106+, has just been defined by us. Subpopulations of MSCs were separated using EasySepH PEPositive Selection Kit. LC3-II was detected by Western Blot. Monocytes transfected with LC3-GFP were treated in different co-cultured system respectively and then LC3+ spots were quantified by fluorescent microscopy. The Microarray was done by CapitalBio Corporation.
RESULTS: The hMSChireg induce an almost complete inhibition of IFN-r secretion of PHA stimulated PBMCs whereas the residual ones induce only partial inhibition (5% vs 39%). Also, hMSChireg can suppress TNF-a production to a much lower level than their counterpoint (41% vs 79%). hMSChireg decrease the expression of IFN-r and TNF-a more effectively (2% vs 19%, 5% vs 19%). In addition, hMSChireg can induce Treg more effectively than the other part of MSCs (5.4% vs 3.3%), hMSChireg treated monocytes up-regulate their LC3-II gene expression while the effect of their counterpoint is weaker. hMSChireg more significantly enhance autophagy of macrophage (4.20 vs. 1.56). gene expression profiles are generated from both hMSChireg and residual MSCs which show that the levels of COX-2, IL-1a, IL-1b, IL-6, IL-8 and IDO1 are significantly up-regulated in hMSChireg with an increased ability to secrete PGE2.
CONCLUSION: MSChireg, as a unique subpopulation of MSC, more effectively suppress Th1 polarization of CD4+ T cells and induce Treg and at same time more significantly enhance autophagy. This indicates that MSChireg may not only contribute to inhibit excess inflammatory but also ameliorate the defective innate immunity in IBD. However, even under inflammatory conditions only a proportion of MSC can be detected in the intestine, suggesting that additional mechanisms of immune suppression may be active. In addition, enhancing binding of MSChireg enhances their migration to the inflamed colon and in turn may also be expected to potentiate their immunosuppressive effects in vivo. So we hypothesize that MSChireg could lead to a more rapid clinical response and a dose reduction of cells, which could have profound effects on current treatment development programs.
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Disclosure of Interest: None Declared
Keywords: IBD, immunoregulatory, in vitro, Mesenchymal stem cells

P1400 CHARACTERIZATION OF PERIANAL CROHŃS DISEASE - RETROSPECTIVE COHORT STUDY

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INTRODUCTION: Perianal manifestations of Crohńs Disease (PMCD) are multiple and may be a therapeutic challenge. Its prevalence is variable with differing results depending on the type of study, length of follow up and the kind of considered perianal lesions. Most studies focus only on fistulas and abscesses and are of an era prior to the introduction of anti-TNF.
AIMS&METHODS: AIM: Characterization of the perianal manifestations in a cohort of patients with Crohńs Disease (CD).
METHODS: Retrospective cohort study with 921 patients with CD. Five PMCD were analyzed: fistulas, abscesses, anal stenosis, ulcers of the anal canal and anal fissures. Other variables: sex, current classification of CD (Montreal Classification), time of follow up, type of PMCD, past and current medical-surgical treatment and response to medical-surgical treatment.
RESULTS: 249/921 (26.3%) patients have at least one PMCD. Baseline characteristics: Average age of diagnosis: 31,2yrs. Male sex: 46%. Average time of follow up: 15,2yrs. Current Montreal Classification: B1 39.1% B2 36.6% B3 24.3% L1 39.1% L2 29.0% L3 31.9% (+L4 3.4%). Rectal involvement: 46.4%. In 41.6% of cases the PMCD preceded the diagnosis of CD. Average number of perianal manifestations: 2.5/patient. PMCD characterization: 9.1% fissures; 9.1% ulcers of the anal canal; 43% fistulas (complex fistulas in 74% of cases); 36.8% abscesses: 2% anal stenosis (4 post-hemorrhoidectomy). Medical therapy in the diagnosis: 71.9% isolated thiopurine, 2.3% anti-TNF: 0.89% combined therapy. Present medical therapy: Anti-TNF: 9.4%; Anti-TNF + thiopurine 25.1%; Thiopurine: 43.5%; MTX; 2.6%; MTX + anti-TNF 4.3%. Surgical/endoscopic approach: anorectal stenosis dilation (n=8). Fistuletomy (n=70). Protectomy (n=10, 8 with previous ulcers of the anal canal), advancement flap (n=9). Response to medical-surgical treatment: none 6.4%, partial response 13.2%, complete response 70.2%, in evaluation 9.9%.
CONCLUSION: In this cohort 26.3% of the patients with CD have at least one of the 5 PMCD studied. The suppurative complications are the most common, although a high number of ulcers of the anal canal have been documented. The fistulas are mainly complex requiring a medical/surgical approach. Presently the majority of the patients are undergoing treatment with thiopurines or combination therapy with anti-TNF. This is one of the largest studies of characterization of perianal Crohńs Disease.
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Disclosure of Interest: None Declared
Keywords: CROHŃS DISEASE, Perianal Crohńs Disease

P1401 PATIENTS' PERCEPTIONS OF PSYCHOLOGICAL SURVEYS IN INFLAMMATORY BOWEL DISEASE.

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INTRODUCTION: With treatment advances, life expectancy in inflammatory bowel disease (IBD) is normalising and thus there is an increasing focus on disability and quality of life (Qol). This has resulted in a multitude of tools to measure patient reported outcomes. Despite this, little is known about patients' perceptions regarding QoL research and which aspects they consider most important
AIMS&METHODS: To explore patient perceptions of IBD QoL research.
387 IBD patients were approached, of whom 341 (88%) (median age 36 years; 175 male) completed a comprehensive questionnaire that included validated instruments to assess depression, anxiety, quality of life, self-esteem, body image and sexual satisfaction. Patients were asked to provide feedback regarding the study, specifically questions they did or did not like and the introduction of such questions at routine clinic visits. Free text boxes were provided for comments. Statistical analysis was performed in SPSS vs 20 and using grounded theory coding of qualitative responses.
RESULTS: 83% of patients reported liking the study. Reasons for liking the study included, 'to express feelings', that 'it covered all aspects of daily life both physically and emotionally' and that it 'might help others'. Additional recurring themes included; the survey made them feel 'less alone', and being 'easier to express emotions in a survey'. 17% disliked the questionnaire. The majority reported that is was 'too long' while others commented that it was 'repetitive', 'too personal' or that they 'don't like doing surveys'. When asked if they would like any of these questions asked at regular clinic, 75% reported yes and 25% reported no. When given an option of which questions they would like asked, the most popular related to work/daily activities in 54%, mood and feelings in 54%, body image in 27% and sexual health in 16%. There was little correlation between liking the study and wanting questions asked at clinic, (r, 0.14, p=0.02). Linear regression identified education as being associated with liking the questionnaire, (p=0.03), while older age, body image disturbance and disability were associated with wanting questions asked at clinics, ($p<0.001$, $p<0.001$, p=0.009).
CONCLUSION: Most patients are interested in participating in QoL research. Patients appreciate the opportunity to address psychosocial concerns and to help others, indicating a high degree of altruism among IBD patients. Areas of particular interest were activities of daily living and mood. This highlights the importance of QoL research in care for patients with IBD, and also suggests that there are few predictable variables to identify patients who are more invested in QoL issues than others.
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Disclosure of Interest: None Declared
Keywords: Inflammatory bowel disease (IBD), quality of life

P1402 PSORIASIS PHENOTYPE IN INFLAMMATORY BOWEL DISEASE: A CASE-CONTROL PROSPECTIVE LONGITUDINAL STUDY

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INTRODUCTION: Psoriasis has been associated with Inflammatory Bowel Disease (IBD). However, whether IBD is associated with specific phenotypes of psoriasis is unknown.
AIMS&METHODS: In a case-control prospective longitudinal study, we aimed to assess the psoriasis phenotype in patients with IBD, when compared with non-IBD control patients (non-IBD C). At this purpose, from January 2011 to April 2013, dermatological assessment was performed in 188 consecutive IBD patients under follow up. Dermatological assessment was focused in detecting the presence of psoriasis (present/absent) and in defining characteristics of psoriasis (localization, phenotype) including severity (mild/moderate/severe). In order to define psoriasis phenotype, each IBD patient with psoriasis was matched for gender, ethnicity and age (±5 years) with one non-IBD patient with psoriasis, referring to the same University/Hospital. Data were expressed as median and range and differences between groups assessed by the T test.
RESULTS: Dermatological assessment was performed in 188 IBD patients (85 F, age 45.5 yrs, range 18-85; IBD duration 9 yrs, range 1-46). Among these 188 patients, there were 72 UC (35 M, age 47, range 23-85; UC duration 6 yrs, range 1-40; UC extent: distal 26, left-sided 11, pancolitis 31, ileal pouch 3, ileostomy 1) and 116 CD (69 M, age 44, range 18-80; CD duration 10 yrs, range 1-46; CD colitis 8, ileo-colitis 24, ileitis 34, neo-terminal ileum 45, ileostomy 2, jejunum 1,

distal ileum + jejunum 2). Non-IBD C included 50 patients (31 M, age 47, range 18-75). Among the 188 IBD patients, psoriasis was detected in 48 (26 %; 28 CD, 20 UC). In the IBD group, the median age and IBD duration were comparable in patients with or without psoriasis (age 50.5 range 23-72 vs 44 range 18-85; IBD duration 8 yrs range 1-45 vs 9 yrs range 1-41; p=ns for both). Mild psoriasis was detected in a higher proportion of IBD patients (40/48; 83%) than non-IBD C (28/50; 56%;$p < 0.001$). Scalp psoriasis and sebopsoriasis were the more common psoriasis phenotype in IBD (16/48; 33%), followed by inverse psoriasis (7/48; 15%) and by palmo-plantar psoriasis (5/48;10%). Psoriatic arthritis was detected in 9/50 (18%) non-IBD-C and in 4/48 (8%) IBD patients (p=n.s.). In 4/48 (12%) IBD patients, psoriasis developed after anti-TNFs (palmo-palmar 3, sebopsoriasis 1).
CONCLUSION: Results from a cohort of IBD patients matched with non-IBD control patients suggest that specific phenotypes of psoriasis may be associated with IBD.
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Disclosure of Interest: None Declared
Keywords: crohn's disease, non IBD controls, phenotype, Psoriasis, ulcerative colitis

P1403 SCREENING FOR MELANOMA AND NON MELANOMA SKIN CANCER IN IBD PATIENTS BEFORE TREATMENT WITH THIOPURINES AND ANTI-TNFS: A PROSPECTIVE COHORT STUDY.

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INTRODUCTION: Recent evidences suggest an increased risk of Non Melanoma Skin Cancer (NMSC) using thiopurines in IBD and preliminary observations suggest an increased melanoma risk by using anti-TNFs.
AIMS&METHODS: In a prospective study, we aimed to assess the frequency of NMSC and melanoma in a cohort of IBD patients screened for skin cancer before thiopurines or anti-TNFs. From January 2012 to April 2013, consecutive IBD patients in follow up, with clinical indication to use thiopurines or anti-TNFs were screened by one experienced dermatologist. Dermatological assessment was performed before (T0), 6 (T6) and 12 mos (T12) after immunomodulators (IMM). Dermatological assessment was focused in detecting NMSC or melanoma. Results were expressed as median and range.
RESULTS: Dermatological assessment has currently been performed in 61 IBD patients (32M, age42, range 20-70; IBD duration 7yrs, range 1-30). IBD group included 15 UC (9M, age39, range 23-70; duration 6 yrs, range 1-17; UC distal 2, left 2, extensive11) and 46 CD (23M, age 42, range 20-67; duration 8,5yrs, range 1-30; CD colitis 2, ileo-colitis 10, ileitis 13, neo-terminal ileum 21). Combined therapy (1 azathioprine, AZA+Infliximab, IFX; 2 AZA+adalimumab, ADA) was initiated by 3/61(5%) patients. Monotherapy included AZA in 26/61(43%) IBD(7 UC,19 CD), 6-mercaptopurine in 2/61 (3%) IBD(1UC,1CD) and anti-TNFs in 36/61 (59%) patients (8 UC,28CD), including IFX in 18/61 (29%)(6UC,12 CD), ADA in 18/61(29%) patients (2UC,16CD). Before IMM, 1/61(1.6%) patients showed NMSC, while no melanotic cancers were detected. At T0, all patients were treated with local photolyase aimed to prevent skin cancer. At T6, dermatological assessment has been performed in 19/61 (31%) patients, as 8 (13%) discontinued therapy (intolerance in 7: AZA 5, ADA 1, IFX 1; pregnancy in 1, IFX); 2 (3%) were lost to follow up; 2 (3%) died (cirrhosis or sepsis), while 30 (49%) patients are continuing the follow up. At T12, 45/61(74%) patients are therefore in follow up; in 1(2%) patient no lesions were detected, while 4/61(7%) patients discontinued IMM due to intolerance (1AZA,2ADA,1IFX). No cases of NMSC or melanoma were detected at 6 or 12 mos (1NMSC detected only at T0).
CONCLUSION: In a cohort of IBD patients from a Mediterranean area, dermatologic screening before immunomodulators showed a low frequency of NMSC and no melanoma. Dermatologic screening and photoprotection are however reccomended during IMM in IBD patients already showing a higher risk of skin cancer.
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Disclosure of Interest: None Declared
Keywords: Inflammatory bowel disease (IBD), Melanoma, Non Melanoma Skin Cancer, thiopurine

P1404 FREQUENCY AND PREDICTORS OF NEGATIVE CALPROTECTIN IN IBD IN TERTIARY CENTER

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INTRODUCTION: Fecal calprotectin (f-cal) is a sensitive marker of intestinal mucosal inflammation. It might be a more sensitive predictor for disease activity and risk of relapse than mucosal healing
AIMS&METHODS: The aim of this study was to analyze the f-cal levels in IBD patients in a tertiary IBD center. Furthermore, we analyzed predictive factors of negative f-cal. cohort consisted of 134 IBD patients, 83 with Crohn's disease (CD) and 51 with Ulcerative colitis (UC). Demographic and clinical characteristics of the disease and concomitant medication were determined in every patient. F-cal levels were measured using cut-off value for negative f-cal < 50ug/g. We also analyzed the prevalence of undetectable f-cal levels using cut-off value $< 7,8$ug/g. Predictors of negative f-cal were analyzed.
RESULTS: Negative f-cal was detected in 54/134 (40,2%) IBD patients, 35/83 (42,2%) CD patients, 19/51 (37,3%) UC patients. Undetectable f-cal was present in 36/134 (26,4%) of IBD patients, in 23/83 (27,7%) of CD patients and in 13/51 (25,5%) UC patients. In IBD patients on biologics (n=77), those on concomitant AZA had negative f-cal in 21/41 (51,2%) as compared to those without AZA 10/36 (27,8%); p=0,036. Undetectable levels of calprotectin were present in 16/41 (39,0%) patients trated with biologics on AZA and in 5/36 (13,9%) patients without AZA; p=0,013. Amongst CD patients treated with biologics (n=54), the concomitant AZA therapy was associated with negative f-cal in 16/27 (59,3%) patients compared to 7/27 (25,9%) patients; p=0,013. Inflammatory behaviour was associated with significantly lower rate of negative f-cal 7/27 (25%) in comparison to stricturing and fistulising CD 28/56 (50%);p=0,03.
CONCLUSION: The results of this study indicate a rather low frequency of negative f-cal in IBD patients. Biological therapy with concomitant AZA shows the highest rate.
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Disclosure of Interest: None Declared
Keywords: Fecal calprotectin, inflamatory bowel disease

P1405 THE RISK OF COLITIS-ASSOCIATED CANCER IN ULCERATIVE COLITIS PATIENTS – A SINGLE CENTER STUDY

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INTRODUCTION: Epidemiological data and molecular insights hint at an increased risk for colitis associated cancer (CAC) in patients suffering from ulcerative colitis (UC) [Eaden Gut 2001]. However, since recent studies propose decreasing time-trends for CAC [Söderlund Gastroenterology 2009], the aim of our study was to determine the prevalence of CAC in a German referral center, as well as to characterize the risk profil of affected UC patients.
AIMS&METHODS: A cohort with a total of n=434 UC patients visiting our clinic between the years 2002 and 2013 was evaluated. Data analysis was performed by univariate logistic regression. Impact of clinical parameter was evaluated by Odds ratios (OR) and 95% confindence intervals (CI), significance was assessed by Wald-test.
RESULTS: Mean patient age at UC diagnosis was 45.7 ± 15.1 with manifestation profile 47.2% pancolitis, 44.4% left-sided colitis and 8.4% proctitis. Disease duration in 56.6% of patients was between 0-8 years, in 21.1% between 9-15 years and in 22.2% more than 15 years. Overall, CAC was detected in ten patients (2.3% of the total cohort). Of these, six patients suffered from pancolitis and eight suffered from UC longer than 15 years. Thus, UC disease duration was strongly associated with the risk for CAC (P=0.004); disease duration between 9-15 years: OR of 2.5 (95% CI 0.1-41.1), more than 15 years: OR of 21.1 (95% CI 2.5-171.3). Furthermore, the risk of dysplastic polyps was also significantly related to disease duration (P=0.02); disease duration between 9-15 years: OR of 1.6 (95% KI 0.5-4.8), more than 15 years: OR of 4.1 (95% KI 1.7-10.1). Established antiinflammatory medication (e.g. 5-ASA, anti-TNF-a) significantly reduced the risk for dysplastic polyps and CAC (P=0.03, OR of 0.3, 95% CI 0.1-0.8; and $P < 0.05$, OR 0.2, 95% CI 0.07-0.9).
CONCLUSION: The rate for CAC found in our relatively large, retrospective, single-institution cohort study contradicts the findings of recent studies and confirms historical data [Eaden 2001]. The risk for dysplastic polyps and CAC is strongly associated with longer disease duration and the extent of colitis. Furthermore, antiinflammatory therapy led to a significant risk reduction for dysplastic polyps and CAC.
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Disclosure of Interest: None Declared
Keywords: colitis-associated cancer, surveillance, ulcerative colitis

P1406 SMOKING CESSATION AND THE COURSE OF CROHN'S DISEASE IN THE BIOLOGIC ERA: A MULTICENTER PROSPECTIVE STUDY

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INTRODUCTION: Even though the negative impact of tobacco smoking on Crohn's disease (CD) phenotype and complications is well established, the clinical usefulness of smoking cessation in ameliorating disease activity has been evaluated by one single prospective study that took place before the era of widespread and early use of anti-TNF and immunosuppressant drugs. Our aim was to evaluate the current clinical benefit of quitting smoking in CD patients prospectively followed after a complete smoking cessation.
AIMS&METHODS: 1170 patients from 14 IBD centers were included. The subjects presented various smoking status and were followed every 3 months. All included smokers were advised to quit smoking and different smoking cessation strategies were proposed according to the clinical practice of each

participating center. Patients not exposed to tobacco before inclusion (non- and former smokers), current smokers and quitters were prospectively compared regarding differences in their disease outcomes.
RESULTS: Subjects with complete data regarding their disease outcomes along with a study follow-up larger than 1 year were included in the present analysis (134 current smokers, 326 non-smokers and 67 quitters). At present, this cohort has 39 months (interquatile range of 18-42) of global study follow-up with a median of 18 months of smoking-free time for the quitters. In comparison with non-smokers, current smokers presented more disease activity (43% vs. 32%, $p<0.05$), more severe disease flare-ups with subsequent hospitalization (15.6% vs. 7.4%, $p<0.05$) and a trend towards an increased need for anti-TNF drugs (16.5% vs. 8.8%, p=0.06). Surprisingly, no differences with respect to disease activity, complications and different therapeutic requirements were found between current smokers and patients who achieved a complete smoking cessation.
CONCLUSION: In this multicenter prospective study, current smokers present a more severe disease course when compared to patients not exposed to tobacco. With the present follow-up, no differences in disease activity, complications and treatment were found between ongoing smokers and patients who quit.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, environmental factors, smoking, smoking cessation, tobacco

P1407 A 7 YEARS STUDY ON EPIDEMIOLOGIC ASPECTS OF INFLAMMATORY BOWEL DISEASE IN THE NORTH EAST OF ITALY.

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INTRODUCTION: Several studies confirm that the incidence and prevalence of inflammatory bowel disease (IBD) are increasing with time. Moreover the distribution of these results is extremely heterogeneous according to different geographic areas considered. Great interest causes this evaluation since the IBD are chronic diseases that require continuing therapy and assistance. It is not clear if the trend is justified by environmental risk factors or if it is secondary to a greater diagnostic accuracy.
AIMS&METHODS: The aim of this study was to determine the change of prevalence of IBD, ulcerative colitis (UC) and Crohn's disease (CD), in the residing population in our Sanitary District 9 Veneto in the last seven years. A retrospective study of prevalence was performed in an area on 500,000 inhabitants from 2005 to 2011 evaluating the IBD registry of the National Health System and considering all new registered exemptions.
RESULTS: 353 new exemption for IBD have been reported during the observation period. The prevalence of IBD detected in 2005 was 100,36/100.000 inhabitants of which 25,46/100.000 CD and 74,89/100.000 UC; no statistically significant difference between males and females (p=ns). In 2011, however, the prevalence of IBD was 179.13/100.000 inhabitants of which 59,63/100.000 CD and 119,5/100.000 UC, being the male population higher than the female one (p=0,028). In a cohort of 398 cases followed for 5 years no difference in the average age of death in comparison to the general population was found (IBD men 72,1±16,6 yrs, women 79,3±10,2 yrs vs general population men 74,2±16 yrs, women 81,2±15 yrs, p=ns). The most frequent cause of death is represented by cardiovascular disease (8 cases), followed by cancers not related to IBD (6 cases), other (3 cases). One patient died of complications related to UC diagnosed in late age.
CONCLUSION: The prevalence rate of IBD in the studied district corresponds to the data detected in the countries of northern Europe. A progressive increase in the diagnosis of IBD in the last years has been demonstrated, namely 179/100.000 inhabitants in 2011 opposite to 100/100.000 at baseline (2005). At the same time, leasting the years CD increased from 25/100.000 to 56/1000.000. The life expectancy in IBD is similar to that of the general population and the causes of death are not related to IBD.
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Disclosure of Interest: None Declared
Keywords: Epidemiology, Inflammatory bowel disease (IBD)

P1408 THE DIAGNOSTIC ACCURACY OF FECAL CALPROTECTIN IN POUCHITIS

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INTRODUCTION: Total proctocolectomy with ileal pouch-anal anastomosis (IPAA) represents the most common surgical procedure for intractable ulcerative colitis (UC), although up to 50% of the patients undergoing surgery will develop pouchitis. The diagnosis of pouchitis requires both pouch endoscopy and biopsy. Searching for non invasive markers which correlate with the degree of the mucosal inflammation is becoming more and more important.
AIMS&METHODS: The aim of our prospective study was to compare fecal calprotectin and matrix metalloproteinase (MMP)-9 in patients with and without pouchitis assessed by clinical, endoscopic and histological scores and to evaluate the diagnostic accuracy of fecal calprotectin and MMP-9 in pouchitis. Stool and blood samples were collected in 27 IPAA patients before control endoscopy. Pouchoscopy was performed and biopsies from the reservoir were taken for histology. Pouchitis was defined as Pouchitis Disease Activity Index (PDAI) > 7 points. The presence of cuffitis was evaluated by endoscopy. Demographics, pouch wear time, inflammatory laboratory parameters and medications used at the time of the study were recorded. Calprotectin and MMP-9 were quantified by use of enzyme-linked immunosorbent assay.
RESULTS: Pouchitis was detected in 22% of the patients. Cuffitis was presented in 8 cases. Fecal calprotectin and MMP-9 was significantly higher in patients with vs. without pouchitis (616.4 vs. 118.5, p=0.02 and 23.5 vs. 3.95, p=0.04), but none of them correlated with cuffitis. The cut-off value for fecal calprotectin and MMP-9 in the diagnosis of pouchitis revealed to be 370 μg/g and 5 ng/ml respectively. None of the examined inflammatory laboratory markers correlated significantly with pouchitis. The pouch wear time did not influence the development of the pouch inflammation.
CONCLUSION: Fecal calprotectin and MMP-9 proved to be reliable markers for the determination of pouch inflammation which may be helpful in the diagnosis of pouchitis and in the differentiation between pouchitis and cuffitis.
Disclosure of Interest: None Declared
Keywords: calprotectin, MMP9, pouchitis

P1409 FEASIBILITY OF ENDOSCOPIC ASSESSMENT AND TREATING TO TARGET TO ACHIEVE MUCOSAL HEALING IN CROHN'S DISEASE

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INTRODUCTION: Current evidence suggests that treatment strategies focused on controlling symptoms do not alter the course of Crohn's disease (CD). Mucosal healing (MH) as a treatment target is of growing interest because it is associated with improved outcomes. We therefore evaluated utility of "treating to target" according to endoscopic findings to reach MH.
AIMS&METHODS: The medical records of 199 patients with CD followed in a single inflammatory bowel disease unit from 2011 to 2012 were reviewed through April 2013. After an initial assessment, endoscopic outcomes were reviewed in all patients with baseline endoscopic lesion. Cumulative incidence of MH (disappearance of all baseline ulcerations) and endoscopic improvement (disappearance of deep ulceration) were estimated using a Kaplan-Meier method. Independent predictors and factors associated with MH were identified using a Cox proportional hazards model.
RESULTS: At baseline, the median age was 38 (IQR75 25-52) and median disease duration was 6.8 years (IQR75 1.5-18.5). Previous treatment included immunosuppressives, TNF antagonists, and surgery for 58 (52.7%), 58 (52.7%) and 42 (38.1%) of patients, respectively. A total of 68 patients (out of 174 patients) underwent repeat endoscopic assessment, representing a total of 163 procedures (including baseline assessments). The median time between two procedures was 26 weeks (IQR75 18.1-38). Second and subsequent assessments were a priori planned to assess response to adjusting therapy and 56 patients were asymptomatic at the time of assessment. After a median follow up of 62 weeks, 34 patients (50%) achieved MH and 41 (60.3%) patients had endoscopic improvement. The cumulative probabilities of endoscopic improvement were 11%, 38% and 61% at 24, 52 and 76 weeks respectively and cumulative probabilities of mucosal healing were 16%, 47%, and 70% at 24, 52 and 76 weeks respectively. None of baseline factors were independently predictive of mucosal healing including prior or current use of immunosuppressives and TNF antagonists. Importantly, independent factors associated with mucosal healing were a median time between endoscopy under 26 weeks (HR=2.13;95%IC 1.04-4.47, p=0.038) and any therapeutic change in case of absence of MH (including biologics introduction/optimization/switch or immunosuppressive introduction/switch)(HR=3.2; 95%IC 1.46-8.04, p=0.003).
CONCLUSION: We demonstrate that repeated objective measurement of disease activity and adjusting therapy to the target of MH is feasible and highly effective. Randomized trials that evaluate treat-to-target algorithms are needed to determine if this treatment strategy can change the course of the disease.
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Keywords: Crohn's disease, endoscopy, mucosal healing, treat to target

P1410 A SCORE USING TISSUE EOSINOPHIL COUNT AND IMMUNOHISTOCHEMICAL MARKER OF CD30 MAY DISCRIMINATE CROHN'S DISEASE FROM ULCERATIVE COLITIS

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INTRODUCTION: Routine histopathological examination from colonoscopic biopsies sometimes are not useful to differential diagnosis of colonic involvement by Inflammatory Bowel Diseases (IBD). The development of new immunohistochemical tools may be helpful to overcome this limitation.
AIMS&METHODS: To evaluate the relevance of CD30 expression by Immunohistochemistry, eosinophil count and histopathological features in differential diagnosis of IBD.
185 IBD patients (105 CD/ 80 UC), were evaluated at a specialized center in a university hospital. Diagnosed according to Lennard-Jones criteria, reviewed by a gastroenterologist expert and corroborated by five years follow up. Patients were all treatment naïve at the time of collection of the biopsies. The samples were taken from affected areas in the colon and examined by an experienced gastrointestinal pathologist. Study approved by the local IRB.
RESULTS:

	CD (105)	UC (80)	p
Eosinophils – median (P25 – P75) most altered segment	42 (25,5 – 63,5)	107 (67 – 123)	<0,001
CD30 – median (P25 - P75)	3 (2 – 6)	33 (24 – 52)	<0,001

Using standard pathological criteria, the accuracy was 69.1% in the differential diagnosis between CD and UC. Assessing the most altered segment the median of eosinophils was 42 (25.5 – 63.5) in CD and 107 (67 – 123) in UC ($p < 0.001$). Assuming a cutoff ≥ 70 eosinophils, the sensitivity was 78.3% and specificity of 71% favoring the UC diagnosis, the area under the ROC curve was 0,767 (CI 95%: 0,696–0,838). After total count of $CD30^+$ cells in 10 high-power fields a median of 3 cells (2-6) in CD and 33 cells (24-52) in UC ($p < 0,001$). The cutoff determined by ROC curve was 15 (S = 97.5%, E = 94.3%, LR + = 17.1;-RV = 0.03, area under the curve: 0.967, 95% CI: 0.941 - 0.993). A value was assigned to each variable based on the statistical power of each, making a total sum of 10 points to build a histopathological score for the CD diagnosis. If the sum of the variables is ≥ 5 achieved 100% specificity and a sensitivity of 86.8%. Considering the cutoff of 4 points the score comes to a sensitivity of 95.3%, and reduces the specificity of 100% to 94.9%.

CONCLUSION: The use of routine assessment of the histopathological features in association with the $CD30^+$ cells count provides a high accuracy for CD and UC differential diagnosis. All parameters assessed here are easily performed, of low cost and accessible by most pathological laboratories. Further studies are warranted to validate our findings.

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Disclosure of Interest: None Declared

Keywords: CD30, Crohn's disease, diagnosis, ulcerative colitis

P1411 MOTIVATIONAL INTERVIEWING IN THE OUTPATIENT VISIT: A USEFUL TOOL IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Motivational interviewing (MI) is a patient-centered counselling style developed for eliciting behaviour change by helping patients (pts) to modify their lifestyle. MI was applied for substance/alcohol abuse, smoking cessation, weight loss, management of chronic pain. The strategy at the base of this approach is comprised of some basic skills: the ability to ask open ended questions, the ability to provide affirmations, the capacity for reflective listening, and the ability to periodically provide summary statements to the pts.

AIMS&METHODS: We report data on MI applied to inflammatory bowel disease (IBD) pts at their first outpatient visit (June '12-February '13). We decided, also, to supplement MI counselling using the aid of explanatory pictures. We evaluated all consecutive IBD pts referred for the first time to our outpatient clinic. At the end of visit pts filled out a questionnaire, anonymously and in a separate room, comparing the visit with their prior experience.

RESULTS: 45 pts (23 males [51%]), with a mean age of 36.1±15.2 yrs and a median disease duration of 12 months (range 1-120), were evaluated. Twenty-one pts were affected by Crohn's disease (47%), 19 by ulcerative colitis (42%), and 5 by indeterminate colitis (11%). Sixty-seven percent of pts (30/45) were previously evaluated by a gastroenterologist while the remaining 33% (15/45) only by their general practitioner (GP). At final analysis a high rate of pts (60%, 27/45) reported a good overall satisfaction but when we analyzed pts previously evaluated by a gastroenterologist 11/30 (37%) reported a complete dissatisfaction. This rate increased to 47% (7/15) in pts evaluated only by GP. Twenty-seven/45 pts (60%) reported a unsatisfactory communication skills of the physician or physicians lack of empathy (30% marked "zero empathy"). Younger pts (<40 yrs) had a significant dissatisfaction rate compared to older pts (p=0.017, OR 5.4;95% CI 1.26-22.9); no differences were found considering level of education or employment status. After MI all pts (100%) reported a good satisfaction rate without lack of empathy (32/45 pts [71%] marked "excellent empathy") due to the fact that they felt they had complete answers to their questions. All pts, also, liking the use of explanatory pictures. The mean duration of the visit was 41.5±8.7 minutes.

CONCLUSION: Our experience showed as MI can be very well appreciated by IBD pts. It is a quite time-consuming technique but considerably useful at the first visit and in younger pts. Explanatory pictures help pts to better understand their clinical condition. MI can help physicians, especially gastroenterologists, to move from "cure" to "care" with their IBD pts.

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Disclosure of Interest: None Declared

Keywords: counselling, Inflammatory bowel disease (IBD), MOTIVATIONAL INTERVIEWING

P1412 MICRORNA MIR-UP1 SERVES AS A BIOMARKER FOR THE COURSE OF INFLAMMATION IN EXPERIMENTAL COLITIS AS WELL AS IN CROHNS DISEASE.

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INTRODUCTION: Crohns disease is a chronic-remittent disease with the risk of disabling complications due to uncontrolled inflammation. A patient-tailored use of anti-inflammatory therapy is needed. However, overtreatment of patients bears the risk of severe side-effects such as opportunistic infections. Sensitive markers to non-invasively follow the course of the disease are still missing. Recent studies demonstrated a specific expression pattern of micro-RNAs (miRNA), involved in many biological processes, in Crohns disease. Aim of our study was to evaluate miR-up1 to monitor the course of inflammation in experimental colitis as well as in Crohns disease patients and to investigate its potential role as a biomarker for disease activity.

AIMS&METHODS: Experimental Colitis was induced in C57BL/6 WT mice by administration of 3% dextran sodium sulphate (DSS) in drinking water for 7 or 10 days, respectively, with daily measurement of body weight. On day 14, mice were sacrificed and histological damage was assessed according to the Dielemann Score. Expression of miR-up1 was determined by qRT-PCR in murine colonic samples and murine peripheral blood as well as in human blood from Crohns disease patients with acute flare and healthy controls (n=4 per group).

RESULTS: On day 14, DSS-treated mice revealed a significant loss of body weight as compared to control mice (20.8 g ± 2.9 vs. 27.6 g ± 1.6; P=0.006). Moreover, histological damage in DSS treated mice was markedly increased as compared to controls and still partially elevated in recovering mice (0.50 ± 0.19 (controls) vs. 21.71 ± 8.16 (colitis) vs. 14.54 ± 2.81 (recovery)). Most severe inflammation was located in the distal colon. Accordingly, mucosal expression of miR-up1 in the distal colon of colitic mice was significantly increased as compared to healthy controls (0.51 ± 0.08 vs. 0.38 ± 0.01; P=0.04). Furthermore, miR-up1 expression in the whole colonic tissue correlated strongly with the severity of histological damage ($r^2 = 0.73$; $P < 0.05$). In human blood from Crohns disease patients with acute flare, miR-up1 expression was significantly increased as compared to healthy controls (0.25 ± 0.17 vs. 1.9 ± 1.15; P=0.03).

CONCLUSION: We demonstrate that miR-up1 expression in colonic tissue monitors the course of DSS-colitis with a positive correlation to the histological damage. In addition, our preliminary data proofs a markedly increase of miR-up1 expression in peripheral blood of Crohns disease patients with acute flare. Therefore, miR-up1 might serve as a bio-marker to follow the course of inflammation in DSS-colitis as well as in Crohns disease patients.

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Disclosure of Interest: None Declared

Keywords: colitis, diagnostic, inflammation, miRNA

P1413 ACCURACY OF FECAL CALPROTECTIN IN THE ASSESSMENT OF POST-OPERATIVE ENDOSCOPIC RECURRENCE IN PATIENTS WITH CROHN'S DISEASE

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INTRODUCTION: Endoscopic post-operative recurrence is frequent in Crohn's disease (CD) and is highly predictive of further clinical recurrence. AIMS: i) to assess the performance of fecal calprotectin (fCal) to discriminate in CD patients who had undergone an ileo-colonic resection those who experienced an endoscopic recurrence from those who did not; ii) to determine the best threshold of fCal capable to distinguish between CD patients with or without a post-operative endoscopic recurrence.

AIMS&METHODS: At least one ileo-colonoscopy was performed in 28 consecutive patients with CD who had undergone a curative resection of the distal ileum and proximal colon (2 colonoscopies were performed in 5 of them) during the previous year. Post-operative endoscopic recurrence was defined as a Rutgeerts endoscopic severity index $\geq$i2. Just before the beginning of the colon cleansing, a fecal sample was collected in the patients for routine fCal measurement by ELISA (Bühlmann, Suisse). Concentrations of fCal were compared in patients who experienced an endoscopic recurrence and in those who did not using the Mann-Whitney test. The accuracy of fCal to discriminate between patients in endoscopic remission (i0, i1) from those in endoscopic recurrence (i2, i3, i4) was determined by constructing a ROC curve and sensitivities, specificities, positive (PPV) and negative predictive values (NPV) were also calculated using various fCal levels as cut-off points.

RESULTS: Among the 33 ileo-colonoscopies performed, a postoperative endoscopic recurrence was assessed in 10 patients (all in clinical remission) with a Rutgeerts score i2 (n=3), i3 (n=3), i4 (n=4). FCal concentrations were significantly higher in patients with an endoscopic recurrence compared with those without (368 ± 333 mg/g *vs* 106 ± 79 mg/g ; $p < 0.001$). The AUC of fCal to discriminate between patients with or without a post-operative endoscopic recurrence was 83 %. The respective accuracies of fCal to diagnosis post-operative endoscopic recurrence according to fCal threshold are summarized in the Table.

Accuracies Cut-off	Sens	Spec	PPV	NPV
[fCal]=100 mg/g	89 %	50%	60%	92 %
[fCal]=150 mg/g	66%	87 %	66 %	87 %
[fCal]=200 mg/g	55 %	87 %	62 %	84 %
[fCal]=250 mg/g	33 %	87 %	50 %	78 %

CONCLUSION: FCal using a cut-off of 100 mg/g had the best sensitivity and NPV to distinguish CD patients in clinical remission who experienced a post-operative recurrence from those who did not. If these results are confirmed in a larger population sample size, finding a fCal concentration above this cut-off might allow to avoid performing some ileo-colonoscopies in the CD post-operative setting.

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Disclosure of Interest: None Declared

Keywords: calprotectin, IBD Monitoring

P1414 POPULATION PHARMACOKINETIC EVALUATION OF INFLIXIMAB REVEALS PATIENT FACTORS THAT INCREASE INFLIXIMAB CLEARANCE AND SHORTEN HALF-LIFE IN INFLAMMATORY BOWEL DISEASE PATIENTS

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INTRODUCTION: Infliximab (IFX) is an effective therapy for inflammatory bowel diseases (IBD: ulcerative colitis (UC) and Crohn's disease (CD)), but may be associated with significant side effects as well as loss of response (LOR). One mechanism of LOR is increased IFX clearance (CL), resulting in short half-life and decreased troughs. Few evaluations of the pharmacokinetics (PK) of IFX in IBD are published.

AIMS&METHODS: Aim: To investigate factors affecting IFX PK variability in IBD.

Methods: IBD patients were prospectively recruited and IFX serum concentrations as well as antibodies toward IFX (ATI) were measured by ELISA during therapeutic drug monitoring (TDM). Demographic, clinical and laboratory data were recorded. Disease activity was defined according to clinical activity scores. IFX data were evaluated using population modeling (Nonmem Version 7.2 Icon Development).

RESULTS: IFX concentrations (n=75) from 38 patients (CD: 12, UC 17, IBD-undetermined: 9) were evaluated. Baseline (mean ± SD) demographics were: weight 69.4±13 kg, age 37±12.2 yrs., Males: 29, BMI 22.8±4.2 kg/cm, CRP 19.4±3 mg/L, albumin 4±0.6 g/dL. Positive ATI at baseline were present in 1 patient, and developed in 14. Disease activity was moderate in 22 and severe in 10 patients. Patient factors significantly associated with high IFX CL were: low albumin, high body weight, and the presence of ATI ($p \leq 0.001$). IBD type did not affect IFX CL. Typical (ATI negative, weight 70 kg, ALB 4 g/dL) CL was 0.617 L/day. Over the range of albumin (2.4-5 g/dL), CL would be 1.12-0.47 L/day. Over the range of weights (45-112 kg), CL would be 0.22-0.40 L/day. ATI formation was associated with a 25% increase in IFX CL. The estimated median effective half-life was 9.8±2.2 days. Simulations investigating alternative dose strategies suggested more reliable measurable concentrations over the dose interval were achieved when the dose interval was shortened than increasing administered dose. After induction, IFX concentrations declined during maintenance with 8 week dosing.

CONCLUSION: IFX CL is significantly influenced by patient factors (albumin, weight, ATI). Decreasing the dose interval for IFX is the suggested dose adjustment strategy, particularly for low albumin patients. Higher starting doses may benefit low weight patients. PK models and TDM may ensure patients have measurable concentrations over entire dose interval. Thus, individualized rather than fixed dosing may improve outcomes for IBD patients treated with IFX.

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Keywords: anti infliximab antibodies measurement, loss of response, monitoring, pharmacokinetics/Pharmacodynamic relationship

P1415 DIFFERENTIAL DIAGNOSIS BETWEEN INTESTINAL TUBERCULOSIS AND CROHN'S DISEASE BY ILEOCOLONOSCOPIC FINDINGS

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INTRODUCTION: Proper differential diagnosis between intestinal tuberculosis (ITB) and Crohn's disease (CD) remains challenging problem.

AIMS&METHODS: The aim of this study was to develop simple and valuable models for distinguishing these diseases based on the ileocolonoscopic findings. Between January 2003 and January 2010, 202 consecutive patients with ulcers on ileocolonoscopy (106 ITB, 96 CD) were enrolled. Ileocolonoscopic features of these patients were retrospectively reviewed following predetermined criteria. Patients were randomly allocated to a training or a validation set at 2: 1 ratio. Parameters which were significant on univariate analysis were subsequently tested by a classification and regression tree (CART) analysis and logistic regression analysis.

RESULTS: On univariate analysis of the training set, transverse shape ulcer, scars, pseudodiverticulum, patulous ileocecal valve, focal distributions, and ascending colon involvement were more frequently observed in patients with ITB than in patients with CD. Whereas, longitudinal shape ulcer, skip lesion, aphthous lesion, cobblestone appearance, pseudopolyp, segmental or diffuse distributions, and involvement of terminal ileum, transverse colon, descending colon, sigmoid colon, or anorectum were more common in patients with CD than ITB. The CART generated a tree model algorithms which are constructed with three variables including anorectal involvement, presence of aphthous lesion, and patulous ileocecal valve. The CART model made correct diagnosis for ITB or CD in 56 of 68 patients (82.4%). Whereas, stepwise multiple logistic regression analysis identified four independent predictive factors for discriminating ITB or CD : aphthous lesion, pseudopolyp, ascending colon involvement, anorectal involvement. The calculation formula (1.4 - [2.92 × aphthous lesion] - [1.89 × pseudopolyp] + [2.10 × ascending colon involvement] - [3.59 × anorectal involvement] < 0) predict CD with an accuracy of 88.2% (60/68).

CONCLUSION: The novel calculation formula and the decision tree model may be useful for initial differentiation between ITB and CD.

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Disclosure of Interest: None Declared

Keywords: Crohn' disease, Differentiation, ileocolonoscopy, tuberculosis

P1416 PERIANAL ADENOCARCINOMA AND SQUAMOUS CELL CARCINOMA IN CROHN'S DISEASE

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INTRODUCTION: Adenocarcinoma (ADK) and squamous cell carcinoma (SCC) of the anus and/or low rectum can occur in Crohn's disease (CD) patients with perianal lesions.

AIMS&METHODS: To describe characteristics of ano-rectal cancers in CD patients with perianal lesions, to estimate the incidence in a single center cohort and to identify risk factors. Cases of anal/low rectal cancers were collected in GETAID centers and the CESAME cohort, and retrospectively analyzed. Inclusion criteria were diagnosis of CD and histologically proven cancer located in anus or low rectum. The following characteristics were registered: age, sex, disease duration, smoking status, perianal lesions duration and type, histopathology, treatment and outcome. Disease-free and overall survival (OS) was analyzed. Actuarial rate of ano-rectal cancer was calculated in a single center cohort (MICISTA). The link between variables and cancer was assessed by log rank analysis.

RESULTS: 40 cases (26F/14M) were identified: ADK (n=29,72%), SCC (n=7,18%), high-grade dysplasia (n=2), neuroendocrine carcinoma (n=1) and rectal lymphoma (n=1). Median age at cancer diagnosis was 42 years (21-74). Median delay between diagnosis of CD and cancer was 19 years (3-37). Median delay between perianal lesions occurrence and cancer was 10 years (0-37). The median delay between diagnosis of stenosis and cancer was 3 years (0-18); it was significantly shorter in SCC (0.4 years) as compared to ADK (4 years). Diagnosis was often difficult and made on the specimen of proctectomy in 8 cases (20%). Mean follow-up was 1.2 years (0-13) for the all population. At the time of analysis, 19 patients had recurrence after treatment with a median disease-free survival of 32 months (5-131) and 13 patients died with a median OS of 52 months (18-180). In the single center cohort (20 cases out of 4908 patients), the actuarial rate of ano-rectal cancer was 0.8% at 20 years and 1.8% at 30 years. In univariate analysis, rectal and colon location, perianal lesions and no tobacco were identified as risk factors. Only rectal location and perianal lesions were significant in multivariate analysis.

CONCLUSION: Perianal ADK and SCC in CD have a poor prognosis and occur more frequently in patients with perianal lesions and rectal involvement. Patients with stenosis may be at a higher risk of ADK. Strategy of surveillance should be considered in high-risk patients.

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Disclosure of Interest: None Declared

Keywords: anorectal cancer, Perianal Crohńs Disease

P1417 DEVELOPMENT OF A NEW IMMUNOASSAY FOR THE ACCURATE DETERMINATION OF ANTI-INFLIXIMAB ANTIBODIES IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: The formation of antibodies to infliximab (ATIs) is closely associated with the loss of response to infliximab in patients with inflammatory bowel disease (IBD). Within the strategy of therapeutic drug monitoring, serum ATI levels have been mainly assessed by immunoassays based on the double-antigen format, in which ATIs were captured by immobilized infliximab or protein A on a carrier. However, in these assays, the presence of infliximab can interfere with the binding of labeled infliximab to the captured ATI leading to

false-negative results. In the present study, we developed a novel immunoassay for ATIs which enables measurement in the presence of infliximab.
AIMS&METHODS: The new assay based on the dissoziation of immune complexes between infliximab and ATI at low pH-values and the use of biotinylated and peroxidase labeled infliximab preventing the re-formation of immune complexes. The presence of ATIs in the samples positive by the new method but negative by the conventional method was confirmed by Western blot analysis. ATI levels were measured using the novel immunoassay and the conventional method in 29 patients with Crohn's disease (CD) under infliximab maintenance therapy. The serum infliximab trough levels were determined by enzyme-linked immunosorbent assay.
RESULTS: ATIs were detected in 7 out of 29 patients (24.1%) by the new method, but the conventional method detected only 1 patients (3.4%) who had the two highest ATI titers assayed by the new method. In the new method, the addition of infliximab to the samples dose-dependently blocked the detection of ATIs. Patients positive for ATIs had significantly lower serum trough levels of infliximab ($P < 0.01$) and significantly higher clinical activity scores ($p < 0.001$) as compared with patients negative for ATI.
CONCLUSION: The new method makes it possible to measure serum ATI levels in the presence of infliximab and anti-adalimumab antibodies (data not shown). This method is useful for deciding the optimal management strategies for IBD patients with loss of response to TNFalpha-antibodies.
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Keywords: ATIs, drug monitoring, IBD, Infliximab

P1418 DETAILED INFORMATION ABOUT ULCERATIVE COLITIS FROM MAGNIFIED ENDOSCOPIC FINDINGS AND MIRNAS EXPRESSION ANALYSIS

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INTRODUCTION: Although the number of patients with ulcerative colitis (UC) is steadily increasing, the pathogenesis of UC is still unclear. We focused on their details about magnified endoscopic findings and miRNA expression patterns.
AIMS&METHODS: 1) Forty-eight UC patients underwent magnifying colonoscopy. Magnified endoscopic observation was compared with clinicopathological characteristics including clinical course within 2 years. We classified CV (crystal violet)-magnified chromoendoscopic findings into 3 grades as follows: CV-Grade 1(G1) is normal or slight irregular arrangement of round to oval pits; CV-G2, opening of intervening round to oval pits; CV-G3, irregular dilatation or disappearance of pits.2) We included 6 patients with UC and 3 healthy controls in the study. In UC patients, we obtained endoscopic biopsy samples from the inflamed mucosa at the anal side and normal-appearing mucosa at the oral side in each UC case. In healthy controls, biopsies were obtained from the rectal mucosa. Using RNA extracted from the biopsied samples, we examined mucosal miRNA expression profile of UC by miRNA microarray.
RESULTS: 1) In pathological findings, the frequency of severe inflammatory cells infiltration was 84% in CV-G3 patients *vs* 24% in CV-G1/2 ($p < 0.001$). In the similar way, crypt abscess was shown in 74% *vs* 27% ($p=0.005$) and Goblet cell depletion was in 95% *vs* 38% ($p < 0.001$). 75% of CV-G3 patients experienced relapse within 2 years, whereas only 20% of CV-1/2 patients experienced relapse ($p < 0.05$). 2) Expressions of 19 miRNAs in the active lesions were significantly down-regulated by more than 2-fold compared to the less inflamed oral-side mucosa. And 24 miRNAs were decreased compared to healthy controls. miR-371-5p expression of the active lesion was significantly suppressed compared to the unaffected mucosa and healthy controls. Five miRNAs of the endoscopically inflamed UC lesions were significantly up-regulated compared to unaffected UC mucosa. And 8 miRNAs were increased compared to healthy controls. Among these miRNAs, miRNA-155 and -223 were upregulated in active lesions *vs* oral side ($P < 0.01$). Their expression levels were well matched with magnified endoscopic or pathological severities.
CONCLUSION: Observation with magnified endoscopy could be rather predictive with respect to the disease activity and relapse in UC. The current study shows the potential involvement of miRNAs in the pathogenesis of ulcerlative colitis, some of which demonstrating a possible association with inflammation. Confirmation of the relations between endocopic findings and specific miRNAs requires further studies.
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Disclosure of Interest: None Declared
Keywords: magnified endoscopy, miRNA, Ulcerlative colitis

P1419 CHARACTERIZATION OF INCIDENT CASES OF CANCER IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN A MULTICENTER CASE-CONTROL STUDY

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INTRODUCTION: Cancer in Inflammatory Bowel Disease (IBD) is a relevant clinical issue
AIMS&METHODS: To characterize, in a case-control, multicentre study, incident cases of cancer in IBD. The role of severity of IBD *vs* thiopurines (IMM) and anti-TNFs was evaluated. From Jan 2012-Apr 2013, characteristics of incident cases of cancer in IBD patients (pts) from 15 IBD centers were recorded. Each IBD pt with cancer (IBD-K) was matched with 2 IBD pts with no cancer (IBD-C) for IBD type (CD/UC), gender, age (±5yrs). Statistical analysis: Data (median, range), Chi-squared, T test, univariate analysis.
RESULTS: Incident cases of cancer were reported in 63 IBD pts (32 M;age 59,16-82), more frequently in CD (CD-K)(n=37;59%) than in UC (UC-K)(n=26;41%;p=0.01). IBD duration was comparable between IBD-K (12yrs,1-50 *vs* 11-35) and their matched 126 IBD-C (64M, age59,15-81). In IBD-K (n=63) cancer involved: 23 GI tract (8CD,15UC), 14 genitourinary (8CD;6UC), 6 skin (2melanoma in CD,1IMM, noanti-TNF;3NMSC in 3CD, 3IMM,2IMM+anti-TNF;1Kaposi,1UC noIMM); 6 lung (3CD,3UC),5 breast (4CD,1UC), 3 lymphoma (3 CD,3M,2IMM+anti-TNF), 6 others (5CD;1UC). Colon cancer diagnosed in 18 IBD (5IMM,4 anti-TNFs,3both): 5CD (IMM+antiTNFs 1),13UC (IMM4, antiTNF 3, both 2). GI cancers were more frequent in UC (58%) *vs* CD (22%;$p < 0.001$), while lymphoma and skin cancers in CD vs UC (8% *vs* 0%, $p < 0.0001$;14% *vs* 4%$p=0.03$). Cancer was more frequent in total (n=14;54%) vs distal (n=10;38%;p=0.03) and subtotal UC (n=2;8% $p < 0.001$), and in stricturing (46%) vs fistulizing (22%;$p < 0.001$) CD (inflammatory 32%;p=0.05). IMM and anti-TNFs use was observed in a comparable proportion of IBD pts developing or not cancer (IMM:IBD-K *vs* IBD-C:33% *vs* 40%;Anti-TNFs:IBD-K vs IBD-C 30% *vs* 39%; p=n.s).
CONCLUSION: Findings from a case-control study suggest a higher frequency of cancer in CD than in UC and that IBD severity, including extensive UC, may influence the overall cancer risk. IMM and anti-TNFs may influence specific cancer histotypes.
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Disclosure of Interest: None Declared
Keywords: Anti-TNFs, cancer, case-control study, Incident cases of cancer, Inflammatory bowel disease (IBD), Thiopurines

P1420 DEEP REMISSION IN FISTULIZING PERIANAL CROHN'S DISEASE: A CONTRAST-ENHANCED MAGNETIC RESONANCE IMAGING (MRI) STUDY IN 49 CONSECUTIVE PATIENTS ON LONG TERM ANTI-TNF-ALPHA MAINTENANCE THERAPY.

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INTRODUCTION: Fistulizing perianal Crohn's disease is a challenging clinical condition difficult to treat. Response to treatment like anti-TNF-alpha is based on a simple clinical evaluation of fistula drainage. MRI evaluation makes possible to evaluated fistula tract activity and to assess remission beyond symptoms.
AIMS&METHODS: The aim of our study were to describe clinical and imaging course of patients with perianal fistulas on long-term maintenance anti-TNF-alpha, to determine the rate deep remission and to search for clinical or imaging features associated with perianal fistula healing. All patients with fistulizing perianal Crohn's disease treated from 2000 to 2012 by anti-TNF and evaluated by MRI at diagnosis and at the end of the study were included. The data analysis was retrospective. The clinical response evaluation was based on Present's criteria and MRI evaluation on Van Assche's score and presence or not of contrast enhancement of fistula tracts. Deep remission was defined as the absence of symptoms associated with the absence of MR sign of inflammatory activity (hyper T2 signal and contrast enhancing of tracts). Characteristics of patients in deep remission were compared to others in univariate and in multivariate analysis.
RESULTS: Forty nine patients, median age 33±2 years were included. All received anti-TNF-alpha (infliximab n=43) associated with azathioprine in 63% of cases. MRI and clinical evaluation were done after a median anti-TNF exposure of 40±3 months. Clinical remission, response and non response were observed in respectively 53%, 20% and 27% of patients. Improvement, stabilization and worsening of MRI score were observed in respectively 61%, 16% and 23% of patients. Among the 26 patients in clinical remission 10 had persisting inflammation on MR. Deep perianal remission was observed in 32.7% of patients. In univariate analysis deep remission was associated with the absence of rectal involvement, the absence of anti-TNF switch or surgery requirement and the loss of contrast enhancement of fistula tract on intermediate MRI evaluation. In multivariate analysis, only the absence of endoscopic rectal involvement (OR=4.6;CI 95%:1-20) was predictive of deep remission.
CONCLUSION: Deep perianal remission is achieved in one third of patients on anti-TNF. Only the absence of rectal involvement was predictive of deep remission. The place of MRI lesions monitoring beyond symptoms needs further investigation but seems a promising approach.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, Perianal fistula, Perineal MRI

P1421 MUCOSAL HEALING DOES NOT CORRESPOND TO HISTOLOGICAL HEALING IN ULCERATIVE COLITIS

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INTRODUCTION: Ulcerative colitis (UC) is a chronic inflammatory disease limited to the large bowel mucosa, thus mucosal healing (MH) assessed by endoscopy could be a potential curative target in the therapy of these patients. In fact, MH demonstrated to modify the natural history of the disease, reducing the need for surgery and the risk of colorectal cancer. MH lower the risk of disease reactivation, but some patients relapse in spite of the presence of MH. It is reasonable to think that the microscopic disease activity beyond MH could explain these cases.
AIMS&METHODS: Our aim is to assess how many patients with MH have a microscopic disease activity and what kind of lesions are the most frequent in these cases.
We used Mayo endoscopic score to assess endoscopic activity. 25 patients with MH defined as Mayo score=0 were enrolled. For each patient microscopic disease activity has been evaluated by an expert pathologist based on the presence of acute or chronic inflammatory cell infiltrate, superficial infiltrate, transmucosal infiltrate, basal plasmacytosis, basal lymphoid aggregates, stromal changes, lamina propria eosinophils, crypt branching, crypt distortion, crypt atrophy/depletion, cryptitis, crypt abscesses, surface irregularity, mucin depletion, erosions and Paneth cell metaplasia.
RESULTS: No patients showed absence of histological lesions, whereas in all patients a chronic inflammatory infiltrate persisted, as superficial infiltrate in 90% of cases. In 70% of cases an acute inflammatory infiltrate could be demonstrated. 60% of patients showed mucin depletion, 50% of patients showed basal plamacytosis, basal lymphoid aggregates and lamina propria eosinophils. 30% of patients showed crypt distortion, cryptitis and Paneth cell metaplasia. 20% of patients showed crypt atrophy or depletion and erosions. Only 10% of patients had crypt abscesses and transmucosal infiltrate. No patients showed surface irregularity and stromal changes.
CONCLUSION: A microscopic disease activity persist in all patients with MH, thus the endoscopic remission does not correlate with histological healing. Further studies are required to assess if persistent histological lesions could predict clinical relapse.
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Disclosure of Interest: None Declared
Keywords: histologic severity, mucosal healing, ulcerative colitis

P1422 RISK MARKERS FOR EARLY ATHEROSCLEROSIS IN YOUNG PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: An increased cardiovascular risk in patients with Inflammatory Bowel Disease (IBD) has been reported. Research data on surrogate markers of early atherosclerosis and endothelial dysfunction in this setting are conflicting.
AIMS&METHODS: Aim of the study was to assess the prevalence of increased intima media thickness (IMT) and of raised indexes of arterial stiffness in young adults with IBD. Consecutive IBD patients (age 15 – 45 years) and healthy controls (HC) comparable for age and sex were enrolled. Data on clinical and demographic features, cardiovascular risk factors, personal and familial history of cardiovascular events, concomitant therapies were registered on a database. Left and right carotid IMT was evaluated using high resolution B-mode ultrasonography. Arterial stiffness was assessed by measurement of carotid-femoral PulseWave Velocity (PWV) and Augmentation Index (AI).
RESULTS: Fifty patients with IBD, median age 34 (IQR 14), 25 males, were recruited, together with 20 HCs. 36 patients had Crohn's disease (CD), 14 ulcerative colitis. Median duration of disease was 4 years (IQR 6). IBD was active in 12 patients (10 CD, 2 UC). 13 were on steroids, 23 on immunomodulators, 12 on anti-TNF therapy (9 adalimumab, 3 infliximab). 14 patients presented extra-intestinal manifestations. Most of them were non-smokers (64%); 44% of the IBD patients had a familial history of cardiovascular events; one had hypertension, one diabetes. There were no significant differences between patients and controls when comparing smoking habits, BMI, lipid profile, blood pressure values. Right and left carotid IMT were significantly higher in patients compared to controls (0.5 versus 0.4 for both; p = 0.03 and0.015 respectively), 7 patients and no HC had evidence of atherosclerotic plaques. Carotid-femoral PWV median values were significantly higher in IBD patients than in controls (8,45 versus 8,3, p=0.007), as well as AI (122% in IBD, 112,5 in healthy controls; p= 0.005). There was no association between type of IBD, disease activity and duration and both IMT and PWV, which instead were related to increasing age (p < 0.005).
CONCLUSION: In a homogeneous Mediterranean cohort of young adults with IBD, early onset of atherosclerosis and alteration of arterial elastic properties were common, regardless of disease activity and of treatment. Evaluation of young IBD patients should include initial assessment and possibly monitoring of IMT and arterial stiffness to keep cardiovascular risk under control.
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Disclosure of Interest: None Declared
Keywords: arterial stiffness, atherosclerosis, IBD, intima media thickness

P1423 BOWEL CONTRAST-ENHANCED ULTRASOUND PERFUSION IMAGING IN THE EVALUATION OF CROHN'S DISEASE PATIENTS UNDERGOING BIOLOGICAL THERAPY

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INTRODUCTION: Evaluation of inflammatory activity in patients with Crohn's disease (CD) represents a crucial aspect of treatment planning and monitoring. High-resolution bowel ultrasound has emerged as one of the most important imaging techniques in the diagnosis and follow up of these patients since it is a non-invasive method that easily allows repeated examination and provides both morphological and functional analyses. In particular, microvasculature activation and angiogenesis induced by inflammation are the basis for the enhanced visualization of inflamed bowel walls evidenced by contrast enhanced ultrasound (CEUS).
AIMS&METHODS: Our aim was to prospectively evaluate the modification in bowel wall microvasculature of CD patients treated with biological therapy.
Ten patients (6 males and 4 females; mean age±SD, 34±12 years) with a clinically active Crohn's disease (CDAI score >150) involving the terminal loop of small bowel (wall thickness > 5 mm), were enrolled in this study. Clinical assessment, laboratory tests and CEUS were performed at baseline and after 7, 15, 30 and 60 days of treatment with adalimumab or infliximab. Bowel wall microvasculature and contrast uptake were assessed by perfusion analysis in regions of interest (ROI) with a quantification software (Q-Lab, Philips). Variations between baseline and different time-points were calculated for three CEUS functional parameters (peak intensity, PI; area under the curve, AUC; slope of wash in, P_w) and were correlated with CDAI.
RESULTS: Before the beginning of the specific treatment all patients revealed diffuse transparietal enhancement after contrast agent injection. In 8 patients both P_w and AUC were significantly lower after 15 and 30 days from the beginning of treatment ($p<0.05$) and were correlated with a reduction of CDAI score ($p<0.05$). In the remaining 2 patients no significant vascularity changes were found during the follow up in spite of a mild reduction of CDAI score. After two months, 2 patients showed a new increase in P_w and AUC, even though the clinical findings continued to be negative. Both these patients developed clinical recurrence within 3 months.
CONCLUSION: According to the preliminary results of our study, the quantification of the terminal bowel loop vascularity after contrast agent injection might become a useful modality not only for assessing the efficacy of biological therapy but also a reliable predictor of relapse during the follow up. In particular, changes in perfusion parameters might suggest a closer clinical control and treatment revaluation also for patients in clinical remission.
Disclosure of Interest: None Declared
Keywords: inflamatory bowel disease, therapy monitoring, Ultrasound

P1424 ENDOSCOPIC AND HISTOLOGICAL ACTIVITY AS PREDICTORS OF RELAPSE IN PATIENTS UNDERGOING SURVEILLANCE COLONOSCOPY FOR ULCERATIVE COLITIS

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INTRODUCTION: Mucosal healing has shown to correlate with improved long term outcomes in patients with inflammatory bowel disease. Histological inflammation is often noted in endoscopically normal mucosa.
AIMS&METHODS: We aimed to investigate the predictive role of endoscopic and histological inflammation on disease relapse in UC patients in clinical remission.
We conducted a retrospective review of adult patients in clinical remission who underwent surveillance colonoscopies in our institution from January 2008 to December 2011. Electronic records were reviewed for endoscopy reports and subsequent clinical care. Data was recorded on age, gender, duration and extent of the disease, medications, steroid use in last 6 months, Mayo endoscopic score, Geboes grades and follow up data for any flares till date. Relapse was defined as patients symptoms requiring steroid treatment or escalation to current treatment in subsequent 12 months following colonoscopy.
Statistical analysis: Rate of clinical relapse and the predictive value of the variables of interest were assessed using SPSS version 17. All variable analysed in univariate fashion and included in multivariate analysis if p was less than ≤0.3. Multivariate analysis was based on an automated backward logistic selection process. P values <0.05 were considered significant.
RESULTS: 406 patients underwent surveillance colonoscopy during the study period of which 317 (Male: 172 Females: 145) met the inclusion criteria. 57 patients (Males 29, females 28) relapsed within 12 months (Table 1 provides the baseline characteristics). On univariate analysis age (OR 0.96 95%CI 0.94-0.98), Geboes grade ≥2 (4.53, 2.40-8.52) and Mayo score ≥1 (3.72, 2.05-6.73) were significantly associated with relapse. Duration of disease (p=0.09), use of immunomodulators (p=0.29) and recent steroid use (p=0.3) were included in the multivariate analysis. On multivariate analysis Geboes score of ≥2 (5.11, 2.73-9.59) and age (0.97, 0.97-0.99) were predictive of clinical relapse.

Variables	Flare up (n=57)	No flare (n=260)
Age (mean ± SD)	51.2 ± 14.6	57.9 ± 12.5
Endoscopic score ≤1	22	182
Endoscopic score ≥2	35	78
Geboes grade <2	33	224
Geboes grade >2	24	36

CONCLUSION: Histological activity and younger age are significant predictors of disease relapse in patients undergoing surveillance endoscopy. Endoscopic activity with standard white light endoscopy did not predict clinical relapse. Better non-invasive markers of disease relapse are required for patients with ulcerative colitis.
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Disclosure of Interest: None Declared
Keywords: Geboes grade, relapse, surveillance colonoscopy, ulcerative colitis

P1425 LUMINAL NITRIC OXIDE (NO) IS AN EARLY PREDICTOR OF COLECTOMY IN CORTICOSTEROID-TREATED ACUTE COLITIS

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INTRODUCTION: NO is known to be up-regulated in inflammatory conditions and can be used as a marker of inflammatory activity. We analysed rectal NO before and after three days of glucocorticosteroid (GCS) therapy in hospitalized patients with severe acute colitis.
AIMS&METHODS: The aim of the study was to study the levels of rectal NO in relation to GCS response and colectomy. Fifty hospitalized patients with acute severe colitis, i.e. Mayo score >10 or Harvey Bradshaw index >10, together with bloody stools were studied. Their median age was 41 years (range 20-78). All patients were given treatment with GCS directly upon admission to the hospital and monitored for the subsequent 30 days. Rectal NO levels were measured with a balloon catheter and analysed as parts per billion (ppb) in rectal gas by chemiluminescence before therapy onset and at day 3 of treatment. Rectal NO levels were compared to clinical activity index and and C-reactive protein (CRP). Values are given as means ± SEM.
RESULTS: The GCS non-responders had significantly lower NO levels than the GCS responders at both baseline and day 3 ($p<0.05$). Furthermore, even lower NO levels were found in patients who were later subjected to colectomy ($p<0.01$) at both baseline and day 3. Using an upper cut-off level of 2239 ppb, the sensitivity and specificity was 86% and 81%, respectively. In ROC analysis, the area under the curve 0.88 and the likelihood ration 4.8. Kaplan-Meier analysis showed that patients with base3line NO levels lower than 2239 ppb were at significantly higher risk of colectomy within one month from onset of GCS treatment ($p<0.0001$). Twelve out of 18 (67%) patients with NO <2239 ppb were colectomized, whereas the corresponding number in patients with NO >2239 ppb was two out of 32 (6%) and odds ratio of 10. CRP levels did not differ between responders and non-responders to GCS therapy, neither did disease activity indices.
CONCLUSION: Rectal NO is a sensitive surrogate marker that is feasibly and conveniently measured. Rectal NO displays reliable predictive properties for colectomy over a 1-month period in patients with acute severe colitis treated with systemic GCS.
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Keywords: acute colitis, C-reactive protein, Inflammatory bowel disease (IBD), nitric oxide

P1426 CORRELATION BETWEEN SEVERITY OF ENDOSCOPIC LESIONS AND CLINICAL ACTIVITY IN A COHORT OF CROHN'S DISEASE PATIENTS FOLLOWED UP FOR 5 YEARS AFTER ILEO-COLONIC RESECTION

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INTRODUCTION: Ileocolonoscopy (IC) represents the gold standard for assessing Crohn's Disease (CD) recurrence. Small Intestine Contrast Ultrasonography (SICUS), is a non invasive technique visualizing small bowel lesions in CD. The predictive role of severe endoscopic recurrence at 1 year for subsequent clinical recurrence at 3 years has been demonstrated, while the longer term predictive role of IC for predicting the clinical outcome of CD patients (pts) after surgery is undefined.
AIMS&METHODS: In order to assess this issue, in a prospective longitudinal study, we aimed to assess, in a cohort of CD pts undergoing ileo-colonic resection, possible correlations between the endoscopic score of recurrence at 1 year and clinical activity assessed yearly for up to 5 years. At this purpose, from July 2003 to Feb. 2012, 40 CD pts undergoing ileo-colonic resection were enrolled. IC and SICUS were performed at 1 yr and pts were prospectively followed up for 5 years, with clinical activity (CDAI) assessed yearly for 5 years. At 1 year, recurrence was assessed by IC (Rutgeerts≥2) and SICUS (wall thickness≥5 mm). Data were expressed as median (range). Correlations between the endoscopic score and CDAI were assessed by the Spearman correlation test.
RESULTS: CD group included 40 pts (23M, age 30 yrs, range 16-69), with stricturing (25/40; 63%) or penetrating CD (15/40; 37%). Among risk factors for recurrence, 16 (40%) pts were smokers, familial history of IBD was shown by 3 pts (8%). The Table summarizes the proportion of pts with endoscopic and SICUS findings compatible with recurrence at 1yr and with clinical recurrence in the 5 years follow up

Recurrence	1 yr Clinical (n=40)	IC (n=40)	SICUS (n=40)	2 yrs Clinical (n=40)	3 yrs Clinical (n=40)	4 yrs Clinical (n=40)	5 yrs Clinical (n=40)
Total N (%)	3 (7.5%)	31 (78%)	24 (60%)	10 (25%)	5 (13%)	3 (7.5%)	5/40 (12%)

When the severity of endoscopic recurrence at 1 year was correlated with the CDAI score, a significant correlation was observed with the CDAI score at 2 yrs ($p=0.007$; $r=0.41$), while no significant correlation was observed with the CDAI score at 1, 3, 4 and 5 years ($p=0.23$;$r=0.19$;$p=0.52$;$r=0.10$;$p=0.86$;$r=0.02$;$p=0.41$;$r=0.13$, respectively). In our study population, a low frequency of clinical recurrence was observed at 5 years (16/40; 40%).
CONCLUSION: In a cohort of CD patients followed up for 5 years after ileo-colonic resection, the severity of endoscopic recurrence at 1 year was predictive of clinical relapse at 2 years, but not at subsequent longer term follow up.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, recurrence

P1427 FREQUENCY AND OUTCOME OF TUBERCULOSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE RECEIVING INFLIXIMAB IN OUR TERTIARY CENTER

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INTRODUCTION: The increasing use of biological therapy may be responsible for the increasing risk of tuberculosis (TB) infection in inflammatory bowel disease (IBD).
AIMS&METHODS: The **aim** of our retrospective study was to determine the frequency and outcome of TB infection in our IBD patients receiving infliximab. Using our database we assessed the data of IBD patients who has been receiving infliximab in the past 10 years in our tertiary centre to select those with TB infection. Before infliximab administration all patients were screened to exclude active TBC with chest x-ray, physician examination and with the history of TB infection.
RESULTS: Active pulmonary TB was diagnosed in 3 of 237 patients (2 with ulcerative colitis, one with Crohn's disease, mean age at the diagnosis of TB: 39 years) treated with infliximab (1.3% of patients, 0.84/100 patient-years). One of the patients developed relapse of previous TB. Every patient developed TB after the third infliximab infusion. Two received concomitant thiopurine, one concomitant prednisolone therapy at the time of infliximab therapy. Specific anti tuberculosis therapy (rifampicin+isoniazid+ pyrazinamide+ethambutol) was administered with good response. At the present every patient is in clinical remission, although one of them underwent an ileostomy operation due to severe perianal fistulosis.
CONCLUSION: The acceptable frequency of TB infections is less than 1/100 patients in IBD during anti-TNF therapy using adequate screening procedures. In our tertiary center the frequency of TB infections is within an acceptable range, although it might be further decreased by using special methods, etc. Quantiferon test in questionable cases. The response to anti tuberculosis therapy in anti-TNF induced TB infection was good.
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Disclosure of Interest: None Declared
Keywords: inflammatory bowel disease, infliximab, tuberculosis

P1428 RISK OF ISCHEMIC HEART DISEASE IN PATIENTS WITH ULCERATIVE COLITIS.

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INTRODUCTION: Systemic inflammation is associated with development of atherosclerosis and ischemic heart disease (IHD) [1]. Patients with ulcerative colitis (UC) have a high risk of being diagnosed with IHD, especially within the first year after UC diagnosis, potentially reflecting ascertainment bias [2]. We found it's quite interesting since there are not many studies on this topic and they are mainly retrospective.
AIMS&METHODS: we conducted a longitudinal cohort study of patients with UC compared with non-UC population. A total of 186 UC patients and 214 matched controls were followed-up of about 5.8 years. The primary outcome was the development of cardiovascular events. Traditional and nontraditional IHD

risk factors were assessed. Using regression analysis, we estimated the incidence rate ratios (IRRs) for IHD with 95% confidence interval (CI) and impact of each risk factor on the outcomes.
RESULTS: patients with UC had an increased risk of IHD (IRR=1.84; 95% CI 1.79 to 1.89) compared with controls. The risk of IHD was particularly high in the first year after UC diagnosis (IRR=2.26 95% CI 1.34 to 3.18). During follow-up period after UC diagnosis, the risk of IHD was 1.43 (95% CI 1.31 to 1.55). UC patients had significantly lower rates of traditional IHD risk factors (hypertension, diabetes mellitus, smoking, dyslipidemia and body mass index (BMI) $\geq$ 30; $p<0.01$). Among nontraditional risk factors, an elevated C-reactive protein (CRP), serum tumor necrosis factor-alpha (TNF-α) and IL-6 levels were a risk factor for IHD development in UC group (IRR = 4.13; 95% CI 3.16 to 5.08). The risk of IHD was lower among UC patients using 5-aminosalicylic acids (IRR=1.27; 95% CI 1.06 to 1.48) than among non-users (IRR=1.61; 95% CI 1.26 to 1.94) ($p < 0.05$), especially among oral corticosteroid users. Also patients treated with thiopurines and TNF- α antagonist or surgically tended to have reduced IRRs for IHD.
CONCLUSION: an increased incidence of events was noted in UC patients despite having lower rates of traditional risk factors. Additionally, the increased long-term risk of IHD in UC may be related to chronic inflammation. It is required further investigation into how to reduce IHD risk in UC patients.
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Disclosure of Interest: None Declared
Keywords: ischemic heart disease, ulcerative colitis

P1429 CYTOMEGALOVIRUS (CMV) AND EPSTEIN BARR VIRUS (EBV) SPECIFIC ELISPOT ASSAYS DETECT FREQUENT REACTIVATION OF CMV AND EBV IN ULCERATIVE COLITIS

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INTRODUCTION: Patients suffering from Ulcerative Colitis (UC) are often immunosuppressed as a result of the disease, treatment or poor nutrition, rendering these patients susceptible to the reactivation of latent viral infections such as CMV or EBV. However, reliable non-invasive tools to assess the reactivation of pathogenic viruses are missing, especially since reactivation mainly occurs in the gut mucosa and not necessarily results in viremia.
AIMS&METHODS: We hypothesized that the detection of CMV- and EBV-specific CD8 effector T cells should permit the distinction between dormant and reactivated viral infection. Peripheral blood was obtained from 13 female and male UC patients; peripheral blood mononuclear cells (PBMC) were isolated and single cell resolution *ex vivo* ELISPOT measurements of CMV- and EBV-antigen triggered release of IFN-γ, Granzyme B (GzB) and Perforin (PFN) were employed to identify actively ongoing T cell responses towards these viruses. Detection of effector T cells, delineated by GzB and PFN production, determined antiviral activity and was correlated with disease activity indices (Colitis Activity Index).
RESULTS: CMV- and EBV-specific T cells were found to be in an activated state in a significant number of UC patients, in particular during flare-ups of the disease (EBV reactivity was detected in 6 of 13 patients, CMV reactivity in 5 of 13 patient. While CMV reactivity was associated with greater disease activity with significantly less CMV reactive patients being in clinical remission (0% vs. 63%, $P<0.05$), EBV reactivity was not associated with active disease (remission rates 33% vs. 43% for EBV reactive/nonreactive, respectively). Additionally, reactivity against CMV was associated with longer disease duration. Interestingly, PCR analysis on serum failed to detect CMV DNA during flares.
CONCLUSION: Our data show that during active UC there is a flare of T cell activity against CMV and EBV in a substantial proportion of patients, suggesting viral reactivation not detected by serum CMV DNA PCR. While it remains open whether viral reactivation is a cause or consequence of IBD, our data suggest that CMV reactivation is of clinical significance while EBV reactivation appears to be a bystander phenomenon. Monitoring of antiviral effector T cells with ELISPOT analysis can provide novel insights into the role of viral infection in UC as well as in other cases of immunosuppression in which patient care critically depends on sensitive and reliable detection of a reactivation of viral infection.
Disclosure of Interest: None Declared
Keywords: CMV, ulcerative colitis

P1430 PREDICTIVE VALUE OF FAECAL CALPROTECTIN IN PATIENTS UNDERGOING COLONOSCOPY: A COST-EFFECTIVE ANALYSIS

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INTRODUCTION: Faecal calprotectin (FC) is a sensitive surrogate marker of intestinal inflammation in patients presenting with gastrointestinal (GI) symptoms without an established diagnosis.
AIMS&METHODS: The aim of this study was to assess the role of FC to direct endoscopic inestigations in lower GI Symptoms and its cost-effectiveness, which has not been well studied. We retrospectively analysed FC tests and colonoscopies performed at a tertiary referral centre over a 3 year period. Electronic patient records were used to collect clinical information, laboratory, endoscopy and histology results
RESULTS: A total of 648 patients had both FC and a colonoscopy during this period. There were 258 male (40%): 390 female (60%). Median ages were 52.6 and 55.2 years, respectively. 120 patients were diagnosed with histology-confirmed inflammatory bowel disease (IBD), 88 with diverticular disease (DD), 46 with adenomas, 45 with irritable bowel syndrome (IBS), 17 with colorectal cancer (CRC). 246 were normal and 86 (13%) patients with a range of other diagnoses were excluded because of small numbers in each group.
The median FC concentration was significantly elevated in Ulcerative Colitis (UC) and Crohn's Disease (CD) patients compared to normals. There was no difference between the FC values of DD, Adenomas, and IBS patients compared to normals. Kruskal-Wallis' test showed a highly significant difference between the groups (X^2 =140, $P<0.0001$).
Table: 1

Working Diagnosis	Number (%)	FC (Median)	95% CI
UC	72 (11%)	215	120 – 420
CD	48 (7%)	218.5	138 – 475
IBS	45 (7%)	17	09 – 28
CRC	17 (3%)	57	48 – 133
Diverticular Disease	88 (14%)	29.5	16 – 45
Adenomas	46 (7%)	28.5	09 – 50
Normal	246 (38%)	27	21 – 35

As a screening marker of IBD, receiver operating characteristics (ROC) curve analyses with a pre-determined cut-off level of 60 µg/g stool for a normal test, showed a sensitivity of 78%, specificity of 68% and a negative predictive value of 85% for IBD. At the same FC level, the sensitivity of FC for CRC was only 47% and hence cannot be used as a screening marker of CRC.
In patients, aged less than 40 years with a normal calprotectin, colonoscopy could be avoided in the absence of alarm symptoms. Using this approach would result in a 12% reduction in total colonoscopies and its associated complications and a cost saving of 90% in this age group (assuming FC and colonoscopy costs of €45 and €450, respectively).
CONCLUSION: Our findings indicate that FC is significantly elevated in IBD but not in IBS patients, compared to normal controls. In young patients with no alarm symptoms and a normal FC, colonoscopy can be avoided and this strategy considerably reduces healthcare costs.
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Disclosure of Interest: None Declared
Keywords: colonoscopy, cost-effectiveness, Faecal Calprotectin (FC), Inflammatory bowel disease (IBD), Irritable bowel syndrome

P1431 A SYSTEMATIC REVIEW OF DE NOVO IBD IN SOLID ORGAN TRANSPLANT RECIPIENT

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INTRODUCTION: De novo inflammatory bowel disease (IBD) arises following solid organ transplant (SOT) unbelievably although increased immunosuppression during post-transplantation, but not infrequently as there is increasing recognition of de novo IBD in this entity recently. It has an incidence that is an order of magnitude higher than that seen in the general population worldwide but the magnitude of this risk has yet to be determined.
AIMS&METHODS: MEDLINE, Cochrane Library, and EMBASE and international conference abstracts are searched and all case reports and cohort studies are included as randomized controlled trials would be difficult for this entity.
RESULTS: 2837 A review of the current literature to date yields a total of 78 reported cases of de novo IBD among 7555 transplants, 58 are in orthotopic liver transplantation (OLT) patients, 13 in kidney, 5 in heart, 1 in BMT and 1 in small bowel transplantation. These cases manifest as UC more commonly than CD as these cases are labeled as ulcerative colitis (UC) in 51, Crohn's disease (CD) in 19 and indeterminate colitis in 8 patients. Over 65% of cases following OLT occur when the indication for transplant is PSC or autoimmune hepatitis. The mean lag time between transplant and IBD diagnosis was 63.0 (10.1-240.0) months. The annual incidence is estimated around 0.2%. Among liver recipients, the annual incidence is much higher at 100 per 100,000 vs. 5.8 per 100,000 in the non-liver organ recipients, and cumulative rates are substantially higher among patients with PSC or AIH (30%) relative to others (10%) following OLT. These cases following OLT are more likely to occur in those patients who has experienced a CMV infection or who has a CMV mismatch, while CellCept and tacrolimus exposure seem be related with those after kidney transplantation.
CONCLUSION: De novo IBD is not limited to OLT recipients. These cases occur in OLT recipients at a rate much higher than the general population and other SOT recipients. It pose management difficulties post-operation since patients diagnosed with de novo IBD require additional medications beyond their transplant immunosuppression for treatment, recognition of this entity has important clinical implications. Interrogations of larger transplant databases would yield some information which could contribute to confirm previously identified risk factors.
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Disclosure of Interest: None Declared
Keywords: IBD, immunosuppression, organ transplant, systematic review

P1432 EXTERNAL VALIDATION OF ILEOCOLONOSCOPY BASED SCORING SYSTEM FOR DIFFERENTIAL DIAGNOSIS BETWEEN INTESTINAL TUBERCULOSIS AND CROHN'S DISEASE

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INTRODUCTION: To aid endoscopic differential diagnosis between intestinal tuberculosis(ITB) and Crohn's disease(CD), ileocolonoscopy based scoring system has been proposed.[1]
AIMS&METHODS: The aim of this study was to perform an external validation of this scoring system. A total of 202 consecutive patients with ulcers on ileocolonoscopy(106 ITB, 96 CD) were enrolled. Ileocolonoscopic features of these patients were retrospectively reviewed following predetermined criteria. A score of +1 was assigned to the four endoscopic parameters(anorectal lesions, longitudinal ulcers, aphthous ulcers, and cobblestoning) that are characteristic of CD, and a score of –1 was given to the other four parameters(involvement of <4 segments, patulous ileocecal valve, transverse ulcers, and scars or pseudopolyps) that are characteristic of ITB. Putative diagnosis for CD was made when the sum of the scores for the eight parameters was greater than zero, whereas the diagnosis for ITB was made when that sum was less than zero. Moreover, the diagnosis was regarded as indeterminate when the score was zero.
RESULTS: The mean value for the sum of the scores was 1.05 in patients with CD and –1.73 in patients with ITB($P<0.001$). Four parameters(anorectal lesions [68.8% vs 5.7%], longitudinal ulcers[40.6% vs 10.4%], aphthous ulcers[77.1% vs 22.6%], and cobblestoning [22.9% vs 2.8%]) were significantly more common in patients with CD than in ITB. Four other parameters(involvement of <4 segments[87.7% vs 46.9%], patulous ileocecal valve[25.5% vs 8.3%], transverse ulcers[53.8% vs 16.7%], and scars or pseudopolyps[47.2% vs 32.3%]) were more frequently observed in patients with ITB than in CD. Using ileocolonoscopy based scoring system, the diagnosis of either ITB or CD for this population could have been made correctly in 157 patients(77.7 %), incorrectly in seventeen patients(8.4%), and would not have been made twenty-eight patients(13.9%).
CONCLUSION: Ileocolonoscopy based scoring system is a simple and useful method for initial differentiation between ITB and CD.
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Disclosure of Interest: None Declared
Keywords: Crohn' disease, Differentiation, ileocolonoscopy, tuberculosis

P1433 POTENTIALLY HARMFUL RADIATION EXPOSURE RATE AMONG INFLAMMATORY BOWEL DISEASE PATIENTS IS NOT REDUCED IN THE ERA OF BIOLOGICALS

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INTRODUCTION: In the past years, the radiation exposure from diagnostic procedures performed to diagnose the complications of inflammatory bowel disease (IBD) has been documented in several studies. This exposure seems to achieve the level of potentially harmful radiation exposure rate, i.e. equal or more than 50mSv, in about 8% of IBD patients. It has been suggested that the use of anti-tumour necrosis factor (antiTNF) biologicals might reduce the radiation exposure in IBD patients. However, it is not clear whether the proportion of IBD patients with high radiation exposure is also reduced in the era of antiTNF treatment.
AIMS&METHODS: Aim of the study: To assess the rate of potentially harmful cumulative radiation exposure among IBD patients using antiTNF.
Methods: All patients with current antiTNF treatment for whom the information on radiation exposure was available were included and the information on radiation exposure was retrieved from medical reports. The cumulative radiation exposure was calculated based on the radiological standards for each diagnostic procedure. The potentially harmful radiation exposure was considered to be equal or more than 50 mSv.
RESULTS: In total, 120 IBD patients (58% males; mean age 40 years, range 19 to 74 years; 76 Crohn's disease and 44 ulcerative colitis; mean disease duration 10 years, range 1 to 46 years) were included.
The radiological procedures with radiation exposure of the abdomen were abdominal and pelvic CT (74 CT in 46 patients), CT colonography (one patient), CT enteroclysis (25 examinations in 23 patients), abdominal X-ray (18 X-rays in 15 patients), irigography (3 examinations in 3 patients) and ERCP (one patient). The majority of patients (67 patients, 55.8%) had at least one diagnostic procedure involving radiation, with the mean cumulative radiation exposure of 33 mSv (range 5 to 140mSv). Ten patients (8.3%) reached the potentially harmful cumulative radiation exposure of 50mSV or more.
CONCLUSION: The potentially harmful cumulative radiation exposure rate resulting from diagnostic radiological procedures for IBD remains high in the era of antiTNF biological therapy.
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Keywords: inflammatory bowel disease, radiation

P1434 LONG TERM ADALIMUMAB EFFICACY IN STEROID-DEPENDENT CROHN'S DISEASE PATIENTS

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INTRODUCTION: Adalimumab (ADA) is effective in the induction of steroid-free remission in patients (pts) with steroid-dependent Crohn's disease (CD). We have already reported data on efficacy and prognostic factors of response to ADA in 110 steroid-dependent pts. At week 6, 91% of pts have had a clinical benefit. At the end of the follow-up (mean 14.6 months), 80.9% of responders have maintained the clinical benefit. Only higher induction regimen was related to remission at week 6. At the end of the follow-up, none of the variables were associated with remission.
AIMS&METHODS: All the 110 pts treated in the previous study were followed up for a further 24 months and the following variables were evaluated: maintenance of clinical benefit, ADA discontinuation, mucosal healing, dosage exalation, surgical treatment.
RESULTS: At the end of the follow up (mean 38.6 $\pm$ 8.6 months) 54 pts (49%) were still in maintaining treatment with ADA with significant clinical benefit, 56 pts stopped treatment because of ineffectiveness (35), side effects (15) or mucosal healing (6). Among no responders 16 pts were then treated with infliximab and 11 of them had a clinical response. During the follow up 26 pts received a new induction dosage with 160/80 mg of ADA because of lack of efficacy and 13 of them (50%) had a clinical response. Twenty-eight pts received a 40 mg weekly mainteining treatment and 14 of them (50%) had a clinical response. Mucosal healing were reported in 15 of 60 pts who underwent colonoscopy (25%). At the end of the follow up 19 pts were operated on. At univariable analysis a lower induction regimen (80/40 mg) were associated with a best response to infliximab ($P < 0.001$, OR 6, 95% CI, 1.01–35.91) while 160/80 mg induction regimen with a lower risk of surgery respect to 80/40 mg (p=0.04, OR 0.311 95% CI 0.969 - 0.998). At the end of follow-up 15 pts (13.6%) developed side effects that determined discontinuation of the treatment.
CONCLUSION: Half of the steroid dependent CD pts treated with ADA maintained a clinical benefit after a mean follow up of about 3 years and 25% of them obtained a mucosal healing, without high risk of side effects. The higher induction regimen (160/80 mg) was confirmed to be the best strategy to maintain a long term efficacy of ADA avoiding surgery. In case of lack of efficacy a new induction dosage or a weekly maintaining treatment are to consider a therapeutic option before discontinuing ADA.
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Disclosure of Interest: None Declared
Keywords: adalimumab, Crohn's disease, long term follow up, steroid dependent

P1435 SERIAL INTRALESIONAL INJECTIONS OF INFLIXIMAB CAN MODIFY COLONIC STRICTURING PROCESS

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INTRODUCTION: Mucosal healing with antiTNF-treatments develops as a surrogate marker of disease modification. However, complete healing process is only achieved in 40-50% of the IBD patients on anti-TNF maintenance therapy, with partial mucosal healing seen in nearly 25-30% of the cases.
The persistance of colonic mucosal lesions can lead to complications as intestinal strictures, especially in the rectosigmoid location, that often leads to obstruction and surgery. Higher antiTNF concentrations given through local injection could favor healing and prevent complications.
AIMS&METHODS: The aims of our study were: to analyze the presence of inflammatory strictures in the recto-sigmoid area in CD patients on antiTNF treatment and to assess the effect of local treatment with Infliximab in the disease outcome.
Ninety eight CD patients who have been treated with antiTNF for severe or refractory disease were followed up during 4 years, analyzing the cases with persistence of inflammation and stenosis of the rectosigmoid region while the other colonic areas were healed. Nine patients with persistent recto-sigmoid stricturing disease refractory to sistemic antiTNF were injected with Infliximab circumferentially (concentration: 5mg/mi; 100mg per session), using a standard sclerotherapy needle trhough the channel of a gastroscope or pediatric colonoscope. The injection process was performed every 4 months until the healing was achieved.
RESULTS: We have found 16 patients that have showed a good clinical response to antiTNF treatment, with mucosal healing of the colonic mucosa but with persistance of inflammatory stricture in the rectosigmoid area. (16%)
Nine patients were treated during the follow-up period with serial intralesional injections of infliximab with the following results: 4 patients (44%), showed complete mucosal healing (in one case combination with balloon dilation was needed); 4 patients (44%), presented reduction in their inflammatory component, with an increase in caliber of the stenosis; and 1 case (12%), was operated two months after the single injection, because of intestinal obstruction.
Of the seven patients not treated, 5 (72%), were operated during the follow-up period.

CONCLUSION:
1-Rectosigmoid location, where strictures are frequent, could be an area of difficult healing with antiTNF systemic treatment.
2-Intralesional injection of infliximab is able to stop or slow down the stricture process formation.
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Disclosure of Interest: None Declared
Keywords: AntiTNF, Local injection, Mucosal healing

P1436 EFFECTS OF ANTI-TNF-A AND STEROID TREATMENT ON MACROPHAGE ACTIVATION ESTIMATED BY SOLUBLE CD163 LEVELS IN INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Activated macrophages shed the hemoglobin-haptoglobin scavenger receptor CD163 from their surface into the circulation. We used soluble sCD163 as a marker of macrophage activation to investigate the *in vivo* macrophage activation in patients with inflammatory bowel disease (IBD) and the modulation of these macrophages by anti-inflammatory treatment.
AIMS&METHODS: We included 58 Crohn's disease (CD) patients and 40 ulcerative colitis (UC) patients; 90 healthy individuals served as controls (HC). All patients had active disease at inclusion and were followed for 7 weeks during treatment with either anti-tumor necrosis factor a (anti-TNF-α) or prednisolone. We measured plasma sCD163 levels at baseline, day 1 (anti-TNF-α treated) and 1 and 7 weeks after treatment initiation. Furthermore, using flow cytometry, the CD163 expression was measured on circulating CD14+ monocytes in 21 CD patients receiving anti-TNF-α treatment.
RESULTS: The baseline levels of sCD163 were similarly elevated in both CD (1.99 [1.80-2.18] mg/l) and UC patients (2.07 [1.82-2.32] mg/l) compared with HC (1.51 [1.38-1.63] mg/l), p=0.001, respectively. Anti-TNF-α treatment induced a rapid decrease in sCD163 levels in CD and UC patients at day 1 after initiation of treatment. Such rapid decrease was not observed in patients treated with prednisolone. In UC patients, anti-TNF-α treatment normalised sCD163 comparable to HC levels, whereas CD patients had constitutively increased sCD163 levels. We observed no changes in CD163 expression on circulating CD14+ monocytes during anti-TNF-α treatment.
CONCLUSION: This study demonstrates increased macrophage activation with elevated sCD163 levels in IBD patients. Anti-TNF-α reduced sCD163 levels acutely suggesting an effect on macrophage activation in IBD per se.
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Disclosure of Interest: None Declared
Keywords: IBD, macrophages

P1437 THERAPEUTIC DRUG MONITORING OF INFLIXIMAB IN INFLAMMATORY DISEASE PATIENTS IN A TEACHING HOSPITAL SETTING: PRELIMINARY RESULTS OF A PROSPECTIVE COHORT STUDY

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INTRODUCTION: Infliximab (IFX) trough levels correlate with clinical remission and endoscopic improvement of inflammatory bowel disease (IBD) and antibodies to infliximab (ATI's) are responsible for suboptimal IFX trough levels to a large extent. Although therapeutic drug monitoring (TDM) of IFX is advocated, this is not routinely implemented in clinical practice. We therefore conducted a prospective cohort study in our total IBD-population treated with IFX.
AIMS&METHODS: Patient demographics, medication- and clinical history were collected from the electronic hospital information system and blood was drawn for determination of IFX trough levels and ATI's. Subsequently, disease activity indices (Crohns disease activity index (CDAI) and Truelove Witts disease activity index (TWDAI) for Crohn's disease (CD) and ulcerative colitis (UC) respectively) and quality of life scores were obtained.
RESULTS: 110 patients were included in this study: 50 male / 60 female, 65 CD (59%) / 45 UC (41%), median age 40 years (range: 18-86). Individual IFX levels varied from <1.0 microg/ml to 38.8 microg/ml. In 19 (17%) patients IFX trough levels were not detectable. In this subgroup 11 patients (58%) had developed ATI's.
CONCLUSION: TDM of IFX in IBD-outpatients in a teaching hospital setting revealed large inter-individual differences in IFX trough levels. Above all, IFX trough levels were not detectable in a significant part of IBD-patients. TDM is indicated to reveal this group of patients. Individualizing IFX treatment of these patients may lead tot improvement of therapeutic dosage and less ATI formation. Further investigation is necessary to determine financial impact.
Disclosure of Interest: None Declared
Keywords: anti infliximab antibodies measurement, infliximab, therapeutic drug monitoring, trough levels

P1438 INCREASED RISK OF ACUTE MYELOID LEUKEMIA AND MYELODYSPLASTIC SYNDROMES IN PATIENTS WHITH PAST EXPOSURE TO THIOPURINES FOR INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Immunosuppressive thiopurines like azathioprine are associated with an increased risk of leukemogenesis. We assessed the risk of myeloid disorders (MD), such as acute myeloid leukemia (AML) and myelodysplastic syndromes (MS) in French patients with inflammatory bowel disease (IBD).
AIMS&METHODS: We performed a prospective observational cohort study of 19,486 patients with IBD, enrolled from May 2004 to June 2005, who were followed up until December 31, 2007. The incidence of MD in the general population, used for reference, was determined from the French Network of Cancer Registries.
RESULTS: During the 49,736 patient-years follow-up, 5 patients were diagnosed with incident MD, consisting of 2 AML and 3 MS. Four (one patient with ongoing treatment and 3 patients with past exposure) out of 5 patients were exposed to thiopurines. The risk of MD was not increased among the overall IBD population, compared with the general population, with a standardized incidence ratio (SIR) of 1.80 (95% confidence interval [CI] 0.58-4.20). The risk of MD was not increased among IBD patients with ongoing thiopurine treatment (SIR = 1.54, 95 % CI = 0.05-8.54), while those with past thiopurine exposure had an increased risk of MD (SIR = 6.98, 95% CI 1.44-20.36).
CONCLUSION: Past exposure to thiopurines increases the risk of MD by 7-fold among IBD patients. This finding should be part of risk assessment when initiating azathioprine either alone or in combination with anti-TNF therapy in IBD patients.
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Keywords: Acute Myeloid Leukemia, Inflammatory bowel disease, Myelodysplastic Syndrome, Thiopurines

P1439 DIETARY HABITS AND INFLAMMATORY BOWEL DISEASE OUTCOMES: A TUNISIAN MONOCENTRIC STUDY.

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INTRODUCTION: Preliminary studies suggest that lifestyle changes, dietary adjustments and specific supplements could be useful additions to treatment in patients with Crohn's disease and ulcerative colitis.
AIMS&METHODS: AIM: to examine the influence of dietary habits in a cohort of Tunisian patients with inflammatory bowel diseases on their disease course.
Patients and Methods : Patients with Crohn's disease or ulcerative colitis diagnosed at least 2 years ago were evaluated. They were enrolled from either inpatient or outpatient clinics. Prospective registration of alimentary habits was conducted through a recall questionnaire to provide informations on the daily intake of nutrients during a 1-week period. Retrospective analysis of clinical data on the disease outcome was carried out. We investigated correlations between dietary habits and the need for surgery, immunosuppressors or immunomodulators and the occurance of an acute severe flare, defining a severe course disease. Statistical analysis was performed with SPSS software version 21.0.
RESULTS: Seventy consecutive patients were colliged: 36 patients having Crohn's disease (51,4%), and 34 patients having ulcerative colitis (48,6%). Male to female ratio was 0,71. Severe Crohn's disease was noted in 68% of patients: there were 13 patients who had severe acute colitis, 24 patients had underwent surgery and 48 patients have been put on immunosuppressors or immunomodulators. Patients who had severe acute colitis had slightly a higher intake per week of tea (237ml vs 148ml, p=0,05) and significantly less intake of coffee (30ml vs 191ml, p=0,028). Patients who underwent intestinal resection consumed per week significantly more pulses (72,6g vs 36,88g, p=0,015), more cereals (487,5g vs 322,9g, p=0,025) and more tea (250g vs 145,9g, p=0,022). They had also significantly a higher intake per week of carbohydrate (71,2% vs 53,74%, p=0,039) and considerably less consumption of coffee (0,1ml vs 186,9ml, p=0,034) and less intake of protein (9,75g vs 14,32g, p=0,032). Overall, cheese consumption was significantly less common in patients with a severe engineering (5,1% vs 22,6%, p= 0,03).
CONCLUSION: A high consumption of coffee and cheese and a great intake of protein may be associated with favorable outcomes in patients with inflammatory bowel diseases. Our findings should be confirmed on prospective studies evaluating the influence of diet on the disease course of inflammatory bowel disease.
Disclosure of Interest: None Declared
Keywords: dietary habits, inflamatory bowel disease

P1440 SAFETY AND EFFICACY OF BOLUS ADMINISTERED FERRIC CARBOXYMALTOSE (500 MG) IN THE TREATMENT OF IRON DEFICIENCY ANAEMIA IN IBD PATIENTS

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INTRODUCTION: Iron deficiency anaemia (IDA) is a common haematological complication in IBD with potentially serious clinical consequences and often requires intravenous (IV) iron therapy. Ferric carboxymaltose (FCM) is a stable, non-dextran iron formulation which can be administered intravenously in large single doses to treat IDA.
AIMS&METHODS: To evaluate safety and effictiveness of multiple or single bolus IV injections of 500 mg FCM administered within 2 minutes compared to standard infusions (15 min) of 500 mg FCM in IBD patients with IDA. Secondary endpoints were improvements in haemoglobin and iron indices. Adult IBD patients with haemoglobin values less than 12 g/dL and ferritin less than 30 µg/L or transferrin saturation less than 16% received 500 mg FCM either as a single bolus injection in 2 minutes (n = 40) or intravenous infusion over 15 min (n = 41).
RESULTS: The increase in haemoglobin and iron indices was similar in both FCM groups. Both groups also reported similar incidences and types of adverse events, all known for FCM, and no serious adverse events were reported. Furthermore, transient, unsymptomatic hypophosphatemia not associated with adverse events or clinical sequelae occurred in similar rates in both groups.
CONCLUSION: FCM administered in single doses of up to 500 mg within 2 minutes is safe, well tolerated and associated with improvements in haemoglobin and iron indices comparable to administration of FCM via infusion.
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Disclosure of Interest: D. Jacobsen: None Declared, M. Wiesenthal: None Declared, F. Hartmann: None Declared, A. Dignass: None Declared, G. Virgin Other: employee of Vifor, J. Stein: None Declared
Keywords: Iron Deficiency Anaemia, treatment

P1441 CLINICAL PREDICTORS OF IMMUNOMODULATION AND PHENOTYPE PROGRESSION IN CROHN'S DISEASE

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INTRODUCTION: Crohn's disease (CD) has a progressive course with decreasing frequency of inflammatory pattern [B1] and increasing frequency of stenotic [B2] and/or penetrating [B3] phenotype.
AIMS&METHODS: Evaluate clinical criteria for earlier initiation of immunomodulators or anti-tumor necrosis factor alpha (antiTNFα), as well, as earlier change of the phenotype (B1 to B2 or B3). Cross-sectional study of 736 patients with CD followed in the inflammatory bowel disease outpatient clinic.
RESULTS: Azathioprine was started earlier in male patients (63 months [47.4, 78.6] *vs* 71 months [52.8, 89.2], p=0.005) and in patients with involvement of the upper gastrointestinal tract [L4], regarding patients with ileocolic [L3], colonic [L2] or ileal [L1] involvement (51 months [31.3, 70.6] *vs* 60 months [43.6, 76.4] *vs* 71 months [32.4, 109.6] *vs* 84 months [66.1, 101.8], p=0.026). AntiTNFα therapy was started earlier in patients diagnosed before 40 years old (p=0.004) and in patients with perianal disease (197 months [145.0, 249.0] *vs* 341 months [276.0.; 406.0] p < 0.001). The change in phenotype was earlier in patients with L4 location in respect to L1, L2 or L3 (95 months [58.6, 131.4] *vs* 138 months [99.3, 176.7] *vs* 174 months [128.2, 219.8] *vs* 253 months [200.0, 306.0], p < 0.001), as well as, in male patients (128 months [99.0, 157.0] *vs* 195 months [154.7, 235.3], p=0.004).
CONCLUSION: Diagnosis before 40 years old, the involvement of the upper gastrointestinal tract, perianal disease and male gender are associated with an increased need for immunomodulation and earlier progression of phenotype.
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Disclosure of Interest: None Declared
Keywords: anti TNF therapy, azathioprine, Crohn's disease

P1442 IMMUNOMODULATION CHANGES PHENOTYPE AND NEED FOR SURGERY IN CROHN'S DISEASE

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INTRODUCTION: In Crohn's disease (CD) there is cumulative structural damage. Early in the disease, it is characterized by a nonstenotic, nonpenetrating behaviour (B1), with progression, over time, to fibro-stenosing (B2) and/or penetrating (B3) phenotype, with frequent need for surgery.
AIMS&METHODS: To evaluate whether treatment with immunomodulators or anti-tumor necrosis factor-alpha (antiTNFα) changes the progression of disease and/or need for surgery in CD. Cross-sectional study in patients with CD followed in the inflammatory bowel disease outpatient clinic.
RESULTS: 736 patients with CD (368 female) were followed during 12.3 years (± 8.4). Of these patients, 87% had B1 phenotype at diagnosis and 24% of them progressed to phenotype B2, 20% progressed to B3 and 49% required surgery. Patients who maintained B1 phenotype initiated earlier either azathioprine either antiTNFα than those who progressed to B2 or B3 (respectively, 25 months [0 – 371] *vs* 56 months [0 – 420], p < 0.001 and 67 months [0 – 364] *vs* 102 months [0 – 395], p < 0.001). The median time till change of phenotype (B1 to B2 or B3) was higher in patients under azathioprine (361 months [306.3, 415.7] *vs* 72 months [47.8, 96.2], p < 0.001), as well as, in those under antiTNFα (141 months [130.4, 167.8] *vs* 61 months [86.2, 100.9], p < 0.001). This was also observed after exclusion of patients with less than 3 years (p < 0.001 for azathioprine and for antiTNFα) and 5 years of follow-up (p < 0.001 for azathioprine and for antiTNFα). Patients who were never submitted to surgery due to CD started either azathioprine either antiTNFα earlier than the ones who were operated (respectively, 19 months [0 – 420] *vs* 70 months [0 – 394], p < 0.001 and 50.5 months [0 – 364] *vs* 103.5 months [0 – 395], p < 0.001). The median time to first surgery was higher in patients under azathioprine (361 months [306.3, 415.7] *vs* 71 months [47.6, 94.4], p < 0.001), as well as, in those under antiTNFα (271 months [84.7, 104.9] *vs* 108 months [74.6; 141.4], p < 0.001).
CONCLUSION: Treatment with immunomodulators and/or antiTNFα changes the phenotype of the disease and the need for surgery in CD.
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Disclosure of Interest: None Declared
Keywords: anti TNF therapy, azathioprine, CROHŃS DISEASE

P1443 MACROCYTIC ANAEMIA SECONDARY TO SULPHASALAZINE IN PATIENTS AFFECTED BY ULCERATIVE COLITIS AND CROHN'S COLITIS: IS A REAL ISSUE?

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INTRODUCTION: Anaemia is a multifactorial complication of inflammatory bowel disease (IBD) with a wide prevalence of 9–74%. Sulphasalazine (SASP) inhibits methylene-tetrahydrofolate reductase, impairing folate absorption and subsequently affecting erythropoiesis. Megaloblastic anaemia during SASP therapy has been reported, but not quantified.
AIMS&METHODS: Our retrospective study evaluated the presence of macrocytic anaemia related to folate deficiency in patients (pts) treated with SASP, affected by ulcerative colitis (UC) or Crohn's disease (CD) colitis. A total of 1226 UC and CD pts were analyzed retrospectively. Eighty seven per cent of pts were excluded from the final analysis. One hundred sixty out of 1226 pts (13%) were analysed. One hundred thirty-nine UC pts (85 M; median age 50; median disease duration 132 mos; 61% extensive colitis, 16% left UC, 23% distal UC) and 21 CD pts (11 M; median age 36; median disease duration 28 mos; 38% penetrating behaviour, 62% non penetrating non structuring) were considered.
RESULTS: In UC group 4/139 pts had concomitant diseases possibly interfering with folate absorption (celiac disease in 1 and microcythemia in 3). Ninety-three per cent of pts were in remission with a median follow-up of 42 mos. SASP duration therapy was 48 mos; concomitant treatments possibly interfering with folate absorption were proton pump inhibitors in 10% of pts, immunomodulators in 17 % of pts, hypoglycemic agents in 5% of pts, anticonvulsivants in 0,7 % and NSAIDs in 6% of pts. Fourty-three out of 139 pts (32%) had anaemia (28/43 with normal MCV, 12/43 with reduced MCV, 3/43 with increased MCV). Nine out of 139 pts (6 %) had macrocytosis without anaemia. Only 9/43 pts (21%) were taking folate supplementation and 7/43 (16 %) iron supplementation. In colonic CD group 1/21 pts was affected by microcythemia. Eighteen out of 21 pts were in remission with a median follow-up of 34 mos. SASP duration therapy was 24 mos; concomitant treatments possibly interfering with folate absorption were proton pump inhibitors in 5% of pts, immunomodulators in 24% of pts. Five out of 21 pts (24%) had anaemia (3/5 with normal MCV, 1/5 with reduced MCV, 1/5 undefined). Only 1/5 pts (20%) was taking folate supplementation and 1/5 (20%) iron supplementation. Only 1/5 (20%) pts had macrocytosis without anaemia. Folate levels were normal in both groups but only 3/48 pts with anaemia (6 %) had only folate deficiency.
CONCLUSION: In our retrospective study considering UC and colonic CD pts treated with SASP, a low rate of macrocytic anaemia was found and few patients underwent folate supplementation.
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Disclosure of Interest: None Declared
Keywords: Anaemia, colitis, Folate deficiency

P1444 THE FFA2 ANTAGONIST GLPG0974: OPPORTUNITY TO TREAT NEUTROPHIL-DRIVEN INFLAMMATION

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INTRODUCTION: Free fatty acids (FFA) have been shown to act as direct signalling molecules through activation of several GPCRs. FFA2 is activated by short chain fatty acids (SCFA) such as acetate, propionate or butyrate. FFA2 is mainly expressed on immune cells (neutrophils, monocytes, B lymphocytes), enterocytes, entero-endocrine cells and adipocytes. FFA2 has been shown to play a major role in SCFA-induced neutrophil activation and migration. Studies in FFA2 knock-out mice suggest an important contribution of FFA2 to the development and control of inflammation. In IBD patients, FFA2 expression in colon biopsies was shown to be upregulated and was reduced after successful treatment with Remicade.
We identified GLPG0974 as a potent and selective antagonist of human FFA2. *In vitro*, it potently inhibits acetate-induced calcium flux in HEK293 cells and acetate-induced human neutrophil migration. In a human whole blood assay, GLPG0974 inhibits acetate-stimulated neutrophil activation, as evidenced by CD11b activated epitope [AE] expression. It is highly selective for FFA2 over the close homologues FFA1 and FFA3, as well as other non-related GPCRs.
AIMS&METHODS: The safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of GLPG0974 were evaluated in healthy volunteers after single (SD) and multiple administrations for 14 days (MAD). The PD was assessed by flow cytometric measurement of neutrophil activation (CD11b[AE] expression) in whole blood upon *ex vivo* stimulation by acetate.

RESULTS: Single doses up to 250 mg and multiple doses up to 400 mg daily were safe and well-tolerated.
GLPG0974 administered under fed conditions as capsules or oral solution, was slowly absorbed with a median t_{max} of about 3 h and eliminated with a mean $t_{1/2}$ of about 5.5 h. The GLPG0974 PK was dose proportional over the 50 to 400 mg daily dose range.
After single administration, GLPG0974 substantially inhibited acetate-stimulated neutrophil activation in whole blood compared to baseline. In general, the inhibitory effect peaked at 2 h post dose. The PK/PD data showed a clear relationship between drug exposure and PD effect. In the MAD study neutrophil activation was inhibited to the same extent as observed in the SD study. The inhibitory activity was sustained for at least 12 h after dosing.
CONCLUSION: Inhibition of neutrophil migration into the gastro-intestinal tract may prevent neutrophil-induced tissue damage as observed in ulcerative colitis. A Proof-of-Concept study is initiated to evaluate the safety and efficacy of GLPG0974 in patients with this condition.
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Keywords: CD11b[AE], FFA2, GLPG0974, pharmacodynamics, safety

P1445 ADALIMUMAB ACHIEVES COMPLETE REMISSION AT 52 WEEKS IN JAPANESE PATIENTS WITH INTESTINAL BEHÇET'S DISEASE

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INTRODUCTION: Behçet's disease (BD) is a chronic, relapsing, multisystem inflammatory disease with oral, dermatologic, genital and intestinal involvement. Elevated serum levels of tumor necrosis factor (TNF) are observed in pts with active disease.[1] The aim of this study was to evaluate the efficacy and safety of adalimumab (ADA), a fully human anti-TNF monoclonal antibody, through 52 weeks (wks) in intestinal BD.
AIMS&METHODS: In this open-label, uncontrolled study, 20 Japanese pts with intestinal BD with typical ileocecal ulcers (≥1cm), refractory to corticosteroids and/or immunomodulators and with severe gastrointestinal (GI) symptoms received ADA 160/80mg at wk 0/2, followed by 40mg every other week (eow) for 52 wks. Dose escalation to 80mg eow was permitted for flare or inadequate response. GI symptom severity was graded from 0 (no symptoms) to 4 (most severe). Ulcer healing was compared to baseline: graded from 0 (healing) to 3 (no change or worsening). The primary endpoint was proportion of pts with marked improvement (MI; defined as reduction of both scores to ≤1) at wk 24; proportion of pts with complete remission (CR; defined as reduction of both scores to 0) was a key secondary endpoint. Non-responder imputation was used for missing data.
RESULTS: 17 pts completed the study; 2 pts and 1 pt discontinued due to adverse events (AEs) and personal reasons, respectively. Mean pt age was 42 yrs. No pts had ocular symptoms at baseline. ADA was increased to 80 mg eow in 6 pts. At wks 24 and 52, 9/20 (45%) and 12/20 (60%) pts achieved MI, respectively. CR was noted in 4/20 (20%) pts at wk 24; the same 4 pts achieved CR at wk 52. Other major symptoms of BD (oral aphthous ulcers, erythema nodosum, and genital ulcers) resolved rapidly (at wk 4), which was sustained up to wk 52. The most frequently observed AE was nasopharyngitis (9 pts); other AEs were consistent with previous ADA trials in inflammatory bowel disease, and no new safety signals were observed.
CONCLUSION: In this study, among pts who responded early, ADA induced and maintained complete remission, comprising endoscopic and GI symptom improvement, through 52 wks in Japanese pts with intestinal BD.
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Keywords: adalimumab, intestinal Behçet's disease, remission

P1446 GUT DIRECTED HYPNOSIS FOR PATIENTS WITH INFLAMMATORY BOWEL DISEASES (IBD)

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INTRODUCTION: About 30% of patients with IBD suffers from psychological distress and has a high demand on psychological support. Gut-directed hypnotherapy is suggested to be one of novel treatments for IBD.
AIMS&METHODS: Aim of the study was to evaluate the feasibility and acceptability of this hypnosis for psychological distressed IBD patients in a group setting, and to show possible effects on physical and general wellbeing as well as depression and anxiety. Method: Nineteen patients with IBD received 5-10 sessions of gut-directed-hypnotherapy in group setting (GHT, 6 patients per group) with a mean follow up (FU) of one year. To assess the physical, psychological and general wellbeing, Visual Analog-scales and the Hospital-Anxiety-Depression-Scale were provided at the first and last GHT session, and at FU. Standardized questions were asked to evaluate feasibility and acceptability of GHT.
RESULTS: 17 Patients filled out all questionnaires. At FU there was a significant improvement in physical ($p=.032$), psychological ($p<.0001$) and general ($p=.004$) wellbeing, and a significant reduction of depression ($p<.012$) and anxiety ($p<.0001$). Patients described GHT as a feasible and helpful method and more than 90% would recommend GHT to other IBD patients.
CONCLUSION: GHT is helpful for IBD patients' quality of life and can be offered for psychological distressed IBD patients integrated into a standard treatment plan at tertiary centres. Controlled trials are needed to show possible effects of GHT on the course of the disease.
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Disclosure of Interest: None Declared
Keywords: hypnosis, Inflammatory bowel disease (IBD), psychology, quality of life

P1447 EFFECT OF REMISSION STATUS ON THE ABILITY TO MAINTAIN OR ACHIEVE CLINICAL AND ENDOSCOPIC REMISSION AFTER 12-MONTH MAINTENANCE TREATMENT WITH MMX MESALAZINE IN ADULTS WITH ULCERATIVE COLITIS

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INTRODUCTION: MMX® mesalazine, a once-daily (QD) oral 5-aminosalicylic acid formulation, is effective in induction and maintenance of ulcerative colitis (UC) remission. Little is known about the correlation between achieving remission and long-term outcomes with maintenance therapy following induction.
AIMS&METHODS: This open-label prospective study (NCT01124149) compared long-term outcomes between patients (pts) in complete remission (CR; clinical and endoscopic) and partial remission (PR) after acute therapy with MMX mesalazine. During the induction phase, pts with active mild-to-moderate UC (acute flare or newly diagnosed with modified UC Disease Activity Index [UC-DAI] total score 4-10, endoscopy score ≥1, and Physician's Global Assessment ≤2) received MMX mesalazine 4.8 g/d QD for 8 wks. Pts achieving CR (modified UC-DAI ≤1; rectal bleeding and stool frequency scores of 0; ≥1-point reduction in endoscopy score) or PR (modified UC-DAI ≤3; combined stool frequency and rectal bleeding score ≤1; not in CR) during induction were eligible for enrolment in the maintenance phase: MMX mesalazine 2.4 g/d QD for 12 mos. The primary efficacy endpoint was the proportion of pts in CR after 12 mos of maintenance.
RESULTS: Of 722 pts enrolled, 717 were treated and 639 completed the 8 wk induction; 472 achieved CR or PR. Of 469 pts enrolled in maintenance, 461 were treated and 459 had ≥1 post-dose efficacy assessment. 373 pts completed the 12 mo maintenance; key reasons for early withdrawal were lack of efficacy (n=40) and adverse events (AEs; n=24). Of pts in CR and PR, respectively, at Mo 0 of maintenance, 47.8% (87/182) and 26.0% (72/277) were in CR at Mo 12 ($P<0.001$). Pts with endoscopy scores ≤1 and symptom scores of 0 at Mo 12 are shown in the table. Common treatment-emergent AEs during maintenance were (pts in CR at Mo 0; pts in PR at Mo 0): UC (7.7%; 10.4%); headache (3.3%; 3.6%); influenza (1.6%; 2.9%); and nasopharyngitis (2.7%; 2.2%).

Mo 12 score	Pts in CR at Mo 0 n=182	Pts in PR at Mo 0 n=277
Endoscopy ≤1	139 (76.4%)	176 (63.5%)
Rectal bleeding = 0	119 (65.4%)	158 (57.0%)
Stool frequency = 0	114 (62.6%)	118 (42.6%)

CONCLUSION: The primary endpoint was met: at Mo 12 of maintenance, significantly more pts (22%) were in CR who began maintenance in CR compared with those who began maintenance in PR. No new safety signals were identified.
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Keywords: maintenance treatment, Mesalazine, remission, ulcerative colitis

P1448 FREQUENCY AND CLINICOPATHOLOGICAL FEATURES OF LOSS OF RESPONSE TO INFLIXIMAB IN CROHN'S DISEASE

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INTRODUCTION: Although Infliximab (IFX) has proven to be an effective medication for patients with Crohn's Disease (CD), loss of response (LOR) to the 5 mg / kg dose is a common occurrence. LOR to IFX decrease quality of life of a patient undergoing treatment.
AIMS&METHODS: This study investigated clinicopathological features associated with the LOR to IFX. Fifty-nine CD patients achieved remission after the induction therapy and received regular maintenance therapy consecutively in our institute. None of the patients had received previous biological therapy. Our study protocol was designed to include patients who maintained response to IFX (G-I), and patients who had lost response to IFX (G-II). We evaluated clinical outcome and long term outcome of LOR to IFX in comparison with patients maintained response to IFX.
RESULTS: Loss of response occurred in 25 of the 59patients (42%). We enrolled 34 patients in G-I,25 patients of LOR in G-II. Median disease duration until first IFX was 4.9 years in G-I, 9.4 years in G-II ($p<0.05$), average age was 33.8 years in G-I, 32.2 years in G-II, the ratio of males to females was 27:6 in G-I, 16:9 in G-II (ns). In disease location, colonic type: ileo-colonic type: ileal type was 11:9:11 in G-I, 2:7:16 in G-II ($p<0.05$). In concomitant therapy, enteral nutrition therapy (half elemental diet) was administered in 24.2% in G-I, 36% in G-II (ns), azathioprine was administered in 27.3% in G-I, 64% in G-II (ns). In previous therapy, surgery had been performed in 30.3% in G-I, 48% in G-II, balloon dilation had been performed in 3% in G-I, 20% in G-II. Cumulative admission rate (1year, 3years, 5years) by the Kaplan-Meier method was 21%, 33%, 33% in G-I, 44%, 62%, 80% in G-II($p<0.01$). Cumulative operation rate (1year, 3years, 5years) was 9%, 9%, 9% in G-I, 12%, 16%, and 34% in G-II (ns). Median duration until LOR is 487days in G-II. After drug response is lost, we escalated the dose of Infliximab to 10 mg/ kg in 14 patients, reduced the interval of administration in 7 patients, switched to adalimumab in 4 patients. After we escalated the dose or reduced interaval, mean level of C reactive protein decreased 2.0mg/dl to 1.5mg/dl in G-II. Recent level of C reactive protein was 0.22mg/dl in G-I, 0.54mg/dl in G-II.
CONCLUSION: During the observation period, LOR increase risk of surgery and admission. In Japan, we are not able to measure serum trough levels of IFX and ATIs in common. Our results showed that remission after induction, short disease duration until the introduction of IFX and colonic type CD was protective against loss of response.
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Disclosure of Interest: None Declared
Keywords: Short disease duration, Clinical, Loss of response

P1449 ONSET OF ULCERATIVE COLITIS INDUCED BY THE ANTI-IL-17A MONOCLONAL ANTIBODY THERAPY

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INTRODUCTION: Interleukin (IL)-17A is an important cytokine in the pathogenesis of psoriasis. Th17 cells are involved in the regulation of innate and adaptive immunity mechanisms, activation of T cells and monocytes/macrophages is regarded as an important factor in the pathogenesis of ulcerative colitis (UC). Association between psoriasis and UC is rarely described.
AIMS&METHODS: We reported clinical case with patient, who received fully human anti-IL-17A IgG1κ monoclonal antibody therapy due to plaque type psoriasis and onset of UC.
RESULTS: A 29-year-old man with no previuos history of UC had plaque type psoriasis since the age of 16 years. For 5 months he has been receiving subcutaneous injections of secukinumab (150mg) in the framework of multicenter study. Patient was admitted to our hospital with diffuse cramp type abdominal pain, bloody diarrhea, and temperature 37.4°C. The blood count was normal, C-reactive protein (CRP) was 265.32 mg/l. Ultrasonography revealed mild splenomegaly (13.2 x 5.7 cm). Intestinal infections were excluded. Colonoscopy showed total severe UC (Mayo index 2), confirmed by clinical symptoms (Rachmilewitz index 9) and morphology. CT showed thickened colon ascendens and caecum walls (no transmural lesions) reactive mild lymphadenopathy in ileocaecal region. Patient received mesalazin, methylprednisolon (i/v) and antibacterial therapy. Level of CRP dropped to 34.2 mg/l. The patient recovered and was discharged on 24th day using per oral mesalazin (2400mg/daily), methylprednisolon (32mg/daily, p/o) with recomendation to tee off azathioprine.
CONCLUSION: Biologic therapy still carry the risk to exacerbate other autoimmune process despite of the treatment of specific one. Our clinical case showed particularly rare finding; anti-IL-17A induced ulcerative colitis.
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Disclosure of Interest: None Declared
Keywords: Inflammatory bowel disease, monoclonal antibody therapy, Psoriasis, ulcerative colitis

P1450 HIGH DOSE INFLIXIMAB IN CROHN'S DISEASE: CLINICAL EXPERIENCE, SAFETY, AND EFFICACY

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INTRODUCTION: Standard treatment dose of infliximab (IFX) is ineffective in some Crohn's disease (CD) patients requiring dose intensification by increasing the dosage or shortening interval of treatment.
AIMS&METHODS: To evaluate safety and efficacy of high dose (HD) IFX (> 10 mg/kg every (q) 8 weeks or equivalent) in CD and characterize predictors of response to dose intensification.
Electronic medical records (EMRs) were queried for CD patients who received HD IFX (10 mg/kg q7weeks – 20 mg/kg q4weeks) during 2010-2012. EMRs fulfilling criteria were reviewed for history, medications, and laboratory data. Safety and efficacy of dose intensification was analyzed.
RESULTS: 319 patients with CD were identified; 87 received HD IFX. Of the HD IFX patients, median age at diagnosis and initiation of HD IFX were 16.5 and 28.5 years, respectively. 93% met criteria for moderate-severe or severe-fulminant disease activity; 55% had history of penetrating disease; 58% had ileocolonic involvement. 29% failed at least 1 other biologic therapy including standard dose of IFX. 69% received HD IFX doses between 10 mg/kg q7weeks and 10 mg/kg q4weeks; 31% received between 15 mg/kg q8weeks and 20 mg/kg q4weeks. 46% of patients initiated HD IFX therapy with an immunomodulator. At 4, 24, and 52 weeks of therapy, 20%, 28%, and 18% of patients experienced a full response, and 46%, 30%, and 23% experienced a partial response, respectively. In 58 patients on HD IFX, CRP was reduced from a median of 21.9 mg/L prior to HD IFX to 4.7 mg/L at a median of 16.5 weeks ($p<0.001$). Patients who responded fully or partially at 4 weeks had a higher median baseline CRP than those who did not respond (24.9 vs 3.5 mg/L, p=0.04). 44% remained on HD IFX at the end of followup (median 103.5 weeks). The median length of treatment before discontinuation was 30.5 weeks. 11 cases of infection required hospitalization; none were mycobacterial; 3 of these were in patients receiving combination immunosuppressant therapy. 2 patients developed melanoma and 1 SCC of the skin. Reasons for discontinuation of HD IFX: infection (n=1), infusion reaction (n=2), autoimmune disease (n=2), other (n=16), inadequate response (n=22), and successful de-escalation to standard treatment dose of IFX after a full response to HD (n=6).
CONCLUSION: HD IFX therapy may offer a therapeutic benefit to CD patients who have failed to achieve a response with standard treatment doses or in patients who have failed other therapies. Safety of HD IFX therapy appears to be consistent with the known side effect profile of anti-TNF therapy. Baseline CRP value may be a predictor for clinical response to IFX dose intensification.
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Keywords: anti TNF therapy, Crohn's disease, IBD, inflamatory bowel disease, biological therapy, infliximab

P1451 SAFETY AND EFFICACY OF FUMARIC ACID ESTERS (FAES) IN STEROID DEPENDENT CROHŃS DISEASE

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INTRODUCTION: Fumaric acid esters (FAEs) have been used successfully in the treatment of moderate to severe psoriasis vulgaris and several noninfectious granulomatous skin diseases (i.e. disseminated granuloma annulare, cheilitis granulomatosa, sarcoidosis)
AIMS&METHODS: Here, we report the safety and efficacy of Fumaric acid esters (FAEs) in steroid dependent Crohńs Disease (CD).
RESULTS: Five patients (two male, three female) presented with Crohńs Disease that have proved to be refractory to various therapies, including corticosteroids and TNFalpha-antibodies were treated with FAEs in tablet form (Fumaderm) according to the therapeutic schedule for psoriasis patients (240 mg td). After treatment with FAE (3-4 months), steroid free remission (CDAI $<$ 150, fecal calprotectin $<$ 200 µg/ml, CRP $<$ 5 mg/L) was achieved in three patients. The side effects observed in this trial correspond to the well-known spectrum of adverse effects of FAE (minor gastrointestinal complaints: 1 pt, temporary lymphopenia: 2 pts, temporary flush: 3 pt).
CONCLUSION: On the basis of our findings FAE therapy seems to be a safe and effective regimen for patients with refractory and/or steroid dependent CD. However controlled trials are necessary to fully explore the efficacy, optimal dosage, and safety of FAE in the management of CD.

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Keywords: Crohn's disease, Fumaric acid esters

P1452 THE PROCESSED BLOOD VOLUME PER BODY WEIGHT FOR GRANULOCYTE AND MONOCYTES ADSORPTION SESSION IN PATIENTS WITH CROHN'S DISEASE PATIENTS

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INTRODUCTION: Granulocyte/ monocytes adsorption (GMA) has been introduced as non-pharmacological therapy for active Inflammatory Bowel Disease (IBD) patients refractory to conventional medications. We have already reported that the processed blood volume per body weight (PV/BW) in GMA session is an essential factor for its efficacy in Ulcerative Colitis patients.
AIMS&METHODS: To investigate the essentiality of PV/BW in GMA for Crohn's Disease (CD) patients, we conducted retrospective cohort study in CD patients. This study involved 29 active CD patients who enrolled remission induction therapy with standard GMA sessions (PV:1800ml). Eligible patients were divided into two groups: High BW (HBW: $>$50kg, n=14) and Low BW group (LBW: $<$50kg, n=15). The primary endpoint of this study is the difference in response rate between these two groups. The responder was defined as the patients who decrease CD activity index (CDAI) score more than 70 points after GMA sessions compared pre GMA sessions.
RESULTS: The 29 CD patient's average CD activity index (CDAI) was 273.7±97.55, the average of CD duration was 8.27±6.32 years the average of simple endoscopic score for Crohn's disease (SES-CD) was 17.1±5.73, the average age was 31.3±5.15 old, the average body weight(BW) was 51.5±7.62 kg. The 11 patients had lost response to anti-TNF-α therapy. There were no differences between HBW and LBW groups in these backgrounds. The response rate in LBW group was significantly high compere to HBW group (80 vs 50 %, $p<0.05$). And The responder's BW was lighter than that of non-responder's BW after performing 5th or 10th weekly GMA significantly (P=0.009). We performed GMA dealing with 1800ml blood volume, so the responder's amount of dealing volume per BW was higher than that of non-responder's significantly (P=.0..009). The average of the responder's amount of dealing volume per BW was 37.5±4.73ml/kg, and that of non-responder's was 32.0±3.97ml/kg.
CONCLUSION: These results indicate the PV/BW is essential in CD patient's GMA, as well as in UC patient's GMA. Additional prospective controlled with larger cohorts of patients should strengthen our findings.
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Disclosure of Interest: None Declared
Keywords: Crohn's Disease, Granulocyte/ monocytes adsorption (GMA), The Processed Blood Volume

P1453 THERAPEUTIC EFFECT OF INFLIXIMAB FOR INDUCTION AND MAINTENANCE OF REMISSION IN INTESTINAL BEHÇET'S DISEASE

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INTRODUCTION: Behçet's disease is a multisystem disorder originally characterized by recurrent oral and genital ulcerations, ocular inflammation, and skin lesions. Intestinal Behçet's disease with gastrointestinal ulcers accounts for approximately 3 - 26% of Behçet's disease. The treatment strategies for intestinal Behçet's disease has not been well established because of the number are limited. Recently, Naganuma reported the efficacy of infliximab for inducing and maintening in intestinal Behçet's disease. The aim of this study was to assess the efficacy of infliximab for induction and maintenance of remission in intestinal Behçet's disease in our institution.
AIMS&METHODS: A total of 8 cases with intestinal Behçet's disease were treated in our institution between April 2000 and April 2013. Treatment strategies were as follows: First, corticosteroid was administered for induction of remission. After the remission was obtained, corticosteroid was tapered. Infliximab was administered in cases with recurrence during tapered corticosteroid. In all cases, the clinical courses were followed for $>$2 yr (2.5-13ys).
RESULTS: Patients were composed of 6 men and 2 women, with a mean age of 51 years (range; 21 - 84 years). Six patients complained of right lower abdominal pain, one patient complained of left lower abdominal pain, and one had bloody stool. Total colonoscopy was performed and deep punched-out ulcers in the terminal ileum or the colon were found in all patients. After the administration of corticosteroid, all patients achieved remission at an early time. While corticosteroid tapering, four patients had recurrences and following administration with infliximab was required. Three patients maintained remission with scheduled treatment of infliximab alone, but in one patient withdrawn the infliximab because of miliary tuberculosis was occured during treatment. After withdrawn the infliximab, corticosteroid introduced again and maintainted remission. One patient was also maintained remission with combination therapy of infliximab and methotrexate. Among the remaining 4 patients, maintained remission was obtained.
CONCLUSION: Corticosteroid is effective for induction of remission in intestinal Behçet's disease. Infliximab can be an effective theraphy to induce and maintain remission, especially in steroid-dependent patients. Our findings should be contributed to establish the treatment of intestinal Behçet's disease.
Disclosure of Interest: None Declared
Keywords: infliximab, intestinal Behçet's disease

P1454 ADALIMUMAB VERSUS INFLIXIMAB FOR THE TREATMENT OF MODERATE TO SEVERE ULCERATIVE COLITIS IN ADULT PATIENTS WITH NO PRIOR ANTI-TNF EXPERIENCE: AN INDIRECT COMPARISON META-ANALYSIS

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INTRODUCTION: Adalimumab and infliximab have been approved for the treatment of ulcerative colitis by several regulatory bodies across the globe. Both are viable treatment options when patients become refractory or intolerant to conventional therapy. Since placebo controlled randomized clinical trials for adalimumab were only published recently, the comparative effectiveness of adalimumab versus infliximab has not yet been established via accepted meta-analytic indirect comparison methods.
AIMS&METHODS: An exhaustive search strategy covered major medical databases and recent conventional meta-analyses to identify eligible randomized clinical trials (RCTs). A Bayesian random-effects indirect comparison meta-analysis was performed for five selected and patient-important clinical outcomes at 8 weeks and 52 weeks. Odds ratio (OR) estimates and associated 95% credible intervals (CrI) were produced.
RESULTS: Five eligible RCTs were identified from which data on clinical remission, clinical response, mucosal healing, response on the inflammatory bowel disease questionnaire (IBDQ), colectomy, serious adverse events and discontinuation due to adverse events were extracted at 8 weeks and 52 weeks. For all efficacy outcomes at both time points, the indirect comparison meta-analysis of adalimumab versus infliximab favoured infliximab. At 8 weeks, clinical remission (OR=0.44, 95% CrI 0.23-0.98), clinical response (OR=0.45, 95% CrI 0.23-0.89) and mucosal healing (OR=0.46, 95% CrI 0.25-0.86) were all statistically significant, whereas IBDQ was not. At 52 weeks, OR estimates for all efficacy outcomes favoured infliximab, but none were statistically significant. Adalimumab and infliximab were both similar and with lower adverse event rates when compared with placebo, and the indirect comparison of the two yielded odds ratios close to 1.00 with wide CrIs.
CONCLUSION: Our findings suggest that infliximab is significantly more effective than adalimumab for the treatment of moderately to severe ulcerative colitis at 8 weeks and is numerically more effective at 52 weeks. The two treatments also appear equally safe.
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Disclosure of Interest: None Declared
Keywords: adalimumab, infliximab, ulcerative colitis

P1455 CHRONIC TREATEMENT WITH ALPHA2DELTA LIGAND REDUCE COLONIC INFLAMMATION AND INFLAMMATORY-ASSOCIATED HYPERSENSITIVITY IN MICE

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INTRODUCTION: Abdominal pain is a common feature of patients suffering from Inflammatory Bowel Disease (IBD) or Irritable Bowel Syndrome (IBS) for which current analgesic therapies are still unsatisfactory. Recent studies highlighted the antinociceptive effect of $\alpha2\delta$ ligands, initially commercialized as anticonvulsant, in patients suffering from IBS. However, their impact on inflammation-associated visceral pain has been poorly investigated.
AIMS&METHODS: We proposed to investigate $\alpha2\delta$ ligand beneficial effects on inflammatory-associated colonic hypersensitivity (CHS) and on inflammatory condition in mice. To induce chronic colonic inflammation, we administered 1% DSS in drinking water for 14 days. From day 7 to day 14, pregabalin or its vehicle was administered subcutaneously at 30mg/kg each day. At day 14, mouse colonic hypersensitivity was evaluated by colorectal distension (CRD). Briefly, at day 10, 2 electrodes were implanted into the abdominal oblique muscle, and at day 14, distension probe were inserted at 1cm from the anal margin. Then, electrodes were connected to a Bio-Amp recording system linked to an acquisition interface device. CRD was performed by inflating distension probe from 20µL to 100µL by 20µL increment step. Visceromotor responses (VMR) were quantified as the area under the EMG activity curve during the 10s stimulation period minus the area measured during the 10s baseline. This VMR were correlated with CHS. After CRD, the animals were euthanized and several tissues were collected to investigate $\alpha2\delta$ ligands effects on inflammation level.
RESULTS: Chronic pregabalin treatment alleviated the CHS induced by DSS treatment, as revealed by a decreased VMR to CRD test in pregabalin DSS-treated mice in comparison to control DSS-treated mice. In addition to this antinociceptive, pregabalin treatment reduced neutrophil recruitment and pro-inflammatory cytokine production, showing a new original anti-inflammatory effect of $\alpha2\delta$ ligands treatment
CONCLUSION: In summary, $\alpha2\delta$ ligands showed beneficial effects in the management of visceral hypersensitivity. Moreover, our findings highlight their novel efficacy in inflammatory CHS which could be, in part, due to an anti-inflammatory effect. Finally, this work underlines the interest in studying the clinical relevance of $\alpha2\delta$ ligands in IBD patients in remission to alleviate IBS-like symptoms, particularly abdominal pain, but also to increase length of remission periods by preventing initiation or triggering of acute severe inflammation phases.
Disclosure of Interest: None Declared
Keywords: Alpha 2 Delta ligand, Inflammatory-associated hypersensitivity, Pregabalin, Visceral pain

P1456 ASSESSMENT OF LOSS OF RESPONSE TO INFLIXIMAB THERAPY IN INFLAMMATORY BOWEL DISEASES USING ANTIBODIES TO INFLIXIMAB AND TROUGH LEVELS.

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INTRODUCTION: Currently the management of inflammatory bowel disease (IBD) patients on infliximab therapy who lose response is mostly empirical: an increase of dose up to double or a decrease of treatment intervals represent the common clinical practice, with a consequent increase of drug use and high costs. Measuring trough levels (TL) and antibodies to infliximab (ATI) may be of great benefit in optimizing therapy.
AIMS&METHODS: We aimed to evaluate the relationship between TL and ATI assay with loss of response and infusion reactions in an Italian IBD unit. Sera were obtained from 82 IBD patients on infliximab maintenance therapy from at least 6 months. Patients were classified as being or not in clinical response. The occurrence of acute reactions to infliximab infusions was recorded. ATI and TL were measured by a commercial ELISA (Immundiagnostik AG, Bernsheim, Germany).
RESULTS: ATI were detected in 18 patients (22%), 50% of which were in clinical response as compared to 80% of patients without detectable serum ATI levels (p=0.0271 by χ^2 test). 5/18 (28%) of ATI positive patients had infusion reactions as compared to 2/64 (3%) ATI negative (p=0.0047 by χ^2 test). 60/82 patients had infliximab TL >0,1 µg/ml and 80% of them were in clinical response, as compared with 54% of patients with TL lower than 0,1 ug/ml (p=0.0043 by χ^2 test). Median TL were not significantly different among clinical responders and non-responders.
CONCLUSION: The combination of ATI and infliximab TL assay could help in managing loss of clinical response in IBD.
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Keywords: antibodies to infliximab, infliximab, trough levels

P1457 CCX507, AN ORALLY BIOAVAILABLE SECOND GENERATION ANTAGONIST OF THE CHEMOKINE RECEPTOR CCR9

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INTRODUCTION: The chemokine receptor CCR9 directs the trafficking of inflammatory cells into GI tissue. The therapeutic benefit of CCR9 inhibition was demonstrated by results from the PROTECT-1 clinical trial, in which the orally bioavailable CCR9 antagonist CCX282-B / vercirnon showed efficacy in the treatment (induction and maintenance) of moderate-to-severe Crohn's disease patients, including those with colonic involvement (1).
AIMS&METHODS: CCX507 is a next generation CCR9 antagonist being developed for the treatment of IBD. This molecule potently inhibits the CCL25-mediated chemotaxis of human Molt-4 cells in the presence of 100% human serum with A_2 and A_{10} values of 5.5 and 50.2 nM, respectively (A_2 and A_{10} are analogous to IC_{50} and IC_{90} values, respectively). CCX507 inhibits the CCL25-mediated chemotaxis of retinoic acid stimulated primary human CCR9+ T cells, in the presence of 100% human serum, with A_2 and A_{10} values of 9.7 and 87 nM, respectively. CCX507 also potently inhibits the CCL25-mediated chemotaxis of murine thymocytes, in the presence of 100% mouse plasma, with A_2 and A_{10} values of 12 and 108 nM, respectively. CCX507 does not bind to any other chemokine receptor.
The ability of CCX507 to inhibit the trafficking of T cells into the intestine was determined using an adoptive transfer model in mice. Administration of CCX507 resulted in a significant decrease of CD45.2+ T cells within the IEL population. Analysis of the plasma levels of CCX507 revealed that drug levels in mice that had a significant reduction in CD45.2+ T cell trafficking were consistently maintained above the mouse A_{10} value. Dosing of CCX507 in both the mdr1a-/- and CD4+ CD25- T cell transfer models of colitis significantly reduced disease severity.
RESULTS: CCX507 has successfully completed the single ascending dose arm of a Phase I study in healthy volunteers at doses up to 30 mg. All doses of CCX507 were well tolerated. Modeling of the steady state PK profile indicates that a 30-mg single daily dose of CCX507 will provide good coverage of the CCR9 receptor at the A_{10} level required for maximal pharmacological effects.
CONCLUSION: In summary, CCX507 is a novel, potent, selective and orally bioavailable CCR9 antagonist currently in development for the treatment of IBD.
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Keywords: CCL25, CCR9, Crohn's disease, ulcerative colitis, vercirnon

P1458 SECONDARY NON RESPONSE TO ANTI-TNF IS RELATED TO ANEMIA, INCREASED WHITE BLOOD CELL, HIGH C-REACTIVE PROTEIN AND LOW SERUM ALBUMIN

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INTRODUCTION: Secondary non-response is defined as recurrence of disease activity during maintenance therapy after achieving an appropriate induction response. It can occur in 20-40% of patients during the first year of treatment and is related to the disease and drug metabolism(1,2). Serum levels of Hemoglobin, Hematocrit, White Blood Cell(WBC),Platelets, C-Reactive Protein(CRP), Total Protein and Albumin could provide information about degree of inflammation and indirect signs of disease activity. Albumin an Ant-TNF co-transporter may also be related to the Drug clearance.
AIMS&METHODS: AIMS: Evaluate the serum level of Hemoglobin, Hematocrit, White Blood Cell(WBC),Platelets, C-Reactive Protein(CRP), Total Protein and Albumin in anti-TNF secondary non-response patients. Methods: Between July 2010 and October 2012, 50 Conh s Disease (CD) patients that was in manteinace after responded to induction of Anti-TNF therapy were followed with clinical visits at each 3 months. At visit the patients after a clinical evaluation based on Harvey-Bradswal index, blood samples were collected for laboratory tests: Hemoglobin, Hematocrit, WBC, Platelets, CRP, Total Protein and Albumin. In cases that recurrence was suspected the patients were submitted to entero CT or MRS for confirmation and divided in two Groups – 1. Responder group (RG) – 38 patients with no signs of loss respond.2. Loss response group (LRG) – 12 patients with confirmed loss respond. Non paried t test was used for statistical analyses.
RESULTS: Results: Statistically significant results between RG and LRG (M[SD]xM[SD]) were seen in hemoglobin levels 14,3[1,20]x11, 9[2,64]p=0,03, hematocrit 43, 9[4,19]x32, 9[11,7]p=0,02, WBC 6.287[1,61]x 11.150[4,02] p=0,005, CRP 1,89[0,78]x44,1[45,1]p=0.01,Total Protrein 7,37[0,25]x5, 25[1,01] p=0.0002 and Albumin 4,53[0.25]x3, 12[0,73]p=0.0001. Non significant trends were seen in Platelet count (p=0.09).
CONCLUSION: Conclusion: Secondary non-response to Anti-TNF in CD is related to anemia, increased WBC, high CRP and low serum Albumin. These preliminary results warrant further larger studies.
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Disclosure of Interest: None Declared
Keywords: anti-TNF, crohn disease

P1459 EXPERIMENTAL STUDY ON EVALUATION OF THE USE OF MESALAZINE IN RATS SUBJECT TO BOWEL INJURY BY NON-STEROIDAL ANTI-INFLAMMATORY DRUG

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INTRODUCTION: Background: Non-steroidal anti-inflammatory drugs (NSAIDs) often cause damage to the small and large intestine. There is no established treatment so far besides the immediate suspension of the drug. Mesalazine (5-aminosalicylic acid, 5-ASA) is a drug with supposedly anti-inflammatory properties. 5-ASA is the primary therapy used in the induction and maintenance of remission of mild-to-moderate inflammatory bowel diseases, particularly ulcerative colitis1,2,3.
AIMS&METHODS: Aims: To observe and to quantify the inflammatory reaction induced by anti-inflammatory drugs in small and large intestine of mice with and without concurrent use of mesalazine. Methods: Twelve (12) male Wistar rats weighing between 220-250g were used. Each rat was injected intraperitoneally with diclofenac sodium 15mg/kg in the first and third days of the experiment. In the control group (CG): 6 rats were under observation for five days. In Group Mesalazine (MG): 6 mice had mesalazine (oral gavage) po 50mg/kg for 5 days. After 5 days, the mice in both groups were killed. The small and large intestines of the 12 rats were then sent for histological evaluation. Samples were taken from the jejunum (2), ileum (2) and large intestine (4). (Ascending: 1; Transverse: 1; Descendant: 1; and sigmoid
RESULTS: In the control group (CG), the mice showed mild (2) and moderate (4) inflammation in the small intestine, whereas the mesalazine group (MG) mice presented with absent (2) and light (4) inflammation. In the large intestine, MG had three rats with absent inflammation and 3 rats with mild inflammation whereas the CG had 4 rats with mild inflammation and 2 with moderate inflammation. On the analyses of the small intestine, the score was 10 (CG) and 4 (MG) $p = 0.04$ and large intestine 8 (GC) and 3 (GM) $p = 0.09$.
CONCLUSION: The use of mesalazine reduces intestinal inflammation caused by non-hormonal anti-inflammatory drugs.
Disclosure of Interest: None Declared
Keywords: Diclofenac, Large intestine, Mesalazine, NSAID, rats, Small Bowel

P1460 THE TYPE OF IRON DEFICIENCY ANAEMIA, BUT NOT THE UNDERLYING DISEASE, PREDICTS INTESTINAL IRON ABSORPTION IN IBD PATIENTS

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INTRODUCTION: Anemia (A) in patients with inflammatory bowel disease (IBD) is multifactorial, however the two most common causes of anemia in IBD are iron deficiency and anemia of inflammation (ACI). Although the exact pathogenesis of ACI is unknown, one hypothesis suggests that-caused by the effects of inflammatory cytokines-ACI arises in part as a result of an impaired intestinal Iron absorption.
AIMS&METHODS: Recently it has been shown, that the acute phase protein hepcidin impairs intestinal iron uptake. We therefore hypothesized that iron absorption is impaired in patients with active IBD at least in part as an increased hepcidin release by the liver. 71 adult subjects with IBD (31 UC, 40 CD) and 26 healthy controls were recruited until February 2013. After an overnight fast, serum hemoglobin levels, Serum ferritin (SF) and serum markers of inflammation [high-sensitive C-reactive protein (hsCRP) and IL-6] were measured. Serum samples for hepcidin assay were obtained at 8 a.m. and measured by LC-MS. Ferrous sulfate (100 mg) was administered orally, followed by determination of serum iron concentrations hourly for 4 hours. An area under the curve (AUC) for iron absorption was calculated for each patient data set. Patients with anemia were classified as having iron deficiency anaemia (IDA), anaemia of chronic disease (ACD) or according to[1].
RESULTS: There was a significant inverse correlation between the AUC and hsCRP ($p < 0.001$) and the AUC and hepcidin levels ($P = 0.017$). Both in UC and CD patients the difference between baseline and 2-hour serum iron level (D[Fe]2hr) independently of disease location was significantly decreased in ACD (fig. 1).
CONCLUSION: Compared to healthy controls and subjects with inactive disease IBD patients ACD have impaired oral iron absorption, which correlates with disease activity and markers of Inflammation but is independent of disease location and type of IBD
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Disclosure of Interest: None Declared
Keywords: iron absorption, Iron Deficiency Anaemia

P1461 THE USE OF SIROLIMUS FOR REFRACTORY INFLAMMATORY BOWEL DISEASE: A SINGLE CENTRE EXPERIENCE

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INTRODUCTION: Refractory inflammatory bowel disease (IBD) in children is challenging. The primary outcome of this study was to assess the therapeutic efficacy of Sirolimus in children with refractory IBD. Secondary outcomes included Sirolimus tolerance and duration of therapy.
AIMS&METHODS: We retrospectively reviewed medical and nursing records of all patients with IBD on Sirolimus (23 patients) between 2006 and 2012. Clinical response was assessed by PUCAI or PCDAI. All patients had an activity index at baseline and 3 months after induction of Sirolimus. Endoscopic and histological findings before starting Sirolimus were compared to the next available endoscopy at least 3 months later. A total of eight cases were excluded, 6 due to incomplete data and 2 due to short treatment time (less than one month).
RESULTS: 15 cases had severe refractory IBD, 4 were Crohns disease (CD), 11 were Ulcerative colitis (UC), 9 were males. The mean age of onset of disease was 8.7 years. The mean number of years after diagnosis until induction with Sirolimus was 3.1 years. The oral daily dose range was between 0.5mg and 5mg with a targeted serum trough level of 5-10ng/ml. The mean trough level was 7.5ng/ml. 16 patients had failed standard medical therapy and all stayed on conventional treatment while on Sirolimus. 15 patients had received steroids, thiopurines, 5-ASAs, 13 infliximab, 8 adalimumab, 5 methotrexate, 2 tacrolimus and two basiliximab prior to starting Sirolimus. 8/11 patients with UC had a response shown by improvement in their PUCAI score at 3 months, 3/11 had no response. Of the patients who responded 2 achieved remission with concomitant administration of Basiliximab, one was started on Mycophenalate while the fourth child required complete gut rest and parenteral nutrition for 6 weeks. 3/8 responders and 2/3 non responders went on to have Colectomys. 3 CD patients had clinical response to their PCDAI scores. 1 CD patient was successfully weaned off prednisolone, 1 off methotrexate. 5/11 patients with UC achieved histological mucosal healing while 4 patients still had some disease activity. Of the CD patients one achieved mucosal healing while 3 demonstrated ongoing inflammation, No side-effects were reported to Sirolimus in the included patients.
CONCLUSION: Our study was limited by its retrospective design; however we demonstrated clinical and histological response to Sirolimus in children with refractory IBD who failed conventional medical therapy. With careful patient selection, Sirolimus (as an adjunct immunosuppressant) appears to be safe and effective medical therapy to be considered in children with severe refractory IBD.
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Disclosure of Interest: None Declared
Keywords: Inflammatory bowel disease (IBD), peadiatric, Rapamycin, refractory symptom, sirolimus

P1462 DRUG INDUCED LUPUS IN PATIENTS WITH CROHN'S DISEASE TREATED WITH ANTI-TNF AGENTS

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INTRODUCTION: Anti tumour necrosis factor alpha medications have become integral in the treatment of moderate to severe Crohn's disease. Drug-induced lupus erythematosus (DILE) and ANA positivity have been associated with these medications. There is, however, little data available that identifies which patients are likely to develop DILE when placed on these medications, whether the severity of DILE correlates with antibody titre and if the concomitant use of immunotherapies such as thiopurines and methotrexate reduces DILE development.
AIMS&METHODS: Clarify the prevalence of drug induced lupus erythematosus in patients with Crohn's disease being treated with adalimumab or infliximab, and also to further clarify the relationship between antibody titre and severity of lupus symptoms.
Retrospective chart review of 68 patients with Crohn's disease, treated with either infliximab or adalimumab at the Nambour Hospital, between 2002 and 2012 was conducted. Information was obtained from medical records and hospital pathology records. All patients with DILE diagnosed by an immunologist or rheumatologist were included in the study. Patients with DILE were matched with healthy controls, who had no symptoms of DILE and currently receiving anti-TNF medication for crohn's disease.
RESULTS:

	Patients with DILE (n=8)	Controls (n=8)
Mean age (years)	51.5	36.6
Males	3	2
Females	5	6
Concurrent immunosuppression (thiopurines or methotrexate)	0	3
IFX	7	4
Adalimumab	1	4

Table 1: Demographic data
Of the 68 patients treated with infliximab or adalimumab between 2002 and 2012, 9 developed an ANA > 2560 of whom 8 had a positive dsDNA between 9 and 40. All of the 8 patients with a positive ds DNA developed symptoms consistent with a diagnosis of DILE.
The control group had a lower mean age than the treatment group (table 1). The male:female ratio was similar between the two groups (table 1). None of the patients who developed DILE were on concomitant immunsuppressive medication. All the patients who developed symptoms of Drug induced lupus developed a high ANA >2560 and positive dsDNA. Of the eight patients who developed DILE, 5 developed a discoid or malar rash, seven developed arthritis, one developed serositis (pulmonary) and none developed neurological symptoms. Of the eight controls, only one developed a low titre dsDNA, but no symptoms consistent with DILE.
CONCLUSION: Although our study suggests a correlation between ANA and dsDNA positivity and development of DILE, further studies are required to investigate if ANA titre is directly correlated with symptom severity in drug induced lupus, whether concurrent use of immunosuppressant medication with anti-TNF medications is protective against the development of drug induced lupus.
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Disclosure of Interest: None Declared
Keywords: adalimumab, crohns disease, drug induced lupus, Infliximab

P1463 LONG-TERM OUTCOME OF PERIANAL AND ENTEROCUTANEUS FISTULIZING CROHN'S DISEASE TREATED WITH TUMOR NECROSIS FACTOR ALPHA (TNF-A) ANTAGONISTS

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INTRODUCTION: There are only limited clinical observational data about the short and long-term efficacy of anti-TNF-α therapy in patients with perianal and enterocutaneus fistulizing Crohn's disease (CD).
AIMS&METHODS: Our aim was to retrospectively evaluate the outcomes, the complications and the therapeutic success rates of anti TNF α therapy in fistulizing CD.
The records of 69 perianal and 7 enterocutaneous fistulising CD patients were assessed retrospectively. Responses to biological therapy were determined by clinical activity indices. We assessed whether rectal involvement, disease location, disease behaviour and smoking are in association with the response to biological therapy and further surgery.

RESULTS: 14.7% of patients had simple perianal and 8 patients had enterocutaneus fistula at the beginning of anti-TNF-α therapy. Seton drainage was performed in 39 patients. Complete fistula closure was achieved in 38.3% of the patients. In 10.3% were refractory to biologicals. Repeated seton-drainage was needed in 20.6%. After the discontinuation of anti TNF-α, fistulas recurred in 53.9% of the patients. None of the examined parameters showed association with the response to biological therapy and the need for surgery.
CONCLUSION: More than every third patient revealed complete fistula closure. Seton drainage had to be performed in the majority of cases. Frequency of fistula recurrence is high after stopping the therapy.
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Disclosure of Interest: None Declared
Keywords: biologic therapy, inflamatory bowel disease, Perianal Crohńs Disease

P1464 TO EVALUATE THE EFFICACY AND SAFETY OF 6-THIOGUANINE THERAPY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE – A LONDON DGH EXPERIENCE

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INTRODUCTION: Conventional thiopurines (Azathioprine/6-Mercaptopurine) are considered to be safe and effective in the treatment of inflammatory bowel disease (IBD). Unfortunately more than 50% of patients discontinue thiopurine therapy, mainly due to the development of adverse events or therapy resistance[1]. In recent years, 6-thioguanine (TG) has been used as an alternative thiopurine in IBD patients failing to tolerate or to respond to conventional thiopurine therapy. The aim of this study was to evaluate the tolerability, safety and efficacy of 6-thioguanine in the treatment of IBD patients in a London District General Hospital (DGH).
AIMS&METHODS: A retrospective database analysis was performed on all IBD patients who had previously failed to respond or to tolerate conventional thiopurine therapy and were subsequently treated with TG at 20 mg once daily. Rates and reasons for treatment failure were assessed. Clinical features, laboratory values, abdominal imaging and endoscopic remission rates were evaluated.
RESULTS: Total of twelve patients received TG and median treatment duration was 8 months (range 1-12). There were 7(58%) female and 5(42%) male. Mean age was 37 years (range 19-62). 6/12(50%) patients had Ulcerative Colitis (UC) and 6/12(50%) had Crohn's Disease (CD). Indications for initiation of 6-thioguanine therapy were conventional thiopurine intolerance 10(83%) and non-response to treatment 2(17%). Two patients stopped taking treatment within first month due to fear of side effects; one of them wanted to become pregnant. Of 10 patients two failed TG therapy: one due to adverse event (hair loss) and other due to therapy failure. 4/10(40%) patients had partial response, having occasional mild flare ups while further 6/10(60%) patients remained in sustained clinical remission at 6 months on treatment, although one of the patient did not turn up to follow up appointment following 6 months of therapy. Tolerability and efficacy rates were similar in both UC and CD. All patients were closely monitored and no abnormality in liver function tests detected.
CONCLUSION: Our study showed that TG was well tolerated in this selected group of difficult to treat patients. In addition, the use of small dose 20mg daily of TG appears to be relatively safe in IBD patients who failed conventional thiopurine therapy. Well designed prospective trials are required to further evaluate the safety and efficacy of 6-thioguanine.
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Disclosure of Interest: None Declared
Keywords: inflamatory bowel disease, thioguanine nucleotides, thiopurines

P1465 GRANULOCYTAPHERESIS IN STEROID-DEPENDENT AND STEROID-RESISTANT PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE OBSERVATIONAL STUDY

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INTRODUCTION: Granulocytapheresis (GCA) has a mounting importance in the treatment of inflammatory bowel diseases (IBDs); however, the differential effectiveness of this treatment in steroid-resistant and steroid-refractory patients needs further investigation.
AIMS&METHODS: We report the results of a prospective observational experience on the use of GCA in patients with either ulcerative colitis (UC) or Crohn's disease (CD) who were steroid-dependant (SD) or steroid-refractory (SR). In total, 118 patients were evaluated: 83 were affected from UC (55 SD and 28 SR), and 35 from CD (22 SD and 13 SR). All patients were treated with GCA, using the AdacolumnTM system, an adsorption column which selectively binds granulocytes and monocytes, for one session/week for 5 consecutive weeks. Concomitant steroid treatment was not permitted. Disease activity was evaluated by clinical disease index (CAI) in patient with UC and by Crohn's Disease Activity Index (CDAI) in those with CD: a clinical remission was defined as CAI $\leq$6 or CDAI $<$150. All patients were followed for 12 months after the end of GCA.
RESULTS: All patients completed the study; no complications were reported. The remission rates at the end of GCA, 6 and 12 months are reported in Table 1, while the values of CAI and CDAI during the follow-up period are shown in Table 2.

Tab.1

End of GCA 6 months 12 months UC	CD
Overall (n=83) 74% 69% 48%	Overall (n=35) 65% 57% 43%
SD (n=55) 71% 67% 45%	SD (n=22) 63% 54% 41%
SR (n=28) 67% 64% 39%	SR (n=13) 61% 53% 38%

Tab.2

Baseline 6 months 12 months UC (CAI)	CD (CDAI)
Overall 9.5±2.4 3.3±3.9 4.3±3.4	Overall 247±37 100±89 95±85
SD 9.5±2.5 3.3±3.9 4.3±3.5	SD 245±37 110±124 80±80
SR 9.5±2.6 3.4±3.9 4.0±3.	SR 251±42 87±19 116±106

CONCLUSION: On the basis of this large observational experience, GCA appears effective and well tolerated for the treatment of UC and CD in patients who are either SD or SR. GCA might be therefore considered as a useful alternative therapeutic approach in these patients. However, these findings need further validation in randomized multicenter trials, with the aim to shed new lights on the use of GCA for the treatment of IBDs.
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Disclosure of Interest: None Declared
Keywords: Granulocyte–monocyte adsorptive apheresis, IBD, Steroid-dependent IBD, Steroid-resistent IBD

P1466 STEROID SPARING WITH ADALIMUMAB IN CROHN'S DISEASE PATIENTS: A REAL-LIFE EXPERIENCE IN A TERTIARY REFERRAL CENTER

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INTRODUCTION: There is a need for long-term treatment alternatives that maintain clinical remission and reduce exposure to corticosteroids in Crohn's disease (CD) patients. Data regarding the long-term steroid-sparing effect of maintenance medications, including anti-TNF therapies, are limited. Adalimumab (ADA) is a fully human monoclonal antibody that is widely approved for the treatment of CD.
AIMS&METHODS: Aim of the study was to evaluate steroid-sparing efficacy of ADA in a cohort of CD patients in clinical practice. This retrospective study included 73 patients treated with ADA for CD between 2007 and 2013 (male: 41%; median age: 40.5 yrs; median disease duration: 12 yrs; previously exposure to anti-TNFs: 57.5%; combination therapy with azathioprine or methotrexate: 13%; steroid-dependence: 68.5%; median CDAI at ADA initiation: 235). Indication to anti-TNFa treatment included active luminal disease, perianal disease and presence of extra-intestinal manifestations. Steroid-free clinical remission was defined as absence of symptoms of active disease without steroids during maintenance and 1 year after ADA discontinuation.
RESULTS: Overall 62/73 (85%) of the patients achieved clinical remission and steroid sparing during maintenance and one year after ADA discontinuation. For perianal disease, remission was achieved in 9 out of 11 patients. In these patients ADA were used in combination to a surgical approach. Median time of ADA treatment was 17 months (1-59). Eleven patients (15%) did not achieve steroid clinical free remission and needed of budesonide in 10 patients and systemic steroid course in only 1 patient.
CONCLUSION: Our findings suggest that ADA therapy in clinical practice may be effective in terms of long-term efficacy and steroid sparing in our population of CD patients.
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Disclosure of Interest: None Declared
Keywords: adalimumab, Crohn's disease, steroid sparing

P1467 IMMUNE RESPONSE TO INFLUENZA VACCINE AND FREQUENCY OF INFLUENZA VIRUS INFECTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE ON MAINTENANCE IMMUNOSUPPRESSIVE THERAPY

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INTRODUCTION: Influenza vaccination is recommended for immuncompromised patients with inflammatory bowel disease (IBD).
AIMS&METHODS: We evaluated the serologic and clinical immune response to influenza vaccine in immuncompromised IBD patients.158 immuncompromised IBD patients were vaccinated. 62 patients refused vaccination. Split and whole virion vaccines were used. Serum samples for pre and postimmunization

antibody titers for influenza vaccine were collected. Cell-mediated responses to influenza A and B vaccines were evaluated using an INF-γ, IL-2, and TNF-α ELISA. Leukocyte and lymphocyte levels were also assessed.
RESULTS: 25 patients had local, 32 systemic reactions after vaccinations. 7 patients developed influenza-like symptoms. INF-γ, TNF-α, IL-2, leukocyte and lymphocyte levels did not change after vaccination. Significant differences were shown between pre- and post-vaccination influenza A and B antibody titers only in case of split virion vaccines.
CONCLUSION: Influenza vaccines were safe and well tolerated. Influenza vaccination did not influence cell-mediated immune response, but increased influenza A and B postimmunisation antibody titers. Split virion vaccines are more effective than whole virion vaccines.
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Disclosure of Interest: None Declared
Keywords: immunosuppression, inflammatory bowel disease, influenza vaccination

P1468 EARLY AND SUSTAINED REMISSION AFTER TREATMENT WITH SC ADMINISTERED GOLIMUMAB IS ASSOCIATED WITH NORMALIZED HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH MODERATE TO SEVERE ULCERATIVE COLITIS: POSTHOC-ANALYSIS FROM PURSUIT INDUCTION AND MAIN

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INTRODUCTION: -
AIMS&METHODS: To assess impact of early and sustained clinical remission on HRQOL in pts with active UC after SC GLM. Pts with moderate to severe UC defined by Mayo score of 6-12 including endoscopy subscore $\geq$2 with inadequate response or intolerance to conventional UC therapies but naïve to anti-TNF were randomized in the Ph3 portion of PURSUIT Induction to PBO or GLM 200mg,100mg or 400mg,200mg at wks 0 and 2. At wk6,GLM-treated pts who achieved clinical response were randomized to PBO or 50 or 100mg GLM q4w in PURSUIT Maintenance. Disease specific HRQOL was measured using the IBDQ and generic HRQOL was measured using SF-36 and EQ-5D.SF-36 was summarized by PCS and MCS. Normalized QoL was defined as SF-36 PCS or MCS $\geq$50, and IBDQ remission with total score$\geq$170. Clinical remission was defined as a Mayo score $\leq$2 points with no individual subscore$>$1.
RESULTS: Compared to PBO, a significantly greater proportion of GLM-treated pts achieved remission at wk6. GLM-treated pts who achieved clinical remission at wk6 had greater mean improvement in PCS,MCS,EQ-5D and IBDQ than those who did not achieve remission (PCS: 8.0 vs. 2.9, $p<0.001$; MCS: 10.7 vs. 2.6, $p<0.001$; EQ-5D: 21.4 vs. 7.2, $p<0.001$; and IBDQ: 54.7 vs. 17.7, $p<0.001$). Pts in clinical remission were more likely to achieve normalized PCS, normalized MCS, and IBDQ remission than those who didn't achieve clinical remission (PCS: 53.6% vs. 25.3%, $p<0.001$;MCS: 63.6% vs. 31.6%, $p<0.001$;IBDQ: 85.5% vs. 32.2%, $p<0.001$). GLM-treated pts who achieved clinical remission during induction AND maintained clinical remission at wk54 in maintenance were more likely to achieve normalized PCS, and MCS, and IBDQ remission than those who did not (PCS:73.5% vs. 22.7%, $p<0.001$; MCS: 63.3% vs. 28.4%, $p<0.001$; IBDQ remission: 89.8% vs. 22.7%, $p<0.001$). Those who achieved clinical response or mucosal healing demonstrated better improvement in HRQOL than those who didn't achieved these outcomes, but improvements in HRQOL were numerically lower than for pts in clinical remission.
CONCLUSION: Early and sustained clinical remission was associated with normalized HRQOL outcomes and should be considered as treatment goal for pts with moderate to severe UC.
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Keywords: golimumab, PURSUIT, ulcerative colitis

P1469 EFFICACY OF ORAL TACROLIMUS AND INFLIXIMAB INFUSION IN THE TREATMENT OF ACTIVE ULCERATIVE COLITIS IN JAPAN.

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INTRODUCTION: Oral tacrolimus and infliximab infusion have been proven to be effective treatments for active ulcerative colitis (UC). In clinical practice, however, it is still unclear which is the better therapeutic choice.
AIMS&METHODS: We aimed to investigate the efficacy of oral tacrolimus and infliximab infusion in the treatment of moderate-to-severe UC. This was a retrospective survey in which 34 consecutive patients with moderate-to-severe UC were enrolled from September 2009 to March 2013. Nineteen patients were treated with infliximab and fifteen were tacrolimus. The disease activity was evaluated using Ulcerative Colitis Activity Index (UCAI) reported by Seo M, et al. Clinical remission was defined as UCAI score of $<$120 and clinical response was defined as UCAI score of $<$150. Relapse was defined by the persistent UCAI score of $>$150 or lack of efficacy requiring a change in the treatment within 10 weeks after the initial administration. We investigated induction rates for remission and response in the two treatment grroups at week 10. Patients who achieved clinical response were followed-up until March 2013. We investigated relapse rates in the treatment groups using the Kaplan-Meier method. Cox regression analysis was performed to identify predictors for time to relapse.
RESULTS: There was no difference in the induction rates for remission and response between the two groups. In the infliximab group, remission rate and response rate at week 10 were 78.9% and 89.5%, respectively. In the tacrolimus group, remission rate and induction rate were 80.0% and 93.3, respectively. Among 31 patients who had achieved clinical response, 10 (32.3%) relapsed during the mean follow-up period of 77.6 weeks (infliximab group, 29.4%; tacrolimus, 35.7%). Time to relapse was not significantly different between the two treatment groups. Cox proportional-hazards regression analysis revealed that left-sided colitis was an independent predictor for relapse in the infliximab group, while no clinical characteristics predicted relapse in the tacrolimus group.
CONCLUSION: Both tacrolimus and infliximab were efficacious in the treatment of moderate-to-severe UC. In the infliximab group, left-sided colitis was associated with higher relapse rate.
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Disclosure of Interest: None Declared
Keywords: infliximab, tacrolimus, ulcerative colitis

P1470 EFFECTIVENESS OF THE SCREENING FOR LATENT TUBERCULOSIS IN INFLAMMATORY BOWEL DISEASE PATIENTS WITH PREVIOUS BCG VACCINATION

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INTRODUCTION: Screening for latent tuberculosis (LTB) prior anti-tumor necrosis factor (antiTNF) treatment is recommended. The diagnostic yield of different screening methods for LTB may be affected by previous BCG vaccination and the use of immune suppressive medication (IS). Furthermore, there are limited data on the effectiveness of this screening in reduction of TB reactivation during antiTNF treatment.
AIMS&METHODS: We aimed to determine whether the use of IS influences the outcomes of screening for LTB based on tuberculine skin test (TST) and interferon gamma releasing assay (IGRA) methods in a population of inflammatory bowel disease (IBD) patients vaccinated with BCG. We evaluated the incidence of TB reactivation during antiTNF treatment in this population. All consecutive patients with previous BCG vaccination were included. The outcomes of the LTB screening were retrieved from medical records and TB reactivation during antiTNF therapy was noted. The differences between the proportions of IS using patients tested positive for LTB vs. those tested negative were analysed by chi-square test.
RESULTS: In total, 182 IBD patients (99 males/83 females; mean age 38 years, range 18-75 years) were screened for LTB prior the initiation of antiTNF therapy. An induration at TST was found in 24 cases, the average induration was 11 mm, ranging from 4 to 25 mm. Nineteen out of these 24 tests were performed at the moment of the use of IS (79% vs. 92% in the group with negative TST, p=n.s.). Quantiferon Gold test was positive in 12 cases (6.6%), nine of these tests were performed at the moment of the use of IS (75% vs. 93% in the group with negative Quantiferon Gold test, p=0.009.). This test was inconclusive in 4 cases (2%), three of these patients were on IS medication. T-spot was inconclusive in two cases, in six cases the results were negative (5 tests at the moment of the IS use).
LTB was diagnosed in 13 cases (7%) based on positive Quantiferon test (11 cases) and in two patients based on an 18 mm large TST induration. These patients received a six months prophylactic treatment with isoniazid. During the further follow-up of a minimum of antiTNF treatment of 6 months, no clinically overt cases of TB reactivation were observed.
CONCLUSION: The use of immune suppressive medication does not seem to influence the diagnostic yield of tuberculine skin test but it does interfere with interferon gamma releasing assays. Nevertheless, the combination of these two methods results in an effective prophylaxis of TB reactivation during antiTNF treatment also in IBD patients using immune suppressive medication.
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Disclosure of Interest: None Declared
Keywords: anti-tumour necrosis factor, inflammatory bowel disease, tuberculosis

P1471 CUTANEOUS MANIFESTATION DURING ANTI-TNF A THERAPY IN PEDIATRIC INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Anti-TNF antibodies play an important role in the management of IBD, rheumatologic diseases, psoriasis. They have a good safety profile

but many studies have reported some adverse reactions. Skin manifestations are the most common adverse events and occur in 20–25% of patients (pts). There are only few data on cutaneous manifestations during anti-TNFα therapy in IBD children.

AIMS&METHODS: We conducted a retrospective study among pts with IBD receiving Infliximab, (IFX) and Adalimumab, (ADA). Duration of therapy, type and location of skin lesions, time of onset, disease activity, concomitant immunosuppressors(IM) and corticosteroids(CS) at the time of skin manifestation were reported. We evaluated differences between IFX and ADA in terms of frequency of cutaneous manifestations.

RESULTS: 74 pts (40 males, 63 with CD,9 with UC and 2 with undefined-IBD) were enrolled. The mean age at first skin manifestation was 16.3±3.2 years. Forty (54%) pts developed at least one cutaneous manifestation during anti-TNFα therapy: folliculitis (14 pts), psoriasis (14), eczematous and seborrheic dermatitis (5), skin infections (7), acne (12), xerosis cutis (7). In terms of distribution and location of skin lesions, folliculitis mainly affected arms and legs (35%pts), whereas in pts with psoriasis the scalp and pubic region were the mostly involved areas, 48% and 24% of pts respectively. There was no difference between males and females in the development of skin lesions (p=0.6). There was no significant difference in terms of disease activity (p=0.5). The mean duration of anti-TNFα therapy at the onset of skin events was 11.75 months (mts). 17 (43%) pts were on concomitant IM therapy, whereas no pts had been on CS during the previous 3 mts. There wasn't a clear association between a specific anti-TNF-agent and the occurrence of skin lesions, but IFX treated pts developed skin manifestations more frequently than pts receiving ADA (72% vs 42%, respectively). We also observed a longer time of onset of cutaneous lesions in pts receiving ADA (p=0.005).

CONCLUSION: In our pts folliculitis and psoriasiform lesions are the most common cutaneous manifestations during anti-TNF therapy. Skin events are frequent during biological therapy thus remarking the importance of a team management of pediatric IBD also including a dermatologist. In our experience the majority of lesions are easy to treat and are not a reason to stop anti-TNF therapy. Only rarely it's necessary to interrupt therapy for some time.

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Disclosure of Interest: None Declared

Keywords: anti TNF therapy, IBD, Psoriasis, SKIN LESIONS

P1472 IMPROVEMENT IN MARKERS OF BONE METABOLISM WITH ADALIMUMAB IN CHILDREN WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: RESULTS FROM IMAGINE 1

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INTRODUCTION: Objective: To measure changes in bone metabolism in paediatric patients (pts) with moderately to severely active Crohn's disease (CD) treated with adalimumab (ADA) enrolled in the clinical trial IMAGINE 1.

AIMS&METHODS: In IMAGINE 1[1], pts aged 6-17 years with Baseline (BL) PCDAI >30 and CD resistant or intolerant to conventional therapy, including prior infliximab, received open-label induction of ADA at wks 0/2 according to body weight (≥40kg, 160/80mg; <40kg, 80/40mg). At wk 4, pts were randomized to double-blind higher-dose (HD) ADA (≥40kg, 40mg every other week [eow]; <40kg, 20mg eow) or lower-dose (LD) ADA (≥40kg, 20mg eow; <40kg, 10mg eow). Pts experiencing disease flare or non-response could move to blinded weekly dosing after wk 12. Changes in serological markers of bone formation (osteocalcin [OC], bone specific alkaline phosphatase [BSAP]) and resorption (serum type I collagen N-telopeptide [NTx]) from BL were calculated at wk 26 and 52 for LD and HD ADA. Subgroup analyses by prior IFX use, disease severity at BL, and response at wk 4 (defined as PCDAI decrease ≥15 points from BL) were also performed. Last observation carried forward (LOCF) was used to impute missing data. Signed rank test was applied to evaluate changes within each treatment group.

RESULTS: Overall, pts achieved improvement in OC and BSAP with LD and HD ADA at wks 26 and 52 (Table). Increases in OC and BSAP were achieved with both doses at wks 26 and 52 in pts naïve to prior IFX and with severe disease (PCDAI≥40). BSAP improvement was more pronounced in wk 4 responders. Significant change in NTx was observed at wk 26 with HD ADA (Table).

Table. Median BL values of serological markers of bone metabolism and median change from BL at Wks 26 and 52 (LOCF)

	Osteocalcin (μg/L)		BSAP (μg/L)		NTx (nm BCE)	
	LD ADA 20/10mg N=63	HD ADA 40/20mg N=64	LD ADA 20/10mg N=62	HD ADA 40/20mg N=65	LD ADA 20/10mg N=62	HD ADA 40/20mg N=65
Baseline	15.10	13.20	42.80	45.10	25.15	26.60
Week 26	2.5†	2.5†	11.9§	9.0§	1.6	4.3*
Week 52	0.5	2.6†	4.6*	3.1*	-1.3	-0.8

*p<0.05; †p<0.01; §p<0.001 using signed rank test for no change from BL within each treatment group

CONCLUSION: Both HD and LD ADA treatment improved bone metabolism in children with moderately to severely active CD. Pts naïve to IFX derived the greatest treatment benefit.

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Keywords: adalimumab, bone formation, Crohn's disease, paediatric

P1473 OROFACIAL GRANULOMATOSIS AND ENTERAL NUTRITION IN PEDIATRIC CROHŃS DISEASE

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INTRODUCTION: Crohńs disease in children and adolescents can be treated with exclusive enteral nutrition (EEN) as induction therapy. Some patients have oral complaints, suspicious of orofacial granulomatosis (OFG). Symptoms are lip swelling, aphtous lesions, cheilitis and granulomatous inflammation in the mouth. OFG might be a part of Crohn's disease and is believed to be, at least partly, an allergic reaction to benzoates and cinnamon. Diet restrictions and elemental diet (amino- acid formula) are used to treat the condition.

AIMS&METHODS: Retrospectively, we wanted to investigate the efficacy and tolerability of exclusive enteral nutrition in children and adolescents with Crohn's disease and OFG at our institution.

During the period May 2005 to January 2012 we diagnosed altogether 70 patients, 64 with Crohn's disease according to the Porto criteria, 12 with concomitant OFG. 6 patients presented with isolated OFG.

RESULTS: Out of the 64 patients with Crohńs disease, 17 were given 5- ASA, azathioprine and or budesonide. All patients who received 5-ASA, azathioprine and or a course of budesonide remained in remission. 45 patients (70%) received EEN and azathioprine. The disease distribution was more extensive in these patients with significantly higher PCDAI, fecal calprotectin ((median 1041 mg/kg (normal range <50mg/kg), CRP (mean 30 mg/l) and ESR (mean 24 mm/h)) before treatment compared to 632 mg/l, 16 mg/l and 18 mm/t respectively. The 6 patients with isolated OFG had a normal fecal calprotectin as well as normal CRP and ESR at time of diagnosis. In 28 (62%) of the EEN treated patients we observed a complete normalization of the ESR, CRP and fecal calprotectin. Fifteen (54%) of the patients who went into remission with EEN and azathioprine are still doing well with azathioprine as maintenance. All OFG patients, with or without concomitant Crohn's disease, responded well to treatment with exclusive elemental diet with a reduction of lip swelling and resolution of aphtous ulcers and cheilitis. The improvement was evident within a few days. Their symptoms were later controlled with a diet free of benzoates and cinnamon.

CONCLUSION: Exclusive enteral nutrition is efficacious and well tolerated in children with Crohn's disease and OFG. In OFG the liquid diet should be an elemental formula. Benzoate free and cinnamon-free diet is of benefit in OFG patients in order to control the symptoms.

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Disclosure of Interest: None Declared

Keywords: CROHŃS DISEASE, Enteral Nutrition, orofacial granulomatosis

P1474 INFLUENCE OF GENOTYPE ON BIOCHEMICAL MARKERS OF INFLAMMATION IN CHILDHOOD INFLAMMATORY BOWEL DISEASE.

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INTRODUCTION: There is paucity of data on the influence of genotype on biochemical inflammation markers in paediatric inflammatory bowel disease (IBD).

AIMS&METHODS: We aimed to investigate associations between IBD related predefined single nucleotide polymorphisms (SNPs) and the level of biomarkers within the first year after diagnosis in a population based cohort of paediatric IBD patients. A historical population-based cohort including all incident paediatric patients with IBD, diagnosed in Eastern Denmark (January 1. 1998 – December 31. 2006) was created. Multiple regression analysis was used to analyze associations between 52 SNPs and the level of biochemical markers of inflammation (albumin, hemoglobin, c-reactive protein, erythrocyte sedimentation rate, leucocytes) measured at diagnosis, 30 days, 6 months and one year after diagnosis. The analysis was adjusted for age, gender and disease localization.

RESULTS: The cohort consisted of 235 patients. In 190 patients (83 Crohn's disease [CD], 95 ulcerative colitis [UC] and 12 IBD-unclassified [IBD-U]) genotyping and retrieving information on blood sample results within the first year after diagnosis was succesful. Mean age at diagnosis was 12.4 years (range 0.4-15 years). In multivariate analysis three different SNPs (rs6785049, rs10500264,

rs4986791) located on three different genes; Pregnane-X-receptor, SLC7A10 and TLR-4, respectively, were associated with a significant increase of the level of hemoglobin ($p<.0001$) and albumin ($p<.0001$) in patients with CD or UC within the first year after diagnosis. The mean changes in the level of hemoglobin was small (mean change 0.2 mmol/l [range -0.2-0.6] in SNP rs10500264) and (mean change 0.4 mmol/l [range 0.1-0.9] in SNP rs6785049) whereas the changes in the albumin level was more marked. In patients with UC homozygous for the C allele (CC genotype) in SNP rs4986791 the mean increase in albumin (g/l) from diagnosis to one year after diagnosis was 2.5 (from 40.0-42.5) compared to UC patients with the genotype CT 0.5 (from 39.6-40.1).

CONCLUSION: In this pilot study on 190 pediatric patients with IBD, we identified an association between three different SNPs and the level in hemoglobin and albumin within the first year after diagnosis, which suggests a genetic contribution to the inflammatory response in paediatric IBD.

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Keywords: biochemical markers, genotype, inflammatory bowel disease,

P1475 POST-OPERATIVE COMPLICATIONS IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY

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INTRODUCTION: We described in children the incidence of and factors associated with post-operative complications (POC) in inflammatory bowel disease (IBD).

AIMS&METHODS: Using a population-based Registry, among 692 IBD incident cases (532 Crohn's disease (CD) and 160 ulcerative colitis (UC),153 (128 CD) patients (22%) underwent one abdominal surgery. Median age at surgery was 16 yrs [14-17]. Medical charts were reviewed for early (<30 days) and late (≥30 days) POC according to Dindo's criteria(1). Factors associated with POC were assessed using Cox models and expressed as HR with 95%CI.

RESULTS: After 8 yrs [3-12] of follow-up,78 (51%) experienced one POC with a total of 115 POC(median1[1-2]) including 51 patients with one POC and 27 with more than one. POC were significantly more frequent in UC than in CD (72%*vs*45%;p=0.01). Children with UC presented more frequently at least 2 POC than those with CD (45% *vs* 29%;p=0.01). A total of 64 early POC was observed in 47 patients (31%), with 33 infectious. Early POC were more frequent in UC than in CD (83% *vs* 55%;p=0.03). Regarding all POC, their graded distribution was 38% (n=42) for grade 1,35% (n=39) for grade 2, 28% (n=31) for grade 3 and 1.8% for grade 5 (n=2). The frequency of severe POC (grade>2) was similar in CD and UC (28% *vs* 27%). 51 late POC were observed in 39 patients (24%), with 45 non-infectious. The cumulative risk of any POC was 31% (95% CI, 24-39) at 1 mo and 44% (36-52) at 6 mos. Multivariate analysis found that type of IBD was the only factor associated with any POC (HR relative to UC *vs*. CD, 2.2;[1.3-3.8]). Gender, systemic steroid, immunosuppressants (IS) before abdominal surgery were not predictors for POC. In UC, shorter was the time from the diagnosis to the colectomy higher was the risk for POC (HR=1.50[1.01-2.20]). In CD, age at diagnosis <14 yrs was associated with an increased risk for POC (HR=1.8 [1.01-3.10]). Time from IBD diagnosis to abdominal surgery <18 mos (HR=2.7[1.1-6.6]) and parenteral nutrition (HR=2.7 [1.2-6.1]) were associated with an increased risk for infectious POC.

CONCLUSION: 50% of children with IBD experienced at least one POC that occurred either early (31%) or late (24%). Only UC was significantly associated with an increased risk of POC. A short time from diagnosis to surgery was poor prognosis in UC and associated in all IBD with an increased risk for infectious POC. Systemic steroid and IS were not associated with an increased risk of infectious POC.

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Keywords: inflamatory bowel disease, paediatrics, population-based, postoperative complications, surgical treatment

P1476 ANTI-TNF ALPHA THERAPY AND MUCOSAL HEALING: THE KEY TO CHANGE THE STORY OF PEDIATRIC CROHN'S DISEASE?

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INTRODUCTION: Efforts have been made to optimize the use of available therapies to improve Crohn's disease (CD) patients' outcome, but up to now no therapy changed the natural history of the disease. Mucosal healing (MH) appears as a therapeutic goal able to predict sustained clinical remission. Therapy with anti-TNFα antibodies, Infliximab (IFX) and Adalimumab (ADA), have been proven effective in achieving MH with a more potent and rapid effect compared to immumomodulants (IMM). Few studies evaluating MH as a therapeutic goal in pediatric CD are available.

AIMS&METHODS: Aim of our study is to assess the efficacy of IFX and ADA in obtaining MH in a pediatric CD cohort. Secondary aim is to evaluate differences in response in children with early (<1 year) or late (>1 year) disease.

Pediatric CD patients (pts), between 6 and 18 years of age, starting IFX or ADA from January 2009 were enrolled. All pts were naïve to biological therapies but could have been previously treated with corticosteroids, IMM and aminosalycilates.

Pts' characteristics collected at baseline are: age at diagnosis, indication for therapy, age at enrollment, disease duration and location, and concomitant medications. An endoscopic procedure was performed before starting biologics and after 9 to12 months to evaluate MH. Clinical and endoscopic disease activity were assessed by Pediatric Crohn's Disease Activity Index (PCDAI) and Simple Endoscopic Score (SES CD) respectively at time 0 (T_0) and at the time of endoscopic follow-up (FU). Pts underwent anti-TNFα therapy with appropriate induction and maintenance therapeutic schemes.

RESULTS: Thirty-one pts (21 IFX and 10 ADA) were enrolled, 18 males. At enrollment mean age was 12.7± 2.9 years and mean disease duration was 13 ± 15.3 months. Fifteen pts (6 IFX) were in the early disease group, 16 (15 IFX) in the late disease group. At T_0 16 pts (52%) were on IMM, 10 of them were still on IMM at FU. Mean ± SD values of PCDAI and SES CD at T_0 and FU are 30±17.6 and 11.3 ± 11.5, and 15.5± 8.6 and 6.5 ± 7.5 respectively; both values were significantly reduced at FU ($p < 0.05$). Dividing patients on the basis of disease duration prior to therapy introduction SES CD values decreased significantly at FU both in early and in late disease pts, however more significantly in the first group ($p<0.0001$ vs 0.02).

CONCLUSION: In our cohort biological therapy appears effective in achieving mucosal healing in pediatric patients affected by CD, probably more efficaciously if introduced early in the course of the disease. Larger studies with longer FU will highlight the effect of MH on disease evolution.

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Disclosure of Interest: None Declared

Keywords: biologic therapy, Crohn's disease, mucosal healing

P1477 ANTI-TNF DEPENDENCY IN PAEDIATRIC IBD- THE SCOTTISH EXPERIENCE

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INTRODUCTION: Management of paediatric IBD (PIBD) has changed significantly in the last 10 years with the advent of biological agents which are beneficial in the induction and maintenance of remission.

AIMS&METHODS: Recent evidence is emerging on biological dependency and the aim of our study is to identify patients in our national cohort who become dependent on Infliximab (IFX) and/or Adalimumab (ADA) after response to induction therapy. A retrospective case note review was carried out in all PIBD treatment centres in Scotland within our national network. Children <18 year were included who were given Infliximab (IFX) and/or Adalimumab (ADA) in a paediatric centre and dependency was defined as relapse of symptoms requiring repeated infusions to regain complete or partial response. Data was collected from 1.1.00 until 01.03.12 with follow up until 30.9.12 on duration of treatment, clinical response and adverse events.

RESULTS: 65 patients had IFX and/or ADA for at least 12 months - 42 males, 64 with CD and 1 UC. 38 of 65 (58%) had anti-TNF dependency. 49 patients were on IFX for a median of 1.67 years receiving 4- 25 doses with a median of 11. 14 patients failed IFX and proceeded to maintenance ADA. Commonest disease location was colonic (37%) and behaviour was inflammatory (B1 and B1p 81%). 61% were on steroids at baseline and all were on immunomodulators. 98% had response/remission after induction. The most common indications were luminal CD, immunomodulatory failure and steroid dependency. 40% required escalation of therapy, either increased dose or frequency. 55% stopped treatment after 12 months (44% loss of response, 33% successful planned IFX withdrawal and 7% allergic reaction); 45% continued to study end.

16 patients (14 prior IFX) were on ADA for a median of 2.18 years, all had CD and 12 were male; 13 were on ADA at study end, 2 stopped for loss of response and 1 had successful planned ADA withdrawal. IFX failure was most commonly primary non-response, in 7 (44%). 9 (56%) required escalation of therapy to weekly dosing. 81% had a response or remission after induction. No serious adverse events were noted during or after biological therapy.

CONCLUSION: 58% on IFX/ADA at 12 months then become dependent on anti-TNFs, with only a minority having successful planned drug withdrawal. Both drugs appear safe and well tolerated; only 7% stopping IFX or ADA due to allergy or side effects after 12 months. The need for dose escalation and identification of those who can successfully cease biologicals remain major issues.

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Disclosure of Interest: None Declared

Keywords: adalimumab, Inflammatory bowel disease (IBD), inflixmab, paediatrics

P1478 COLONIC ULTRASONOGRAPHY IN PEDIATRIC ULCERATIVE COLITIS: COMPARATIVE STUDY WITH COLONOSCOPY

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INTRODUCTION: Bowel ultrasonography (US) is a non-invasive tool in the evaluation of inflammatory bowel diseases, especially Crohn's disease. There are only few data on its role in Ulcerative Colitis (UC), particularly in children.
AIMS&METHODS: To evaluate the usefulness of bowel US in the assessment of pediatric patients (pts) with UC and compare US findings with clinical and endoscopic data. Thirty pediatric pts (median age 15 years; range 2-21; 14 males) were prospectively enrolled. Eight pts had a clinical suspicion of UC, 22 had an already established diagnosis and showed a disease flare-up. All pts underwent clinical evaluation, bowel US with Color-Doppler examination (Toshiba equipment, 3.5 MHz convex and 7.5 MHz linear transducers) and ileo-colonoscopy. US and endoscopy were carried out by different operators, blind to the results of the other technique. For each patient Pediatric Ulcerative Colitis Activity Index (PUCAI) and Mayo endoscopic subscore were calculated. The US assessed parameters were Bowel Wall Thickness (normal value < 3 mm), BW stratification, vascularity and presence of austrae:each parameter was assigned a value of 0 or 1 depending on the presence or absence of alteration.
RESULTS: 27/30 pts were finally diagnosed as UC. Extension of disease according to Paris Classification was: E2 (left-side colitis) in 12/27 (45%), E4 (pancolitis) in 15/27 (55%) pts. This extension was independently confirmed in 24/27 pts by US, that yielded a 90% concordance (K) with endoscopy for disease extension (CI 0.82-0.96; SE 0.03). Disease activity was mild (PUCAI 10-34) in 7 pts (25%), moderate (PUCAI 35-64) in 12 (45%) and severe (PUCAI >65) in 8 (30%). The mean values of PUCAI, Mayo score and US score respectively were: 40.5 ± 24.4, 2 ± 1 and 3 ± 1. The US score strongly correlated with PUCAI ($r=0.90$, $p<0.0001$) and Mayo index ($r=0.94$, $p<0.0001$). A positive correlation was also found between PUCAI and Mayo score ($r=0.88$, $p<0.0001$). Multiple regression analysis showed that variables making a significant contribution to the final value of Mayo score were BWT ($p=0.0008$), vascularization ($p=0.02$) and stratification ($p=0.02$). The mean BWT in affected colonic segments was 5 ± 2 mm. BWT allowed to discriminate between moderate-severe and mild disese activity ($p=0.001$).
CONCLUSION: Our data show a strong relationship between US and clinical and endoscopic findings, thus suggesting that colonic US might represent a useful first line tool in the evaluation of pediatric UC pts. It allows to assess the extension and activity of disease and to estimate the severity of a flare-up, prior to further invasive tests.
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Disclosure of Interest: None Declared
Keywords: children, ulcerative colitis, ultrasonography

P1479 EARLY RESPONSE TO TREATMENT WITH ADALIMUMAB IN CHILDREN WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: RESULTS FROM IMAGINE 1

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INTRODUCTION: To evaluate adalimumab (ADA) efficacy at week (wk) 4 in paediatric patients (pts) with moderately to severely active Crohn's disease (CD) enrolled in the randomised clinical trial IMAgINE 1.
AIMS&METHODS: In IMAgINE 1[1], pts aged 6-17 yrs with baseline (BL) PCDAI >30 and CD resistant or intolerant to conventional therapy, including prior infliximab (IFX), received open-label induction of ADA at wks 0/2 according to body weight ($\geq$40kg, 160/80mg; $<$40kg, 80/40mg). Proportion of pts in clinical remission (PCDAI$\leq$10) and response (PCDAI decrease $\geq$15 points from BL) were measured at wk 4. Non-responder imputation (NRI) was used for missing data. Median change in C-reactive protein (CRP) levels (mg/dL) from baseline was measured at wk 4. The safety profile for ADA in IMAgINE 1 has been reported previously[1].
RESULTS: At wk 4, 155 (81%) pts responded to induction and 52 (27%) were in clinical remission. Remission and response rates were comparable between the induction dose groups (Table). A numerically higher proportion of IFX-naïve pts were in remission at wk 4 compared to pts who had prior IFX (Table), however the differences were not statistically significant. A decrease in median CRP was observed for both dose groups (-0.6 mg/dL ADA 160/80mg; -1.1 mg/dL ADA 80/40mg) at wk 4, but was not statistically significant between the groups (P=.097).
Table. Efficacy at wk 4 in ADA-treated pts in IMAgINE 1 (NRI)

	ADA 160mg/80mg N=123	ADA 80mg/40mg, N=69	P-value*
Baseline PCDAI score, mean	40.0	42.6	NA
Remission, n/N (%)	36/123 (29)	16/69 (23)	0.36
IFX-naïve	22/65 (34)	12/42 (29)	0.57
IFX-experienced	14/58 (24)	4/27 (15)	0.33
Response, n/N (%)	97/123 (79)	58/69 (84)	0.38
IFX-naïve	56/65 (86)**	35/42 (83)	0.69
IFX-experienced	41/58 (71)	23/27 (85)	0.15

NA: Not applicable. *Chi-square test comparison between dose groups; **$P<0.05$ for IFX-naïve vs IFX-experienced comparison; $P>0.05$ for all other IFX-naïve vs IFX-experienced comparisons.
CONCLUSION: ADA induced clinical remission and response in children with moderately to severely active CD as early as wk 4. The early clinical benefits were comparable for both induction doses, with a trend towards greater benefits observed in anti-TNF naïve patients.
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Keywords: adalimumab, CROHNS DISEASE, paediatric, remission, response to treatment

P1480 SERUM ADIPOKINE LEVELS DURING INFLIXIMAB THERAPY IN PEDIATRIC CROHN'S DISEASE

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INTRODUCTION: Crohn's disease (CD) is an inflammatory disorder of the intestine and the visceral adipose tissue, characterized by adipocyte hyperplasia and increased fat tissue concentrations of TNFα, leptin and adiponectin. In vitro TNFα suppresses the expression of leptin and the anti-inflammatory mediator adiponectin.
AIMS&METHODS: We aimed to investigate the early effect of anti-TNFα therapy with infliximab (IFX) on visceral adipose tissue and assessed serum adipokine levels in pediatric CD. Serum concentrations of adipokines (leptin, adiponectin and resistin) were retrospectively measured with commercially available ELISAs before the 1st, 2nd and 4th IFX infusion (week 0, 2 and 14). Results of 18 CD patients were compared with 15 gender and weight/BMI matched healthy controls (HC). We recorded the mathematically weighted Pediatric Crohn's Disease Activity Index (wPCDAI), laboratory parameters, anthropometric data and treatment response. Wilcoxon signed-rank test was applied to analyze differences between patients and HC and changes during IFX therapy at the 3 time points.
RESULTS: The IFX treated patients included 10 males and 8 females (median age 14.9 years, range 12.2-17.5). The wPCDAI decreased from 26.3 (7.5-72.5) to 15 (0.0-35.0) and 8.8 (0.0-45.0) after 2 and 14 weeks, respectively ($p<0.01$). Baseline resistin levels were higher in patients than in HC: median 14.7 ng/ml (range 5.1-50.5) vs 7.3 ng/ml (0.5-14.5), respectively ($p<0.001$), and decreased with IFX at both time points ($p<0.01$ compared to baseline, n.s. to HC). At baseline leptin levels did not differ from HC, but leptin levels were significantly higher in girls compared to boys ($p<0.0001$). In girls, leptin levels increased after 2 weeks from 9.5 ng/ml (7.6-30.1) to 16.0 ng/ml (7.9-35.2) ($p<0.05$). In boys, leptin increase showed only a trend from 2.0 ng/ml (0.6-12.9) to 2.8 ng/ml (1.7-8.6) (n.s.). Adiponectin baseline levels in patients were not different from HC: 7765 ng/ml (4591-11897) vs 8660 ng/ml (5029-10795) (n.s.). Adiponectin notably peaked 2 weeks after 1st IFX infusion to 9200 ng/ml (4075- 20706), ($p<0.01$) but thereafter fell to 6470 ng/ml (2956-12681), which was lower compared to values in HC ($p<0.05$), at baseline ($p<0.05$) or at 2 weeks ($p<0.001$).
CONCLUSION: TNFα blockade by IFX effectively reduced disease activity and inflammatory markers including resistin in CD and led to an early increase of leptin and adiponectin. Leptin parallels weight gain. We speculate that successful induction therapy with IFX is partially mediated by the anti-inflammatory properties of released adiponectin.
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Disclosure of Interest: None Declared
Keywords: adipokines, infliximab, pediatric IBD

P1481 NOD2, IRGM, AND ORMDL3 POLYMORPHISMS INCREASE RISK OF PEDIATRIC INFLAMMATORY BOWEL DISEASE IN LITHUANIAN POPULATION

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INTRODUCTION: Recent GWAS and meta-analyses have revealed about 163 susceptibility genes/loci for inflammatory bowel diseases (1). However, only a small number of studies were performed in children population.
AIMS&METHODS: The aim of the study was to assess the frequency of *NOD2*, *IL23R*, *ATG16L1*, *IRGM*, *IL10*, *NKX2-3* and *ORMDL3* polymorphisms in a case-control panel of Lithuanian children. Seventy six unrelated IBD children [30 with Crohn's disease (CD) and 46 with ulcerative colitis (UC)] at the age of ≤17 years and 158 healthy controls were genotyped for the following known genetic susceptibility variants: *NOD2* Arg702Trp (rs2066844), Gly908Arg (rs2066845) and Leu1007insC (rs2066847), *IL23R* rs11209026, *ATG16L1* rs2241880, *IRGM* rs4958847, *IL10* rs3024505), *NKX2-3* rs11190140 and *ORMDL3* rs2872507.
RESULTS: Our study revealed that Leu1007insC was strongly associated with CD (21.4% CD vs 4.7% controls, p = 3.687 x 10(-8), OR = 5.54, 95% CI: 2.85-10.75). (16% CD *vs* 2% in controls, p =1,21x10^{-5}, OR=6,56; 95% CI:2,54-16,91). *IRGM* variant also significantly increased risk for CD (16% CD *vs* 7% in controls p=0,033, OR=2,32; 95% CI:1,05-5,14). Whereas, presence of variant *ORMDL3* allele strongly predisposed to UC (50% UC *vs* 33% controls, p= 4,15x10^{-3}, OR=1,99; 95% CI:1,23-3,20).
CONCLUSION: The results of our study revealed that polymorphism Leu1007insC in *NOD2* and *IRGM* variant are associated with increased risk of CD, whereas the *ORMDL3* variant associated with susceptibility to UC in the Lithuanian pediatric population.
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Disclosure of Interest: None Declared
Keywords: Crohn's disease, IRGM, Lithuania, NOD2, ORMDL3, Ulcerative colitis

P1482 LOW DOSE AZATHIOPRINE TREATMENT MONITORED BY THIOPURINE METABOLITES IS SAFE AND EFFECTIVE IN KOREAN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: Azathioprine (AZA) is used to maintain clinical remission in inflammatory bowel disease (IBD). This study evaluated the role of 6-thioguanine nucleotide (6-TGN) and thiopurine S-methyltransferase (TPMT) as predictors of adverse effects and clinical response to AZA, and determined the optimal dose of AZA in Korean pediatric IBD patients.
AIMS&METHODS: One hundred and nine IBD patients (age range, 3 to 21 years) who required AZA to maintain remission were monitored for thiopurine metabolites since September 2010. Of these, 83 cohorts who had received a consistent dose of AZA for at least 3 months prior to September 2010 were selected and followed until October 2011 to assess adverse drug reactions (ADR), disease activity and optimal AZA dose at pre- and post-thiopurine metabolite monitoring period.
RESULTS: The distribution of the TPMT genotype was as follows: 102 patients had *1/*1 (wild type), one had *3C/*3C (homozygote), four had *1/*3C, one had *1/*6, and one had *1/*16 (heterozygote). ADR occurred in 31 patients before thiopurine metabolite monitoring and in only nine patients after monitoring. AZA dose was 1.4 ± 0.31 mg/kg/day at pre-monitoring and 1.1 ± 0.46 mg/kg/day at post-monitoring ($P < 0.001$). However, there were no statistical differences in disease activity between pre- and post-thiopurine metabolite monitoring period ($P = 0.34$).
CONCLUSION: Since monitoring, ADR markedly decreased and the AZA dose was reduced to 1.1 ± 0.46 mg/kg/day with maintaining remission. This dose of AZA was lower than those reported in Western countries.
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Disclosure of Interest: None Declared
Keywords: 6-thioguanine nucleotide, azathioprine, Inflammatory bowel disease, thiopurine S-methyltransferase

P1483 THE DIAGNOSTIC ACCURACY OF COMBINING FAECAL CALPROTECTIN WITH COMMON BLOOD TESTS IN THE INVESTIGATION OF SUSPECTED PAEDIATRIC INFLAMMATORY BOWEL DISEASE

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INTRODUCTION: We have previously shown that FC has better diagnostic accuracy than individual blood parameters in suspected paediatric inflammatory bowel disease (PIBD). However, the diagnostic accuracy of combining FC and blood tests has yet to be established.
AIMS&METHODS: We aimed to determine the diagnostic accuracy of a panel of PIBD biomarkers using a case-control design. Cases of PIBD cared for in Edinburgh have been recorded prospectively since 1997, with FC becoming available as a routine clinical biochemistry test on 01.01.05. All children >1yr and <18yr of age undergoing their primary investigation for suspected bowel inflammation were eligible. A retrospective search of the PIBD database and endoscopy records between 01.01.05-31.12.11 identified all PIBD and non-PIBD (control) cases with FC and blood samples (Hb, WCC, Plt, Alb, ESR, CRP) taken in the 6 months prior to full upper and lower endoscopy. Children with a known gastrointestinal disease or who had undergone previous endoscopy were excluded. Population-based normal blood parameters were used. Statistical analyses were performed using R and GraphPad Prism.
RESULTS: 221 children met the inclusion criteria including 108 cases of PIBD (69 Crohn's disease, 28 ulcerative colitis, 11 IBD-unclassified). The PIBD group were older at endoscopy (12.7yr *vs* 9.9yr) with terminal ileum intubation rates comparable in both groups (p=0.142). Common indications for endoscopy in the control group were abdominal pain, rectal bleeding and diarrhoea; all children had a minimum follow up of 16 months. Median FC level in the PIBD group was 1235ug/g (IQR 684-1667) compared to 60ug/g (20-155) in controls ($p < 0.0001$). Sensitivity and specificity for FC alone (>50ug/g) were 0.97 (95% CI 0.92-0.99) and 0.48 (95% CI 0.38-0.57) compared to the best blood parameter (ESR) at 0.71 (95% CI 0.61-0.79) and 0.86 (95% CI 0.78-0.92). Using *any* abnormal blood test, sensitivity and specificity were 0.85 (95% CI 0.76-0.91) and 0.63 (95% CI 0.52-0.73). Combining an abnormal ESR *or* abnormal FC provided a sensitivity of 0.99 (95% CI 0.93-1.00) with specificities of 0.38 (95% CI 0.28-0.47) and 0.69 (95% CI 0.59-0.77) using >50ug/g and >200ug/g FC cut-off values.
CONCLUSION: FC provides excellent sensitivity and moderate specificity for PIBD but diagnostic accuracy is improved when combining an abnormal ESR (>20mm/hr) and a FC cut-off of >200ug/g; the addition of certain symptoms such as rectal bleeding would likely improve this diagnostic utility. A raised FC and an abnormal ESR should lead to prompt endoscopic assessment of children with suspected bowel inflammation.
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Disclosure of Interest: None Declared
Keywords: calprotectin, diagnostic accuracy, inflammatory bowel disease, paediatric

P1484 LONG-TERM SAFETY OF ADALIMUMAB IN PAEDIATRIC PATIENTS WITH CROHN'S DISEASE

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INTRODUCTION: The safety profile of adalimumab (ADA) in children with moderately to severely active Crohn's disease (CD) enrolled in the clinical trial IMAGINE 1 up to week 52 has been reported previously[1]. Cumulative safety data including the on-going open-label extension (OLE) is presented in this report.
AIMS&METHODS: Patients (pts) who completed IMAGINE 1[1] had the option to continue in the on-going OLE. Treatment-emergent adverse events (AEs) were monitored regularly and by spontaneous reporting. Rates of AEs were assessed per 100 patient-years (PY) of exposure for any pt enrolled in the double-blind clinical trial IMAGINE 1 and followed through the 31 July 2011 cut-off or up to 70 days after the last dose of ADA. Subgroup analysis by prior infliximab (IFX) use was also performed.
RESULTS: 192 paediatric pts had received ADA for CD, totaling 304.1 PY of exposure. As of 31 Jul 2011, 29/192 (15%) pts had up to 3 years of exposure. The most common AE for all pts was injection site reaction; all were non-serious. The most common serious AE (SAE) was flare or worsening of CD. Rates of SAEs, infections and AEs leading to discontinuation were consistent with IMAGINE 1[1]. Serious AEs were experienced by significantly more pts exposed to prior IFX than IFX-naïve pts (Table). No malignancies,TB, demyelinating disease, or deaths were reported.
Table. Overview of Treatment-emergent Adverse Events (AE) as of 31 July 2011

	Any ADA N=192, 304.1 PYs	IFX naïve N=107, 199.7 PYs		Prior IFX N=85, 104.4 PYs	
	Events (E/100PY)	n (%)	Events (E/100PY)	n (%)	Events (E/100PY)
Any AE	2414 (793.8)	107 (100)	1536 (769.2)	82 (96.5)	878 (841.0)
Serious AE	123 (40.4)	38 (35.5)	64 (32.0)	43* (50.6)	59 (56.5)
AE leading to discontinuation	64 (21.0)	22 (20.6)	29 (14.5)	27 (31.8)	35 (33.5)
Opportunistic infection (excluding TB)	2 [a] (0.7)	1 (0.9)	1 (0.5)	1 (1.2)	1 (1.0)
Serious infection	24 (7.9)	12 (11.2)	15 (7.5)	8 (9.4)	9 (8.6)
Injection site reaction	100 (32.9)	23 (21.5)	61 (30.5)	16 (18.8)	39 (37.4)
Hematologic AE	33 (10.9)	12 (11.2)	17 (8.5)	13 (15.3)	16 (15.3)
Hepatic AE	14 (4.6)	10 (9.3)	11 (5.5)	2 (2.4)	3 (2.9)

[a] *Aeromonas* infection and histoplasmosis disseminated; *p<0.05 IFX naïve vs prior IFX (Fisher's exact test)

CONCLUSION: Prolonged ADA treatment, up to 3 years, in children with moderately to severely active CD has a safety profile that is consistent with known ADA data[1] and no new safety signals have been identified.

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Disclosure of Interest: R. Baldassano Consultancy for: AbbVie, Janssen Ortho Biotech, F. Ruemmele Lecture fee(s) from: Shering-Plough, Nestlé, MeadJohnson, Ferring, MSD, Johnson & Johnson, Centocor, Other: Board membership: SAC:DEVELOP (Johnson & Johnson), invited to MSD France, Nestlé Nutrition Institute, invited to Nestlé Health Science, invited to Danane, invited to MeadJohnson, Biocodex, J. Rosh Financial support for research from: AstraZeneca, AbbVie, Janssen, UCB, Lecture fee(s) from: Abbott Nutrition, Prometheus, Consultancy for: AbbVie, Janssen, Soligenex, Other: Board membership: GI Health Foundation, W. Faubion Financial support for research from: AbbVie, Shire Develpoment Inc, Consultancy for: Genentech, Connecticut Children's Medical Center - Safety officer on subcontracted award through NIH for clinical trial, Other: Board membership: Shire Development, Inc - Pediatric UC Advisory Board, Janssen Services LLC - DEVELOP Registry Scientific Advisory Committee, UCB Biosciences Advisory board, J. Kierkus Lecture fee(s) from: AbbVie, Schering-Plough, J. Hyams Lecture fee(s) from: Janssen Orthobiotech; Payment for development of educational presentations: Janssen Orthobiotech, Consultancy for: Janssen Orthobiotech, AbbVie, Other: Expert testimony: Janssen Orthobiotech, A. Lazar Shareholder of: AbbVie, Other: AbbVie employee, Y. Wang Shareholder of: AbbVie, Other: AbbVie employee, S. Eichner Shareholder of: AbbVie, Other: AbbVie employee, R. Thakkar Shareholder of: AbbVie, Other: AbbVie employee

Keywords: adalimumab, Crohn's disease, paediatric, Safety

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00

OTHER LOWER GI DISORDERS III – Poster Area

P1485 HEMOSPRAYTM TREATMENT IS EFFECTIVE FOR LOWER GASTROINTESTINAL BLEEDING

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INTRODUCTION: Acute lower gastrointestinal bleeding (LGIB) is diverse in origin and can be substantial, requiring urgent hemostasis. As this is sometimes not achieved by current modalities such as injection, hemoclip placement and/or thermal therapy, an alternative is much required. Hemospray™ is a promising novel hemostatic agent for upper gastrointestinal hemorrhage. Evidence on the efficacy of Hemospray™ therapy in lower GI bleeding is very limited, based on extrapolations of what happens in upper GI bleeding and in small series of patients.

AIMS&METHODS: We aimed to expand our knowledge on the application of Hemospray™ for the treatment of LGIB in a wide range of conditions to further define the optimal patient population for this new therapeutic modality. From October 2011 to April 2013, all patients endoscopically treated with Hemospray™ for an active LGIB in Sabadell Hospital Spain and Erasmus Medical Centre University Hospital Rotterdam were collected. Data on sex, age, comorbidity, clinical presentation, medication use, procedural details and outcome were prospectively collected, anonymized and analyzed. Hemospray™ was deployed onto the active bleeding site until hemostasis was confirmed.

RESULTS: Nine patients (median age 63 yrs, range 22-79 yrs, 56% male) with LGIB were treated with Hemospray™ (5-30 g) during the referred period. Four patients were on antithrombotic therapy at time of bleeding. LGIB occurred spontaneous in 5 patients (colorectal anastomosis, rectal ulcer, colonic diverticulum, cecal adenocarcinoma, and thrombo-leucocytopenic proctitis) and post-polypectomy in four others. In all cases, successful initial hemostasis was obtained with use of Hemospray™; as monotherapy in 6 cases and as salvage therapy (after failed hemostasis with clips and/or epinephrine) in 3 cases. Rebleeding within 7 days occurred in 2/9 patients (22%), one rectal diverticular bleed and one post-polypectomy bleed in the transverse colon. Both patients were on acetyl salicylic acid. No rebleeding after 30 days occurred. No perforation, symptomatic systemic embolism or bowel obstruction were observed during 30-day follow-up.

CONCLUSION: Hemospray™ is a welcome alternative in the management of colorectal bleeding; as primary or secondary modality but also in a large diffuse bleeding area when only thermal therapy is available. We advise cautious use of Hemospray™ onto spurting bleeds.

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Keywords: cancer bleeding, diverticulum, hemospray, hemostatic powder, lower gastrointestinal bleeding, Polypectomy

P1486 THE ANALYSIS OF RISK FACTORS FOR ISCHEMIC COLITIS IN SAGA UNIVERSITY HOSPITAL IN JAPAN.

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INTRODUCTION: Ischemic colitis is often occurred in the left-side colon because of insufficient blood supply. Several factors causing inadequate intestinal blood flow, use of non-steroidal anti-inflammatory drugs (NSAIDs) and arteriosclerosis, could be risk factors. We evaluated the risk factors for ischemic colitis.

AIMS&METHODS: Between January 1998 and December 2012, 76 patients diagnosed ischemic colitis in Saga University hospital in Japan. Gender and age matched control cases were selected from patients of other diseases hospitalized during the same period. We evaluated the influences of comorbidities such as cerebrovascular disease, ischemic heart disease, hypertension, hyperlipidemia, diabetes mellitus, chronic kidney disease, hyperuricemia and osteoporosis, medications including NSAIDs, antithrombotic agents and bisphosphonate, and habits of smoking, alcohol, and chronic constipation.

RESULTS: Sex ratio of men *versus* women for ischemic colitis was 23:53. Chronic kidney disease and chronic constipation were significant risk factors for ischemic colitis (chronic kidney disease: odds ratio [OR] = 8.474, 95% CI: 2.923-22.844, chronic constipation: OR = 2.041, 95% CI: 1.079-3.862), but the others were not(cerebrovascular disease: OR = 0.609, 95% CI: 0.238-1.559, ischemic heart disease: OR = 1.249, 95% CI: 0.609-2.561, hypertension: OR = 1.098, 95% CI: 0.611-1.971, hyperlipidemia: OR = 1.263, 95% CI: 0.648-2.461, diabetes mellitus: OR = 0.576, 95% CI: 0.238-1.393, hyperuricemia: OR = 2.260, 95% CI: 0.369-13.860, osteoporosis: OR = 0.636, 95% CI: 0.189-2.144, use of NSAIDs: OR = 1.522, 95% CI: 0.511-4.530, antithrombotic agents: OR = 0.828, 95% CI: 0.397-1.726, bisphosphonate: OR = 1.480, 95% CI: 0.091-24.030, habits of smoking: OR = 1.126, 95% CI: 0.555-2.283, alcohol: OR = 0.996, 95% CI: 0.528-1.876).

CONCLUSION: This case-control study revealed that chronic kidney disease and chronic constipation were significant risk factors for ischemic colitis. Other arteriosclerosis risk factors, including hypertension, hyperlipidemia, diabetes mellitus, hyperuricemia and habits of smoking, would not serve as risks of ischemic colitis.

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Disclosure of Interest: None Declared

Keywords: chronic constipation, chronic kideny disease, ischemic colitis

P1487 LIVER CIRRHOSIS IS A RISK FACTOR OF REPEAT ACUTE HEMORRHAGIC RECTAL ULCER OF INTENSIVE UNIT PATIENT

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INTRODUCTION: Acute hemorrhagic rectal ulcer (AHRU) can be found in patients with severe comorbid illness who are long-term bedridden, and per anal suturing is a quick and feasible treatment. However, recurrent bleeding occurs frequently after suture ligation of a bleeder and could be life threatening. But, the risk factor for recurrent bleeding is not well known. Our study tried to clarify the risk factor of repeat AHRU of intensive care unit patient.

AIMS&METHODS: From January 2004 to December 2009, the medical records of 32 patients who were admitted to the intensive care unit (ICU) of the Tri-Service General Hospital, a tertiary referral center in Taiwan, and who underwent per anal suturing of acute hemorrhagic rectal ulcer were retrospectively reviewed.

RESULTS: Of 96 patients who received emergency treatment for acute massive hematochezia, 32 patients were diagnosed as AHRU. 8 (25%) patients had recurrent bleeding following suture ligation of AHRU and underwent reoperation; no patient had recurrent bleeding after the second operation. The duration from the first hematochezia attack to surgery ($P = 0.04$), liver cirrhosis ($P = 0.002$), and coagulopathy ($P = 0.01$) were risk factors for recurrent bleeding after suture ligation of a bleeder. Multivariate logistic regression analysis indicated that liver cirrhosis (OR = 37.77, $P = 0.014$) was an independent risk factor for recurrent bleeding.

CONCLUSION: AHRU could be a major cause of acute massive hematochezia in patients with severe illness. Our data showed that per anal suturing can quickly and effectively control bleeding. We found that liver cirrhosis was an independent risk factor for recurrent bleeding. Therefore, treat the liver cirrhosis patient with AHUR should more aggressively such as early detection and proper suture ligation.

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Disclosure of Interest: None Declared
Keywords: acute hemorrhagic rectal ulcer, intensive care unit, liver cirrhosis, rectal bleeding

P1488 DO SEASONAL TRENDS IN POSITIVITY EXIST WITH THE GUAIAC-BASED FAECAL OCCULT BLOOD TEST?

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INTRODUCTION: Several bowel cancer screening programmes, including the NHS Bowel Cancer Screening Programme (BCSP) in England, use a guaiac-based faecal occult blood test (gFOBt). Seasonal variations in quantitative faecal immunochemical tests for haemoglobin (FIT) positivity have been reported, with lower positivity in spring and summer compared with autumn and winter, thought to be caused by haemoglobin degradation in higher temperatures. This study aims to establish whether this is also observed in gFOBT in southern England.
AIMS&METHODS: Men and women aged 60-69 years are eligible for biennial routine bowel cancer screening. The gFOBt card comprises six windows (or 'spots') onto which the participant is asked to apply two samples from three separate stools. Test cards are returned to a BCSP Hub where each spot is tested to determine 'spot positivity'. Samples usually arrive dry at the laboratory, which is likely to reduce haemoglobin degradation. The number of positive spots determines test positivity. Data for the BCSP Southern Hub (January 2008 to September 2012) were analysed; analysis was limited to the first screening episode.
RESULTS: In total, 8,521,790 spots were analysed. Spot positivity for men (2.50%) was consistently higher than for women (1.65%) and increased with age. Variations in seasonal positivity were similar for men and women. The pattern of spot positivity by month was inconsistent year-on-year and there was no clear evidence that it was different in the spring/summer compared with autumn/winter.
CONCLUSION: Seasonal variation did not appear to account for any fluctuations in spot positivity observed in the gFOBT samples, a strength of gFOBT at a time when more countries and screening programmes are switching to FIT. This suggests gFOBT could be used in hotter, drier climates where FIT are likely to deteriorate faster than gFOBT, reducing the possibility of false-positive test results. More work is required to explore these data further.
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Disclosure of Interest: None Declared
Keywords: colorectal cancer screening, faecal immunochemical test, guaiac faecal occult blood test, Seasonal variation

P1489 DIAGNOSTIC YIELD OF COLONOSCOPY IN THE DIAGNOSIS OF "MELENA" AFTER A NORMAL UPPER ENDOSCOPY

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INTRODUCTION:
"Melena" is common in clinical practice, the source found in upper endoscopy. However, sometimes no lesion is found and a colonoscopy is performed to rule out a lower gastrointestinal source
AIMS&METHODS: Diagnostic yield of colonoscopy in patients with melena after a normal upper endoscopy, and the rate of therapeutic intervention. Patients attended at our Institution (March 2004/ July 2012) with a colonoscopy performed for "melena" with a previous normal upper endoscopy. Colon was divided into right colon (from cecum till the splenic flexure) and left colon (from splenic flexure till rectum). Data recorded: age, sex, comorbidities, Hb level, procedure setting, drug intake, days between upper and lower endoscopy, cecal and ileum intubation, bowel preparation, endoscopy findings, therapeutic intervention and change in patient management. Statistical analyses performed with SPSS (Chicago, IL USA; v13.0)
RESULTS: 220 patients elegible: 134 male (61%)/ 86 female (39%), median age 72,52±12.18. Almost half (44%) were on antiagregant or anticoagulant drugs. Mean Hb level 8.85±2.4. Comorbidities in 82% of pts. 175 (80%) inpatients and 20% outpatients. Bowel preparation was good in 85.5%. Cecum reached in 92% and ileum intubated in 9% of the procedures. Days between upper and lower procedures were 5.51± 5.2. Colonoscopy found a suspected bleeding source in 79 pts (39%). Endoscopic therapy performed in 3 pts (rate 1.4%). A change in patient management after the procedure was done in 44 cases (56.4%)

BLEEDING LESION (79 patients)	RIGHT COLON (50 patients)	LEFT COLON (36 patients)
Tumour	12	13
Arteriovenous malformation	23	5
Advanced polyps	2	4
Bleeding diverticulosis	2	-
Ischemic colitis	2	7
Inflammatory bowel disease	1	3
Radiation colitis	-	2
Other conditions	1	2

CONCLUSION: Our overall diagnostic yield of colonoscopy to investigate melena after a non-diagnostic upper endoscopy was 36%. However, the rate of therapeutic intervention (1.4%) was very low, suggesting that the majority of these procedures are diagnostic only and could be performed on an outpatient setting. A change in patient management was performed in more than a half (56.4%) of the patients with positive findings.
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Disclosure of Interest: None Declared
Keywords: colonoscopy, lower gastrointestinal bleeding

P1490 EFFECTIVENESS OF THE THERAPEUTIC BARIUM ENEMA FOR RECURRENT COLONIC DIVERTICULAR BLEEDING IN SHORT PERIODS

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INTRODUCTION: Many patients with colonic diverticular bleeding experience recurrent bleeds within short periods, even when the source of the bleeding is detected and clipped. In this study we found the therapeutic barium enema to be effective for colonic diverticular rebleeding within 7 days after administration for lower gastrointestinal endoscopy at admission.
AIMS&METHODS: We retrospectively analyzed 218 consecutive cases of colonic diverticular bleeding treated between 2003 and 2010. Lower gastrointestinal endoscopy was performed immediately after admission in all of the cases. Some of these patients received a therapeutic barium enema in addition to conventional methods. Barium sulphate solution was administered using a double balloon enema tip. Next, an additional 600 ml of 60 w/v percentage barium was administered. After confirming that the ascending colon and caecum were filled with barium, the enema tube was clamped and the patient's position was changed every five minutes (prone, left lateral, supine, and right lateral positions) for 2 hours. The enema tube was then withdrawn.
RESULTS: The source of bleeding was identified in 140 (64%) of the 218 patients, and all of these patients underwent endoscopic hemostasis with clipping. After the clipping, 110 patients were observed conservatively (Group A) and 30 patients received additional high-dose barium impaction therapy within 5 days from admission (Group B). In the other 78 patients in whom no bleeding source was detected, 55 were observed conservatively (Group C) and 23 received therapeutic barium enemas within 5 days from admission (Group D). The rebleeding rates within 7 days were as follows: Group A, 37/110 (33.6%); Group B, 3/30 (10.0%); Group C, 13/55 (23.6%); Group D, 1/23 (4.3%). Significant differences were found between Group A and Group B (p=0.0117), and between Group C and Group D (p=0.0450), in log-rank tests by the Kaplan-Meier method to determine the free rates of rebleeding.
CONCLUSION: The therapeutic barium enema effectively prevents recurrent colonic diverticular bleeding in short periods.
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Disclosure of Interest: None Declared
Keywords: diverticular bleeding, therapeutic barium enema

P1491 CLINICAL EVALUATION OF THE HOOD METHOD FOR DETECTING RESPONSIBLE DIVERTICULA AND ENDOSCOPIC BAND LIGATION FOR HEMOSTASIS IN PATIENTS WITH COLONIC DIVERTICULAR HEMORRHAGE

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INTRODUCTION: Although colonic diverticular hemorrhage is a common cause of lower gastrointestinal bleeding, the low detection rate of the responsible diverticulum and insufficient evaluation of endoscopic hemostasis remain unsatisfactory.
AIMS&METHODS: First group comprised 85 patients who underwent conventional colonoscopy for observation and clipping for hemostasis. Second group comprised 53 patients who underwent hood method for observation and endoscopic band ligation (EBL) for hemostasis. We retrospectively evaluated the detection rate of the responsible diverticulum by conventional colonoscopy and hood method, and the results of hemostasis by clipping and EBL.
RESULTS: Regarding diagnosis of colonic diverticular hemorrhage, the hood method was significantly better than conventional colonoscopy for detecting the responsible diverticulum ($p = 0.04$). Although active bleeding was noted in only approximately 30% of cases in both groups, non-bleeding visible vessels were more common in cases receiving the hood method ($P < 0.001$). Regarding endoscopic hemostasis, EBL was significantly better than clipping in the results of hemostasis ($p = 0.01$). In most cases treated with EBL, the responsible diverticulum resolved with scar formation at the original site.
CONCLUSION: Although the hood method is useful for detection of potential non-bleeding visible vessels and consequently improves the detection of responsible diverticula, the detection rate (52%) remains not to be satisfied yet. EBL therapy demonstrated excellent results for endoscopic hemostasis and few complications, and acts as an "endoscopic diverticulectomy", which is available for preventing future rebleeding from the original diverticulum.

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Disclosure of Interest: None Declared
Keywords: colonic diverticular hemorrhage, endoscopic band ligation, hood method

P1492 EFFECTIVENESS OF A NURSE LED ANAEMIA CLINIC IN IDENTIFYING IRON DEFICIENCY AND PLANNING FURTHER INVESTIGATION

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INTRODUCTION: Iron deficiency anaemia (IDA) occurs in 2-5% of adult men and postmenopausal women in the developed world and is a common cause of referral to gastroenterologists. The British Society of Gastroenterology (BSG) guidelines (updated 2011) state that all patients with IDA should be tested for coeliac disease (grade B recommendation) and that all men and postmenopausal women should be considered for upper and lower gastrointestinal tract (GI) investigation (grade A recommendation).
In this clinic, a specialist nurse assesses patients and checks haemoglobin (Hb), MCV, ferritin, and endomysial antibodies (EMA). Appropriate further investigations are then arranged.
AIMS&METHODS: The data from three sequential audits in 2004, 2005, and 2012 was collated and reviewed to assess compliance with BSG guidelines. All three audits used a standardised data collection proforma. The 2004 and 2005 audits used retrospective case note review, while the 2012 audit used an audit proforma prospectively.
RESULTS: A total of 183 patients were referred during the three audit periods (2004, 2005, and 2012). In all audit periods, female patients outnumbered males by a ratio of more than 1.8:1. The mean time from referral to be seen in clinic was 25 days, 28 days, and 13 days respectively. Hb and MCV were checked in all patients and ferritin in 98% – 100%. Among patients referred, IDA was confirmed in 86%, 79%, and 90% respectively. EMA was checked in 89%, 100%, and 97% respectively. Of patients found to have IDA, the proportion sent for both upper and lower GI investigation was 72%, 95%, and 99% (90% attended and completed the investigations). In the 2004 audit, a further 17% underwent gastroscopy only (9% in 2005) and 12% had colonoscopy only (0% in 2005).

Investigation findings:	2004	2005	2012
GORD / benign ulcer disease	36%	13%	30%
Diverticulosis / haemorrhoids	45%	13%	15%
Colorectal cancer	9%	2%	3%
Coeliac disease	3%	6%	5%

CONCLUSION: The nurse led clinic for anaemia has proved to be an effective way to manage the large number of referrals for investigation of IDA. Significant pathology is identified early as a result of the requested investigations (up to 9% colorectal cancers and up to 6% coeliac disease). Notable improvements in the service since 2004 are reduced waiting times and increased compliance with investigation recommendations. The proportion of patients referred who are confirmed to have IDA has also increased.
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Disclosure of Interest: None Declared
Keywords: Anaemia, iron deficiency

P1493 A RANDOMIZED PROSPECTIVE STUDY OF ENDOSCOPIC BIPOLAR HEATER PROBE TREATMENT OF CHRONIC RECTAL BLEEDING FROM RADIATION COLITIS

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INTRODUCTION: Radiation colitis, an insidious, progressive disease of increasing frequency, develops 6 mo to 5 years after regional radiotherapy for malignancy, owing to the deleterious effects of the latter on the colon and the small intestine. Management of chronic radiation colitis remains a major challenge owing to the progressive evolution of the disease, including development of fibrosis, endarteritis, edema, fragility, perforation, partial obstruction, and cancer. Patients are commonly managed conservatively.
AIMS&METHODS: Our purposes were to (1) evaluate efficacy and safety of bipolar heater probe endoscopic coagulation compared to prior medical therapy for bleeding radiation telangiectasia, and (2) consider the impact of treatments on patients' impression of their overall health and activity
Six months of medical management had failed in 2 men and 9 women with chronic, recurrent hematochezia and anemia after radiation treatment of pelvic malignancies. Patients had multiple rectal telangiectasias coagulated with bipolar heater probes CD 120 U with Olympus HPU 20 unit in a randomized, prospective study. Patients followed for 6 months.
RESULTS: Rectal bleeding stopped within four treatment sessions. During 6 months of endoscopic versus medical therapy, severe bleeding episodes diminished significantly for bipolar heater probe versus 6 months of prior medical therapy (79% vs 37%) ; mean hematocrits rose significantly for patients undergoing bipolar heater probe (40.2 vs 30.1) treatment, and their impression of overall health improved. During long-term follow-up, new telangiectasias or rectal bleeding were easily controlled. No major complications resulted.
CONCLUSION: Bipolar heater probe is safe and effective relative to medical therapy for palliation of patients with lower gastrointestinal bleeding from radiation colitis, all patients improved in ability to travel and day to day working and in their overall impression of their health.
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Disclosure of Interest: V. Sharma : none, R. sharma : none, D. Mangal : none
Keywords: bipolar heater probe, Radiation Colitis

P1494 RADIOFREQUENCY ABLATION TREATMENT OF RADIATION PROCTITIS: RESULTS FROM AN EUROPEAN COLLABORATIVE STUDY

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INTRODUCTION: Radiofrequency ablation (RFA) is a new option for treatment of chronic radiation proctitis (RP), noticeably in patients who failed argon plasma coagulation (APC).
AIMS&METHODS: Our aim was to evaluate the feasibility, efficacy and safety of RFA for treatment of RP. Data from patients with RP treated by RFA were retrospectively collected from 5 European centers. Main outcomes measurements were the following: a three-item symptom scale (0 to 10 points, see reference) including diarrhoea (0 to 3), bleeding (0 to 4), and tenesmus/rectal pain (0 to 3), red blood cell (RBC) transfusions (number of RBC packs, number of patients off transfusions), lowest hemoglobin rates, and complications. Wilcoxon matched-pairs signed-ranks test was used to estimate the difference in response in the 6 months before and after RFA treatment.
RESULTS: 13 patients had RFA for treatment of RP (5 female and 8 male patients, aged 63 to 87 (mean age 76 ± 8). Past history included prostate (7), bladder (1), cervix (4), and anus (1) cancers. 3 patients were treated with aspirin, 2 with anticoagulants. 5 patients had received previous APC treatment (1 to 5 sessions), 1 had bipolar coagulation (1 session) and 2 had laser therapy (1 to 5 sessions). RFA was performed with the Halo^{90} ablation catheter and the HaloFlex system (Covidien), with a power of 12 to 15 J/cm^2. Patients received a mean number of 2.0 RFA sessions (range 1-4). Treatment was deemed feasible, quick and easy in all patients. No early complications were recorded. Two patients were referred for additionnal APC treatment. Symptom scores decreased in all patients, from mean score of 4.8 ± 0.7 (range 4 to 6) to 1.4 ± 0.9 (range 0 to 3) ($p<0.001$). Among 10 patients who were transfusion-dependent (mean number of 8.6 ± 8.3 RBC packs, range 2 to 27, over the 6-month before RFA), 8 patients (80%) were off transfusions within the 6 months following RFA. In the 6 months after RFA treatment has been completed, an increase in hemoglobin rate was recorded in all patients (from 7.3 ± 0.9 g/dL to 10.2 ± 1.2 g/dL, mean increase 2.9 ± 1.1 g/dL, $p<0.001$). One patient developed a fibrotic narrowing of the rectum, with no sign of obstruction.
CONCLUSION: RFA allowed a complete treatment of RP in a safely and clinically efficient manner. RFA significantly decreased clinical symptoms and the need for RBC transfusions, and lead to a significant increase of the hemoglobin rate. A prospective evaluation is strongly considered.
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Disclosure of Interest: None Declared
Keywords: Radiation proctitis, radiofrequency ablation

P1495 MEK5/ERK5 EXPRESSION IS INCREASED IN COLON CANCER ADENOMAS AND ADENOCARCINOMAS, AND MEK5/ERK5 SIGNALLING ACCELERATES CELL CYCLE PROGRESSION AND MIGRATION IN SW620 COLON CANCER CELLS

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INTRODUCTION: ERK5 and its direct activator, MEK5, are overexpressed in prostate and breast cancer correlating with an overall poorer disease prognosis, and leading to increased proliferation, metastasis and chemoresistance. In addition, we have previously demonstrated that ERK5 silencing increases colon cancer (CC) cell apoptosis and 5-FU-induced apoptosis, highlighting the relevance of ERK5 signalling in CC.
AIMS&METHODS: In the present study, we evaluated the expression of ERK5 and MEK5 by immunoblotting in 284 human samples of CC, including normal colonic mucosa, tubulovillous adenomas, and adenocarcinomas with proficient or deficient DNA mismatch repair system (pMMR and dMMR, respectively). In addition, we produced a stable cell line model with differential ERK5 activation via lentiviral transduction and cell sorting of SW620 colon carcinomas cells to overexpress constitutively active MEK5 (MEK5AA), dominant-negative MEK5DD, and empty vector control. Next, we evaluated the impact of

MEK5/ERK5 signalling in cell cycle progression and migration by flow cytometry with PI staining, and wound healing assay, respectively.
RESULTS: Our results show that ERK5 and MEK5 are overexpressed in adenomas ($p<0.01$) and pMMR and dMMR adenocarcinomas ($p<0.05$). According to TNM stage classification, tumors classified with (T_4), (N_{1-2}) and (M_1), representing more aggressive tumors, displayed higher ERK5 overexpression ($p<0.05$), suggesting that ERK5 might be relevant in CC progression and to the acquisition of more invasive and metastatic potential. In vitro, we demonstrated that ERK5 overactivation (MEK5-DD) significantly accelerates cell cycle progression ($p<0.01$) and increases cell migration by ~ 2-3 fold from 24 to 56 h ($p<0.001$), in comparison with inactive ERK5 (MEK5-AA) and empty vector control cell lines.
CONCLUSION: Our results suggest that MEK5/ERK5 signalling pathway is important for tumor onset and progression, possibly representing a novel relevant therapeutic target in CC treatment.
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Disclosure of Interest: None Declared
Keywords: Cell Cycle, Colon Cancer, ERK5, Migration, TNM classification

P1496 SMAD7-INDUCED PLASTICITY OF TUMOR-INFILTRATING TH17 CELLS ARMS TNF-ALPHA TO KILL COLORECTAL CANCER CELLS

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INTRODUCTION: Transforming Growth Factor (TGF-)-Beta is deeply involved in colorectal cancer development and the disruption of the TGF-beta signaling in dysplastic cells is required for tumor to grow. Nevertheless, TGF-beta is highly expressed by tumor cells to escape the immune-surveillance mediated by T cells. Accordingly, T cell-specific overexpression of Smad7, an intracellular inhibitor of the TGF-beta signaling, resulted protective in colitis-associated colorectal cancer. However whether Smad7 expression in T cells might influence colorectal cancer growth independently of chronic inflammation and which T cell subset is involved in this process, is currently unknown.
AIMS&METHODS: To address this issue, the immune response against cancer was investigated in T cell-specific Smad7 transgenic mice and wild type littermates subcutaneously transplanted with syngenic MC38 colon carcinoma cells.
RESULTS: Smad7Tg mice resulted resistant to tumor development as compared to Wt and protection was dependent on CD4+ but not CD8+ T cell. Smad7 overexpression in CD4+ T cells induced Tbet and IFN-gamma while inhibited IL17A in Th17 cells. Moreover, the immune environment generated by Smad7 overexpression in CD4+ cells sensitized tumor cells to the TNF-alpha-mediated apoptosis in an IL17A-dependent but IFN-gamma-independent manner.
CONCLUSION: These data underscore the intimate connection between the immune response and cancer development and directly provide a mechanism involving Th17 plasticity induced by Smad7 expression.
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Disclosure of Interest: None Declared
Keywords: cancer immunology, immunity, Plasticity, T cell

P1497 CONTRIBUTION OF LARGE INTESTINAL MICROBIOTA AND BACTERIOCINS TO THE DEVELOPMENT OF COLORECTAL NEOPLASIA

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INTRODUCTION: Sporadic colorectal cancer (CRC) represents an immense problem worldwide. The exact role of all the potential contributors on its aetiology and pathogenesis has not been clarified yet, however, large bowel microbiota play an extremely important role. Bacteriocins are peptides or small proteins, which are produced by bacteria of the *Enterobacteriaceae* family, especially by *Escherichia coli*. Bacteriocins are divided into more groups, colicins and microcins are the most important ones. Bacteriocins have antibacterial, antineoplastic, proapoptotic and probiotic effects.
AIMS&METHODS: We have established completely new methods of bacteriocin typing. Mucosal biopsies were taken in the caecum, transverse colon and rectum within the colonoscopy in patients with colorectal adenoma (17 men, 13 women, mean age 63±9), with colorectal carcinoma (23 men, 7 women, mean age 67±11) and in the controls (average risk population with normal endoscopy findings and with negative history of colorectal adenoma, carcinoma or idiopatic bowel disease; 9 men, 11 women, mean age 55±15). After appropriate microbiological culture bacteriocinogeny of each strain and the genotypes of *Escherichia coli* were investigated by PCR methods.
RESULTS: There were 666 strains isolated and futher investigated. Statistically significant difference in bacteriocinogeny was found out between patients with non-advanced (N-A) and patients with advanced (A) colorectal neoplasia (N-A: 39% vs A: 72%; p=0.010). There was a trend towards statistically significant difference in the frequency of *Escherichia coli* genotype B2: genotype B2 (which is associated with more virulent strains) was found in patients with N-A colorectal neoplasia in 24% vs in patients with A colorectal neoplasia in 52%; p=0.054). Increasing bacteriocinogeny, microcinogeny and colicinogeny & microcinogeny was associated with increasing stage of CRC (assessed according to the TNM classification) – results see in the Table 1.
Table 1:

	I	II	III	IV
Staging	I 6/12	II 10/12	III 26/38	IV 6/6
Bacteriocinogenic strains	(50%)	(83%)	(68%)	(100%)
Colicinogenic strains	3/12 (25%)	4/12 (33%)	20/38 (53%)	4/6 (67%)
Microcinogenic strains	5/12 (42%)	8/12 (67%)	24/38 (63%)	6/6 (100%)
Strains producing colicin and microcin	2/12 (17%)	2/12 (17%)	18/38 (47%)	4/6 (67%)

CONCLUSION: We have confirmed, that large bowel mucosa in patients with advanced colorectal neoplasia is colonised by *Escherichia coli*, which belongs to more virulent strains. Large intestinal microbiota with their products including bacteriocins contribute to the pathogenesis of colorectal neoplasia and CRC.
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Disclosure of Interest: None Declared
Keywords: Bacteriocins, Colorectal neoplasia, Large intestinal microbiota

P1498 LOW MOLECULAR WEIGHT PROTEIN TYROSINE PHOSPHATASE (LMWPTP) IS UPREGULATED IN PRIMARY COLORECTAL CANCER AND AFFECTS CANCER SIGNALING PATHWAYS.

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INTRODUCTION: Cancer cell functions are tightly regulated by protein phosphorylation and dephosphorylation. Enhanced kinase activation and phosphorylation is often observed in colorectal cancer (CRC). Whereas kinases are seen as potential oncogenes, dephosphorylation of proteins by phosphatases is commonly assumed to be tumor suppressive. However, some phosphatases may also stimulate tumor growth and invasion. One of these is low molecular weight protein tyrosine phosphatase (LMWPTP), overexpression of which in cell lines is sufficient for cellular transformation.
AIMS&METHODS: The aim was to investigate the expression levels of LMWPTP in primary CRC specimens, and elucidate its role and signaling targets in CRC cells. LMWPTP expression was analysed on sections from biopsies of low grade dysplasia (LGD; n=9), high grade dysplasia (HGD; n=7), and adenocarcinoma (AC; n=12) by immunohistochemistry. Normal colon tissue (n=2), active ulcerative colitis (n=6) served as controls. This staining was subsequently performed on a tissue microarray (TMA) of 72 patients with colorectal adenoma (N=47) and/or carcinoma (N=164) and their corresponding normal tissue (N=63). To investigate downstream targets of LMWPTP, we manipulated the LMWPTP expression *in vitro* by lentiviral transduction of HCT116 and Caco-2 cells with siRNA against LMWPTP.
RESULTS: In our initial screen LMWPTP expression in intestinal epithelial cells (IEC) was limited to 9% of IEC in non-cancerous tissues. In contrast, expression of LMWPTP significantly increased with subsequent levels of dysplasia (42%, 80% and 100% positive IEC in LGD, HGD and AC respectively). Staining of the TMA confirmed these results: the mean % positive IEC was 27±3% in normal tissues, 64±4% in adenoma and 90±3% in carcinoma ($p<0.001$). There was a significant difference between different cancer-stages within patients (N=15, paired testing; $p<0.001$), however, Dukes stage or patient survival did not correlate with LMWPTP expression. Knocking down LMWPTP in CRC cells reduced phosphorylation of the EGF-receptor and PKB *in vitro* by approximately 50%.
CONCLUSION: LMWPTP expression is drastically upregulated in epithelial dysplasia and CRC. During transformation of IECs, LMWPTP expression increases, suggesting a role for LMWPTP in the pathogenesis of CRC. As LMWPTP knockdown decreases EGFR and PKB phosphorylation, overexpression of LMWPTP in CRC samples may contribute to the enhanced EGF and PKB signaling, known to play a role in CRC development. In conclusion, LMWPTP is overexpressed in CRC, may function as an oncogene, and represent a compelling target for future therapy.
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Disclosure of Interest: None Declared
Keywords: Cancer signaling, Colorectal cancer, Low molecular weight protein tyrosine phosphatase, Phosphatases

P1499 MYOFIBROBLAST-DERIVED SECRETED FRIZZLED-RELATED PROTEIN 1 (SFRP1) CAN INHIBIT COLORECTAL CARCINOMA FIELD CANCERISATION

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INTRODUCTION: Besides frequent mutations of canonical Wnt pathway in colorectal cancer (CRC), intercellular Wnt regulator SFRP1 plays a crucial role in the inhibition of autocrine Wnt loop of epithelial cells. We hypothesized that this effect may appear in genetically/epigenetically altered, but histologically normal adjacent tumour (NAT) areas, and inhibit field cancerisation.
AIMS&METHODS: Our aim was to compare mRNA expression of *SFRP1* in stromal sections of NAT (n=49) and CRC (n=49) areas by Affymetrix microarray chip. To identify the origin of SFRP1, dual fluorescent SFRP1 – α-SMA immunohistochemistry was applied on NAT (n=5) and CRC (n=5) samples. To examine *SFRP1* methylation status of α-SMA+ stromal cells, we examined *SFRP1* methylation status of laser capture microdissected α-SMA+ cells from NAT (n=3) and CRC (n=3) samples with methylation-specific PCR.
RESULTS: *SFRP1* mRNA expression in CRC stroma significantly decreased compared to NAT region ($p<0.001$). This change also appeared at protein level, mainly in stromal α-SMA+ myofibroblasts (CRC: 27,65±18,27 vs. NAT: 85,73±12,61%; $p<0.05$). In line with this, in CRC areas we found significantly increased ($p<0.05$) *SFRP1* DNA hypermethylation in laser capture microdissected α-SMA+ myofibroblasts.
CONCLUSION: Myofibroblast-derived SFRP1 may act as a tumour suppressor and inhibit field cancerisation in NAT areas. Paralell with tumour growth, increased hypermethylation and consequentional underexpression of *SFRP1* in stromal myofibroblast may exert a synergistic effect with the enhanced autocrine epithelial Wnt loop.
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Disclosure of Interest: None Declared
Keywords: colorectal cancer, DNA methylation, field cancerisation, myofibroblast, secreted frizzled-related protein 1

P1500 SYSTEMIC DENDRITIC CELLS IN COLORECTAL CANCER ARE MORE ACTIVATED AND LYMPH NODE HOMING: POTENTIAL ROLE IN DISEASE PROGRESSION AND FUTURE OF CANCER IMMUNOTHERAPY

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INTRODUCTION: Dendritic cells (DC) are antigen presenting cells that migrate to lymphoid tissues to initiate cytotoxic or tolerogenic immune response to cancer antigens. CD40 is a co-stimulatory molecule and a marker for DC activation. Increased CD40 expression on DCs can be associated with maturation and enhanced cytokine production against cancer cells [1]. Activation of DC is accompanied by up regulation of the lymph node migration marker C-chemokine receptor7 (CCR7) [2]. However, DC in cancer are unable to elicit effective immune responses against tumour cells. Previous studies on DC in colorectal cancer (CRC) were on cell lines and animal models. We aimed to determine the phenotype and activation status of systemic DC in CRC patients.
AIMS&METHODS: Peripheral blood mononuclear cells were obtained from CRC patients before any surgical intervention (n=21) together with age and sex-matched healthy controls (n=21). DC were identified as HLA-DR positive and lineage (anti-CD3, CD14, CD16, CD19, CD34 and CD56) negative cells. DC were further classified as CD11c+ myeloid DC (mDC) or CD11c- putative DC (pDC). CD40, CD80, CD86 and CCR7 expression was determined on DC by flow-cytometry.
RESULTS: In CRC, expression of CD40 was significantly higher on all DC (27.59%±2.521 vs 17.30±2.989, p=0.012) compared to control. This increase was driven by the mDC subset, which was significantly increased in CRC (32.36%±4.278 vs 19.50%±2.223, p=0.011). There was also statistically significant increase in CCR7 expression in mDC in CRC patients compared to control (35.42%±3.862 vs 16.00%±2.150, $p<0.0001$). There were no differences in CD80 and CD86 expression between groups.
CONCLUSION: DC in CRC patients are activated and their potential capacity to migrate to lymph nodes is increased. Increased CD40 expression may indicate increase in partially activated DC subpopulation. Our results using fresh DC show contrasting results to previous studies done using monocyte-derived DC, which showed reduced CD40 expression in CRC. Hence, results should be interpreted with caution when using cytokine stimulated DC as they may not resemble DC normally present in blood. Furthermore, increased expression of CCR7 in mDC in CRC could suggest its possible role in cancer metastasis. DC may stimulate either immunogenic or suppressive responses upon migration to lymph nodes. Therefore, further studies are warranted to investigate which immune response DC in CRC are inducing, which is an important step towards creating more suitable anti-tumour vaccines.
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Disclosure of Interest: None Declared
Keywords: cancer immunology, Colorectal cancer, dendritic cell

P1501 ASSOCIATION BETWEEN MICROBIAL DYSBIOSIS AND COLORECTAL CANCER DEVELOPMENT USING APC MIN MICE MODEL.

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INTRODUCTION: Tumor microenvironment of colorectal carcinoma (CRC) is a complex association between non neoplastic and tumoral cells and a large amount of microorganisms. These microorganisms could be linked to cancer by several mechanisms, including chronic inflammation and/or production of carcinogenic metabolites.
AIMS&METHODS: The aim of this study was to analyze the microbiota composition associated to normal and tumoral gut mucosa in multiple intestinal neoplasia (Min) mice, in accordance to tumoral development and compared to that associated to mucosa of wild type (WT) mice. The dominant and subdominant bacterial populations (*Escherichia coli, Bacteroides/Prevotella, Faecalibacterium prausnitzii, and Bifidobacterium*) were quantified in all samples by quantitative PCR using Taqman® probes.
RESULTS: Total mucosa-associated eubacteria were increased in Min compared to WT mice. Interestingly, the level of mucosa-associated eubacteria in Min mice was significantly correlated with the number of colonic tumors. Mucosa and tumors-associated *E. coli* were only detected in the older Min mice (>15 weeks) with a higher level associated to tumoral tissues. Concerning *Bacteroides*, similar levels of mucosa and tumors-associated bacteria were measured in Min mice, and a lower level of *Bacteroides* was detected in mucosa of WT mice. In our experimental conditions, *Faecalibacterium prausnitzii* associated to intestinal mucosa was undetectable. Finally, a decrease of mucosa-associated *Bifidobacterium* was observed on both older WT and Min mice. Moreover, mucosa-associated *Bifidobacterium* was significantly decreased in both normal and tumoral tissues of Min mice presenting more than 2 colonic tumors.
CONCLUSION: Intestinal mucosa-associated microbiota was significantly altered in Min mice compared to WT mice. During tumoral development, dysbiosis was observed in both tumor and adjacent normal tissues of Min mice. This study allows better understanding how gut microbiota dysbiosis is associated with CRC in Min mice model, and may suggest a possible involvement of *E. coli* in colorectal carcinogenesis.
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Disclosure of Interest: None Declared
Keywords: colorectal cancer, microbiota, murine APC model

P1502 INNATE IMMUNITY IN HEREDITARY NON POLYPOSIS COLORECTAL CANCER

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INTRODUCTION: Pattern Recognition Receptors (PRRs), such as TLRs and NLRs, are well known for their pivotal function in innate immunity but their role in cancer immunosurveillance is elusive. Indeed, TLR5, TLR7 and TLR8 agonist have shown a potent antitumor activity and TLR4 signalling was associated to adaptive immunosurveillance in ulcerative colitis. However, TLR4-MyD88 signalling has been linked to tumour growth and progression in mice and it was associated with colorectal cancer poor prognosis.
Hereditary non polyposis colon cancer (HNPCC) is characterized by defects in DNA mismatch repair genes (most frequently MSH2, MLH1, PSM2 or MSH6).
AIMS&METHODS: The aim of the study was to examine TLRs and NODs expression in the healthy mucosa of patients with familiar history of colorectal cancer and to assess TLR4 and MyD88 expression in HNPCC to understand if alteration of mismatch repair genes expression may affect TLR4-MyD88 signalling.
Firstly, a prospective cohort of 63 patients who had colonoscopy for cancer screening or colonic resection for colorectal cancer was enrolled. Colonic biopsies of healthy mucosa were taken to quantify TLRs1-10, NODs and MyD88 mRNA expression by real time RT-PCR. Familial and medical history were retrieved. Secondly, immunohistochemistry for TLR4, MyD88, MSH2, MLH1, MSH6 and PSM2 expression on epithelial cells was quantified in 98 patients operated for colorectal cancer. Non parametric statistics was used.
RESULTS: The mRNA levels of TLR2, TLR4, TLR5, TLR10, NOD1 and NOD2 resulted significantly upregulated in the healthy colonic mucosa of subjects who had a familial history of cancer in comparison to subjects with a negative familial history. In particular, those subjects who had a familial history of colorectal cancer showed an overexpression of TLR4 and TLR8 transcripts (p=0.05 and p=0.02, respectively). By contrast, in the diseased mucosa,TLR4 expression on epithelial colorectal cancer cells was significantly decreased in patients with a single mismatch repair gene defect compared to patients with no defect (p=0.03).
CONCLUSION: TLRs and NODs upregulation in healthy colon of patients with familiar history of cancer and, specifically, that of TLR4 and TLR8 in case of family history of colorectal cancer, might be interpreted as an enhancement of innate immunity cancer surveillance in a high risk setting. Moreover, a

decreased expression of TLR4 in colorectal cancer with a single mismatch repair gene defect suggest a possible impairment of immunosurveillance mechanisms in case of defect of DNA damage repair.
Disclosure of Interest: None Declared
Keywords: HNPCC, immunosurveillance, MyD88, TLR4

P1503 THE PROGNOSTIC VALUE OF CDKN2A HYPERMETHYLATION IN COLORECTAL CANCER: A META-ANALYSIS

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INTRODUCTION: The prognostic value of CDKN2A promoter hypermethylation in colorectal cancer remains controversial. We systematically reviewed the evidence for assessment of CDKN2A methylation in colorectal cancer to elucidate this issue.
AIMS&METHODS: Pubmed, Embase and ISI web of knowledge were searched to identify eligible studies to evaluate the association of CDKN2A hypermethylation and overall survival and clinicopathological features of colorectal cancer patients. Combined hazard ratios (HRs) or odds ratios (ORs) with 95% confidence interval (95% CI) were pooled using a random-effects model.
RESULTS: Overall, CDKN2A hypermethylation in the primary tumor had significant association with an enhanced mortality risk of colorectal cancer patients in the random effects model (combined HR 1. 65, 95% CI 1.29–2.11), despite the exhibition of heterogeneity among studies (I^2 69%, p=0.0004). For the exploration of the source of heterogeneity, meta-regression and subgroup analysis were conducted by study location, publication year, number of patients and methylation rate, REMARK score and ELCWP score. Study location was found to be significantly correlated with the inter-study heterogeneity (p= 0.008) while other covariates was not. Furthermore, subgroup analysis revealed that the significant correlation between CDKN2A hypermethylation and OS was present in Europe (HR 1.49; 95% CI 1.28-1.74) and Asia (HR 3.30; 95% CI 1.68-6.46). We also observed the significant association of CDKN2A hypermethylation and OS of patients in studies with REMARK score greater than 12 (HR 1.75, 1.22-2.51), further confirming the prognostic role of CDKN2A hypermethylation in CRC. Of note, the pooled HR estimate by multivariate analysis was 1.38 (95% CI: 1.02–1.87), suggesting that CDKN2A hypermethylation might be an independent prognostic factor for patients with colorectal cancer.
Additionally, we assessed the association between CDKN2A hypermethylation and clinicopathological features of colorectal cancer patients. As indicated in Table 3, CDKN2A hypermetylation had a significant association with lymphovascular invasion (positive vs. negative: OR 1.68, 95% CI 1.15–2.47), lymph node metastasis (positive vs. negative: OR 1.68, 95% CI 1.09–2.59), and tumor location (proximal vs. distal: OR 2.09, 95% CI 1.34–3.26).
CONCLUSION: This meta-analysis indicated that CDKN2A hypermethylation might be a predictive factor for unfavorable prognosis of colorectal cancer patients.
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Disclosure of Interest: None Declared
Keywords: CDKN2A, Colorectal Cancer, Methylation, Prognosis

P1504 INDIAN HEDGEHOG IS REQUIRED FOR INTESTINAL ADENOMA FORMATION

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INTRODUCTION: Activating mutations in the Hedgehog (Hh) pathway are found in basal cell carcinomas and medulloblastomas. The role of Hh signaling in intestinal tumorigenesis has not yet been clarified. Hh is expressed by enterocytes and signals in a paracrine manner from the epithelium to the mesenchyme. Hh controls mesenchymal factors such as Bone Morphogenetic Proteins and Activins which negatively regulate the proliferation of precursor cells. Since Indian Hedgehog (Ihh) is the major Hh expressed in the intestinal epithelium we decided to study the potential role of Ihh signaling in intestinal adenoma formation.
AIMS&METHODS: In order to study the effect of loss of *Ihh* signaling in sporadic tumorigenesis we conditionally deleted *Ihh* in mice in the intestinal epithelium using the *Cyp1a1Cre* promoter. These mice were crossed with conditional mutant Apc^{15lox} mice to generate $Cyp1a1Cre\text{-}Ihh^{fl/fl}\text{-}Apc^{fl/+}$ mice. At 4-7 weeks of age mice were intraperitoneally injected with 80 mg/kg β-naphthoflavone for 5 days. $Cyp1a1Cre\text{-}Ihh^{+/+}\text{-}Apc^{fl/+}$ littermates served as controls. Four months after recombination, we sacrificed and analyzed the mice (n=15).
RESULTS: *Ihh* expression was upregulated in polyps of $Cyp1a1Cre\text{-}Ihh^{+/+}\text{-}Apc^{fl/+}$ mice as assessed by in situ hybridization. Deletion of *Ihh* resulted in a marked reduction of 90.3% in the number of polyps (17.2 ± 13.65 polyps per mouse vs. 1.7 ± 1.5, $P < 0.01$). The polyp size did not differ between groups. Neither did the number of proliferating or apoptotic cells in the polyps, as assessed by immunostaining for BrdU and cleaved caspase 3. Analysis of Hh responsive cells in the mesenchyme of the polyp showed a decrease of the number of α-sma en desmin double positive cells (smooth muscle cells). COX2 is expressed early in adenoma to carcinoma transition and believed to play an important role in adenoma formation. Stromal cells are known to be a source of COX2. In accordance with this, examination of *Cox2* expression by Q-PCR and immunostaining showed up regulation in polyps of $Cyp1a1Cre\text{-}Ihh^{+/+}\text{-}Apc^{fl/+}$ mice in compared to normal intestinal epithelium ($P < 0.01$, resp. $P < 0.05$). In contrast, *Cox2* expression in the polyps of $Cyp1a1Cre\text{-}Ihh^{fl/fl}\text{-}Apc^{fl/+}$ mice was not significantly up regulated.
CONCLUSION: Surprisingly, in contrast to its role as an anti-proliferative signal in the normal epithelium, *Ihh* acts as a tumor promoter. The expression of *Ihh* is increased in polyps and mice that lack *Ihh* develop fewer polyps. This finding is accompanied by loss of smooth muscle cells in the mesenchyme of the polyp and decreased *Cox2* expression.
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Disclosure of Interest: None Declared
Keywords: Adenoma, COX-2, hedgehog

P1505 THE BONE MORPHOGENETIC PROTEIN PATHWAY EITHER ENHANCES OR INHIBITS THE WNT PATHWAY DEPENDING ON SMAD4 AND P53 STATUS IN COLORECTAL CANCER.

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INTRODUCTION: In intestinal crypt-villus homeostasis, morphogenic signalling pathways such as BMP and Wnt interact to control cell fate. In the normal intestine BMP signalling is responsible for differentiation and apoptosis and inhibits Wnt signalling, which is responsible for proliferation and inducing stemness. In tumourogenesis, cells acquire mutations which result in the disruption of these morphogenic pathways and in changes in pathway crosstalk. We set out to investigate how several of the common mutations found in colorectal cancer might change the BMP-Wnt interaction. With cancer therapy increasingly focussed on the targeted pharmacological modulation of the specific molecular pathways underlying carcinogenesis, understanding of how the major pathways interact and how mutations influence this is of critical importance.
AIMS&METHODS: BMP signalling was activated in a series of 8 CRC cell lines and Wnt activity was measured using a β-catenin reporter assay. HCT116 SMAD4-/- cells, HCT116 R248 cells (p53 mutant) and shSMAD4 in LS174T cells were used to investigate BMP-Wnt interaction dependent on SMAD4 and p53. Expression of Wnt-target genes was evaluated by q-PCR array. MTT assays were performed to study cytotoxic effects of 5-FU in CRC cells. The expression patterns of SMAD4, p53 and β-catenin at the invasive front of 94 stage I/II CRCs were analyzed using immunohistochemistry.
RESULTS: Activation of BMP signalling results in downregulation of Wnt signalling only in SMAD4 positive and p53 WT cell lines. Loss of SMAD4 shifts BMP signalling from inhibiting to enhancing Wnt signalling. In p53 mutant cells Wnt signalling inhibition by BMP is abolished. While BMP signalling significantly increases the sensitivity of SMAD4 positive cancer cells to 5-FU, it reduces 5-FU sensitivity in SMAD4 negative cancers. Pre-treatment of SMAD4 negative cancer cells with a BMPReceptor 1a inhibitor significantly increases chemo sensitivity. Loss of SMAD4 and/or aberrant p53 expression at the invasive front of CRC is correlated with a high expression of β-catenin.
CONCLUSION: Our data suggest that BMP signalling either inhibits or enhances the Wnt pathway based on the SMAD4 and p53 status and can therefore be either tumour-suppressive or tumour-promoting. Inhibition of BMP signalling increases chemosensitivity in SMAD4 negative colorectal cancer, a chemoresistant molecular subtype with a poor prognosis.
Disclosure of Interest: None Declared
Keywords: beta-catenin, BMP, chemosensitivity, p53, SMAD4, Wnt

P1506 SUSCEPTIBILITY FOR COLITIS-ASSOCIATED CANCER DEVELOPMENT IN SAMP1/YIT MICE

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INTRODUCTION: SAMP1/Yit mice, which spontaneously develop transmural, patchy intestinal inflammation in the ileum, are widely recognized as a murine model of Crohn's disease. However, inflammatory colonic lesions are not found in this strain. Although recent studies have revealed dysfunctions of regulatory T cells and interleukin (IL)-10-producing regulatory B cells in these mice, little is known regarding the role of such an immune background in development of colitis-associated cancer.
AIMS&METHODS: We evaluated colitis-associated cancer development in SAMP1/Yit mice and compared our findings to age-matched control AKR/N mice. Experimental colitis was induced in 7-week-old male SAMP1/Yit and AKR/ N mice by administration of dextran sodium sulfate (DSS) for 10 days. The colitis activity parameters body weight, colon length, histological score, and colonic expressions of tumor necrosis factor (TNF)-alpha and macrophage inflammatory protein (MIP)-2 were assessed in inflamed colon tissues obtained from those mice. In addition, a mouse colitis associated cancer (CAC) model was induced by intraperitoneal injection of azoxymethane (AOM) in both strains, then a 3-cycle administration of DSS was given and examinations performed on day 60. The incidence of colitis-associated tumor development, and numbers and size of colonic tumors were determined, and compared between the mouse groups.

RESULTS: There were no differences regarding macroscopic and histological findings of the colon between SAMP1/Yit and AKR/N mice before DSS administration. In the colitis model, body weight loss, colon shortening, histological colonic inflammation severity, and TNF-alpha and MIP-2 expressions were significantly greater in SAMP1/Yit mice than AKR/N mice. As for the CAC model, the incidence of colitis-associated tumors was significantly higher in SAMP1/Yit mice (100%) than AKR/N mice (12.5%).
CONCLUSION: DSS-induced colonic inflammation was greater in SAMP1/Yit mice as compared to AKR/N mice, which may indicate its influence on susceptibility for colitis-associated cancer development.
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Disclosure of Interest: None Declared
Keywords: colitis-associated cancer, regulatory B cells, regulatory T cells, SAMP1/Yit mice

P1507 SERRATED LESIONS SHARE COMMON RISK FACTORS WITH COLONIC ADVANCED NEOPLASMS IN 6,218 CHINESE COHORT

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INTRODUCTION: Few studies have evaluated risk factors and the magnitude of risk for serrated lesions.
AIMS&METHODS: To assess risk factors associated serrated lesions and advanced neoplasms (AN) in a cohort of Chinese population, we analyzed findings from 6,218 consecutive adults aged≥50 years who underwent colonoscopy to the cecum. We quantified the risk of advanced neoplasm (adenoma≥1 cm, a polyp with tubulovillous/villous histology or high-grade dysplasia, or adenocarcinoma) and serrated lesions (hyperplastic polyps or serrated adenomas). Variables examined included family history of colorectal cancer (CRC), smoking, alcohol use, hypertension and body mass index (BMI). Age-adjusted univariate and multivariate logistic regression analyses were performed for each variable to calculate odds ratios (ORs) and 95% confidence intervals (CIs) associated with having serrated lesions and AN compared with having no polyps.
RESULTS: 3,647 subjects (58.8%) had no polyps, 344 (5.5%) had AN, 1486 (23.9%) had adenomas, 532 (8.56%) had serrated lesions. Mean age was 56.65 ±6.15 and 46.8% were male. 21% and 34% of serrated lesions and AN, respectively, were found in the proximal colon. Age ≥50 was associated with risk of serrated lesions and AN. In multivariate analyses after age adjustment, male gender (OR, 1.23; 95% CI, 1.02 – 1.50), current/previous smoking (OR, 1.98; 95% CI, 1.49 – 2.65) and BMI of ≥25 (OR, 1.34; 95% CI, (1.10 - 1.64) were associated with an increased risk of serrated lesions. Male gender (OR, 2.02; 95% CI; 1.57 – 2.59), a family history of colorectal cancer (OR, 1.62; 95% CI, (1.21 – 2.16), current/previous smoking (OR, 1.46; 95% CI, (1.02 – 2.09), hypertension (OR, 1.55; 95% CI, (1.20 – 2.01), and BMI≥25 (OR 1.40, 95% CI (1.10 - 1.79) were positively associated with an increased risk of AN.
CONCLUSION: Age, male sex, smoking and obesity are common clinical risk factors for serrated lesion and advanced neoplasms. Environmental and genetic factors play a role in the pathogenesis of these lesions.
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Disclosure of Interest: None Declared
Keywords: advanced neoplasm, risk factor, serrated lesion

P1508 FTY 720 INHIBIT THE TUMOR FORMATION IN A DEXTRAN SODIUM SULPHATE ENHANCED APCMIN/+ MOUSE MODEL

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INTRODUCTION: Sphingolipids activate multiple signal transduction pathways associated with cancer development. Sphingosine kinase 1 (SphK1) generates sphingosine-1-phosphate (S1P), which is a ligand for S1P receptors and a key molecules in sphingolipid-mediated functions including cell growth, differentiation and survival. Upregulation of SphK1 has been shown to be associated with colitis and colitis-associated cancer. The *Apc* $^{min/+}$ mouse is one of the well-known models of intestinal tumorigenesis. Colitis induced by DSS can enhance formation of colonic tumorigenesis in this model, which is more relevant to human colitis-associated cancer (CAC). In this study, we evaluate the FTY 720, functional S1PR antagonist on colonic tumorigenesis in DSS- *Apc* $^{min/+}$ mouse model.
AIMS&METHODS: The aim of this study is to define the role of regulation of sphk1/sphK2 in murine colitis and CAC.
C57BL/6 and *Apc* $^{min/+}$ mice were used for all experiments. Acute colitis was induced with 3% DSS for 5 days. Mice were treated with PBS or FTY (1mg/kg.i.p) and sacrificed at 8 days.
Histologic assessment of colitis was evaluated after H & E stain. Four-week old *Apc* $^{min/+}$ mice were given 2% DSS and then FTY 720 (1mg/kg.i.p) or PBS was administrated for 5 weeks and sacrificed 24hrs after final dose injection. To determine whether the effects of FTY 720 are due to suppression of inflammation during early CAC induction, same dose of FTY 720 was administrated to mice for 7 days of DSS cycle. Mice were sacrificed 5 weeks after DSS treatment. Tumor formation and size were assessed in the colon. Genetic expression of SphK1/2 was determined using real-time PCR in mice rectum. Immunohistochemistry and Western blots for Sphk1, pAkt, cyclin D1 were performed in mice colon and colonic epithelial cells.
RESULTS: FTY 720(1mg/kg) significantly ameliorated the acute DSS-colitis. Both earlier and delayed treatment of FTY 720 significantly reduced the number (16.1±3.4, 10.8±3.8, 9.8±4.5, $p<0.05$) and size of macroscopic tumors compared to PBS-treated mice (3.32±0.68 mm, 2.78 ±1.3, 2.26±1.17mm, $p<0.05$). Immunoactivies of Sphk1, pAkt and cyclin D1 were significantly suppressed in colonic tumors by FTY 720 treatment. Also Sphk1/Sphk2 gene expression ratio was significantly reduced by FTY 720 treatment (50 folds, $p<0.01$).
CONCLUSION: FTY 720, functional S1PR antagonist suppresses colitis and colitis associated cancer in B6J and *Apc*$^{min/+}$ mice by the modulation of Sphk1 expression and other proliferative signaling pathways. The regulation of Sphk1/Sphk2 expression might be one of the important signaling pathways in the pathogenesis of CAC.
Disclosure of Interest: None Declared
Keywords: colitis-associated cancer, DSS induced colitis, FTY 720, SPHK1/SPHK2, Tumorigenesis

P1509 ASSOCIATION BETWEEN BODY MASS INDEX (BMI) AND PREVALENCE OF COLONIC ADVANCED NEOPLASM

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INTRODUCTION: There is increasing evidence to show the impact of obesity on the incidence of colorectal cancer (CRC). It is important to understand the association of obesity with pre-neoplastic conditions to identify high risk subjects and implement appropriate preventive measures.
AIMS&METHODS: This study assesses the association between colonic advanced neoplasms (CAN) and BMI (and other co-morbidities) among a Chinese population.
CAN is defined as CRC, or any colorectal adenoma which has a size of equal to or larger than 10 mm in diameter, high grade dysplasia, villous or tubulovillous histologic characteristics, or any combination thereof. In addition, BMI(kg/m^2) ≥18.5 to <23 is defined as normal weight; <18.5 as underweight; ≥23 to <25 as overweight; ≥25 as obesity.
Asymptomatic Chinese subjects were recruited into a community colorectal cancer screening program in Hong Kong from June 2008 till December 2012. They were offered either fecal immunochemical test or colonoscopy. The colonoscopic results were recorded and odds ratio of detection of CAN in relationship to BMI and other comorbidities were determined by multivariate regression analysis.
RESULTS: Among 10758 subjects, 4961(46.1%) underwent complete colonoscopy and provided detailed demography and medical history. The mean age was 57.1 (4.9) and male proportion was 47.5% (2357/4961). The CAN detection rate was 5.5% (272/4961). Table 1 shows the results of multivariate regression analysis. When compared to normal weight subjects, the adjusted OR of prevalence of CAN in overweight subjects was 1.47 (95%CI: 1.07-2.02), obese subjects was 1.55 (95%CI: 1.14-2.11). Furthermore, men with overweight [aOR: 1.97 (95%CI: 1.43-2.71)] and obesity [aOR: 2.18 (95%CI: 1.62-2.95)] were associated with a higher risk of CAN. Overweight [aOR: 1.7 (95%CI: 1.01-3.00)] and obese [aOR: 1.93 (95%CI: 1.21-3.08)] subjects with family history of CRC also had a higher risk of CAN.
Table 1
Odds ratios (95% CI) of colorectal advanced neoplasm

	OR (95% CI)	aOR (95% CI)
Underweight	0.87 (0.40-1.91)	1.01 (0.46-2.22)
Overweight	1.63 (1.19-2.23)	1.47 (1.07-2.02)
Obesity	1.81 (1.34-2.44)	1.55 (1.14-2.11)
Age	1.09 (1.06-1.11)	1.07 (1.05-1.10)
Male	1.93 (1.50-2.48)	1.64 (1.28-2.15)
HTN	1.73 (1.34-2.25)	1.32 (1.14-2.11)
DM	1.41 (0.93-2.13)	-
Family history of CRC	1.50 (1.11-2.04)	1.55 (1.13-2.12)
Smokers	1.85 (1.30-2.64)	1.44 (0.98-2.09)

CONCLUSION: To conclude, individual with a high BMI (≥23 kg/m^2), male gender and family history of CRC were associated with a higher risk of CAN. Appropriate screening strategies are needed to determine for these high risk groups of individuals.
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Disclosure of Interest: None Declared
Keywords: Adenoma, advanced neoplasm, BMI, Colorectal cancer, Obesity

P1510 INTRAUTERINE GROWTH RETARDATION ALTERS THE COLONIC EPITHELIAL BARRIER AND INCREASES THE RISK OF COLONIC DISEASES IN ADULT RATS

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INTRODUCTION: Infants born with intrauterine growth retardation (IUGR) are at increased risk for developing metabolic diseases in adulthood such as type 2 diabetes (1). It has been proposed that an adverse intrauterine environment could induce stable epigenetic modulation of gene expression, which in turn, alters the function of metabolic organs later in life (2). Epigenetic and metabolic modifications are also involved in the pathogenesis of inflammatory bowel disease and colorectal cancer but their origins are not completely understood (3).

AIMS&METHODS: The objective of this study was to determine the impact of IUGR upon colonic epithelial barrier and colonic diseases.The rat model of IUGR was obtained by restricting protein intake in pregnant rats. Birth weights of IUGR pups are 15-20% lower than controls. By the age of 5-8 months, colons were collected and colonocytes isolated. Permeability was assessed by mounting colonic tissues in Ussing chambers. Expression of key genes and epigenetic modifications were analysed by immunohistology, western-blot, qPCR and ChIP assays. Susceptibility to colitis was assessed by dextran sodium sulfate (DSS) treatment and colitis induced-carcinogenesis by azoxymethane (AOM) injection. Histological scores and neoplastic lesions were measured.
RESULTS: Proliferation of epithelial cells was decreased in colonic crypts from IUGR rats without modification of apoptosis, suggesting a lower self-renewal of colonic epithelium. IUGR increased intestinal permeability and this effect was associated with disorganisation of tight-junction proteins. Expressions of the transporter (MCT1) and ß-oxidation enzyme (scACAD) of butyrate were down-regulated in IUGR colonocytes suggesting impairment of butyrate utilisation, the main energy source for colonocytes (5). Among the posttraductional modifications of H3 and H4 histones, IUGR induced a drastic loss of H4K16 acetylation, an epigenetic mark of colorectal cancer (5). The severity of DSS-induced colitis was higher in IUGR rats than in controls. Moreover, the number of AOM-induced preneoplastic lesions (MDF) was higher in IUGR rats.
CONCLUSION: Our study suggests that IUGR induces epigenetic and metabolic modifications in colonic epithelium, which could affect the intestinal barrier and predispose to gastrointestinal diseases.
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Disclosure of Interest: None Declared
Keywords: Colorectal cancer, Epigenetics, Inflamatory bowel disease, Nutritional imprinting

P1511 ERBB3 PHOSPHORYLATED BY HEREGULIN PROMOTES ANGIOGENESIS IN COLORECTAL CANCER

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INTRODUCTION: The erbB family, including epidermal growth factor receptor (EGFR), erbB2, erbB3, and erbB4, plays various and distinctive roles both physiologically and pathologically, including cell proliferation, differentiation, migration, and apoptosis. There are multiple mechanisms underlying erbB-mediated tumor progression. We have shown that heregulin stimulates vascular endothelial growth factor (VEGF) secretion via phosphorylation of erbB3 (p-erbB3) using colorectal cancer cell lines in vitro. The clinical significance of phosphorylated erbB3 expression has yet to be explored in colorectal cancer.
AIMS&METHODS: To investigate heregulin, p-erbB3, and VEGF protein expression in human colorectal cancer and determine the relationship between their expression and angiogenesis and patient prognosis.
We examined 155 surgical resections from colorectomy patients. Cellular localization of heregulin, p-erbB3, and VEGF protein in colorectal cancer surgical resections was analyzed by immunohistochemistry. Microvessel density (MVD) was determined by immunostaining for CD34. Immunohistochemical results were compared with clinicopathological factors and patient prognosis.
RESULTS: MVD was higher in heregulin- and VEGF-positive cases than in heregulin- and VEGF-negative cases. In addition, MVD was higher in p-erbB3-positive cases than in p-erbB3-negative cases. Statistically, heregulin expression correlated with p-erbB3 or VEGF expression. In univariate analysis, heregulin and p-erbB3 correlated with worse prognosis in colorectal cancer patients. In multivariate analysis, heregulin and p-erbB3 retained independent prognosis significance.
CONCLUSION: These data suggest that heregulin contributes to colorectal cancer development by promoting angiogenesis via phosphorylation of erbB3.
Disclosure of Interest: None Declared
Keywords: angiogenesis, Colorectal cancer, phosphorylated erbB3, VEGF

P1512 METAGENOME ANALYSIS OF PLASMA DERIVED CFDNA IN HEALTHY PATIENTS AND COLON DISEASES

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INTRODUCTION: There are many theory of the cell free DNA (cfDNA) origin such as apoptosis, necrosis and active secretion; however the exact nucleotide composition is unknown. We are constantly exposed to foreign DNA from various sources like benign or malicious microbes in and on our body, pollens in the inhaled air and as the largest amount with the daily food supply. Here we report a new possible mechanism, which can be contribute the quantity and quality of the cfDNA.
AIMS&METHODS: Our aims were to determine the DNA content of cfDNA by NGS sequencing technology and identify differences among four clinical groups and analyze the unmapped read from NGS sequencing data.
CfDNA was extracted from plasma samples which were collected (TUKEB 2009/037) from 50-50 normal, IBD, colorectal adenoma and -cancer patients. Fractions were separated via electrophoresis and DNA fragments were recovered from the gel slices. Intact DNA above 10kb (1st), the fraction is between 200bp to 10kb (2nd) and nucleosomal DNA (3rd) fractions were separated. Indexed DNA fragment library resequencing was performed on SOLiD IV system. The sequencing yielded 50 nt long reads a total of 86.6 Gbases. Sequence alignments were performed by SHRiMP and Bowtie aligners. We have verified our data using SRA data sets.
RESULTS: We analyzed cfDNA NGS data from own and previously published cohort of over 1000 patients. On average above 70% of the reads were mapped to the human reference genome. The non-aligning reads were aligned to genomes of various other organisms. Significant portion of the sequence tags (0.5-50 ppm) can be mapped back with high confidence to the genome of Enterobacteriaceae (Escherichia coli, Shigella sonnei) and commonly consumed food substances such as potato or rice. The number of tags can be fitted with a log-normal distribution which consistent with our fractionation result, furthermore the time dependent DNA degradation processes and the different absorption efficiency. IBD is a potential promotion factor of the absorption.
CONCLUSION: Though the sporadic occurrence of food related miRNA and DNA in blood has already been reported in previous studies, the presence of fragments which can carry complete genes seems to be novel. Our findings can be change fundamentally our general ideas from the digestion processes and macro molecular transport, furthermore may be contributing to understanding cancer development or making blood based diagnostic markers.
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Disclosure of Interest: None Declared
Keywords: cell free DNA, colorecal cancer, sequencing

P1513 PROGNOSTIC SIGNIFICANCE OF DR-70 LEVELS IN DYSPLASTIC COLON POLYPS

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INTRODUCTION: Background: The AMDL-ELISA DR-70 (fibrinogen degradation products [FDP]) test isthe first in vitro diagnostic cancer test approved by the USFDA to monitor colorectalcancer since 1982 when carcinoembryonic antigen (CEA) was approved. Objective:This study investigated the relationship between DR-70 serum levels anddysplastic colon polyps.
AIMS&METHODS: This is a single center prospective analysis of selected patientswith colon polyps. 50 healthy blood donors and 130 patients with adenomatous polypsdetected by colonoscopy were included in the study. Patients were divided into twogroups (i.e., "low grade" - Group 1a and "high grade" - Group 1b) according to theextent of the dysplasia in the polyp. Blood samples from each participant wereanalyzed for serum CEA and DR-70 levels. Main Outcomes Measures: Prognostic significance of DR-70 levels in dysplasticcolorectal polyps described.
RESULTS: The median DR-70 level was 0.5 ug/ml in the healthy control group and 1.1
ug/ml in Group 1b (i.e., the high grade polyp) ($p<0.001$). DR-70 was higher in Group 1b
as compared Group 1a ($p<0.001$). However, the mean DR70 values for the low grade
polyp group (i.e., Group 1a) and the control group were similar ($p=0.067$).
The median DR-70 level was 0.5 ug/ml in the healthy control group and 1.1ug/ml in Group 1b (i.e., the high grade polyp) ($p<0.001$). DR-70 was higher in Group 1bas compared Group 1a ($p<0.001$). However, the mean DR70 values for the low gradepolyp group (i.e., Group 1a) and the control group were similar ($p=0.067$). Limitations: We did not include CRC patients in the sample population. Moreover, wecould not include serrated adenomas because only five of our patients presented withthis condition. Lastly, the patient sample size, i.e., 130 cases, may not be sufficientlylarge to determine the cut-off level between dysplastic lesions and healthy controls
CONCLUSION: DR-70, a marker used to measure FDP, which is generated by all majorcancers, is a potential marker to identify patients with advanced adenomatous polyps, i.e., precursors of colorectal cancer.
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Disclosure of Interest: None Declared

Keywords: colon cancer screening, colonic polyps, DR-70

P1514 THE SENSITIVITY AND SPECIFITY OF DR-70 IMMUNOASSAY AS A TUMOR MARKER FOR GASTROINTESTINAL CANCERS

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INTRODUCTION: The sensitivity and specificity of DR-70 as a tumor marker for the detection of gastrointestinal cancers was evaluated and compared to that of conventional tumor markers (i.e., CEA and CA 19-9), The relationship between the clinical parameters of the gastrointestinal cancers and the serum DR-70 values versus that of CEA and CA 19-9 was examined.

AIMS&METHODS: Blood sera from 101 patients with gastrointestinal malignancies and 105 healthy blood donors were collected prospectively. The tumor extension and spread was classified using organ-specific TNM classification and histologic grade. All patients and controls were also tested for DR-70, CEA, and CA 19-9 levels.

RESULTS: The median levels of DR-70 were 1.6 μg/mL and 0.5 μg/mL in cancer patients and the healthy control group, respectively ($P < 0.001$). The sensitivity, specificity, and the best cut-off value for DR-70 in patients with malignancy were 97.0%, 95.2%, and < 0.75 μg/mL, respectively. The positive predictive value was 95.1%, and the negative predictive value and the efficacy were 97.1% and 96.1%, respectively. Although the sensitivities of CEA and CA 19-9 were 52.5% and 38.6%, respectively, the sensitivity increased to 66.3% with the combined use of both. The specificities were 94.2% and 99.0% for CEA and CA 19-9, respectively. The serum DR-70, CEA, and CA19-9 levels were higher in cancer patients as compared to the control group ($P < 0.001$).

CONCLUSION: Due to its high sensitivity, specificity, and positive and negative predictive values, DR-70 can be used more frequently as a tumor marker for the diagnosis of gastrointestinal cancers and in the detection of tumor progression and treatment follow-up due to the positive correlation between DR-70 levels and tumor stage.

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Disclosure of Interest: None Declared

Keywords: colon cancer screening, DR-70, markers

P1515 INTERVAL CANCERS IN LYNCH SYNDROME FAMILIES UNDER COLORECTAL SURVEILLANCE

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INTRODUCTION: Mutation carriers in Lynch syndrome (LS) have a lifetime risk for CRC of 52-82% at the age of 70 years(yrs). Several studies reported colorectal cancer (CRC) within an interval of 2 years after a negative colonoscopy, therefore International Guidelines for LS suggest colonoscopic surveillance interval of 1-2 year. Nowadays the effectiveness of a less (2 years) or more intensive (1 year) interval surveillance protocol is still not defined.

AIMS&METHODS: Aim of the present study was to evaluate the most optimal surveillance interval for mutation carriers in LS families.

Among subjects who referred to the Family Cancer Clinic of our Institution LS families with a known deleterious mutation of Mismatch Repair (MMR) genes were selected. All the carriers with at least 2 surveillance examinations were included in the study. All colonoscopies were performed by experienced gastroenterologist and after 2006 Narrow Band Imaging and Magnification were used at each examination. The recommended interval of surveillance was 1-2 years according with International Guidelines.

RESULTS: 71 patients (33 males/38 females) from 30 LS families were included in the study. Mean age at baseline surveillance colonoscopy was 39,8 years (range 18-68 years). 40 patients carried a deleterious mutation of MSH2 gene and 31 of MLH1 gene. After a mean follow up of 61,6 months (range 12-371) and a total of 268 colonoscopies, 4 out of 71 patients (5,6%) developed CRC under surveillance. One out of these 4 patients had a sub-optimal bowel preparation. Mean interval from previous colonoscopy was 24 months (range 16-30 months). Mean age at diagnosis was 40 years (range 32-50 years). Two patients carried a large deletion of MSH2 gene and the other 2 a deleterious mutation of MLH1 gene. None of the patients had a prior history of CRC.

CONCLUSION: In our series interval CRCs were detected in 5,6% of LS under endoscopic surveillance with a mean interval of 24 months, according with previous studies. In three patient CRC was diagnosed at an early stage (T1-T2N0), whereas in one at a more advanced stage (T2N1). In the last case the bowel preparation was suboptimal and the surveillance colonoscopy was performed with a 16 months interval. All patients were asymptomatic and all underwent a high quality colonoscopy with advanced imaging techniques (NBI and magnification). No specific genotype was associated with a more rapid malignant transformation.

In conclusion, in our experience the risk of developing CRC in LS mutation carriers could be reduced by a one year colonoscopic surveillance program rather than every 2 years.

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Disclosure of Interest: None Declared

Keywords: interval cancer, Lynch syndrome

P1516 UPTAKE OF COLORECTAL CANCER SCREENING IN SOUTH EAST LONDON; A PROSPECTIVE QUESTIONNAIRE SURVEY OF DEMOGRAPHIC AND PSYCHOLOGICAL FACTORS

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INTRODUCTION: Colorectal cancer screening is offered in the UK to individuals aged 60-75 years through the self-completed faecal occult blood test (FOBt). Nationally uptake of screening is 60% but only 40% in South East (SE) London. Reasons for this low uptake are unclear.

AIMS&METHODS: This study examined whether demographic and/or psychological factors account for variation in FOBt uptake in SE London. A prospective phone survey was conducted with participants (n=507) two months before being invited for screening. The questionnaire was based on an integrated psychological framework (Michie et al 2005), including constructs such as intentions, emotions and environmental context. Socioeconomic status (SES) was measured combining education, housing tenure and car ownership. Participants reported their ethnic group. Uptake was assessed from screening records. Data were analysed using logistic regression and mediation analysis.

RESULTS: White British (WB), Black African (BA), Black Caribbean (BC) and White Other (WO) ethnic groups were included. Participants' SES varied, though there were more participants from less deprived backgrounds than those from more deprived backgrounds.

Table 1 displays the odds ratios (OR) for FOBt uptake by ethnicity. BA and WO participants were less likely to complete the FOBt than WB participants. However, BC participants did not differ in their likelihood of completing the FOBt compared to WB participants. In terms of SES, those of low SES were generally less likely to complete the FOBt, although this result was marginally non-significant (OR=-0.754, p=0.073).

Table 1: Ethnicity as a predictor of FOBt uptake

Ethnicity	OR	P value
BA	0.318	0.004
BC	1.681	0.259
WO	0.445	0.008

Ethnic differences were mediated by psychological factors, with lower FOBt uptake by BA participants being partly due to their having lower intentions (BA participants vs. WB participants=-0.505, 95% confidence intervals (CI) 0.911-0.215) and greater difficulty planning FOBt completion (BA participants vs. WB participants=-0.168, 95% CI 0.412-0.041). For WO participants, lower FOBt uptake was mediated by greater planning difficulties only (WO participants vs. WB participants=-0.128, 95% CI 0.327-0.011).

CONCLUSION: There were significant differences between ethnic groups in FOBt uptake, which persisted when controlling for SES. These differences appear to result from BA and WO participants having lower intentions and more difficulties planning how and when to complete the FOBt compared to WB participants. Screening uptake interventions may benefit from targeting these factors.

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Keywords: Colorectal cancer screening, Ethnic Groups, Faecal Occult Blood test (FOBt), Psychological factors, Screening uptake, Socioeconomic status

P1517 HIGHER SENSITIVITY FOR THE DETECTION OF ADENOMAS BY A HB/HP BED SITE TEST USING A NOVEL SAMPLING DEVICE

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INTRODUCTION: Point of care diagnostic tests are widely used for the detection of occult blood in the stool to enable an early detection of bowel cancer or adenomas. Due to their higher specificity and sensitivity compared to formerly used biochemical tests, immunochromatographic tests on haemoglobin (Hb) and the haemoglobin/haptoglobin complex (Hb/Hp) in stool samples are regarded as superior. The aim of the study was to compare the sensitivity and specificity of an i-FOB test using a novel or a standard sampling device.

AIMS&METHODS: The new i-FOB test, named ''FD Hb/Hp complex professional'', uses a novel stool sampling system, which enables the testing of a precisely defined quantity of stool independent of its consistency. 245 stool samples from healthy controls and patients with different types of lower GI disease were tested with an i-FOB test using the novel (new test) or a standard (old test) sampling device. All 245 subjects underwent lower GI tract endoscopies including biopsies, healthy controls were defined by the absence of endoscopic or histological abnormalities. Statistical analysis was performed using a chi-squared test.

RESULTS: For the detection of adenomas applying Hb as a marker the sensitivity of the test using the novel sampling device was a lot higher (93%) compared to the old test (57%). The new system detected 9 out of 11 adenomas while the old system detected only 5 cases. Using Hb/Hp as a read out the novel sampling system detected 6 cases with colorectal adenoma compared to 3 cases using the standard sampling device with a sensitivity of 39% vs 28%, respectively. In this series each case of a positive Hb result was paralleled by a positive Hb/Hp finding and specificity was above 99% in every setting..

In all other disease conditions the new and the old test system only showed minor differences.

Furthermore, Hb and the Hb/Hp complex had different detection rates in that in general the sensitivity of Hb as marker was higher compared to the Hb/Hp complex.

Disease	n	New Test Hb	Old Test Hb	New Test Hb/Hp	Old Test Hb/Hp
Colon adenoma	11	9	5	6	3
Colon carcinoma	4	4	4	1	1
Colon polyps	4	4	3	1	1
Colon diverticulosis	9	1	0	0	0
Crohn's disease	6	2	1	2	1
Ulcerative colitis	4	2	1	1	1
Healthy controls	207	2	1	1	1

CONCLUSION: This new test system analysing Hb or Hb/Hp in a precisely defined amount of stool obtained by a novel sampling device, allows a better detection of faecal occult blood derived from colon adenomas and might be also beneficial in other settings characterised by occult bleeding.

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Disclosure of Interest: T. Knittel Consultancy for: Frost Diagnostika, K. Lüthgens Consultancy for: Frost Diagnostika, G. Frost Shareholder of: Frost Diagnostika

Keywords: adenoma detection, adenoma detection rate, adenomatous polyps, Faecal Occult Blood test (FOBt)

P1518 THE COMPARISON OF K-RAS MUTATION IN COLORECTAL MUSCULARIS PROPRIA CARCINOMA ACCORDING TO MORPHOLOGICAL DEVELOPMENTS

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INTRODUCTION: To investigate differential expression of K-ras mutation in depressed-type lesion in comparison with polypoid- or flat types.

AIMS&METHODS: A total of 22800 neoplasms were resected endoscopically or surgically at our unit from April 2001 to June 2012. Of these 347 muscularis propria carcinoma were included. Thirty specimens of MP carcinoma were obtained by surgical resection or endoscopic submucosal dissection. According to their morphological developments, we classified them into three types : polypoid(n=30), flat(n=20), and depressed types(n=34). K-ras mutation was examined using reverse sequence-specific oligonucleotide with polymerase chain reaction method(PCR-rSSO).

RESULTS: Single-base transition from GGT to GAT in codon 12 was detected in ten samples, and twelve samples presented with GGC to GAC transition in codon 13. Our study showed a high frequency of G to A transition of codon 13 mutation of the K-ras gene. K-ras mutation was found in polypoid type by 50.0%(15/30), flat type by 55.0%(11/20), and depressed type by 20.6%(7/34). To explain flat type in detail, eigteen LST-G and two LSTs-NG (pseudo-depressed type) were included in flat-type lesions. Eleven(61.1%) of 18 LST-G had K-ras mutation, while two LSTs-NG had no K-ras mutation(0/2). In summary, the frequency of K-ras mutation was significantly lower in depressed-type lesions and LSTs-NG (pseudo-depressed type) [7/36(19.4%)] as compared to the other types [26/48(54.2%)] of MP carcinomas.

CONCLUSION: Depressed-type lesions and LST-NG (pseudo depressed type) were suggested to come through a distinct genetic pathway.

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Disclosure of Interest: None Declared

Keywords: colorectal muscularis propria carcinoma, k-ras mutation

P1519 HOW RELIABLE ARE IMMUNOHISTOCHEMICAL STAINING FOR DNA MISMATCH REPAIR PROTEINS PERFORMED AFTER NEOADJUVANT CHEMO-RADIATION IN PATIENTS WITH RECTAL CANCER ?

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INTRODUCTION: The use of immunohistochemistry (IHC) for mismatch repair proteins (MMR) is being increasingly used. We aimed to compare the efficacy of IHC staining performed on biopsy specimens obtained at endoscopy with the surgical specimens following neoadjuvant therapy

AIMS&METHODS: 32 rectal cancer subjects had paired pre & post neoadjuvant tissue available for IHC staining for $hMLH_1$, $hMSH_2$, $hMSH_6$, and PMS_2. *Absent* staining was defined as total loss of protein in the tumor. *Focal & weak* staining was defined as no more than moderate intensity staining present in $<10\%$ of the tumor cells. 13 rectal cancer patients that did not receive neoadjuvant treatment served as controls.

RESULTS: The IHC of the *pre* neo-adjuvant biopsies showed that 2 subjects had absent stain for at least one of the MMR proteins and 30 subjects had strong stain for all MMR proteins. Overall, out of 30 subjects with strong pre neoadjuvant staining of all MMR proteins, in only 18 subjects (60.0%) there was also strong staining of all MMR proteins in the post neoadjuvant material. In the post neoadjuvant material, a pattern of *focal & weak* staining emerged in a significant proportion of all MMR proteins [PMS_2 (33.3%); $hMSH_6$ (13.3%); *hMLH1* (10.0%); $hMSH_2$ (6.7%)].

CONCLUSION: Our study suggests that neoadjuvant therapy is associated with the emergence of a false focal staining pattern in all MMR proteins. Therefore, IHC from the pre neoadjuvant endoscopic biopsies should be preferred. We also highlight the importance of obtaining multiple biopsies before chemoradiation is commenced.

Disclosure of Interest: None Declared

Keywords: immunohistochemical staining, LYNCH SYNDROME AND VARIANTS, Neoadjuvant therapy

P1520 COMPREHENSIVE MIRNA EXPRESSION PROFILE ANALYSIS IN ADENOMA-CARCINOMA SEQUENCE

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INTRODUCTION: Recent studies described the changes of the miRNA expression in precancerous lesions and in colorectal cancer. miRNA remain stable in formalin-fixed, paraffin-embedded (FFPE) tissue samples. Several miRNA extraction kits are available, but it is still controversial that total RNA or enriched miRNA isolation kits are better for extraction and investigation of miRNA.

AIMS&METHODS: Our primary aim was to find any viable miRNA by using different extraction protocols.

Our further aims were to identify the miRNA expression alterations between normal colonic tissue (N), tubulovillous adenoma (AD) and colorectal cancer (CRC) FFPET samples after selecting the top isolation method and to find characteristic miRNA patterns between the three clinical groups. Other purpose was to predict gene targets of the most interesting miRNA *in silico*.
miRNA were isolated using High Pure miRNA Isolation Kit (Roche), miRCURY^{TM} RNA Isolation Kit (Exiqon), High Pure RNA Paraffin Kit (Roche), MagNA Pure 96 Cellular RNA LV Kit (Roche) to determine any differences in the 4 extraction methods after deparaffinization of FFPET sections from human N (n=3), AD (n=3) and CRC (n=3) FFPET samples. To analyze the miRNA expression patterns qPCR Human Panel I+II (Exiqon) method detecting 742 human miRNA was performed. Gene target prediction was done using four algorithms.
RESULTS: The High Pure miRNA Isolation Kit showed most of the expressed miRNA on both Panels, moreover the number of expressed miRNA. Different miRNA expressions could be detected in N, AD and CRC samples. Out of the 752 analyzed miRNA, 256 miRNA showed significant ($p<0,05$) differences in the comparison of N vs. AD, furthermore most of them (n=251) were found to be downregulated in AD samples. miR-124 shown significantly decreased 6 times level ($p<0,05$) in AD samples. miRNA showed expression alteration between N vs. CRC cases, most of them were upregulated. miR-31 produced increased expression through N vs. CRC. We found 244 miRNA expression alterations in AD in comparison to CRC samples, moreover 242 miRNA were overexpressed in CRC. miR-99a was found to be most upregulated in CRC group. Predicted mRNA targets were selected from the most significantly up- and down-regulated miRNA and validation was confirmed with all genome expression data.
CONCLUSION: According to our preliminary results, miRNA expression patterns could be determined among the three analysed stages and after further validation with increased sample number, groups of selected miRNA can be suitable for diagnostic classification of pre-cancerous and cancerous lesions.
Disclosure of Interest: None Declared
Keywords: colorecal cancer, CRC, miRNA, mRNA target, Real-time quantitative reverse transcriptase polymerase chain reaction, tubulovillous adenoma

P1521 AFATINIB, A TYROSINE KINASE INHIBITOR, ENCAPSULATED WITH POLYMERIC MICELLES TO IMPROVE THE THERAPEUTIC EFFECT FOR HER2-OVEREXPRESSED TUMORS

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INTRODUCTION: HER2, a receptor protein with tyrosine kinase domain, overexpressed in tumors, including breast tumor, gastric tumor, colorectal tumor, and participated in the cell proliferation of tumor cells. Studies have indicated that tyrosine kinase inhibitor such as afatinib can block HER2 activation, and hence reduce tumor growth. On the other hand, nanoparticles such as polymeric micelles, which possess the enhanced permeability and retention (EPR) effect, were used as a drug carrier to improve the accumulation of drugs in tumor tissues. Therefore, we aimed to encapsulate afatinib with the polymeric micelles for improving the therapeutic effect of HER2-overexpressed tumors in this study.
AIMS&METHODS: The expressions of HER2 in the variety of tumor cells were detected using Western Blotting. A dose-dependent method of afatinib was performed in high-expressed HCT-15 cells and low-expressed MKN45 cells to validate the therapeutic effect of this tyrosine kinase inhibitor response to HER2 expression. Moreover, apoptosis and *in vivo* inhibitory effect were measured after afatinib-encapsulated micelles administration.
RESULTS: We observed that HER2 overexpressed in breast (MCF-7), prostate (PC-3), gastric (AGS), colorectal (HCT-15), and hepatocellular (HepG2) tumor cells as compared to lung cancer cells (A549). We selected high-expressed HCT-15 and AGS cells, and low-expressed MKN45 cells for testing the specific therapeutic effect of afatinib. We found that afatinib had higher inhibitory effect to HCT-15 and AGS cells as compared to MKN45 cells, indicating afatinib specifically inhibited HER2-overexpressed tumors. Furthermore, afatinib-encapsulated micelles led to higher inhibitory effect and apoptosis, demonstrating that micelles help afatinib enter to the HER2-overexpressed tumor cells. In vivo inhibitory assay of HCT-15-induced tumor xenografts demonstrated that afatinib-encapsulated micelles significantly reduced tumor growth as compared to afatinib performance alone.
CONCLUSION: In this study, we demonstrated the specific expression of HER2 in the variety of tumor cells, and created a novel micelles-carried afatinib for the therapeutic application of HER2-overexpressed tumors. The improved therapeutic effect of this micelles-carried afatinib may be applied in clinical practice for prolonging the survival of HER2-overexpressed tumor patients.
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Disclosure of Interest: None Declared
Keywords: Afatinib, HER2, polymeric micelles, tumor

P1522 MANAGEMENT OF POLYP CANCERS WITHIN A NATIONAL BOWEL CANCER SCREENING PROGRAMME

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INTRODUCTION: Endoscopic management of early colonic neoplasia or polyp cancer remains unclear. There are no national guidelines or good quality data to guide clinicians with these difficult lesions.
AIMS&METHODS: The aim of this study is to identify the incidence of early cancer and variation in practice of managing these lesions. Data was prospectively collected in all patients undergoing screening within the Solent Bowel Cancer Screening Programme (BCSP) in the United Kingdom. The database was interrogated to identify all neoplasia. The endoscopists suspicion of cancer was noted from the reports. MDT outcome was recorded, along with final management of the cancer
RESULTS: In total 3976 patients underwent screening colonoscopy between 2007 -2012. N=5768 neoplastic polyps found giving a mean polyp detection rate of 1.5/patient. Cancer was found in 235/3976 (6%) patients. Mean age was 67yrs. 142/235 (60%) were male. 145/235 (62%) had advanced cancer, confirmed at surgery. 90/235 (38%) patients had polyp cancer. 83% of them in rectosigmoid.
1) 13/90 were pedunculated polyps (mean size 23 mm, range 12-35mm)
2) 77/90 were flat polyp cancers (mean size 24mm, range 8-80mm)
See table 1 below
13/13 pedunculated polyp cancers were endoscopically resected. In 6/13 cases cancer was suspected prior to resection. Histology was reported accurately on 12/13 (92%) polyp cancers using Haggitt classification. 1/13 required surgery due to invasive features on histology.
30/77 (39%) of flat or sessile polyp cancers were endoscopically resected. Endoscopist suspected cancer in only 13/30 (43%) cases prior to resection. Histology was reported confidently by Kukuchi levels in 19/30 (63%) of lesions. 9/19 required surgery due to invasive features on histology. In 11/30 (37%) cases the histology report was inconclusive due to a poor quality EMR specimen. This led to surgery in all 11 patients but no residual disease or LN involvement was found.

Size(mm)	Pedunculated	Flat	Total
0-10	0/13 **0%**	17/77 **22%**	17/90 **19%**
11-20	6/13 **46%**	27/77 **35%**	33/90 **37%**
>20	7/13 **54%**	33/77 **43%**	40/90 **44%**

Table 1: Breakdown of polyp cancer size and morphology

CONCLUSION: 1) The in-vivo endoscopic diagnosis of cancer prior to resection is suboptimal and can be improved
2) Post EMR histology reporting is inconclusive in a large proportion of flat polyps leading to unnecessary surgery
3) Clinical care could be improved by optimising in-vivo diagnostic skills and resecting large flat lesions in single piece by ESD.
Disclosure of Interest: None Declared
Keywords: cancer, colon cancer screening, Polyp

P1523 FROM SURGERY TO THE DELIVERY OF ADJUVANT THERAPIES IN STAGE III COLORECTAL CANCER PATIENTS: THE ROLE PRE-OPERATIVE NEUTROPHIL TO LYMPHOCYTE RATIO.

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INTRODUCTION: The role of adjuvant chemotherapy [AC] is established in stage III colorectal cancer but a significant proportion do not proceed with therapy after colorectal resection. Preoperative neutrophil to lymphocyte ratio (NLR) has been found to be an independent negative prognostic outcome marker in patients with colorectal cancer (CRC) [1,2]. In an era of increasingly personalised cancer treatment, we assessed whether NLR might determine the likelihood of proceeding with adjuvant therapy.
AIMS&METHODS: All patients diagnosed with stage III CRC undergoing curative elective resection from 2006 to 2011 were assessed from a prospective database. Demographics, operative factors and postoperative outcomes were recorded. Data fields were complete for all patients in the study. Univariate analysis determined predictors of failure to initiate AC that were then submitted to multivariate analysis to determine independent predictors. Factors including sex, age, operation type (laparoscopic versus open), 30-day major morbidity [Clavien-Dindo (CD)≥3], Enhanced Recovery protocol, TNM stage, ratio of positive lymph nodes, vascular invasion, tumour site, Charlson morbidity score, preoperative albumin and preoperative NLR were assessed. Emergency presentations and operations were excluded.
RESULTS: 271 patients were analysed. Median age of 68.5 years [IQR, 57.25-77.00]. 177 patients (57%) were male. Multivariate regression analysis identified NLR>3 (OR 0.42, (95% CI 0.23-0.78) P=0.006) and age ≥65 years (OR 0.13, (95% CI 0.06-0.26); P<0.001) as independent prognostic factors for failure to proceed with AC. NLR> 3.0 was significantly associated with age, higher T and N stage and a low pre-operative albumin level.
CONCLUSION: In this prospective cohort study, preoperative NLR> 3.0 and age were independent predictors of failure to proceed to adjuvant chemotherapy: NLR>3.0 was related to > 50% reduction in the likelihood of starting therapy. Preoperative NLR may assist clinicians where individual risks need to be considered before initiating adjuvant therapy, particularly in older patients.
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Disclosure of Interest: None Declared
Keywords: adjuvant chemothrapy, Colorectal cancer, Neutrophil to Lymphocyte ratio

P1524 POST POLYPECTOMY ENDOSCOPIC SURVEILLANCE: DO DIFFERENT SPECIALISTS MEET THE INTERNATIONAL GUIDELINES ON COLORECTAL CANCER PREVENTION?

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INTRODUCTION: The "US Multi-Society Task Force on Colorectal Cancer and American Cancer Society" suggests specific guidelines for the colonic post polypectomy follow-up. However, some relevant publications concluded there is a low adherence by physicians to such international guidelines.
AIMS&METHODS: To assess if in our Hospital different specialists (gastroenterologists, surgeons and clinicians) meet the surveillance intervals suggested by the guidelines.
We carried out a restropective clinical record analysis of patients who underwent a surveillance colonoscopy after polypectomy from July 2011 to April 2012 at a University Hospital. All patients included were treated and followed in our institution. We reevaluated the previous therapeutic colonoscopy that caused the follow-up and then we compared the surveillance period suggested by the guidelines based on these reports with the period observed in our data base. Patients with incomplete colonoscopy, submucosal invasion histology, serratum adenomas, and/or inadequate colonic cleansing were excluded. Whether patients influence physician decisions on the timing of the surveillance colonoscopy is unknown.
RESULTS: We analyzed 331 post polipectomy surveillance colonoscopy. Only 24% of the studies were carried out according to the guidelines. The percentage of surveillance colonoscopies performed before the period suggested by the guidelines, discriminated on physician specialty was: Gastroenterologists (GE) in 59%, Surgeons (SO) in 83% and Clinicians (CN) in 75%. The percentage of colonoscopies performed according to the guidelines was: GE in 34%, SO in 17% and CN in 22%. And the percentage performed after the period was: GE in 7%, SO in 0% and CN in 3%. We also compared the surveillance intervals based on the polyp findings observed in the previous colonoscopy (table).

	On time intervals	Anticipated intervals	Average months (Anticipated)	Delayed intervals	Average months (delayed)
Rectal hyperplastic polyps	3%	97%	51	0%	0
1 or 2 small tubular adenomas with low grade dysplasia	15%	85%	33	0%	0
3 to 10 adenomas or one >1 cm or any with villous features or high-grade dysplasia	36%	59%	22	5%	16
>10 adenomas on a single examination	67%	33%	12	0%	0
large sessile adenomas that are removed in piecemeal	47%	0%	0	53%	12

CONCLUSION: Although patients evaluated by gastroenterologists showed the best rates of adherence to the guidelines, all specialists showed a strong trend to shorten the follow-up intervals. This situation led to an overuse of resources and an unnecessary increase in health care costs
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Disclosure of Interest: J. Pizzala: None Declared, M. González: None Declared, I. Oría: None Declared, M. Sobrero: None Declared, P. Carrillo: None Declared, P. Daffra: None Declared, M. Giménez Villamil: None Declared, J. De paula Financial support for research from: Danone reserch, C. Macías Gómez: None Declared
Keywords: polypectomy, surveillance colonoscopy

P1525 THE CLINICOPATHOLOGICAL CHARACTERISTICS OF TUMORS WITH A NEGATIVE COLONOSCOPY WITHIN THE PREVIOUS TEN YEARS.

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INTRODUCTION: Total colonoscopy(TCS) is considered to have the highest sensitivity for colorectal cancer(CRC). A 10-year interval is recommended according to adenoma-carcinoma sequence, however, considering the presence of de-novo cancer and missing rate, the appropriate interval of screening TCS has been unknown.
AIMS&METHODS: The aim of this study is to evaluate the characteristics of CRCs of following a previous negative TCS. Records of patients who underwent an endoscopic resection or operation of invasive carcinoma at our hospital, from 2002 to 2010, were reviewed retrospectively. The patients were divided into two groups. GroupA included patients with a negative colonoscopy within the previous one to 10 years. GroupB included patients without a previous colonoscopy or with a previous colonoscopy more than 10 years prior. Tumor stage (classified by TNM classification), tumor location (left or right-sided), size were analyzed.
RESULTS: A total of 2208 resected invasive carcinomas were available to analyze. GroupA contained 2151 lesions, GroupB contained 57 lesions. In each groups, tumor staging were as follows ; GroupA T1 703(32.7%), T2 305(14.2%), T3 922(42.8%), T4 221(10.3%). GroupB T1 24(42.1%), T2 8(14%), T3 20(35.1%), T4 5(8.8%). In each groups, average of tumor size were 39.4±24.3mm and 25.6±19.7 in diameter. In GroupA, 1537(71.5%) tumors were located at left-side colon, meanwhile 33(57.9%) in GroupB. Tumors in Group B were smaller and tend to be located in right-side colon compared to GroupA.
CONCLUSION: The clinicopathological characteristics between GroupA and B were similar. It would be necessary to analyze prognosis of each group in order to evaluate the appropriate interval of colonoscopy.
Disclosure of Interest: None Declared
Keywords: colorecal cancer, total colonoscopy

P1526 INTERVAL CANCERS DIAGNOSED AFTER THE FIRST COLORECTAL CANCER SCREENING PROGRAMME IN THE FINISTERE DISTRICT (FRANCE) : CHARACTERISTICS AND ANALYSIS OF SURVIVAL

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INTRODUCTION: Several trials have shown that screening for colorectal cancer (CRC) by fecal occult blood tests (FOBTs) can reduce CRC mortality. However, interval cancers are the major limitation of the FOBT. The objective of this study was to analyze the characteristics and the survival of the interval cancers diagnosed in the two years after a negative FOBT at the end of the first CRC screening programme organized in the Finistere area between September1st 2004 and September 1st 2006.
AIMS&METHODS: All CRC diagnosed in individuals aged 50-74 years and registered in the database of the Finistere registry of digestive cancers were cross-referenced with the database of the Cancer Prevention Coordination Centrer (ADEC 29) to analyze their screening status. CRC diagnosed in the screening population were classified into four groups according to their screening status : screen-detected by FOBT (203 CRC), screen-excluded for medical reasons (53 CRC), individuals who had declined the screening, called non-responder (478 CRC) and the interval cancers (114 CRC). In each group 3 years-overall and specific survival were estimated using the Kaplan-Meier method. The log-rank test was used for univariable comparisons of time-to-event end points. End of follow-up date due to death or censoring was 1st September 2011.
RESULTS: The participation rate of the first screening programme was 48 %. Among 102 978 persons who had performed the FOBT, 96 316 had a negative test. Among these persons, 114 interval cancers were diagnosed within 2 years. The stage distribution of interval cancers and cancers diagnosed in the non responder group were similar with 48 % of stages III and IV. The 3 years-overall cumulative survival rates in the four groups were :

		Overall cumulative survival rates (%)		
	Number	1 year	2 years	3 years
Screen detected group	203	95.6%	92.1%	89.1%
Screen-excluded group	53	94,3%	88,7%	88,7%
Non responder group	478	85.9%	75.8%	70.1%
Interval cancers	114	89.3%	79.3%	72.0%

The survival of patients with interval cancers was not statistically different from the survival in the non responder group. The overall survival at 3 years was 72 %, whereas it was 89.1 % for patients with CRC detected by FOBT ($p < 0.0001$).
CONCLUSION: FOBT improve CRC prognosis in the screen detected group. Prognosis of interval cancers is similar to prognosis of cancers detected in subjects who did not answer the screening program. The high number of interval cancers constitutes a limit which justifies the replacement of the FOBT by a more sensitive screening test as the immunological test.
Disclosure of Interest: None Declared
Keywords: colorectal cancer screening, interval cancer

P1527 THE RISK FACTORS FOR DEVELOPING METACHRONOUS NEOPLASMS DURING SURVEILLANCE AFTER INITIAL RESECTIONS OF COLORECTAL ADENOMAS AND INTRAMUCOSAL CARCINOMAS

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INTRODUCTION: The object of the study was to investigate the risk factors for developping metachronous colorectal adenomas and carcinomas during colonoscopic follow-up after initial resections.
AIMS&METHODS: The study included 403 patients (mean age 66.2+-9.9yr, M:F= 1.55:1) with initial endoscopic resections of colorectal adenomas and/or intramucosal carcinomas with repeated follow-up colonoscopys after at least one year interval (a median follow-up period 73.9 months). They were classified into 225 patients with no recurrent lesions during surveillance (group A) and 178 with subsequent resections of recurrent lesions (group B). The patients in group B were subclassified into 109 with recurrent non-advanced lesions (group B-1) and 69 with recurrent advanced lesions (larger than 10mm in size, adenoma with high grade dysplasia or carcinoma) (group B-2). The number, maximum size, location, configulation, histology of colorectal tumors in initial resections were statistically compared with each other groups.
RESULTS: The mean number of lesions at initial resection in group A,B,B-1, and B-2 were 1.38, 1.94, 1.95, and 1.93, respectively. Many more lesions were resected in group B than group A ($p<0.001$), although no difference between group B-1 and B-2. The size of lesions in group A,B,B-1, and B-2 were 8.46mm, 9.41mm, 9.18mm, and 9.61mm, respectively. Larger lesions were resected in group B than group A ($p<0.05$), although no difference between group B-1 and B-2. The location of lesions in group A and B were 58.2%, 48.9% in left-sided, 28.9%, 23.6% in right-sided, and 12.9%, 27.5% in bilateral, respectively. Right-side shift in group B comapred to group A was observed ($p<0.005$), although no difference between group B-1 and B-2. The configulation of lesions in group A and B were 65.5%, 58.1% (sessile), 19.8%, 30.3% (pedunculated), 8.5%, 7.1% (LST), and 6.2%, 4.5% (flat), respectively. Pedunculated lesions were more frequent in group B than group A ($p<0.05$), although no difference between group B-1 and B-2. High-grade adenomas or carcinomas in the resected lesions were found 27.6%, 36.0%, 29.4%, and 43.5% in group A, B, B-1, and B-2, respectively. The statistical difference was observed between group B-1 and B-2 ($p<0.05$).
CONCLUSION: Increasing number, increasing size, right-sided location, and pedunculated shape of lesions at initial colonoscopies were the risk factors associated with recurrent lesions during surveillance. In contrast advanced pathology at initial colonoscopies were the risk factors for recurrent advanced lesions.
Disclosure of Interest: None Declared
Keywords: Colorectal adenoma, surveillance colonoscopy

P1528 CZECH COLORECTAL CANCER SCREENING PROGRAM AT THE POINT OF SWITCH TO THE POPULATION BASED PROGRAM – FEASIBILITY STUDY

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INTRODUCTION: The opportunistic National Colorectal Cancer (CRC) Screening Program in the Czech Republic (3.8 million inhabitants aged over 50) was introduced in 2000. To asymptomatic individuals aged 50 – 54, the annual fecal occult blood test (FOBT) is offered, followed by FOBT+ colonoscopy, if positive. At age of 55, there is a choice of either FOBT biannually or screening colonoscopy in 10 years interval. Since the beginning of 2013 only immunochemical FOBT (FIT) is recommended. The participation of target population has reached the 25.0% level in year 2011. But according to results of preventive colonoscopies performed in years 2011 – 2012 it seems that this kind of program settings has reached its maximum.
AIMS&METHODS: Feasibility study of switch to population based program has been performed, concerning the colonoscopy capacity
RESULTS: In 2011, there have been 528,476 FOBTs performed. Because of 6.1% FOBT positivity, 32,237 patients have been indicated for colonoscopy. The nationwide network of 160 specialized endoscopic units (Centers for Screening Colonoscopy) has been set. In case of target population participation increase by 10%, 20% and 30%, in each Center 20, 40 and 60 patients will be examined annually in addition. If FIT with lower cut-off level (and therefore higher positivity) will be used, the capacity of each Center needs to be increased significantly, as described in the table. In case of combination of highest participation increase (30%) and highest FOBT positivity (13%) expected, the need of 89,313 preventive colonoscopies per year will rise. Concerning the solution of this prediction, the important fact is that only 12% of all colonoscopies were performed within the CRC screening program, 20% were therapeutical and 68% diagnostic or follow-up examinations.

FOBT positivity	Number of FOBT+ colonoscopies	Increase	Colonoscopies per one Center per year in addition
6,1%	**32 237**	**0**	
7,0%	36 993	4 756	30
8,0%	42 278	10 041	63
9,0%	47 563	15 326	96
10,0%	52 848	20 611	129
11,0%	58 132	25 895	162
12,0%	63 417	31 180	195
13,0%	68 702	36 465	228

CONCLUSION: The switch to population based CRC screening program in the Czech Republic is feasible only if adequate FIT with reasonable cut-off level will be used and all colonoscopies will be indicated rationally
This project has been supported by the Czech Ministry of Health grant No. NT 13673
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Disclosure of Interest: None Declared
Keywords: colorectal cancer, Czech Republic, population based screening program

P1529 CERTIFIED COLON CANCER TREATMENT CENTERS IN BRANDENBURG/GERMANY: DO THEY PROVIDE BETTER QUALITY ?

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INTRODUCTION: A network of certified colon cancer treatment centers (CCCTC) have arisen in Germany (to date approx. 270 centers). The establishment of such a center is associated with a considerable effort for the hospital implementing it. For the first time an analysis is underway in Brandenburg, to determine if a change in the treatment quality can be detected.
AIMS&METHODS: Between 2009 and 2011 eight colon cancer treatment centers have been certified in Brandenburg. In 2011, 39% of 1427 patients with colon cancer operations were cured in these centers.
According to the index numbers of Onkozert, relevant treatment criteria are compared for four groups of clinics (CCCTC; hospitals with >50 operated colorectal carcinomas (CRC) and 20-49, respectively; other). The groups are reviewed with respect to the homogenicity of age and UICC-stage. In the cancer registry of Brandenburg about 95% of all CRC cases are registered.
RESULTS: In all 4 hospital groups one criteria was achieved without difference: 90% R0-resection of CRC in all primary cases. The demanded neoadjuvant chemotherapy treatment in rectal carcinomas UICC II/III has been administered to 80% of patients, but occurred more often in CCCTC and with a considerable difference between the individual departments. In smaller departments the share of adjuvant therapy is larger, so that multi-modal therapies are altogether administered similarly often. The quality of the TME-rectal preparation after Mercury do not differ in the department groups, but the documentation is suboptimal.
The quota of 80% of chemotherapy in patients with colon carcinoma UICC III was not reached in all the groups (CCCTC 56%, no chemotherapy because of justified reasons 33%). The index number of patients (95%) with 12 lymph nodes examined post-operative, is only reached by the CCCTC. The departments with 20-49 operations reached 80%. The 5-year survival rate for colorectal carcinoma UICC III lies with 69,2% slightly lower than the 70% demanded by the S3-guideline.
CONCLUSION: The portion of treated patients in CCCTC in Brandenburg is above the national average. A difference in treatment quality in 2011 for CCCTC can only be detected in the number of lymph nodes examined post-operative. The quality of CRC treatment has risen state wide.
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Disclosure of Interest: None Declared
Keywords: certified treatment centers in germany, Colorectal cancer treatment, quality control

P1530 FACTORS THAT PREDICT CLINICAL OUTCOMES TO PRUCALOPRIDE IN THE MANAGEMENT OF CHRONIC CONSTIPATION

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INTRODUCTION: Chronic constipation (CC) is a prevalent disorder with traditional management focussing on lifestyle measures and laxatives. Prucalopride (Resolor), a selective 5-HT_4 receptor agonist, has efficacy in treatment of CC (1,2). However, factors that predict clinical response are incompletely understood.
AIMS&METHODS: Our aims were to identify baseline factors, either physiological or psychological, that may predict positive clinical outcomes in patients taking prucalopride for CC. A single centre, prospective open label trial was undertaken in consecutive patients with CC, defined as less than 2 spontaneous complete bowel movements (SCBM) per week, who were commenced on prucalopride from November 2011-October 2012. Validated questionnaires were used to assess the severity of symptoms (patient assessment of constipation symptoms (PAC-SYM)), somatic symptoms (patient health questionnaire-12), anxiety/depression and the personality trait of neuroticism (big five inventory-neuroticism scale (BFI-N)). Patients were excluded if they did not wish to complete the questionnaires. Other investigations, such as colonic transit studies (CTS), were undertaken as clinically appropriate. At follow up, clinical response was defined as the proportion of patients achieving 3 or more SCBM per week.

RESULTS: 84 patients (82 female, mean age 50 years, range 18-83) had a mean SCBM per week of 1.6 (range 0.5-2). No patients were excluded. At a mean follow up of 4.8 weeks (range 4-8) 41/84 (48.8%) patients achieved clinical response. 7/84 (8.3%) did not tolerate treatment due to side effects. In an intention to treat analysis, mean SCBM per week increased from 1.6 to 3.2 (p=0.01) with mean PAC-SYM scores reducing from 27.7 to 20 (p=0.001). Logistic regression analysis demonstrated that BFI-N (odds ratio 8.7, 95% confidence interval (CI), 1.99-64, $p<0.01$) and slow transit constipation (STC) (odds ratio 1.4, 95% CI, 1.20-2.1, $p<0.01$) were independently associated with positive treatment outcomes.
CONCLUSION: Prucalopride is a useful, generally well tolerated, treatment for the management of CC in secondary care. These data suggest that efficacy could be enhanced by targeting patients with STC and in those who have higher neuroticism scores. Further work is now warranted to confirm these findings in a larger cohort of patients.
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2. Tack et al, Gut 2009
Disclosure of Interest: A. Farmer Lecture fee(s) from: Lecture fees from Shire (manufacturers of prucalopride), P. Harvey: None Declared, Q. Aziz: None Declared
Keywords: chronic constipation, prucalopride

P1531 INCREASED SMALL BOWEL AND COLONIC VOLUMES WITH IMPAIRED MOTILITY IN CHRONIC CONSTIPATION (CC): SIGNIFICANT DIFFERENCES BETWEEN SLOW TRANSIT CONSTIPATION (STC) AND IBS WITH CONSTIPATION (IBS-C) SHOWN BY NOVEL MRI TECHNIQUE

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INTRODUCTION: Many CC patients are dissatisfied with treatment reflecting our current inability to accurately target underlying mechanisms. Our aim was to exploit our new MRI techniques to noninvasively assess colonic function.
AIMS&METHODS: 29 patients (ages 18-68, F:M =27:2) with CC unresponsive to simple laxatives including 19 STC and 10 IBS-C were compared with 11 previously reported healthy volunteers (HV). Whole gut transit (WGT) was assessed from an MRI scan showing the distribution of 5 marker pills ingested 24 h before. A validated Transit Score (TS) was converted to WGT time in hours[1]. Patients then ingested 1 litre of macrogol (MCG) followed by hourly MRI scans for 4 h and scored bowel symptoms from 0-10 (none-severe). Colonic movements were assessed using a motility index based on colonic wall movement. Hypersensitivity index were scored using bloating symptom/ascending colon (AC) volume.
RESULTS: Mean (SD) See Table 1. Both STC and IBS-C had significantly greater WGT time than HV. STC but not IBS-C had greater fasting small bowel water content (SBWC) and AC volumes and reduced motility index 2 h after MCG ingestion than HV. Furthermore STC showed impaired response to MCG with longer time to first bowel movement, reduced stool frequency on study day, greater distension of the colon and reduced motility index compared with IBS-C and HV groups. The hypersensitivity score at 2 h following MCG ingestion were higher in IBS-C compared to STC and HV.
Table1:

Mean (SD)	HV	IBS-C	STC	P value(1-way ANOVA), *=p<0.05 compared to HV, **=p<0.05 compared to IBS-C
WGT (hr)	30±25	64±38*	106±42*,**	<0.0001
SBWC (ml)	83±64	131±118	196±144*	0.0213
Fasting AC (ml)	193±84	215±75	330±94*,**	0.0002
AC volume at 2 hours following MCG ingestion (ml)	357±153	364±190	618±180*,**	0.0002
Motility index at 2 hours following MCG ingestion	80±48	72±46	29±37*,**	0.0054
Time to first bowel movement(min)	117±62	114±92	674±1130*,**	0.0027
Bowel frequency on study day	9±3	6±3	3±1*,**	0.0002
Hypersensitivity index (l^{-1})	6±5	22±16*	12±7*,**	0.0018

CONCLUSION: Despite similar symptoms STC differ from IBS-C showing impaired motility reflected in increased fasting SBWC and AC volumes and after MCG challenge, greater AC distension, more discomfort, lower motility and delayed bowel response. IBS-C colonic motility is similar to HV but IBS-C report more discomfort despite similar distension suggesting hypersensitivity.
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Keywords: constipation, Irritable bowel syndrome

P1532 HISTOPATHOLOGIC FEATURES OF SURGICAL SPECIMENS IN PATIENTS WITH CHRONIC INTESTINAL PSEUDO-OBSTRUCTION IN JAPANESE POPULATION

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INTRODUCTION: Chronic intestinal pseudo-obstruction (CIPO) is an intractable disease in which clinical symptoms of intestinal obstruction appear without any mechanical cause. According to the diagnostic criteria, diagnosis is based on typical clinical manifestations, radiological evidence of distended bowel loops with air-fluid levels, and exclusion of any organic obstruction of the gut lumen. Although not mandatory, highlighting the pathologic abnormalities (i.e. myopathy, neuropathy, mesenchymopathy) is also an essential clue for diagnosis and understanding the mechanism of this intractable disease. However, no histopathological diagnostic algorithm has been established. The aim of our study is to clarify the proportion of each disease type using immunohistochemistry and propose the algorithm most effective for the classification of each subtype.
AIMS&METHODS: Thirty-two patients with a prior diagnosis of CIPO, 9 males and 23 females, mean age of 46.2 (15 to 75) years at diagnosis and 50.2 (19 to 75) years at surgery, with available full-thickness biopsy (FTB) samples were enrolled in this study. All specimens were stained with hematoxylin and eosin (HE), and a systematic immunohistochemical study, using smooth muscle α-actin (SMAA), HuC/D antibody, and CD117 (c-kit) antibody, was performed with reference to previous studies. Absence of expression on the muscularis propria was considered to be an abnormal finding in SMAA staining. Neuropathy was defined as a pathologic defect in both ganglia and ganglion cells. ICC abnormality (mesenchymopathy) was defined as a severe defect or a total absence of ICC network. The proportion of each subtype and overlap ratio are calculated.
RESULTS: Of all the 32 patients, myopathy was observed in 10 patients (31.3%), neuropathy in 17 patients (53.1%), and mesenchymopathy in 10 patients (31.3%). In 17 neuropathy patients, 4 patients also showed myopathy and 3 patients showed mesenchymopathy. No overlap was observed between myopathy and mesenchymopathy.
CONCLUSION: This is the first study to clarify the proportion of each disease subtype using systemic immunohistochemistry. Hu C/D and CD117 immunostaining unveiled undetected abnormalities on standard histology in 83% of cases. To obtain efficient differential diagnosis, Hu C/D staining should be performed at first to diagnose neuropathy. After the exclusion of neuropathy, CD117 staining should be conducted to diagnose mesenchymopathy. Because of no overlap between myopathy and mesenchymopathy, the rest are to be diagnosed as myopathy.
Disclosure of Interest: None Declared
Keywords: CIPO, full-thickness biopsy, imunohistochemistry

P1533 PERIPHERAL TRANSCUTANEOUS NEUROMODULATION IN THE TREATMENT OF IDIOPATHIC FUNCTIONAL CONSTIPATION: PRELIMINARY RESULTS OF A PILOT STUDY

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INTRODUCTION: Transcutaneous tibial nerve stimulation is a possible alternative to sacral nerve stimulation. It is non-invasive, cheap and well tolerated.
AIMS&METHODS: The aim of the study was to assess the efficiency of posterior tibial nerve (PTN) transcutaneous electrical nerve stimulation (TENS) in the treatment of idiopathic functional constipation.
This prospective study assessed 30 patients (26 women; mean age 57±17 years) with functional idiopathic constipation, resistant to maximal therapy, treated with TENS. TENS was done on PTN route, with self-adhesive electrodes 2 times a week for 6 weeks. One session lasted for 30 minutes. Number of the bowel movements per 2 weeks was the primary outcome. KESS (Knowles – Eccersley-Scott Symptom scoring system) constipation score, laxatives, suppositories and enemas used as well as Gastrointestinal Quality of Life Index (GIQLI) was evaluated pre- and post-treatment. Anorectal physiologic studies and colonic transit time were also performed in each patient.
RESULTS: After 6 weeks 14 patients (46.6 %) had a $\geq$ 50% increase in stool frequency and reported a significant symptomatic improvement. Overall two week stool frequency increased from 4.37 ± 2.44 pre-treatment to 7.63 ± 3.76 post-treatment ($p<0.001$) and the use of laxatives decreased ($p<0.05$). KESS constipation score improved significantly ($p<0.001$) after the treatment.
The effect was seen in 3 (33%) of 9 patients with slow transit constipation. Colonic transit had normalized in 1 patient after the treatment. Four patients (36%) of 11 with functional obstructive defecation benefited from treatment. The best results were observed in normal transit constipation group – the effect was seen in 7 out of 9 patients (77 %). Slow colonic transit together with dyssinergic defecation was seen in 1 patient and there was no effect after the treatment.
There was a statistically significant improvement in all four GIQLI subscales. The score of symptom subscale increased from 51.7 ± 6.3 pre-treatment to 56.87 ± 7.46 post-treatment ($p<0.001$), emotion subscale - from 9.13 ± 4.49 to 11.57 ± 3.87 ($p=0.001$), physical functioning – from 15.8 ± 4.77 to 17.57 ± 4.49

(p=0.006) and social functioning subscale – from 13.1 ± 2.48 to 13.4 ± 2.42 (p= 0.039).

CONCLUSION: The first results of this study are encouraging. Posterior tibial nerve transcutaneous electrical stimulation may be a new and easy-to-use therapeutic option to treat functional idiopathic constipation.

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Disclosure of Interest: None Declared

Keywords: constipation, tibial nerve stimulation

P1534 ENTEROPATHY IN PATIENTS WITH DIABETES MELLITUS TYPE 2: THE ROLE OF ENDOTHELIAL DYSFUNCTION AND LIPID PEROXYDATION

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INTRODUCTION: The problem of treatment patients with diabetes mellitus (DM) type 2 is caused by the high frequency of comorbid diseases that potentiate the polysystemic risk of complications, including the gastro-intestinal tract (GIT). The formation and progression of enteropathy on the background of the insulin-independent DM are associated with the combination of injuring factors, first of all, intestinal dysbiosis and diabetic autonomic neuropathy with the development of gastrointestinal motor-evacuation function dyscoordination. However, some pathogenetic mechanisms of DM type 2 and enteropathy combinations are studied insufficiently.

AIMS&METHODS: The aim was to determine the endothelial dysfunction role in the enteropathy development in DM type 2 patients.

Materials and methods. The study involved 74 enteropathy patients with DM type 2, including 41 (55.4%) women, 33 (44.6%) men, the mean age 56.4 ± 9.8 years and the duration of DM type 2 was 7-10 years. The DM type 2 was in subcompensation phase: the level of HbA1c ≤7.5% without ketoacidosis. To correct carbohydrate metabolism patients received combined glucose-lowering therapy. The level of nitrite, the total nitric oxide synthase (NO-synthase) activity, the malon dialdehyde (MDA) and the catalase were determined in the blood serum.

The enteropathy with the obstipation syndrome was diagnosed in 49 (66.2%) patients with DM (group I); with the diarrhea syndrome – in 25 (33.8%) (group II).

RESULTS: The imbalance of the free radicals generation and their inactivation was noticed in patients with DM type 2 in combination with enteropathy: increased concentration of the MDA in groups I and II in 1.2 and 1.4 times respectively, while reducing the catalase activity in 1.3 times ($p<0.05$). The reduction of the nitrite concentration in 1.48 times in blood serum of group II patients was detected on the background of increased in 1.6 times ($p<0.05$) total NO-synthase activity, with a tendency to change these parameters in patients of group I. The increase in the total production of NO-synthase, primarily inducible, promotes the high-power NO release, with its metabolism in an aggressive free radical – peroxynitrite, which has a direct damaging effect on the organism.

CONCLUSION: DM type 2 associated with the reduction of endothelial NO-synthase, leading to a decrease production of NO in the vascular endothelium, including the intestinal mucosa, which can be considered as a risk factor for enteropathy. The maximum lipid peroxydation processes activity and endothelial dysfunction in DM type 2 is noticed on the background of enteropathy proceeding with the diarrhea syndrome.

Disclosure of Interest: None Declared

Keywords: efficacy, enteropathy, diabetes mellitus type 2, pathogenesis, diarrhea syndrome, endothelial dysfunction, lipid peroxydation

P1535 NALOXEGOL SYMPTOM RESPONDER RATES IN PATIENTS WITH OPIOID-INDUCED CONSTIPATION: RESULTS FROM 2 PROSPECTIVE, RANDOMIZED, CONTROLLED TRIALS

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INTRODUCTION: Opioid-induced constipation (OIC), a side effect associated with chronic use of opioid analgesics for pain management, is characterized by straining, hard stools, and incomplete evacuation of stool. The objective of this analysis was to examine the efficacy of the peripherally acting, μ-opioid receptor antagonist naloxegol (NGL) in OIC patients using multiple OIC response criteria.

AIMS&METHODS: Two phase 3 randomized, double-blind, 12-week studies (KODIAC-04 [K04, NCT01309841] and KODIAC-05 [K05, NCT01323790]) were conducted. Oral NGL (12.5 mg, 25 mg) or placebo was given once daily to outpatients with noncancer pain and OIC. OIC symptom data were further analyzed in patients who had an NGL treatment response (primary endpoint), defined as ≥3 spontaneous bowel movements [SBMs]/wk with ≥1 SBM/wk increase over baseline for ≥9 of 12 wks and ≥3 of the last 4 wks of treatment. A pre-specified analysis of NGL symptom responders was defined as those who met the above criteria plus additional symptom improvement criteria (improvement and no worsening from baseline) in ≥1 of the following: straining score by ≥0.5 point; Bristol Stool Scale score by ≥1 point; number of days with complete SBM by ≥1 day). Differences between treatment groups in each study were analyzed by the Cochran Mantel-Haenszel test stratified by response to laxatives at baseline.

RESULTS: The NGL 25-mg group showed an improvement in the primary endpoint compared to placebo in both studies (K04, $P=0.001$; K05, $P=0.021$) with improvements maintained when symptoms were incorporated into response (K04, $P=0.003$; K05, $P=0.006$, respectively). For NGL 12.5 mg compared to placebo, significance for the primary endpoint was seen in K04 ($P=0.015$) but not K05 ($P=0.202$), and response incorporating symptoms was $P>0.05$ in both studies.

Table. Naloxegol Response Rates for Weeks 1–12 in Patients With Response as per SBMs vs SBMs + Symptoms

	Number (%) of Patients Responding			
	K04		K05	
Treatment Group	Response: SBMs	Response: SBMs + Symptoms	Response: SBMs*	Response: SBMs + Symptoms*
Placebo	63 (29.4)†	54 (25.2)†	68 (29.3)	53 (22.8)
12.5 mg	87 (40.8)‡§	71 (33.3)‡	81 (34.9)	65 (28.0)
25 mg	95 (44.4)†§	83 (38.8)†§	92 (39.7)§	80 (34.5)§

*n=232; †n=214; ‡n=213; §$P<0.025$ vs placebo.

CONCLUSION: When using a stringent definition of treatment response that incorporates SBM frequency and symptom improvement criteria, NGL 25-mg response rates were higher versus placebo ($P<0.01$) in both studies.

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Keywords: naloxegol, opioid-induced constipation, opioids, peripherally acting mu-opioid receptor antagonist, responder analysis, symptoms

P1536 POLYETHYLENE GLYCOL SHOULD BE USED IN PREFERENCE TO LACTULOSE IN THE TREATMENT OF CHRONIC CONSTIPATION

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INTRODUCTION: Constipation is a common clinical problem. Lactulose and Polyethylene Glycol (PEG) are both commonly used osmotic laxatives that have been shown to be effective and safe treatments for chronic constipation. However, there is no definitive data as to which provides the best treatment.

AIMS&METHODS: To identify and review all relevant data in order to determine whether Lactulose or Polyethylene Glycol is more effective at treating chronic constipation and faecal impaction.

We searched the MEDLINE, EMBASE and CINAHL databases, and the Cochrane Central Register of Controlled Trials for all randomised controlled trials (RCTs) comparing the use of lactulose and polyethylene glycol in the management of faecal impaction and chronic constipation.

Studies were included if they were randomised controlled trials which compared lactulose with polyethylene glycol in the management of chronic constipation.

Data on study methods, participants, interventions used and outcomes measured was extracted from each study. Data was entered into the Cochrane Review Manager software (RevMan 5.1) and analysed using Cochrane MetaView.

RESULTS: In the present meta-analysis, we considered for the first time all twelve randomised controlled trials so far performed.

The twelve trials enrolled a total of 1046 participants and were conducted between 1997 and 2012. The trials were conducted in seven different countries. Participant age ranged from 3 months to 70 years. Adults only were recruited for 4 studies. Six trials reported stool frequency per week.

Singularly taken, all showed that PEG resulted in a higher stool frequency per week when compared with Lactulose. Three trials reported form of stool on the Bristol Stool Scale, all reported a higher Bristol Stool Score when using PEG compared with lactulose (softer stool). Four trials reported relief of abdominal pain. Two favoured PEG in this outcome; one found Lactulose and PEG to be comparable in this outcome. Three trials reported on use of additional products, all favoured PEG as requiring less use of additional products.

CONCLUSION: The findings of our work indicate that Polyethylene glycol is better than lactulose in outcomes of stool frequency per week, form of stool, relief of abdominal pain and the need for additional products. On subgroup analysis, this is seen in both adults and children, except for relief of abdominal pain. Polyethylene Glycol should be used in preference to Lactulose in the treatment of Chronic Constipation.

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Keywords: constipation, medical treatment

P1537 HOW SAFE IS PRUCALOPRIDE FOR THE TREATMENT OF CHRONIC CONSTIPATION? A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Available therapies for chronic constipation (CC) have limited efficacy. Gastrointestinal prokinetics represent an attractive option, but both cisapride and tegaserod, the two agents with proved efficacy in CC, have been withdrawn because of cardiac adverse events. Prucalopride is the first selective, high-affinity 5-HT_4 agonist, without any significant activity towards other (5-HT and non 5-HT) receptors or channels (e.g. hERG) at the therapeutic doses.
AIMS&METHODS: To perform a systematic review and meta-analysis of the large clinical trials using prucalopride to treat patients affected by CC in order to assess its safety. MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials as well as abstracts from the major American, European and Asian meetings were searched up to November 2012. Large ($\geq$ 250 patients) randomized controlled trials (RCTs) in adult patients with CC, treated with prucalopride, were included. Risk of bias for RCTs was assessed as described in the Cochrane handbook. Relative risks (with 95% CI) were computed using a random effects model in order to provide a more conservative estimate. The outcomes assessed were adverse events, drop-outs due to adverse events as well as Increase of QTc > 450 ms from baseline at week 12. Results were analyzed only if, for each variable considered, data were available from at least 3 RCTs.
RESULTS: Five studies, comparing different doses of prucalopride to placebo, were identified. They included more than 2500 patients, most (up to 92.5 %) of whom were female. All studies were at low risks of bias. The results are shown in Table 1.

	Prucalopride 2 mg daily versus Placebo	Prucalopride 4 mg daily versus Placebo	Prucalopride 4 mg daily versus 2 mg daily
Adverse Events during the 12 weeks of treatment	RR: 1.21 (95% CI: 1.06 to 1.37)	RR: 1.12 (95% CI: 1.04 to 1.19)	RR: 0.98 (95% CI: 0.92 to 1.04)
Drop-Out due to Adverse Events during the 12 weeks of treatment	RR: 1.81 (95% CI: 0.82 to 4.02)	RR: 2.53 (95% CI: 1.61 to 3.96)	RR: 1.61 (95% CI: 0.84 to 3.09)
Increase of QTcF > 450 ms from baseline at week 12	RR: 0.77 (95% CI: 0.41 to 1.43)	RR: 0.59 (95% CI: 0.07 to 4.62)	RR: 0.77 (95% CI: 0.12 to 4.59)
Increase of QTcB > 450 ms from baseline at week 12	RR: 0.88 (95% CI: 0.61 to 1.27)	RR: 0.93 (95% CI: 0.40 to 2.16)	RR: 0.93 (95% CI: 0.43 to 1.99)

CONCLUSION: At the recommended therapeutic doses (2 mg daily), prucalopride is safe for treating CC. The most frequently reported adverse effects were headache and GI events, which occurred mainly on the first day(s) of treatment. Furthermore, there were no significant changes in QT_c interval even when the 4 mg dose was compared to placebo.
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Keywords: chronic constipation, prucalopride, treatment

P1538 HOW EFFECTIVE IS PRUCALOPRIDE FOR THE TREATMENT OF CHRONIC CONSTIPATION? A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: Chronic constipation (CC) is a challenging condition that impairs quality of life and, because of its high prevalence and chronicity, consumes significant healthcare resources. Prucalopride is the first selective, high-affinity 5-HT_4 agonist, with a predominantly enterokinetic effect, translating into a significant clinical efficacy.
AIMS&METHODS: To assess the efficacy of prucalopride to treat patients affected by CC performing a systematic review and meta-analysis. MEDLINE, EMBASE, the CCRCT as well as abstracts from the major American, European and Asian meetings were searched up to November 2012. Outcome assessed are shown in Table 1. Outcomes were measured as Relative Risk of improving with prucalopride or as Raw Mean Difference (RMD), both computed using a random effects model in order to provide a more conservative estimate. When I2 statistic was > 25%, heterogeneity between studies was considered significant.
RESULTS: Five studies, comparing different doses of prucalopride to placebo, were identified. They included more than 2500 patients, most of whom were female. The results are shown in Table below.
CONCLUSION: • Prucalopride is effective for treating CC and also improves significantly the quality of life.
• The two regimens tested (i.e. 2 mg and 4 mg daily) provide a similar clinical benefit, with no evidence of dose-response effect.
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Table: P1538

	Pru 2 mg daily vs. Placebo	Pru 4 mg daily vs. Placebo	Pru 4 mg daily vs. Pru 2 mg daily
Pts with ≥3 SCBMs at week 4	RR: 2.21 (95% CI: 1.68 to 2.88)	RR: 2.34 (95% CI: 1.53 to 3.56)	RR: 1.18 (95% CI: 0.73 to 1.77)
Pts with ≥3 SCBMs at week 12	RR: 2.45 (95% CI: 1.95 to 3.08)	RR: 2.23 (95% CI: 1.73 to 2.88)	RR: 1.01 (95% CI: 0.83 to 1.22)
Pts with ≥1 SCBMs at week 12	RR: 1.82 (95% CI: 1.59 to 2.08)	RR: 1.78 (95% CI: 1.51 to 2.09)	RR: 1.04 (95% CI: 0.91 to 1.17)
Pts with ≥1 SBMs at week 12	RR: 1.72 (95% CI: 1.57 to 1.87)	RR: 1.76 (95% CI: 1.56 to 1.96)	RR: 1.02 (95% CI: 0.89 to 1.16)
Pts rating their treatment as extremely or quite a bit effective at week 12	RR: 2.23 (95% CI: 1.66 to 2.99)	RR: 1.87 (95% CI: 1.53 to 2.30)	RR: 0.98 (95% CI: 0.83 to 1.42)
Improvement ≥1 PAC-SYM at week 12	RR: 1.78 (95% CI: 1.48 to 2.14)	RR: 1.53 (95% CI: 1.11 to 2.10)	RR: 0.92 (95% CI: 0.72 to 1.17)
Number of bisacodyl tablets taken at week 12 (RMD)	-8.25 (95% CI: -11.66 to -4.84)	-9.11 (95% CI: -12.24 to -5.98)	-0.12 (95% CI: -2.34 to 2.10)
Number of enemas taken at week 12 (RMD)	-0.50 (95% CI: -0.76 to -0.24)	-0.50 (95% CI: -0.86 to -0.19)	0.01 (95% CI: -0.21 to 0.24)

Disclosure of Interest: L. Gatta: None Declared, R. Kerstens Other: employee of Shire-Movetis and own stock in Shire, C. Scarpignato Other: Consultancy for: Shire
Keywords: chronic constipation, Meta-analysis, prucalopride, treatment

P1539 SOLITARY RECTAL ULCER SYNDROME: THE ROLE OF ANORECTAL PHYSIOLOGY TESTS IN REFRACTORY CASES

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INTRODUCTION: Since physiology of the solitary rectal ulcer syndrome (SRUS) is not known properly, a complete success does not attained. However; it is argued that success may be obtained using biofeedback treatment the effectiveness of which has been proven in functional anorectal disorders. The aim of the study was to examine the correlation between clinical and demographic characteristics and anorectal physiology tests among the patients diagnosed as SRUS in a tertiary referral center.
AIMS&METHODS: 18 cases diagnosed as SRUS were included in the study through the results of colonoscopic and histopathological examinations. Demographic data regarding age, sex, medical and operational history, rectal bleeding, rectal pain and defecation frequency and type of stool (Bristol Stool Scale) were collected. Anorectal manometry, balloon expulsion and rectal sensitivity tests were performed.
RESULTS: 62% of the cases were women (11/18), mean age was 41±14 (18-70) years. 17 cases (94%) had rectal bleeding. All of the cases described one or more defecation complaints such as incomplete evacuation, excessive straining or assistance with finger as well as unsuccessful medical treatment. Seven cases had unsuccessful operation due to the SRUS diagnosis. Fourteen cases (77%) were diagnosed as functional constipation according to Rome III criteria. According to Bristol Stool Scale; it was found out that 9 of the cases (50%) had type 1 stool, 5 cases (27%) had type 3-4 stool and ineterestingly 4 cases had type 6-7 stool without any laxative medication. The anorectal manometry demonstrated that 11 cases (61%) had dyssynergia. Eleven cases (61%) presented prolonged balloon expulsion time. Rectal sensitivity decreased in 4 (22%), increased in 4 (22%) and was normal in 10 of the cases (56%). Anal canal resting pressure was low in 3 cases (16%) while the rest was normal. There was no difference among those cases in whom dyssynergic defecation compared to normal defecation patterns in terms of gender (p=0.08) whereas it was seen that cases with dyssynergic defecation were older (46±9 vs 32±15) (0.04).
CONCLUSION: It was proved that anorectal coordination disorder was accompanied by mostly SRUS diagnosed with clinical and anorectal physiology tests. It was suggested that anorectal physiology worsened as disease-age increased due to the fact that cases with dyssynergic defecation were older than those cases with normal defecation patterns. Performing anorectal physiology tests at the time of diagnosis for SRUS may help uncover underlying anorectal coordination disorder and may correct pathology of the disease using biofeedback method.
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Disclosure of Interest: None Declared
Keywords: anorectal manometry, Rectal Ulcer

P1540 PATIENT PERSPECTIVE ON CONSTIPATION'S CHARACTERISTICS, IMPACT ON QUALITY OF LIFE AND FACTORS AFFECTING TREATMENT CHOICE. AN INTERNATIONAL INTERNET SURVEY

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INTRODUCTION: Constipation is a common gastrointestinal disorder which is often chronic and associated with an impaired quality of life (QoL). Laxatives are a treatment of choice after failure of lifestyle and dietary changes. However different laxatives can be used and factors affecting the choice of laxative are poorly studied.
AIMS&METHODS: The objective of this survey was to assess the characteristics of the patients' constipation, impact on QoL and factors associated with laxative choice.
In December 2011, a market research survey was conducted by Norgine Ltd in 9 European countries, Australia and South Africa. Participants >18 years who had been using laxatives (medicinal or natural product) in the last year answered 30 questions, describing the characteristics of the constipation, impact on quality of life and factors affecting choice of laxatives.
RESULTS: 766 respondents were surveyed (women 73%, 52% in the 25–44 years age group). Constipation duration was >6 months (e.g. chronic) in 78% and >5 years in 41%. It was judged severe (with faecal impaction) in 18% and moderate but persistent in 34%. An impact on QoL was reported in 98% (large or very large in 36%), on physical wellbeing (80%), diet (55%), appetite (41%), sleep (35%), concentration at work (32%) and social life (31%). Respondents were most commonly ''irritated'' by their constipation (51%), followed by ''embarrassed'' (41%), ''stressed'' and ''concerned'' both in 38%. Overall, the most commonly used laxatives were herbal/natural product 44% followed by Macrogols 42% (PEG+electrolytes (PEG+E-Movicol®) 24%, others 18%), stimulant laxatives 37%, fibers 34%, lactulose 25% and others 11%.
One third of respondents had been taking their current laxative for more than one year. In respondents taking PEG+E, two thirds only took it when they had symptoms, and 60% took one sachet or less per day. Reasons for switching were most commonly because a perceived lack or loss of efficacy 47%, followed by doctors recommendation in 34% and side effects in 23%.
The most important qualities sought in a laxative were that it works well (39%) and quickly (27%), with limited side-effects (32%).
CONCLUSION: The results of this international survey show that the severity of constipation impacts patients' QoL. Herbal/natural products and Macrogols were the most used treatments. The determinants in laxative choice were efficacy, propensity for side effects and medical recommendation.
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Disclosure of Interest: P. Jouet Other: Travel costs, UEGW registration costs, M. Bellini: None Declared, M. Halphen Other: Norgine employee, J. M. Sabate: None Declared
Keywords: constipation, laxative, quality of life, survey

P1541 HOME ELECTRIC STIMULATION IS BETTER THAN STANDARDIZED BIOFEEDBACK TRAINING FOR WOMEN WITH FECAL INCONTINENCE

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INTRODUCTION: Home electric stimulation (HES) and standardized biofeedback training (SBT) are effective treatments for fecal incontinence (FI). Studies that randomized incontinent women to treatment by these 2 methods only are missing.
AIMS&METHODS: To compare effectiveness of HES and SBT in women suffering from FI.
Consecutive women suffering from FI were randomized to HES or SBT only for a period of 6 weeks. Patients were evaluated by a questionnaire regarding their demographics, medical and childbearing history. Subjective measures of outcome included the Fecal Incontinence Grading Scale (FIGS), quality of life questionnaire (SF-36) and a diary for the assessment of bowel movements before and after treatment. Objective measure of outcome included the pelvic floor muscle (PEM) contraction assessed by surface electromyography (EMG).
RESULTS: A total of 36 women with FI were randomized to HES or SBT (18 in each treatment group). Groups were matched by mean age: 65.5±13.5 years, mean BMI (kg/m^2): 26.2±3.9, mean disease duration: 1.42±0.8 yrs, mean number of births: 2.7±1.3 and reports of obstetric trauma (25%). Only patients that received HES reported a significant improvement of FIGS (p=0.0015) and a significant drop in the number of leaked solid and liquid stool (p=0.012, p= 0.07, respectively). SF-36 scores were not affected significantly by treatment in both groups. A significant improvement of PEM contraction was achieved in 89 % of patients from both groups.
CONCLUSION: Home electric stimulation only was found to be more efficient than standardized biofeedback training only if assessed by both subjective and objective measures.
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Disclosure of Interest: None Declared
Keywords: Biofeedback Training, Home Electric Stimulation

P1542 EFFICACY AND SAFETY OF PRUCALOPRIDE IN THE TREATMENT OF CHRONIC CONSTIPATION: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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INTRODUCTION: Chronic constipation is a very common functional gastrointestinal disorder which can be associated with significant impairments in quality of life for some people with the condition. Its management has, traditionally, been based on dietary and lifestyle changes and the use of a variety of laxative agents. Prucalopride, appears to be highly selective for the serotonin 5-HT4 receptor and is, therefore, a potent stimulator of gut motility.
AIMS&METHODS: The main objective of this meta-analysis is to test the clinical efficacy and safety of the selective and high affinity serotonin-4 (5-HT4) receptor agonist prucalopride in the management of chronic constipation. Articles were identified through MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials and internet electronic databases. We searched abstracts, lists of review articles and retrieved studies by manual and internet search strategies. Two reviewers independently assessed trial quality and extracted data. Analyses were performed using the Mantel-Haenszel test. Random effects models were used when heterogeneity was noted.
RESULTS: A total of six (6) studies with total sample size of 3616 patients were included. The outcome in the improvement of mean number of stools per week showed that there was no significant difference between the prucalopride and placebo group (OR 0.78; 95%CI 0.96 to 2.53, *p* 0.38). However the overall effect leans toward the study treatment (prucalopride). The test for heterogeneity was not significant. The numbers of adverse events were more common with prucalopride than with placebo (RR 1.22; 95% CI 1.14 to 1.32, p <0.00001).
CONCLUSION: Prucalopride has no significant effect compared to placebo for the treatment of chronic idiopathic constipation. The drug appeared safe, but adverse events were significantly common, particularly headache, nausea and diarrhea, and patients should be warned of these potential side effects of treatment.
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Disclosure of Interest: None Declared
Keywords: constipation, prucalopride

P1543 PERINEAL RETRAINING FOR FECAL INCONTINENCE: INCREASING THE NUMBER OF SESSIONS RAISES THE CHANCE TO SUCCESS

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INTRODUCTION: Fecal incontinence (FI) is a frequent complaint that deeply affects quality of life (QoL). Perineal retraining (PR) may improve conservative treatment for FI. The best modalities of PR have to be determined to raise the chance to success in FI.
AIMS&METHODS: Our aims were to determine the number of PR sessions useful to improve FI and to identify clinical factors which could predict chance to achievement. We interested to patients who benefited from PR in a randomized assessor blinded clinical trial (the ORALIA trial) in 8 centers. In this study, patients were randomly assigned to standard conservative treatment (SC group) or to PR including biofeedback in addition to medical treatment. Patients in failure in the SC group benefited from PR in 2nd line. PR was performed in an outpatients setting according to optimized and standardized procedures based on 20 sessions of 30 mn within a 4-month period with 2 to 3 sessions per week for the 1st month and 1 to 2 per week thereafter. The physiotherapist tested anal squeeze by muscular testing at each session. Statistical analyses were performed in Statistical Analysis System software 9.2 (SAS Institute, NC).
RESULTS: 104 patients benefited from PR, as 1st line for 67 and 2nd line for 37. Data about all the 20 sessions were available for 62 patients (59%). Anal squeeze quality, cough reflex squeeze and capacity to differ stool evacuation were improved after 10 sessions and between 10 and 20 sessions ($p<0.001$) (Table).

	1st session	10th session	20th session
Squeeze quality: (n,%)			
Nothing	5 (8%)	0 (0%)	0 (0%)
Incomplete squeeze	42 (68%)	17 (28%)	10 (17%)
Complete squeeze	15 (24%)	45 (72%)	52 (83%)
Cough reflex squeeze (n,%)	19 (31%)	39 (63%)	52 (84%)
Capacity to differ stool evacuation (mn)	5.7±11.6	8.3±13.1	13.8±17.3

The following clinical factors were analyzed: age, sex, 1st or 2nd line PR, history of anorectal surgery, anal squeeze time and strength, FI incidents, Wexner score, QoL. Multivariate analysis failed to determine a clinical factor that could predict the chance to achieve FI improvement with PR.
CONCLUSION: There is a significant improvement between 1st and 10th and between 10th and 20th session of PR in FI. PR should not be stopped after 10 sessions even if there is no initial improvement. This study did not allow identifying predictive factors of success of PR in FI. Consequently, PR should be tried in any case of FI.
Disclosure of Interest: None Declared
Keywords: Biofeedback Training, fecal incontinence, ORALIA, perineal retraining

P1544 CLINICAL AND PATIENT RELATED RISK FACTORS ASSOCIATED WITH A PERSISTENT DISEASE COURSE IN NEW CHRONIC CONSTIPATION PATIENTS

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INTRODUCTION: Up to 90% of patients with constipation report symptoms on a long-term basis. However, the natural history may differ between patients and can be divided in a non-persistent and persistent disease course. Information on factors associated with the natural history of chronic constipation (CC) are scarce.
AIMS&METHODS: We aim to identify demographic and clinical factors associated with a persistent disease course in new CC patients. New CC patients were retrospectively identified and followed up in a Dutch health insurance database (~1.2 million subjects) between January 2005 and December 2010. Subjects with laxative prescriptions for a cumulative ≥90 days within a period of one year and/or with a Diagnosis Related Group (DRG) of chronic constipation were identified. Only subjects who met these criteria, with absence of CC in the preceding year, were regarded as *new* CC patients. Patients with colorectal cancer, irritable bowel syndrome or with less than one year of follow-up after CC diagnosis were excluded. A persistent disease course was defined as constant laxative use (without pauses of >90 days) until the end of follow-up. Others were defined as having non-persistent disease. Data on demographics, reimbursed prescriptions and DRGs were used to identify potential risk factors. Adjusted hazard ratios (HR) and 95% > confidence intervals (95% > CI) were estimated for potential risk factors using Cox proportional hazard models.
RESULTS: A total of 18,416 new CC patients were identified (mean age 64.0 ± 17.9, 64% female) of which 15% had persistent disease. Independent factors associated with an increased risk for persistent disease were older age (HR 2.10, 95% > CI 1.87-2.35 for >70 vs. <50 years), male gender (HR 1.29, 95% > CI 1.20-1.40) and the use of opioids (HR 1.51, 95% > CI 1.40-1.64) and psycholeptics (HR 1.17, 95% > CI 1.08-1.26). The use of calcium antagonists was associated with a decreased risk of persistent disease (HR 0.91, 95% > CI 0.84-0.99). Urbanization level, a non-Dutch nationality, the use of beta-blocking agents and antidepressants, and a diagnosis of hypothyroidism, Parkinson disease or multiple sclerosis were not associated with disease course, although non-Dutch older patients tended to have an increased risk for persistent disease (HR 1.20, 95% > CI 0.99-1.47).
CONCLUSION: Only a minority of new CC patients develops a persistent disease course, but, if present, it is associated with older age, male gender, and use of opioids and psycholeptic medication. Results of this study may help identifying CC patients who are at an increased risk of developing persistent disease.
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Disclosure of Interest: None Declared
Keywords: clinical characteristics, constipation, natural history, risk factors

P1545 A COMPARATIVE STUDY OF THREE-DIMENSION HIGH-RESOLUTION SYSTEM AND WATER-PERFUSION SYSTEM IN ANORECTAL MANOMETRY

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INTRODUCTION: The detailed differences of comprehensive motility parameters of anorectal function between the three-dimension high-resolution manometry (3D-HRM) and water-perfusion mamometry (WPM) were not clear.
AIMS&METHODS: To compare the characteristics between three-dimension high-resolution manometry (3D-HRM) and water-perfusion mamometry (WPM) in anorectal function evaluation.
63 subjects were enrolled in the study (46 chronic constipation patients and 17 healthy volunteers). All of them underwent anorectal manometry (ARM) by both 3D-HRM and WPM. WPM was performed using 8-channel water-perfusion catheter with side holes spaced at 1-cm interval and diameter of 4.7mm. 3D-HRM was performed using 256 (16*16)-channel solid-state catheter with diameter of 10mm, displaying in topographic and three-dimension form using analysis software. Measurements of anal sphincter pressure at rest, during voluntary contraction, during forced defecation, and rectal sensory thresholds were compared.
RESULTS: Anal sphincter and rectal pressures recorded by 3D-HRM tended to be higher (anal resting pressure: 94.8±26.3 vs 63.9±21.4mmHg, P=0.000; anal squeezing pressure: 218.3± 61.1 vs 174.5± 50.9mmHg, P=0.000; defecation anal pressure: 76.4±31.4 vs 44.5±20.1mmHg, P=0.000; defecation rectal pressure: 43.7±20.8 vs 35.1±20.4mmHg, P=0.033) and urge defecation thresholds tended to be lower (128.6±52.4 vs 157.7±73.5ml, P=0.017) than those recorded with WPM. The two methods showed to be significantly correlated in the aspects of anal resting pressure (r=0.575, P=0.000), anal squeezing pressure (r=0.610, P=0.000), defecation anal pressure (r=0.568, P=0.000), anal relax ratio (r=0.573, P=0.000), first defecation threshold (r=0.621, P=0.000), urge defecation threshold (r=0.595, P=0.000) and maximal tolerated threshold (r=0.663, P=0.000). Also, there were weak correlations in the length of high pressure zone (r=0.390, P=0.002) and defecation rectal pressure (r=0.419, P=0.002). However, there was no correlation in minimum relaxation volume (MRV) for rectal anal inhibitory reflex (RAIR) (r=0.156, P=0.255) between the two methods. 3D-HRM could find paradoxical puborectalis contraction during defecation, but WPM could not provide the message.
CONCLUSION: In addition to MRV, all pressure and sensory parameters were consistent between 3D-HRM and WPM, but 3D-HRM provided more detail information of anorectal anatomy.
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Disclosure of Interest: None Declared
Keywords: anorectal manometry, comparative study, three-dimension high-resolution manometry, water-perfusion mamometry

P1546 SHORT- AND LONG-TERM EFFICACY OF TREATMENT WITH TEMPERATURE-CONTROLLED RADIOFREQUENCY ENERGY (SECCA) IN PATIENTS WITH FAECAL INCONTINENCE

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INTRODUCTION: Controlled delivery of radio frequent energy (Secca) has been suggested as treatment for faecal incontinence (FI). The supposed mechanism of action of Secca is shrinkage and remodelling of the mechanical properties of the anorectum.

AIMS&METHODS: To evaluate the short- and long-term efficacy of Secca treatment for faecal incontinence (FI). Between 2005 and 2010, 31 patients who failed conservative management for FI received Secca at our outpatient clinic. FI was scored using the Vaizey score (VS). Follow up was performed after 6 months, 1 yr, 3 yrs, 5 yrs and 7 yrs. Anal sonography and anal manometry was performed at 3 months and compared with baseline. Using decreases in VS compared to baseline, patients were assessed as having a good clinical response (≥ 50% reduction in VS), a moderate clinical response (≥ 20- < 50% reduction) or no clinical response (< 20%). Initial response to Secca was measured at 6 months as having good or mild clinical response. Regarding long-term results, 7 respectively 10 patients were not yet available for 5 and 7 yr follow up. Impact of FI on experienced QOL was measured using the FIQL.
RESULTS: All 31 patients, (mean age 61 yrs, 30 females) received Secca. Mean length of FI was 10 yrs. Twenty-one patients (68%) had an anal sphincter defect. From baseline to 7 years follow up, mean VS was 18 (SD 3) at baseline, 14 (SD 4) at 6 months, 14 (SD 4) at 1 year, 14 (SD 4) at 3 years, 13 (SD 6) at 5 years, (for all $P < 0.001$) and 14 (SD 6) at 7 years, ($P=0.02$). During follow-up, 17/31 (55%), 13/31 (42%), 10/31 (32%), 6/23 (26%) and 4/13 (31%) of patients still experienced a good or a moderate clinical response. An achieved good or moderate clinical response was maintained up to 5 years, ($P < 0.001$), but lost statistical significance at 7 years of follow up, ($P=0.06$). No increases in anorectal pressure were found in any patients. FIQL scores coping and embarrassment temporarily improved (up to 6 months) in those with an initial response to Secca. No predictive factors for achieving success could be demonstrated.
CONCLUSION: Secca is a safe, minimally invasive procedure for FI. A good and moderate clinical response was achieved in 55% of patients after 6 months which decreased to 30% after 3 years and remained stable up to 7 years. No increased anal pressures or anorectal function alteration became apparent.
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Disclosure of Interest: None Declared
Keywords: fecal incontinence, radio frequent energy (Secca), treatment

P1547 ANAL INCONTINENCE, SEXUAL COMPLAINTS AND ANORECTAL FUNCTION IN PATIENTS WITH A THIRD DEGREE ANAL SPHINCTER RUPTURE: LONG TERM FOLLOW-UP

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INTRODUCTION: Anal incontinence (AI) affects activities of daily life and can have a devastating effect on the physical and emotional wellbeing. The primary cause of AI in women is vaginal delivery. With this study we aim to evaluate the long-term alteration of anorectal function in women after primary surgical repair of a third degree obstetrical anal sphincter injury (OASI) in relation to clinical outcome.
AIMS&METHODS: Women who suffered a third degree OASI between 1998 and 2008 in our hospital and underwent anorectal function evaluation (AFE) consisting of anal manometry and anal endosonography three months post-partum were included. These women were invited to participate in the present study by sending them standardized questionnaires regarding complaints of AI (Vaizey/Wexner), urine incontinence (UI) (ICIQ), sexual function (FSFI) and quality of life (QOL) (Rand-36) and were asked to undergo additional AFE.
RESULTS: Sixty-six women underwent AFE three months post-partum. With a mean OASI follow-up of 5.0 years (2.4-11.4), 40 women (61%) with a mean age of 38 years (SD 4.7), participated for follow up regarding complaints of AI and UI. Prevalence of AI was 63% (flatus), 50% (liquid stool) and 20% (solid stool). UI was present in 48% of women. Of these 40 women, 32 (80%) also returned questionnaires regarding QOL and sexual function. Overall sexual function was lower (total FSFI of 23) than the sexual dysfunction cut-off value of 26.55, ($P < 0.05$). Compared to control values, all FSFI subscales were lowest in women with larger OASI, ($P < 0.001$). Sixteen women (20%) underwent additional AFE. Women with combined internal anal sphincter (IAS) and external anal sphincter (EAS) injury ($n = 6$) reported more pronounced anal incontinence and had lower anal pressures than women with isolated EAS injury ($n = 10$), ($P < 0.05$). Mean maximal basal pressure (MBP) was 40 (SD 13) respectively 53 (SD 12) mmHg, and mean maximal squeeze pressure (MSP) was 25 (SD 11) respectively 39 (SD 13) mmHg, ($P=0.04$ for both MBP and MSP).
CONCLUSION: Women with a combined IAS and EAS defect had the most severe complaints and the lowest anal pressures. Special attention should be paid to women with these large combined anal sphincter defects, since anorectal function will deteriorate more and AI and sexual dysfunction are more prominent later in life.
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Disclosure of Interest: None Declared
Keywords: anal incontinence, anal manometry, anal ultrasound, obstetric labour complications, sexual symptoms, third degree anal sphincter rupture

P1548 CAN WE USE A SHORTER TEST PERIOD BEFORE DEFINITIVE SACRAL NEUROSTIMULATION FOR FECAL INCONTINENCE?

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INTRODUCTION: Sacral neuromodulation may be proposed for fecal incontinence after failure of medical treatment and biofeedback. A 3-week test period is usually proposed. The length of the test period is a compromise between the variability of soiling frequency and the risk of material-related infection
AIMS&METHODS: The purpose of this study was to present a week-by-week analysis of response during the screening period in order to determine whether early response is predictive of the final implantation decision
PATIENTS AND DESIGN: From May 2010 through July 2012, 12 patients completed an exploitable bowel-movement-soiling diary before and during the test period.
RESULTS: After one week, 50% of patients (6/12) had a 50% reduction in soiling frequency. This percentage reached 66.7% (8/12) at two weeks and 83.3% (10/12) at three weeks. Among those patients whose soiling frequency fell off rapidly, the decline was considerable (89% reduction) and remained so for the next two weeks (92% and 97% reduction). The decline was also considerable (83%) when the response took longer (2 or 3 weeks). Retention time for urgency episodes increased 5.4 [0:22.5] minutes the first week, 3.1 [-9:+9.5] the second week, and 16.3 [4.1:36] minutes the third week. Urgency frequency fell off by 1.4 [-5.3:+4.3] episodes per week the first week (22.2% reduction), 1 [-6.3:+6.7] the second week (26.4% reduction) and by 3.3 [-9.3:+1] the third week (59.6% reduction). There were no problems with infection
CONCLUSION: Rapid improvement in soiling frequency during the first screening week was sustained the next two weeks so that early implantation could be proposed in half of the patients without waiting for the end of the 3-week screening period.
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Disclosure of Interest: None Declared
Keywords: fecal incontinence, sacral neuromodulation, Screening test

P1549 SCREENING THE ANAL DYSPLASIA IN HIV-POSITIVE PATIENTS: HOW EFFICIENT IS HIGH-RESOLUTION ANOSCOPY?

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INTRODUCTION: Human immunodeficiency (HIV) and Papillomavirus (HPV) virus are major co factors of developing anal dysplasia. Annually anal screening is recommended in HIV positive subjects because of a high-risk of anal dysplasia. The high-resolution anoscopy (HRA) has been shown to improve the exploration of the anal mucosa by magnifying the macroscopic changes. It is recommended to patients presenting anal dysplasia on cytology (low or high grade squamous intra-epithelial lesion: LSIL or HSIL, and atypical squamous cell of undetermined significance: ASCUS). Its interest remains under debate in the anal screening of dysplasia. The aim of this study was to evaluate the HRA performances in HIV-positive patients with abnormal cytology, using biopsies on both identified lesions and normal mucosal appearance as a gold standard.
AIMS&METHODS: Between October 2010 and April 2013, 70 HIV-positive patients (M/F: 66/4, aged 47.6 ± 10.1years) with anal dysplasia on cytology underwent 107 HRA. The tinctorial and macroscopic aspects of the anal canal were used to characterize the abnormal areas: acetowhite, iodonegative, mucosal punctuations, warty raised, mosaic pattern, vascular abnormalities and miscellaneous. Biopsies were systematically made on both abnormal and normal areas.
RESULTS: Macroscopic lesions were associated to ASCUS in 14.4%, LSIL in 56.7% and HSIL in 28.4%. Histological anal intra-epithelial neoplasm (AIN) was more frequently observed in association to mucosal punctuations (48.1%), warty raised (55%) and mosaic pattern (50%). No statistical significance was observed in association with vascular abnormalities. Macroscopic lesions were associated to AIN in 34/55 (61.8%) and to high-grade AIN (AIN 2-3) in 21/55 (38.2%). Acetowhite & iodonegative areas were statistically associated to AIN in 20/46 (43.5%) & 18/46 (39.1%) respectively: both abnormalities were reported I, 11/46 (24%) of AIN 2-3. AIN lesions were observed in 6/42 (15%) of patients with normal tinctorial aspects, in 17/38 (44.7%) of those without macroscopic lesion and in 35/107 (32.7%) of normal areas (AIN 2-3 in 18/107 (16.8%)). As compared to histology, sensitivity and specificity of HAR were 34/51 (66.7%) & 10/27 (37%) to detect AIN and 21/51 (41.2%) & 17/27 (63%) to detect AIN 2-3 respectively.
CONCLUSION: A normal HRA doesn't rule out the presence of AIN. Both abnormal and normal areas have to be biopsied. This technique may be preferred to detect and to treat macroscopic changes rather than to screen dysplasia.
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Disclosure of Interest: None Declared
Keywords: anal dysplasia, high-resolution anoscopy, Human Immunodeficiency Virus

P1550 PROGRESS OR REGRESS? NATURAL HISTORY OF ANAL DYSPLASIA IN HIV-INFECTED PATIENTS.

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INTRODUCTION: Anal screening is justified by the high incidence of anal dysplasia and carcinoma in Human Immunodeficiency Virus (HIV) infected patients. High-grade anal intra-epithelial neoplasm (AIN) may progress to invasive cancer within a short period of time. The aim of our study was to assess the temporal change of dysplasia and to identify factors associated to a pejorative evolution.
AIMS&METHODS: Between October 2010 and April 2013, 176 HIV-positive patients (M/F: 165/11; aged 47.4 ± 10.6 years) were screened, using anal cytology. In case of abnormal findings (low or high grade squamous intra-epithelial lesion: LSIL or HSIL, and atypical squamous cell of undetermined significance: ASCUS), biopsies were performed to identified low or high-grade AIN (AIN 1 or AIN 2-3). Follow-up program was a 12-month interval in those with a normal cytology, a 3-to-6 month interval in case of abnormal histology (AIN 1 and AIN 2-3 respectively). The mean duration of follow-up was 41.2 ± 40.9 months.
RESULTS: Anal cytology at inclusion was normal cytology in 75 (43%), ASCUS in 30 (17%), LSIL in 52 (30%) & HSIL in 17 (9.6%). At the end of

follow-up, new HSIL or AIN 2-3 was reported in 35/159 (22%) patients: invasive cancer was encountered in 1/159 (0.6%). In contrast, 40/101 (39.6%) down-staged their initial anal status. Median period to reach high-grade dysplasia was 39.1 weeks (23.5-52.6, CI 95%) and period to regress was similar (33.9 weeks - 14.1-52.8, CI 95%). A previous Human Papillomavirus (HPV) infection ($p=0.02$), previous anal HSIL ($p<0.01$), endo-anal condylomas at inclusion ($p<0.01$), high-risk HPV infection ($p<0.0003$) and HPV 16 infection ($p<0.0001$) were associated to progression to high-grade dysplasia.
CONCLUSION: Almost one-third of HIV-positive patients develop high-grade dysplasia of the anal canal but dysplasia may also regress in a similar proportion. These features of natural history have to be taken into account in intervention studies.
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Disclosure of Interest: None Declared
Keywords: anal dysplasia, Human Immunodeficiency Virus

P1551 NOVEL MEASURES OF ANAL FUNCTION USING HIGH-RESOLUTION ANAL MANOMETRY (HRAM) OUTPERFORM CONVENTIONAL MANOMETRIC MEASURES IN FEMALE PATIENTS WITH FAECAL INCONTINENCE (FI)

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INTRODUCTION: Anal manometry is the most widely used investigation of function in patients with FI, however its impact on clinical management remains uncertain and evidence correlating findings with symptom severity are limited. The development of HRAM has enabled new analyses of manometric recordings with potential to provide better biomarkers of disease for treatment stratification and monitoring.
AIMS&METHODS: To develop and assess the utility of new derived measures of global anal sphincter function using HRAM, and to compare findings with conventional anorectal manometry (ARM) in female healthy volunteers (HV) and females with FI.
82 HV (median age 45 [18-68]) and 71 consecutive patients with FI (age 55 [22-81]; St Mark's FI score >5), underwent HRAM using a 12 channel solid-state catheter, and ARM at the same appointment. Data were collected using customized software (v9.1: MMS BV). New measures of resting tone, squeeze pressure and 30 sec endurance squeeze area (ESA.30 = an area under the curve calculation of pressure changes across the whole anal canal during prolonged squeeze) were determined using HRAM. Results from both techniques were correlated with St Mark's score using regression analysis. Data from HVs were used to derive normal ranges for new measures and their utility tested in patients with FI.
RESULTS: Normal ranges (5^{th}-95^{th} percentile) for anal resting pressure, maximum squeeze increment and ESA.30 using HRAM were 34-101 mmHg, 45-315 mmHg and 515-4795 mmHg.sec, respectively. New HRAM derived measures of squeeze pressure outperformed those of conventional ARM (Table 1A), with ESA.30 ($R^2=0.34$; $P<0.0001$) the best overall. Novel HRAM indices were better discriminators of abnormal sphincter function compared to conventional measures (Table 1B) with ESA.30 the best measure: LROC AUC = 0.87 (very good). Based on normal ranges, yields of positive test results in FI were much higher for HRAM than conventional ARM (conventional squeeze = 23% vs. HRAM ESA.30 = 55%).

1A - St Mark's FI score (all subjects)	R^2	*coeff (95% CI)*	*P*	
Conventional ARM max squeeze incr.	0.1	-2.2 (-3.5-0.83)	0.002	
HRAM max average anal squeeze incr.	0.31	-7.7 (-9.7- -5.7)	**0.0001**	
HRAM ESA.30	0.34	-111 (-137 - -85)	**0.0001**	
1B. FI vs. HV	R^2	*OR (95% CI)*	*P*	*LROC AUC*
Conventional ARM max squeeze incr.	0.07	0.98 (0.97-1.0)	0.023	0.68
HRAM max average anal squeeze incr.	0.29	0.98 (0.97-0.99)	**0.0001**	**0.84**
HRAM ESA.30 (mmHg)	0.32	0.998 (0.997-0.999)	**0.0001**	**0.87**

CONCLUSION: Derived measures of anal sphincter function using HRAM outperform conventional ARM measures and may provide better disease biomarkers.
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Disclosure of Interest: E. Carrington Other: Non financial collaboration with MMS B.V. for software development, E. Tangenberg Other: Employee of MMS B.V., A. Meek Other: Employee of MMS B.V., C. Knowles Other: Non financial collaboration with MMS B.V. for software development, S. M. Scott Other: Non financial collaboration with MMS B.V. for software development
Keywords: anal sphincter function, anorectal manometry, faecal incontinence, fecal incontinence, high resolution anal manometry

P1552 12 MONTH OUTCOME AND PATIENT SATISFACTION WITH STRUCTURED GASTROENTEROLOGICAL EVALUATION FOR CHRONIC GASTROINTESTINAL SYMPTOMS FOLLOWING PELVIC RADIOTHERAPY

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INTRODUCTION: 17000 patients are treated with pelvic radiotherapy annually in the UK.50% develop chronic GI symptoms.The structured approach to management used in this service evaluation has been shown to identify treatable diagnoses and improve symptoms in the short term. We report the first 12 month outcome data for the effect of structured GI evaluation on symptom burden and patient satisfaction.
AIMS&METHODS: 56 patients with GI symptoms$\geq$6 months after radical pelvic radiotherapy underwent structured GI assessment as part of a service evaluation. They were assessed using the following questionnaires:inflammatory bowel disease questionnaire(IBDQ);Vaizey incontinence questionnaire (VIQ); and the CTCAE pelvic symptom questionnaire.12 month assessments were compared to the previously reported baseline and 6 month assessments to determine if the improvement in symptoms was sustained. Patient satisfaction with the service was assessed at 12 months by an in-house questionnaire.
RESULTS: 40 patients(71%)completed the 12 month assessment and 37(66%)completed the patient satisfaction questionnaire. The initial statistically significant improvement in GI symptoms from baseline to 6 months in parallel to GI evaluation was sustained up to 12 months in all questionnaires(IBDQ $p=0.019$,IBDQB and CTCAE rectum bowel subset $p<0.0005$)except the VIQ($p=0.098$). There was also a clinically significant improvement as defined by an increase in IBDQ score of$\geq$0.5 points per question. Total IBDQ and IBDQB score increased by 25 and 11 points respectively between baseline and 12 months.97% of patients found the appointments convenient,97% felt their problems were understood;86% were satisfied with the outcome and 89% with the service. Dissatisfaction related to communication(n=3), travel(n=2)and ongoing symptoms(n=3).
CONCLUSION: The clinically and statistically significant improvement in GI symptoms found in parallel to structured GI evaluation for chronic GI symptoms following pelvic radiotherapy was sustained over 12 months follow up. These data suggest that structured investigation on the basis of the BSG guidelines can lead to a sustained improvement in symptoms and is acceptable to patients. Further research is essential to optimise patient care.
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Disclosure of Interest: None Declared
Keywords: gastrointesinal assessment, gastrointestinal symptoms, pelvic radiotherapy, toxicity

P1553 DEVELOPMENT OF RADIATION-INDUCED PROCTOPATHY: THE ROLE OF HYPOXIA-INDUCED FACTOR

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INTRODUCTION: Radiotherapy is a current standard for prostate cancer patients treatment. Side-effects such as rectal bleeding, diarrhea and urgency occur in a third of treated cases. Mucosal and submucosal areas in the rectum of such patients suffer a rapid inflammatory process, which evolves into moderate to severe inflammation with blood vessels damage, ischemia and finally to fibrosis. Hypoxia inducible factor (HIF-1-alpha) and other angiogenic factors have been related to radiation-induced late rectal injury, suggesting that radiation-induced hemorrhagic proctopathy could be treated by targeting such molecular factors.
AIMS&METHODS: Our aim was to define the mechanism through which radiotherapy induces proctopathy evaluating the role of HIF-1-alpha expression in radiation-induced proctopathy.
Patients were examined by rectosigmoidoscopy before and 4 weeks after radiotherapy, and biopsy samples of the rectal mucosa were collected in both occasionswere for histological diagnosis and CD31 immunohistochemistry analysis to evaluate angiogenesis. Endoscopic findings were classified using the Vienna Rectoscopy Score (VRS: 0=normal; 1=reddening, single angiectasia and oedema; 2=more than One angiectasias). Moreover, total protein content was extracted from the rectum samples and western blot analysis was performed to evaluate HIF1-alpha levels before and after radiotherapy.
RESULTS: Twenty-five patients were enrolled in the study. Rectosigmoidoscopy performed 4 weeks upon the termination of a 3-month radiotherapy revealed no mucosal damage in 13 patients, while proctopathy with VRS grade 1 lesions was present in 12 patients (48%). Molecular analysis showed up-regulation of HIF-1-alpha in 9 out of 25 patients, while in the rest of the samples HIF-1-alpha was either slightly down-regulated (6/25) or unchanged (10/25). Interestingly, significant association was observed between the presence of mucosal damage and HIF-1-alpha up-regulation (two-tailed Fisher: p=0.04). In particular, 77% of the cases (7/9) with higher post-radiotherapy levels of HIF-1-alpha showed VRS grade 1 lesions; when HIF-1-alpha was not up-regulated, mucosal damage was observed only in 31% of cases.
CONCLUSION: About half of the patients who underwent pelvic radiotherapy in our study developed radiation-induced proctopathy. In this setting, presence

of higher levels HIF-1-alpha was associated with a more severe mucosal acute inflammation.
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Disclosure of Interest: None Declared
Keywords: HIF-1-alpha, Hypoxia-induced factor, Radiation proctitis

P1554 HIGH PREVALENCE OF ANAL CANAL INFECTION WITH HUMAN PAPILLOMA VIRUS IN FRENCH MEN AND WOMEN WITHOUT RISK FACTORS.

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INTRODUCTION: Currently the incidence of anal canal (AC) cancer increases by 2% each year and the sex ratio tends towards 1. Human papilloma virus high risk genotypes (HPV HR) are now well recognized as the causal agents for this cancer, with a large overrepresentation of HPV type 16. Concomitant infection with HIV is the main risk factor. However, only few data are available on the presence of HPV in AC and in the non-HIV population.
AIMS&METHODS: The aim of this study was to analyse prospectively the prevalence and the distribution of HPV genotypes in the AC of patients without risk factor for AC cancer. Secondary objectives were to evaluate 1) the relevance of cytology for screening HPV 2) the prevalence of precancerous lesions and 3) the study of viral parameters: viral load, DNA integration. Enrolment was proposed to all patients who underwent a colonoscopy under general anesthesia, whatever the indication, in the gastroenterology unit of a French university hospital. Two AC smears were taken for each patient in order to 1) look for HPV DNA by real time PCR and 2) perform cytological examination and immunocytochemistry with p16/Ki67 double staining.
RESULTS: Sixty two patients were enrolled (men: 60%; women: 40%) between 2011/12/01 and 2012/05/01. The prevalence of HPV infection was 19% (13% in men and 29 % in women). The prevalence of HPV HR was 16% and HPV HR 16 was predominant. Several genotypes were often found in one patient. Seventy % of patients carrying HPV in AC were women. When HPV HR 16 was found, viral load was low (60-120 copies/1'000 cells) and HPV DNA was not integrated to host cell genome. Cytological analysis revealed only few abnormalities. Preliminary data showed a positive p16/Ki67 double staining in a few HPV HR + samples.
CONCLUSION: This study, one of the rare ones describing AC infection with HPV in non-HIV patients, reports a prevalence of 1/5 subjects. The higher prevalence in women indicate that gynecologic current or past infection is likely to play a role. Our study is ongoing with the recruitment of 1'000 patients to get an accurate estimation of HPV prevalence in AC. These results may help guide prevention strategies against AC cancer through better understanding of HPV-related lesions and appropriate HPV screening and vaccination.
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Disclosure of Interest: None Declared
Keywords: Anal Canal, epidemiology, human papilloma virus

P1555 CHRONIC SACRAL NERVE STIMULATION: EFFECTS ON RECTAL EPITHELIAL BARRIER AND ON NEUROMUSCULAR TRANSMISSION IN A PORCINE MODEL

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INTRODUCTION: Sacral nerve stimulation (SNS) is a validated treatment option for fecal incontinence although the mechanism-of-action remains unknown. In a pilot study we previously showed that short-term SNS induced a significant reduction in rectal mucosal paracellular permeability together with a concomitant decrease of mucosal thickness and an increased mucosal secretion (1). The objective of this work was to determine the impact of a long-term period of SNS on the intestinal epithelial barrier in a preclinical model.
AIMS&METHODS: The objective of this work was to determine the impact of a long-term period of SNS on the intestinal epithelial barrier in a preclinical model. Fourteen pigs were implanted for bilateral S3 root stimulation. Seven pigs received a seven-day permanent stimulation (Medtronic *041828-004*, Minneapolis, USA; 14 Hz, 210ms) whereas the remaining animals received no stimulation. Rectal biopsies were performed before and after seven days. Intestinal epithelial permeability (Ussing chambers), mucosal-tight-junction and cytokines mRNA expression, IL-6 production in an organotypic culture model, and *ex vivo* neuromuscular transmission in rectal muscle strips were assessed.
RESULTS: No severe advert effect occurred in animals. Intestinal epithelial permeability was not modified after seven-day stimulation compared with baseline. The stress-induced (PAR-2) significant (n=7; p=0.03) increase of epithelial permeability observed in controls at D7 did not occur in SNS group. Likewise a significant decrease of ZO-1 mRNA expression was observed at D7 in controls which did not occur in SNS group (n=7; p=0.25). Cytokine overexpression was not observed in the mucosa in either group. SNS decreased IL-6 production in the organotypic culture model. In the stimulated group, the area-under-the-curve of the electrical field stimulation-induced contractile response was significantly increased as compared with D0 (p=0.03).
CONCLUSION: Despite no occurrence of changes in physiologic conditions, chronic SNS modified the properties of the intestinal epithelial barrier, mainly by inhibiting the stress-induced increase of permeability. Neuromuscular transmission was modified by SNS, leading to neuronal hyper-excitability. These results add evidence to the reinforcement of the intestinal epithelial barrier induced by SNS.
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1. Neurogastroenterol Motil 2012;24, 267–e110
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Disclosure of Interest: None Declared
Keywords: Animal model, Intestinal epithelial barrier, paracellular permeability, Sacral nerve stimulation

P1556 WICH LESIONS SHOULD BE BIOPSIED DURING HRA? PROSPECTIVE DESCRIPTIVE STUDY OF SIMPLE MORPHOLOGICAL CRITERIA

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INTRODUCTION: High-resolution anoscopy (HRA) is a useful screening tool for anal intraepithelial neoplasia (AIN), although reputedly challenging for interpretation of suspected lesions.
AIMS&METHODS: The purpose of this study was to identify straightforward descriptive criteria predictive of the histological grade of suspected lesions visualized during HRA. All patients undergoing HRA from November 2010 through March 2012 with a biopsy of a suspected AIN lesion were included prospectively. All procedures were performed by senior proctologists. The characteristic features of the suspected lesion were noted. The characteristic features were compared with the histology findings.
RESULTS: Biopsy specimens were obtained from 168 suspected AIN lesions found in 103 patients (68% men) aged 49.8±9 years; 57.3% of patients were HIV-positive. Histologically, the lesions were classed: high-grade AIN (57.7%); low-grade AIN (35.6%); non-dysplastic tissue (23.8%, including 11.9% considered normal). The epithelium was irregular in 68.5% of the high-grade lesions and in 37.9% of the low-grade lesions. Similarly, the vascularization was irregular in 61.4% of the high-grade lesions and in 37.9% of the low-grade lesions. A flat surface was noted for 41.4% of the high-grade lesions versus 17.2% for the low-grade lesions. 91.4% and 94.8% of the high-grade and low-grade lesions respectively were acetowhite versus 70% of the normal specimens. Lugol's iodine staining was negative for 62.9% of the high-grade lesions versus 31% of the low-grade lesions. Combining the different criteria produced positive predictive values as follows:

Group	High-grade AIN n=70	Low-grade AIN n=58	PPV for high-grade AIN
I. Acetic acid-positive (single criterion)	64 (91.4%)	56 (94.6%)	43.2%
II. Acetic acid-positive + Lugol-negative + irregular epithelium	46 (65.7%)	20 (33.9%)	62.2%
III. Acetic acid-positive + Lugol-negative + irregular epithelium + irregular vascularization	35 (50%)	14 (23.7%)	68.6%

CONCLUSION: Several simple morphological criteria significantly associated with high-grade AIN are found less often in low-grade lesions. Combining morphological criteria provides a satisfactory PPV for guiding HRA biopsies.
Disclosure of Interest: None Declared
Keywords: anal cancer screening, anoscopy

P1557 ANORECTAL CONDYLOMA IS ASSOCIATED WITH ONCOGENIC HUMAN PAPILLOMAVIRUS INFECTION IN THE ANUS OF HIV-INFECTED MEN WHO HAVE SEX WITH MEN

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INTRODUCTION: High-risk oncogenic human papillomavirus (HPV) types are responsible for the majority of HPV-caused cancers.
AIMS&METHODS: To elucidate the prevalence of oncogenic HPV infection in the anus and its association with anorectal condyloma in HIV-infected men who have sex with men (MSM). MSM with HIV infection who underwent colonoscopy were prospectively enrolled in this single-center study. Anorectal condyloma was diagnosed based on endoscopic findings and confirmed by biopsy. A Dacron swab was used to obtain samples of anal canal cells for detection of HPV DNA by polymerase chain reaction (PCR). PCR and genotyping was conducted by standard methods. Associations between

oncogenic HPV infection (strains 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 66), anorectal condyloma, and other factors were determined by univariate and multivariate logistic regression analyses.
RESULTS: A total of 122 patients were enrolled. Median age and CD4 count were 42 (IQR 37–52) years and 362 (IQR 121–577) cells/mm^3, respectively. Of the patients, 85 (70%) were on antiretroviral therapy (ART), and 76 (62%) had a HIV viral load of <200 copies/ml. Of 100 patients infected with HPV, 90 (74%) were infected with oncogenic HPV, and 18 (15%) patients had biopsy-confirmed anorectal condyloma. Anorectal condyloma was found to be marginally associated with oncogenic HPV infection (OR 7.219, 95% CI 0.920–56.65, p=0.060), and this tendency persisted after adjustment for age, CD4 count, and ART (adjusted OR 6.162, 95% CI 0.761–49.91, p=0.088). On the other hand, older age was associated with a lower frequency of oncogenic HPV infection (OR 0.952, 95% CI 0.918–0.987, p=0.007).
CONCLUSION: The prevalence of oncogenic HPV infection is high in MSM patients with HIV infection. Regular screening for anal cancer is warranted in HIV-infected MSM, especially those with anorectal condyloma.
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Disclosure of Interest: None Declared
Keywords: Anal canal cancer, Anorectal condyloma, HIV infection, Oncogenic HPV infection

P1558 QUALITY OF LIFE AMONG THE CASES WITH FUNCTIONAL CONSTIPATION

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INTRODUCTION: For the functional diseases such as functional constipation; enabling the patients to cope with the disease and helping them lead a life of quality should be the main objective of the treatments. We aimed at exploring clinical and demographic characteristics that affected quality of life among the cases with chronic functional constipation.
AIMS&METHODS: 268 cases who were admitted to our Constipation Outpatient Clinic were diagnosed with functional constipation according to Rome III criteria were included in the study. Constipation Quality of Life Questionnaire (CQLQ) was filled in by the cases after registring of the demographics, constipation features (stool frequency, consistency, amount, urge for bowel movement, need to strain, feeling of incomplete evacuation) and type of stool using Bristol Stool Scale were obtained.
RESULTS: 75% of the cases were women (201/268) and mean age was 45.1±1.1 years. 47% had infrequent defecation (<3 weekly), 33.6% had straining for 1-5 minutes, 43.3% had the sensation of incomplete evacuation, 39.6% defined to make pressure around anus, 31.3% had the feeling of incomplete evacuation. According to the Bristol Stool Scale, 104 patients (38.8%) had type 1 stool. Mean CQLQ was found to be 92.9±1.2. No correlation existed between mean CQLQ scores and age (p=0.4), sex (p=0.8), educational status (p=0.3), marital status (p=0.4), defecation frequency (p=0.07), incomplete defecation (p=0.15), defecation assisted with finger (p=0.06), straining (p=0.1), the feeling of incomplete evacuation (p=0.06), type of stool (p=0.1). Mean CQLQ scores were found to be considerably higher among those without feeling of incomplete evacuation than those with (99.8±17 vs 91.9±19.6 p=0.02) and among those with abdominal distension than those without (94±18.8 vs 83.6±23.9 p=0.01). The subscale of worries and concerns was significantly higher among those with defecation once a month (p=0.024), those with no feeling of incomplete evacuation, those who defecated assisted with finger (p=0.01) and abdominal distension (p=0.005); the subscale of physical discomfort was significantly higher among those aged 15-40 (p=0.021), those with hard defecation (p=0.009); the subscale of psychosocial discomfort was significantly higher among those without no sensation of obstructed anus (p=0.025) and the subscale of satisfaction was significantly higher among those aged ≥60 (p=0.045) and those with incomplete evacuation (p=0.005).
CONCLUSION: Quality of life worsened due to functional constipation. Worsening was higher in subscale of worries and concerns. Since improving quality of life was the main objective of the treatment in functional constipation, CQLQ could be used as an objective criterion in the evaluation of the treatment response.
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Disclosure of Interest: None Declared
Keywords: constipation, Qualıty Of Lıfe

P1559 THE IMPACT OF SPHINCTER EXERCISES ON ANORECTAL PHYSIOLOGY, FREQUENCY OF INCONTINENCE AND QUALITY OF LIFE IN PATIENTS WITH FUNCTIONAL FECAL INCONTINENCE

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INTRODUCTION: Fecal incontinence greatly affects social activity and quality of life and may even lead to social isolation. We aimed to examine the effects of sphincter exercise on anorectal physiological tests, frequency of incontinence and quality of life in patients presenting with fecal incontinence.
AIMS&METHODS: A total of 19 functional fecal incontinence patients [14 female, 5 male; mean age: 53±17 (median 56)], whose anorectal physiological tests were compatible with fecal incontinence were prospectively followed on a regular program of sphincter exercises during 3 months. Patients with abnormal electromyography (EMG) activity of the anal sphincter and subjects with a history of anorectal surgery were excluded. Frequency of defecation, incontinence, anal resting pressure and anal squeeze pressure, rectal sensation and quality of life were compared after the exercise program. Chi-square and t test were used in statistical analysis.
RESULTS: 5 (26%) patients had passive, 10 (52%) patients had urge, 4 (21%) patients had leakage type incontinence. Frequency of incontinence decreased from 7/week to 1 /week (p: 0,00009), from 25 /month to 7 /month (p=0,0001), endurance squeeze time improved from 17,5 sec to 24, 9 sec (p=0,016) following an exercise program of 92±5 days and median 18 times/day. In rectal sensation test, desire to defecate volume increased from 57,6 mL to 79,4 mL (p= 0,009) and urge to defecate volume increased from 107,8 mL to 137,3 mL (p=0,008) after exercise. Weekly and monthly bowel movements, anal resting and squeeze pressure, first sensation of content in the rectum and maximum tolerable volume to defecate did not change significantly. Following exercise, physical role (p=0,007), pain (p=0,003), general health (p=0,002), vitality (p=0,009) and mental health (p=0,004) improved according to the quality of life scales. Sex and differences in defecation patterns did not have a significant association with anal resting and squeeze pressures and endurance squeeze time.
CONCLUSION: Sphincter exercises decrease frequency of fecal incontinence and improve quality of life; by increasing endurance squeeze time, desire to defecate and urge to defecate volumes.
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Disclosure of Interest: None Declared
Keywords: Functional fecal incontinens, Sphincter exercises

P1560 EFECTIVENESS OF TREATMENT WITH BOTULINUM TOXIN TYPE A VERSUS BIOFEEDBACK IN PATIENTS WITH DYSSINERGIC DEFECATION

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INTRODUCTION: Efficacy with TBA and BRT are not compared universally the biofeedback therapy is often used only with qualified personal. Botulinum toxin in the muscle diminish the activity of motor neurons alfa and reduction of aferent signal and feedback with reduction of muscular contraction, affect the perception in the region due to the brain-gut axis allows bi-directional input, links emotional and cognitive centers of the brain with peripheral functioning of the GI tract and viceversa, then the motor reactivity could be modified by botulinum toxin similar to biofeedback
AIMS&METHODS: Prospective randomized study,33 patients with dyssinergic defecation referred to motility service at Hospital Issste, Jalisco, México(dec 2010-dec 2011). Diagnosis of DD:clinical Rome III, anorectal manometry and balloon expulsion test, TTC. **Excluded:** Pregnant, altered colonic and anorectal region.**Anorectal manometry**:Air catheter four balloon spaced 0.5 cms (Sierra Inst®).**Protocol performance:**stationary pull-through technique recording anal pressure, mean squeeze pressure, RIAR, cough, bear-down manouver, Group A (BTA) 16 patients, incobotulinum toxin 80 U diluted at 0.4 cc injected at each side of puborectalis muscle once a time. Group B (BFB) (17 patients), eigth sesions twice a week. Clinical and manometric evaluation:four months. Dyssinergic defecation by anorectal manometry was made if basal pressure increase 10mmHg, three attempts. Ballon expulsion test at least 1-3 min. Primary outcomes variable was expulsion baloon test and clinical improvement.
RESULTS: Baloon expulsión: Significant difference in the median from 180 to 20 seconds. This represents an improvement in time to allow evacuation. The analysis of variables of the 17 patients evaluated with botulinum toxin type A, showed improvement in expulsion balloon test. The rest and intrarectal pressure did not differ with treatments.
CONCLUSION: BTA is safe and an option to treat dyssinergic defecation. We do not have infraestructure for Biofeedback treatment. The difference in results between the groups in this study has been demonstrated the feasibility of their use as initial therapy in patients with disturbed defecation with severe chronic constipation refractory to standard treatments.
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Disclosure of Interest: None Declared
Keywords: ano rectal function, chronic constipation

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00

OESOPHAGEAL, GASTRIC AND DUODENAL DISORDERS III – Poster Area

P1561 MALLORY-WEISS SYNDROME: IS IT POSSIBLE TO PREDICT A COMPLICATED OUTCOME?

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INTRODUCTION: Mallory-Weiss Syndrome (MWS) is a common cause of upper gastrointestinal bleeding, which usually has a benign outcome; however, some cases may have a complicated course.
AIMS&METHODS: The aim of this study was to identify predictive factors of a complicated clinical course in an inpatient population, defined as hemodynamic instability on admission (tachycardia/hypotension), blood transfusion, bleeding recurrence or death. We retrospectively analyzed all consecutive admissions in our Gastroenterology unit due to MWS between 2006 and 2012. Data collected included symptoms, precipitating factors, pharmacological and medical records, vital signs and analytic results at admission, endoscopic findings, treatments and outcomes. Statistical analysis was performed with SPSS ® v20.
RESULTS: We included 121 patients (mean age 65 ± 17 years, 84.3% males). Hemodynamic instability on admission was present in 40% of patients, with male having a higher risk (OR 6.1). Univariate analysis identified the following predictors of transfusion requirement (received by 42% of the patients): melena (OR 2.7), tachycardia (OR 2.62), lower systolic arterial tension (123vs135mmHg), longer time between bleeding onset and endoscopy (28vs11hours) and higher values of blood urea nitrogen (49.8vs29.8mg/dl). Independent predictors for transfusion identified by multivariate analysis were: tachycardia, melena, higher blood urea nitrogen and time to endoscopy. There was bleeding recurrence in 6.6% (n=8) of patients. Statistical analysis didn't identify any predictor of recurrence. No deaths related with MWS were recorded in this series.
CONCLUSION: This study highlights the benign course of MWS, despite relatively high frequencies of hemodynamic instability and transfusion requirements. The authors emphasize the importance of individual risk assessment of each patient, taking into account the absence of unequivocal predictive factors of bleeding recurrence.
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Disclosure of Interest: None Declared
Keywords: Blood transfusion, Mallory-Weiss syndrome, Predictive factors, Recurrence

P1562 IS ENDOSCOPIC THERAPY SAFE FOR UPPER GASTROINTESTINAL BLEEDING IN SUPRATHERAPEUTIC ANTICOAGULATED PATIENTS WITH SUPRATHERAPEUTIC INTERNATIONAL NORMALIZED RATIO?

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INTRODUCTION: Rebleeding is the most important predictive factor of mortality for patients with upper gastrointestinal bleeding (UGIB). The purpose of this study was to evaluate the safety of endoscopic therapy for UGIB in anticoagulated patients with supratherapeutic international normalized ratio (INR).
AIMS&METHODS: 192 anticoagulated patients who underwent endoscopic treatment for UGIB were enrolled in the study. Patients were divided into two groups based on the occurrence of rebleeding within 30 days of the initial therapeutic endoscopy; no-rebleeding group (without rebleeding, n=168) and rebleeding group (with rebleeding, n=24).
RESULTS: The overall rebleeding rate was 12.5% among enrolled patients. The supratherapeutic INR at the time of presentation (P=0.047) and bleeding from gastric cancer (P=0.025) were significantly related to rebleeding in a univariate analysis, while melena as a presenting symptom (P=0.003) and bleeding from gastric ulcer (P=0.020) were significant factors related to no-occurrence of rebleeding. In multivariate analysis, presenting symptoms except melena (hematemesis, hematochezia, or others) (P=0.008, OR=3.9, 95% CI=1.4–10.8) and bleeding from gastric cancer (P=0.024, OR=6.1, 95% CI=1.3-29.3) were significant risk factors predictive of rebleeding. The supratherapeutic INR at the time of endoscopic therapy had the increasing tendency of rebleeding in univariate analysis (P=0.052), but did not reveal the significant association with rebleeding in multivariate analysis (P=0.192, OR=4.3, 95% CI=0.5-37.8). The rebleeding group revealed the significant differences of success of initial endoscopic therapy (P=0.006), additional interventions to control bleeding (P=0.006), length of hospital stay (P=0.017), transfusion requirements (P=0.001), and bleeding-related (P=0.009) or all-cause mortality (P=0.010), comparing to the no-rebleeding group. There were no significant differences of therapeutic outcomes between patients with INR less than or equal to 3.0 and with INR more than 3.0.
CONCLUSION: The supratherapeutic INR at the time of endoscopic therapy did not affect rebleeding and therapeutic outcomes. The endoscopic therapy should be considered the anticoagulated patients with supratherapeutic INR.
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Disclosure of Interest: None Declared
Keywords: Anticoagulation, Rebleeding, Upper gastrointestinal bleeding

P1563 COMPARISON OF THE GLASGOW BLATCHFORD AND ROCKALL SCORES IN THE PREDICTION OF CLINICAL END-POINTS AFTER UPPER GASTROINTESTINAL BLEEDING

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INTRODUCTION: The Glasgow Blatchford Score (GBS) is increasingly being used to predict intervention and outcome following upper gastrointestinal bleeding (UGIB).
AIMS&METHODS: The aim of this study is to compare the GBS with both the admission and full Rockall scores in predicting clinical end-points following UGIB. Retrospective study including patients with UGIB, admitted to the department of Hepato-Gastroenterology, Hassan II University Hospital, of within two years. Admission history, clinical and laboratory data, endoscopic findings, treatment and clinical follow-up were recorded. Using ROC curves, we compared the three scores: GBS and the admission and full Rockall scores in the prediction of death, endoscopic intervention and transfusion.
RESULTS: 284 patients were included. The average age was 51 years. Thirteen (4.5%) died, 72 (25.3%) had endoscopic intervention and 116 (66%) required transfusion. The comparison of the GBS with admission Rockall score and full Rockall score, shows that this one was higher than admission Rockall score (AUROC 0.705 vs 0.530) and full Rockall (AUROC 0.705 vs 0.537) in predicting need for a transfusion, and lower than both the admission Rockall score (AUROC 0.655 vs 0.735) and full Rockall score (AUROC 0.655 vs 0.772) in predicting endoscopic intervention. For predicting death, the GBS was higher than admission Rockall score (AUROC 0.801 vs 0.776) and comparable to full Rockall score (AUROC 0.801 vs 0.812).
CONCLUSION: Comparing the three scores,GBS was superior to both Rockall scores in predicting a transfusion's need and death.
Disclosure of Interest: None Declared
Keywords: Upper endoscopy, upper gastrointestinal bleeding

P1564 RISK SCORING SYSTEMS IN PREDICTING OUTCOME IN PATIENTS WITH UPPER GASTROINTESTINAL BLEEDING

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INTRODUCTION: Rockall and Glasgow-Blatchford score can be used in stratifying the risk in patients with upper gastrointestinal bleeding (UGIB).
AIMS&METHODS: AIM
The importance of scoring systems in predicting outcome in patients with upper gastrointestinal bleeding
MATERIAL AND METHOD
299 patients with UGIB admitted in RIGH Cluj Napoca's Emergency Department between November 2012 - March 2013 were included in the study. Upper endoscopy was performed in all patients and they were followed prospectively until discharge.
Pre-endoscopy Rockall score, post-endoscopy Rockall and Glasgow-Blatchford score were determined; rebleeding episodes, death and the need for blood transfusion were recorded.
RESULTS: The mean time from admission to endoscopy was 4h 38 min, and the average admission time was 8 days.
Rebleeding occurred in 7.69 % of the patients. The mean scores for the patients who had at least one more bleeding episode while they were admitted, compared to those who did not, were: pre-endoscopy Rockall score 2.39 vs 2.83; post-endoscopy Rockall score 4.70 vs 4.76; Glasgow-Blatchford score 11.83 vs 11.42 ($p > 0.05$).
Death occurred in 13.71% of the patients. The mean scores for the patients who died compared to those who survived were: pre-endoscopy Rockall 3.83 vs 2.64; post-endoscopy Rockall 5.76 vs 4.60; Glasgow-Blatchford 13.63 vs 11.11 ($p < 0.05$).
Regarding the need for blood transfusion, the patients were divided into 4 categories: A – no need for transfusion; B - a need between 1 to 5 units of blood; C- 6 to 10 units; D – more than 10 units of blood needed. The mean pre-endoscopy Rockall scores were 2.43; 2.91, 3.19 and 3.80 (p=0.021); mean post-endoscopy Rockall scores were 4.29; 4.89, 5.31 and 6 (p=0.023); mean Glasgow-Blatchford scores were 8.98; 12.54, 12.62 and 14.20 (p=0.000).
CONCLUSION: The pre-endoscopy Rockall, post-endoscopy Rockall and Glasgow-Blatchford scores were significantly higher in patients who died compared to those who survived.
All of these 3 scoring systems were higher in patients who needed blood transfusions, and there was a correlation between these scores and the number of blood units needed.
None of these scores correlated with the occurrence of a new bleeding episode.
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Disclosure of Interest: None Declared
Keywords: Glasgow-Blatchford score, Rockall score, upper gastrointestinal bleeding

P1565 THE ROLE OF EARLY ENDOSCOPY VS URGENT ENDOSCOPY IN UPPER GATROINTESTINAL BLEEDING

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INTRODUCTION: Upper gastrointestinal bleeding (UGIB) is one of the major emergencies in gastroenterolgy. The endoscopy is recommended to be performed in the first 24 hours.
AIMS&METHODS: The aim of the study is to follow the influence of endoscopy timing on hospitalization period, mortality rate and rebleeding risk in patients with UGIB.
Material and method. It is a prospective study done in a tertiary medical service with permanent access to Endoscopy Department, for 5 months interval (between November 2012 and March 2013). 294 patients with UGIB were included in the study. In all patients the endoscopy was performed in the first 24 hours after admission. The patients were followed the whole duration of hospitalization. According to the time interval after the endoscopy was done, the patients were divided in 2 groups: urgent endoscopy - first 3 hours (UE) and early endoscopy – 3-24 hours (EE).
RESULTS: In the studied group of 294 patients, 163 of them had UE (55.44%), while 131 had EE (44.56%). The mean age was 62.5 years (min 19 years, max 94 years), with a predominance of male patients (68.71%).
13.9% of the patients died during hospitalization period. The mortality rate was lower in patients with UE compared with EE group (13.5% versus 14.5%), without statistic significance (p=0.804).
Rebleeding episodes occur in 7.82 % of the patients, more frequently in patients with UE compared to EE group (8.59% versus 6.87%), without statistic significance (p=0.585).
Even the hospitalization period is slighty prolonged in patients with EE vs UE group (8.24 days vs 7.96 days), this was not significantly influenced by the endoscopy timing (p=0,74).
CONCLUSION: Urgent endoscopy compared to early endoscopy has not been significantly superior regarding the mortality rate, rebleeding episodes and hospitalization period in patients with UGIB.
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Disclosure of Interest: None Declared
Keywords: early endoscopy, upper gatrointestinal bleeding, urgent endoscopy

P1566 EFFICACY OF LONG-ACTING RELEASE OCTREOTIDE IN RECURRENT BLEEDING FROM GASTROINTESTINAL ANGIODYSPLASIA: A RETROSPECTIVE STUDY OF 98 CONSECUTIVE CASES

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INTRODUCTION: Management of recurrent bleeding due to gastrointestinal angiodyplasias (GIADs) is a clinical challenge, mainly because it occurs in elderly patients. The inaccessibility or numerosity of the lesions as well as the patient comorbidities, strongly limit the suitability of endoscopical or surgical procedures. The rarity of bleeding due to GIADs, the heterogeneity of the patient population and the natural course of the disease critically hamper to plan prospective studies.
AIMS&METHODS: To assess the efficacy and safety of long-acting release (LAR)-octreotide in definitively control recurrent bleeding due to GIADs.
Medical records of consecutive patients diagnosed with GIADs from January 2000 to December 2008 were retrieved for the study. All patients received octreotide 0.1 mg three times/day SC for 28 days and, starting from the 14th day LAR octreotide 20 mg IM monthly for 6 months.
RESULTS: Ninety-eight out of 147 patients were eligible for the analysis. The history of bleeding before starting therapy lasted at least two years and the mean follow-up was 78 months (range 36-120 months). In respect to the observation period before starting therapy, during the follow-up the mean hemoglobin level increased ($p < 0.0001$), and the number of bleeding episodes, patients requiring blood transfusion, unit of transfused red cells and number of hospitalizations decreased ($p < 0.0001$, $p < 0.0001$, $p < 0.0001$ and $p < 0.0001$, respectively). Overall, 72/98 (74%) patients did not have overt bleeding nor presented recurrent anemia during the whole follow-up, and in particular 40/98 after the first cycle of therapy (full responders) and 32/98 by the third cycle of therapy (relapsers), while the remaining 26/98 patients required continuous therapy (poor responders). At multivariate stepwise analysis, chronic antiplatelet therapy (OR, 5.7; 95% CI 2.0 to 16.0; $p = 0.001$), overt bleeding (OR, 7.5; 95% CI 0.7 to 78; $p = 0.09$) and multiple sites of GIADs (OR, 4.0; 95% CI 1.4 to 11.4; $p = 0.009$) were the only covariates independently associated with poor response to therapy.
CONCLUSION: LAR octreotide is a safe and effective treatment in controlling recurrent bleeding due to GIADs, even definitely stopping bleeding in a substantial percentage of the cases. Therefore, LAR octreotide is useful to global well-being, health-related quality of life and public health cost streamlining.
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Disclosure of Interest: None Declared
Keywords: gastrointestinal angiodysplasia, gastrointestinal bleeding, long-acting release octreotide

P1567 OUTPATIENT MANAGEMENT OF LOW-RISK PATIENTS WITH UPPER GI BLEEDING: CAN WE SAFELY EXTEND THE GBS IN CLINICAL PRACTICE?

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INTRODUCTION: The pre-endoscopy Glasgow Blatchford Score (GBS) accurately predicts outcome in patients presenting with upper GI bleeding (UGIB).[1] A GBS of zero identifies low-risk patients in whom out-patient management is recommended.[2] There is debate whether this low-risk score can be extended above zero. The aim of this study was to prospectively assess the introduction of a protocol for out-patient management of patients with UGIB and GBS <2.
AIMS&METHODS: After adjusting our hospital UGIB protocol to avoid admission if GBS <2 (unless required for other reasons), we undertook hospital educational meetings and introduced the new protocol in December 2011. A research nurse prospectively collected demographic and outcome data on consecutive patients presenting with UGIB during the 12 month period to December 2012. All data were cross referenced with the A&E Information System. An endpoint of death, endotherapy, transfusion or HDU/ITU admission within 30 days was used to define adverse outcome. The negative predictive value of GBS <2 was calculated with 95% confidence intervals.
RESULTS: 516 patients presented to our hospital with UGIB during the study period. 180 (34.9%) had GBS <2 (109 GBS=0 and 71 GBS=1).89 (49.4%) were managed as outpatients, of whom none had an adverse outcome within 30 days. Of the 91 (50.6%) managed as inpatients, 76 (83.5%) had other acute morbidities requiring inpatient care, of whom one died within 30 days from an unrelated malignancy. Of the 15 admitted without other acute morbidities, one was discharged for out-patient endoscopy but readmitted with a Mallory-Weiss tear requiring transfusion. The overall negative predictive value of GBS <2 in predicting adverse outcomes at 30 days was 98.9% (95% CI: 96.0% to 99.9%)
CONCLUSION: GBS <2 had a high negative predictive value for adverse outcomes in clinical practice. This suggests outpatient management of patients with UGIB and GBS <2 is safe.
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Disclosure of Interest: None Declared
Keywords: Glasgow Blatchford Score, Upper gastro-intestinal bleeding

P1568 LEFT-SIDED PORTAL HYPERTENSION – A COMPLEX CLINICAL PROBLEM

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INTRODUCTION: Sinistral or left-sided portal hypertension (LSPH) is an uncommon entity in our clinical practice. Among its multiple aetiologies, chronic pancreatitis is the most common, and among its various manifestations, gastric variceal bleeding is the most worrying.
AIMS&METHODS: Characterization of a series of patients with an established diagnosis of LSPH with a retrospective analysis of epidemiological, clinical, endoscopic and imaging characteristics of the identified cases.
RESULTS: Included 9 patients, 8 male, with a mean age of 52±9 years (42-68), with an established diagnosis of LSPH, confirmed with CT scan and/or Endoscopic Ultrasonography. Median follow-up of 7 months (3 to 108). Eight patients had pancreatic disease (chronic pancreatitis - 4; sequelae of acute necrotizing pancreatitis – 1; pancreatic tumor – 3) and the other had an arteriovenous malformation involving the splenic artery and vein. None of the patients had evidence of liver disease and only two of them had abnormal liver biochemical parameters, secondary to biliary obstruction due to pancreatic mass and chronic pancreatitis. The diagnosis of fundal varices was established in all patients by endoscopy and/or CT scan, but only two had gastrointestinal bleeding, and emerging obliteration of gastric varices with cyanoacrylate was necessary in one of them. Splenomegaly was observed in two patients and thrombocytopenia in three. Regarding the definitive treatment, two patients underwent splenic artery embolization (those who had gastrointestinal bleeding) and one was submitted to splenectomy, although there was recurrence of LSPH in this one.
CONCLUSION: Left-sided portal hypertension is a rare clinical syndrome, usually secondary to pancreatic pathology and with subtle clinical manifestations, but occasionally can lead to life-threatening gastric variceal bleeding. The therapeutic approach is not consensual, may have significative risks and the results are not always satisfactory.
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Disclosure of Interest: None Declared
Keywords: Gastric varices, Portal hypertension

P1569 EVALUATION OF ENDOSCOPIC BAND LIGATION IN THE MANAGEMENT OF ACUTE NON-VARICEAL UPPER GI BLEEDING

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INTRODUCTION: Acute nonvariceal upper-GI bleeding (NVUGIB) is a challenging emergency condition. Early endoscopic therapy has recommended as the first-line treatment for upper gastrointestinal bleeding as it has been shown to reduce recurrent bleeding.
AIMS&METHODS: Aims of the study determine the various causes of non variceal gastrointestinal hemorrhage and discuss the role of band ligation.. Between November 2006 and December 2012, 184 patients were treated with EBL who had NVUGIB were included for the study. Bleeding lesions included Dieulafoy's ulcer, Mallory- Weiss tear, duodenal ulcer, post surgical anastomosis bleed and gastric ulcer after polypectomy. After basic life support was provided, all patients underwent emergent and elective endoscopy.
RESULTS: These comprised 123 (66.8%) males and 61 (33.2%) females. The mean age was 48.2±6.4years for males and 40.6±2.2years for females.

Mallory-Weiss tear and Dieulafoy's lesion constituted the majority of bleeding lesions 64 (34.9%) and 48(26.1%) respectively requiring EBL. Other causes were: pre-pyloric ulcer 23(12.5%); duodenal ulcer 17(9.2%); ulcers in antrum 14(7.6%); post polypectomy bleed 11(6%); Anastomosis bleed 3(1.6%); malignant lesions 4(2.2%). Bleeding stopped after endoscopic therapy in 96.5% of patients. The single failure was in bleeding from a pre pylori lesion. Injection sclerotherapy with 1:10000 adrenaline solution and EBL was not successful
CONCLUSION: EBL provides safe and effective modality for hemostasis in NVUGIB. EBL could be considered as a primary or alternative method of choice for treatment of endoscopic hemostasis in patients with NVGIB.
Disclosure of Interest: None Declared
Keywords: Band ligation, hemorrhage, NVUGIB

P1570 FEATURES OF THE ABDOMINAL HEMODYNAMIC IN PATIENTS OF THE ASTHENIC CONSTITUTION

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INTRODUCTION: The abdominal hemodynamics is one of the factors defining structural and functional features of the alimentary system.
AIMS&METHODS: Research objective: To estimate features of the abdominal hemodynamics in patients of various constitutional types
Materials and methods. 121 patients of the asthenic constitution and 43 patients of the normosthenic constitution (group of control) were included in the research. An average age was 22,28 ±3,7 years. Patients were comparable according to their age and sex, they had no acute or chronic diseases. The computer angiography of the abdominal aorta and ultrasonic dopplerography of the portal vein, the general hepatic artery, the upper mesenteric artery, splenic artery on an empty stomach and after alimentary assay were executed. For the description of data the median (Me) with the indication of interguartile scope was used. Mann-Whitney U Test was applied to detect the differences between groups.
RESULTS: Results. In patients of the asthenic constitution smaller mass of the body was registered (p=0,0017), body mass index (p=0,0001). At the computer angiography smaller diameters of the abdominal aorta were found: 17,0 mm [15,3-18,0mm] at the level of Th 12, 21,00 mm [19,0-22,0] (p=0,0001) in control, 13,00 mm [12,4-13,8mm] at the level of L4, 16,50 mm [15,0 - 17,0 mm] (p=0,0001)in control. In patients of the asthenic constitution low volumetric rates of blood flow were defined against a background of smaller diameter of vessels: on the portal vein on an empty stomach (p=0,0314) and after alimentary assay (p=0,0443), on the arteries after an alimentary assay (p=0,00070; p=01430; p=0399). The body mass index Indicators correlated with the diameter, volumetric rate of the blood flow on the upper mesenteric artery (r=0,43; r=0,34); on the general hepatic artery (r=0,34; r=0, 36), with a linear rate of the blood flow on the portal vein r=-0, 35).
CONCLUSION: Conclusions: Patients of the asthenic constitution were established to have a reliable decrease of the diameter of an abdominal aorta becomes perceptible, smaller indicators of a volume blood flow on the visceral vessels were registered. Features of the abdominal blood flow in patients of the asthenic constitution can determine the trophological status of patients.
Disclosure of Interest: None Declared
Keywords: abdominal hemodynamics, asthenic constitution

P1571 GASTRIC ANTRAL VASCULAR ECTASIA: CLINICAL FEATURES, ASSOCIATIONS AND PROGNOSIS

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INTRODUCTION: Gastric antral vascular ectasia (GAVE) is a rare disorder characterised by upper GI bleeding, chronic iron-deficiency anaemia and endoscopic findings of columns of red tortuous vessels along the longitudinal folds of the antrum of the stomach. Although the pathogenesis of this condition is largely unknown, it is associated with a number of medical conditions including portal hypertension and scleroderma. There have been few studies analysing the prevalence of the associated conditions in a cohort of GAVE cases, and none in a sample size of greater than 15.
AIMS&METHODS: This is a retrospective cohort study of all patients diagnosed with GAVE an Milton Keynes district general hospital between November 2007 and November 2012. Information was gathered from electronically stored patient records.
RESULTS: 20 patients were identified, 50% of cases were male. Average age at diagnosis overall was 65 years. The most common symptom that lead to a diagnosis of GAVE was of iron deficiency anaemia. 45% of cases had a co-existing diagnosis of liver cirrhosis (n=9), 35% chronic renal failure, 25% (n=7) had diabetes (n=5), 20% had rheumatologic disease (n=4) and in half of these the condition was scleroderma, 11% of the cohort had thyroid function abnormalities (n=2). Patients were followed up for a mean period of 1.9 years and in this period one patient had an acute GI bleed. Argon Plasma Coagulation was performed in 5 cases and the remaining cases were treated medically. Following APC the haemoglobin increased by an average of 3.75g/dL.
CONCLUSION: GAVE is an important differential diagnosis in the setting of iron deficiency anaemia on a background of cirrhotic liver disease or portal hypertension, especially in patients in their sixties or older. This cohort confirms the associations in previous studies but also notes that acute bleed risk is low and that APC appears an effective treatment modality
Disclosure of Interest: None Declared
Keywords: Bleeding, Gastric antral vascular ectasia

P1572 THE ROLE OF ENDOSCOPY AND HISTOPATHOLOGY OF THE UPPER GASTROINTESTINAL TRACT IN THE MANAGEMENT OF PATIENTS WITH ORGANIC AND FUNCTIONAL DYSPEPSIA

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INTRODUCTION: Upper gastrointestinal endoscopy with histopathological evaluation provides essential tool to differentiate the organic and functional causes of dyspepsia.
AIMS&METHODS: The aim of this study was to assess the frequency and type of endoscopic and histological changes in patients with dyspepsia. A retrospective study was performed on 212 patients with dyspepsia, at the age of 18-84 years, who underwent gastroscopy. Patients were divided into two age groups: ≤ 45 years (group I,60 patients) and ≥ 40 years (group II,152 patients). Biopsy specimens were taken from the gastric and duodenum for histological examination. The presence of *H.pylori* infection has been established.
RESULTS: 1 patient (61 years) was diagnosed with gastric cancer (0.5%) and 1 person was diagnosed with Crohn's disease (0.5%)(group I). Peptic ulcer was found in 10 patients (4.7%). Reflux esophagitis was found in 18 patients (8.5%). The most common inflammatory changes of esophagus were mild inflammation - Grade A classification Los Angeles. A more advanced form and Barrett's esophagus was found only in patients > 45 years of age. In 25% of patients in group I and 5.3% in group II, gastric mucosa appeared to be normal. The most common endoscopic change was gastritis (74%). The most frequent type of gastritis were erythematous-exudative (23.6%) and atrophic (18.4%). Erosive gastritis was present in 15% of patients. The percentage of associated *H. pylori* infection, was slightly more than 30%. The main location of *H. pylori* infection was antrum. The patients with *H. pylori* infection had mainly a moderate degree of inflammation (55.2%). Atrophy, metaplasia, and dysplasia were significantly frequent in patients > 45 years of age. In no one of the group ≤ 45 years of age there was dysplasia or metaplasia of the third degree. The majority of patients (77.4%) had normal duodenal mucosa. In 3.3% of the respondents stated histological typical for celiac disease(I - 8.3%, II-1.3%). Microscopic examination of all samples taken from the duodenum, in the absence of endoscopic lesions, showed the presence of inflammatory infiltrates of varying degrees of severity, regardless of gastric *H. pylori* infection.
CONCLUSION: It seems that during endoscopy in patients with dyspepsia, regardless of macroscopic changes, routine biopsies from different parts of the stomach and the duodenum are appropriate. Celiac disease should be considered in the differential diagnosis of the causes of dyspepsia. Further histological study of microscopic duodenitis in patients with dyspepsia, may be needed and helpful.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, dyspepsia

P1573 GASTRIC GHRELIN AND SEROTONIN (5-HT) SIGNALING IN PATIENTS WITH FUNCTIONAL DYSPEPSIA (FD)

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INTRODUCTION: Background:
Circulating serotonin and ghrelin levels were suppressed in FD patients(Cheung et al. 2013). However, the role of serotonin and ghrelin signaling in patients with FD remains unclear.
AIMS&METHODS: Aim:
To compare the gastric mucosal expression of Ghrelin, 5-HT modulators between FD patients and healthy controls.
Methods:
Consecutive adult patients with FD (Rome III criteria) and age-and-sex matched asymptomatic healthy controls were recruited for upper endoscopy after an overnight fast. Subjects with GERD and IBS as predominant symptoms, diabetes mellitus, current *H. pylori* infection and recent use of NSAID or PPI were excluded. Mucosal biopsies from the gastric corpus were obtained for quantitative assay of mRNA Ghrelin, OCT-1, TpH-1 and GNB3 using Real Time-PCR. The Generalized Estimating Equation (GEE) approach was used to examine the differences in gene expression between patients and controls.
RESULTS: Results:
46 [M:F=14:32, mean age: 35.5(9.7)] FD patients were matched with 23 healthy controls [M:F= 8:15, mean age: 36.7(10.4)] respectively. FD patients had PDS as predominant symptoms (PDS: 44, EPS:2). Compared to healthy controls, FD patients had significantly higher relative mRNA expression of GNB3 (FD: 0.11± 0.02, Control: 0.06 ± 0.0, 1.9 fold, p=0.006) while no significant differences were observed in TpH-1 (FD: 6.9 ± 0.1 X 10-3, Control: 7.4 ± 2.3 X 10-3, 0.9 fold, p=0.798) and OCT-1 (FD: 6.9 ± 2.1 x 10-4, Control: 2.2± 0.6 x 10-4, 1.3 fold, p=0.481), Serotonin 4 receptor (FD:3.7± 0.5 X 10-4, Control: 4.2± 1.0 X 10-4, 0.9 fold, p=0.68)and ghrelin (FD: 13.0 ± 1.9, Control: 14.5± 3.6, 0.9 fold, p=0.77). However, Gastric TpH-1 mRNA in patients significantly correlated with epigastric burning (R = 0.33, p=0.04) and bloating(R=0.34, p=0.03). Gastric OCT-1 mRNA also significantly correlated with FD global symptom score (R=0.35, p=0.03), Bloating (R=0.32, p=0.05) and postprandial fullness (R=0.32, p=0.05) in patients with FD.
CONCLUSION: Conclusion:
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Alternations in ghrelin and serotonin signaling in the gastric mucosa may contribute to the aberrant circulating plasma levels and the pathophysiology of FD. Modulation of ghrelin and serotonin system may provide a therapeutic option for FD.
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Disclosure of Interest: None Declared
Keywords: Functional dyspepsia, ghrelin, serotonin

P1574 ALARM SYMPTOMS ARE NOT ASSOCIATED WITH THE CLINICALLY SIGNIFICANT FINDINGS IN UPPER ENDOSCOPY IN AMBULATORY SETTING

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INTRODUCTION: The demand of esophagogastroduodenoscopies (EGDS) is steadily increasing and could hardly be satisfied. According to guidelines the presence of alarm symptoms is unequivocal indication for EGDS. Though, there are some doubts if the presence of alarm symptoms yields in much more clinically significant findings.
AIMS&METHODS: Aim. To evaluate the correlation of alarm symptoms and clinically significant findings found on EGDS in the routine clinical practice in ambulatory setting.
Methods. A prospective study performed in 4 hospitals in Lithuania: Hospital of Lithuanian University of Health Sciences (tertiary level), and 3 secondary level hospitals. Alarm symptoms that were evaluated as an indication to perform EGDS were: dysphagia, odynophagia, anemia, signs of upper GI bleeding (suspicion of melena), weight loss, recurrent vomiting, fever. The following endoscopic findings were considered as a clinically significant: erosive esophagitis, gastric ulcer, duodenal ulcer, gastric or duodenal polyps, malignant tumors.
RESULTS: Data from 502 patients (mean age- 55.6±16.7) were analysed: 204 (41%) males and 298 (59%) females. Mean age of males – 54.1±16.3, of females – 56.6±16.9 years, $p>0.05$. Alarm symptoms were found in 77 (15%) patients: in 28 (13%) female and in 39 (19%) males, $p<0.05$. Mean age of patients with alarm symptoms - 58.2±18.6, without alarm symptoms - 55.1±16.3, $p>0.05$. Clinically significant findings found in 176 (35%) patients. Malignant tumor found only in 2 (0.4%) patients. Mean age of patients with clinically significant findings was 55.7±17.0, without clinically significant findings - 55.4±16.4, $p>0.05$. Among patients with alarm symptoms, clinically significant findings was found in 28 (36%) patients, among patients without alarm symptoms – in 148 (35%), $p>0.05$. Duodenal or gastric ulcer was found in 4 (33.3%) out of the 12 patients with melena, and in 22 (4.5%) out of 490 patients without melena, $p<0.01$. We did not find any differences in clinically significant findings if the patients were referred to upper endoscopy by gastroeneterologist or not gastroenterologist.
CONCLUSION: There is no correlation between the age and alarm symptoms and clinically significant findings in our cohort. The presence of alarm symptoms in our cohort was not asocciated with the clinicaly significant findings. Only the presence of signs of upper gastrointestinal bleeding was asociated with more frequent detection of peptic ulcer. There are extremely low prevalence of malignancies in our studied cohort, therefore the role of alarm symptoms in the malignant disease must be clarified in much larger sample size.
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Disclosure of Interest: None Declared
Keywords: Alarm symptoms, Upper gastrointestinal endoscopy

P1575 UPPER GASTROINTESTINAL MUCOSAL INJURY AND SYMPTOMS IN LOW DOSE ASPIRIN USERS

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INTRODUCTION: It is well known low-dose aspirin(LDA) not only increases the risk of gastrointestinal(GI) mucosal injury but also worsens the quality of life(QOL) because of the symptoms like dyspepsia. Previous studies have mostly investigated the upper GI(u-GI) mucosal injury in individual organs, but there are few reports which were investigated plural organs at the same time.
AIMS&METHODS: To reveal the clinical features of LDA related u-GI mucosal injury, we investigate frequency, severity and symptom of reflux esophagitis(RE), gastric erosions and/or ulcers(GE), and duodenal erosions and/or ulcers(DE) individually between patients of LDA users(LDA) and non-LDA users(C). Data were extracted from the records of subjects who underwent u-GI endoscopy at our department between April 2008 and December 2012. Among 8280 patients answering Frequency of Scale for severity of GERD(FSSG) and SF8 QOL were analyzed after excluding proton pump inhibitor or histamine type 2 receptor antagonist users. Frequency of u-GI mucosal injury was compared between LDA and Control. Among patients who were diagnosed to have mucosal injuries, symptom and QOL was compared between LDA and Control. FSSG items were classified into a total score(TS), reflux score(RS), dyspepsia score(DS). SF8 has a physical component summary(PCS) and mental component summary(MCS).
RESULTS: Number of LDA and C was 501 and 7779, respectively. Frequency of RE in LDA:C was 10.2%(n=51): 9.6%(n=750)(p=0.69), GE was 36.5%(n=183): 26.7%(n=2076)($p<0.001$). DE was 5.4%(n=27): 4.6%(n=355)(p=0.39). Regarding symptom and QOL, TS, RS and DS of RE were LDA:C = 6.2±6.2: 8.0±7.1(p=0.07), 3.5±3.8: 4.4±4.3(p=0.16) and 2.7±2.9: 3.6±3.3(p=0.05). TS, RS and DS of GE were 5.5±6.1: 6.9±6.7(p=0.006), 2.9±3.4: 3.5±3.9(p=0.04) and 2.6±3.1: 3.4±3.4(p=0.002). TS, RS and DS of DE were = 6.0±5.7: 6.6±6.3(p=0.64), 3.1±3.9: 3.3±3.7(p=0.77) and 2.9±2.3: 3.3±3.2(p=0.56). PCS and MCS of RE were 47.0±10.8: 49.6±6.7(p=0.01) and 50.3±9.3: 48.3±7.4(p=0.07). PCS and MCS of GE were 47.6±7.9: 49.0±6.6(p=0.01) and 50.0±7.0: 48.3±7.4(p=0.005). PCS and MCS of DE were 48.7±11.6: 49.5±7.2(p=0.59) and 48.4±11.6: 48.3±8.1(p=0.95).
CONCLUSION: Frequency of gastric mucosal injury was significantly high in LDA user comparing to non-LDA user, however frequency of esophageal and duodenal mucosal injury was similar in LDA user to non-LDA user. Regarding symptoms, LDA user complained significantly less symptom score on DS with reflux esophagitis and TS, RS, DS with gastric mucosal injury. QOL was not impaired at all in upper GI mucosal injuries in LDA users. These results give us the important clinical information that symptom based management was not appropriate in LDA user in terms of upper GI mucosal injuries.
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Disclosure of Interest: None Declared
Keywords: Aspirin, gastrointestinal symptoms

P1576 OSTEOPOROTIC FRACTURE RISK ASSESSMENT IN GASTROENTEROLOGY INPATIENTS: A MISSED OPPORTUNITY TO SCREEN?

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INTRODUCTION: In the general population, a majority of fragility fractures occur in patients with bone mineral densities (BMD) in the osteopaenic rather than osteoporotic range, suggesting that factors other than BMD need to be taken into account when determining both the need for screening and anti-osteoporosis treatment. The Fracture Risk Assessment (FRAX) score, developed by the WHO, is a free web-based clinical scale assessing the 10-year fracture risk and need for lifestyle advice/reassurance, dual X-ray absorptiometry (DEXA) scanning or preventive treatment.
AIMS&METHODS: We sought to compare the screening and management of osteoporosis in patients with gastrointestinal and liver diseases admitted to our hospital with treatment recommendations according to FRAX scores.
Consecutive inpatients [n=100: 37% female] admitted to our ward between January and March 2013 were included; 8 patients were subsequently excluded because they were already prescribed a bisphosphonate. The proportions of patients in whom a DEXA scan was planned/completed and those treated with a bisphosphonate were recorded. FRAX scores for hip and other major osteoporotic fractures, as well as subsequent treatment recommendations were prospectively derived using the UK specific web-based calculator [1]. Differences between observed and recommended treatments were sought using Chi-squared analysis.
RESULTS: The median age [range] of the sample was 52 [18-87] years; the median [range] predicted 1 year survival according to the Charlson co-morbidity index was 89% [64%>98%]. The mean [SEM] vitamin D level was 36.3 [5.0] and 65% [60/92] patients were deemed to be vitamin D deficient. The mean [SEM] 10 year risk of major osteoporotic fracture and hip fracture was 8.9% [2.9] and 3.5% [2.4] respectively. Overall, according to FRAX guidance; 64% [59/92] patients required no treatment; DEXA scans were recommended in 21% [19/92] patients; and based on clinical risk factors alone, 15% [14/92] patients should have been receiving a bisphosphonate: compared with 98%, 0% and 2% respectively observed in our current practice ($p < 0.0001$).
CONCLUSION: Patients admitted with gastrointestinal and liver diseases are frequently vitamin D deficient and at high risk of future osteoporotic fracture, however, few are adequately assessed and/or treated for osteoporosis. The web-based WHO FRAX tool is a readily available, easy to use, free and rapid way of assessing fracture risk based on clinical factors alone that could be utilised in the gastroenterology inpatients to predict those patients who need DEXA scans and/or consideration for specific treatment of osteoporosis.
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Disclosure of Interest: None Declared
Keywords: Fracture, FRAX

P1577 INAPPROPRIATE USE OF PROTON PUMP INHIBITOR: AN ASIAN PERSPECTIVE

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INTRODUCTION: There are growing concerns that the use of proton pump inhibitors(PPI) may be inappropriate in many instances and do not conform to evidence based indications. The purpose of this point prevalence study was to investigate the frequency, indications and appropriateness of PPI use in hospitalized patients on a randomly chosen day.
AIMS&METHODS: The total number of in-patients on a randomly chosen day was documented. The number of in-patients on any form of PPI on the same day was determined. The indications for maintaining the patients on PPI were obtained from the electronic medical records. The list of accepted indications for PPI use was adapted from the Food and Drug Administration (FDA) approved list and these were cross-referenced with the indications documented from the medical records.
RESULTS: A total number of 1025 in-patients were studied. 477 (46.5%) were using PPI, of which 219(45.9%) fulfilled FDA approved indications. The remaining 258(54.1%) did not fulfill FDA approved indications. 208(43.2%) were not indicated based strictly on the FDA criteria and 52 (10.9%) had borderline indications based on expert consensus or other guidelines other than the FDA. The most prevalent indication for inappropriate PPI usage was uninvestigated anaemia in stable patients with no clinical evidence of GIT bleeding. The most

common borderline indication for PPI usage was endoscopic findings of gastropathy/gastritis.

NON-INDICATIONS FOR PPI (BY FDA)	TOTAL =206
Anaemia (no evidence of GI bleed/clinically stable)	71(34.5%)
Aspirin or antiplatelet or NSAIDs (<65yrs)	45(21.8%)
No apparent indication(in records)	24(11.7%)
Corticosteroids	15(7.3%)
Warfarin	14(6.8%)
Malignancy	14(6.8%)
Bone fractures	5(2.4%)
Others (Nasogastric tube feeding, nil per oral status, on low molecular weight heparin, musculoskeletal chest pain, bone fracture, foreign body removal in throat, high gastric residual volume, post tonsillectomy)	18(8.7%)

CONCLUSION: PPI usage is pravelent in hospitals. Less than half of the total PPI usage amongst hospitalized patients has evidence-based indications to support their use. Overuse of PPI has a negative impact on health care cost and may lead to certain adverse effects. Steps to curb inappropriate PPI use should address a few factors including indications to initiate PPI, reassessing need for on-going use while in hospital or upon discharging patients and upon out-patient reviews

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Disclosure of Interest: None Declared

Keywords: hospitalized, inappropriate, indications, patients, proton pump inhibitor

P1578 ALARMINGLY POOR ADHERENCE TO LOW-DOSE ASPIRIN CAN BE IMPROVED BY CONCOMITANT PROTON-PUMP INHIBITOR USE: A LARGE COMMUNITY-BASED STUDY

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INTRODUCTION: Low-dose acetylsalicylic acid (ASA) is the mainstay of cardiovascular (CV) risk management in high-risk populations. Adherence with ASA therapy is of critical importance as poor adherence or discontinuation leads to an increased risk of major CV events. ASA-associated upper gastrointestinal (GI) adverse events are important reasons for decreased compliance with ASA therapy. Concomitant treatment with proton-pump inhibitors (PPIs) reduces the incidence of GI symptoms but there are no studies evaluating the effects of this strategy on ASA compliance. We studied the effect of concomitant PPI use on compliance with ASA therapy in community practice.

AIMS&METHODS: We designed a population-based, retrospective cohort study using data from the Medi-Cal Research database in California. Medi-Cal data include details of all medication use, including over-the-counter medications. Patients aged $\geq$ 18 years who had at least one claim for an incident 30-day supply of low-dose aspirin (325 mg or less per day) formed the study population. Among these patients, a group of PPI users was identified, based on prescription claims during the 12 months following cohort entry. Patients who had no PPI use during the 1-year study follow-up served as controls. We calculated the actual number of days that each patient had "possession" of aspirin during the 12 months of study period. This ratio (number of days of aspirin possession/365 after first aspirin ingestion) was defined as the Medication Possession Ratio (MPR). All analyses were adjusted for comorbidities, GI symptoms, and concomitant NSAID and clopidogrel use.

RESULTS: A total of 80, 623 patients took aspirin with concomitant PPI and 237, 031 took aspirin without any PPI, during the study period. Only 50.6% of the cohort had a 50% or greater compliance with ASA (MPR>= 0.5). Multivariate logistic regression analyses adjusted for age, gender, comorbidity, concomitant NSAID and clopidogrel use and history of GI complaints showed that concomitant PPI use was significantly associated with the likelihood of >=50% adherence to low-dose aspirin, relative to the non-PPI group (OR 1.47, 95% CI 1.43-1.49, $p<0.0001$). Sensitivity analyses showed that high compliance (>=70%) was also significantly more likely in patients on concomitant PPIs (OR 1.33, 95% CI 1.31-1.36, $p<0.0001$).

CONCLUSION: Adherence to low-dose aspirin used for CV risk management in community practice is poor, but may be improved significantly by concomitant PPI use. It is likely that this increased adherence with ASA will translate to a more favorable CV outcome.

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Keywords: Aspirin, compliance, PPI

P1579 PROPOFOL SEDATION FOR DIAGNOSTIC ESOPHAGOGASTRODUODENOSCOPY COMPARED TO MIDAZOLAM: A RANDOMIZED COMPARISON IN SINGLE CENTRE

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INTRODUCTION: Sedative medications are commonly used even in scheduled endoscopic examinations. Although midazolam is widely supervised by endoscopists, propofol is recently favored for rapid acting and metabolized character.

The aim of this study is to compare propofol with midazolam for outpatients' diagnostic esophagogastroduodenoscopy (EGD).
AIMS&METHODS: One hundred and six healthy patients aged 20 to 69 years requesting sedation at diagnostic EGD from October 2012 to May 2013 were randomly assigned to propofol (n=54) or midazolam (n=52). Medications were given by bolus injection and the dose was adjusted by bodyweight (P:0.6-1mg/kg, M:0.03-0.05mg/kg). Supplementary doses were tolerated up to 50% of the initial doses. Before the start of the study, endoscopists and nurses were trained in administering propofol sedation under the supervision of an anesthesiologist. Sedation level and patients' acceptability during procedures, recovery time and patients' satisfaction were assessed. Sedation level and acceptability were evaluated by American Society of Anesthesiologists (ASA) responsiveness levels and gagging reflux on a four-point scale, respectively.
RESULTS: There was no statistical difference between both groups. Among more than 80% patients in both groups, sedation level was moderate to deep without respiratory depression and gagging reflux was absent or mild. The majority of patients rated procedures as good or excellent. Among propofol sedated patients, 91% could walk out just after procedures finished while 85% of midazolam group required wheelchair to leave ($p<0.01$). Mean full recovery time was 4.7 minutes with propofol sedation, which was significantly shorter than midazolam sedation (24min, $p<0.01$). No major incidence was reported after procedure until 24 hours later.
CONCLUSION: Propofol sedation provided adequate sedation level, good acceptability and satisfaction as same as midazolam during diagnostic EGD. Furthermore, propofol sedation might be unnecessary for preparing recovery room and excessive visual task. (Clinical trial registration number: UMIN000009142)
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Disclosure of Interest: None Declared
Keywords: esophagogastroduodenoscopy, Propofol sedation, randomized controlled trial

P1580 WEEKEND VS. WEEKDAY ADMISSION FOR URGENT EGD DUE TO UPPER GASTROINTESTINAL BLEEDING, 10-YEARS SINGLE-CENTER EXPERIENCE

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INTRODUCTION: Acute upper gastrointestinal bleeding (UGIB) is one of the most common cause of hospital admissions for acute care and indication for urgent esophagogastroduodenoscopy (EGD). The aim of this study was to estimate whether outcomes for patients subjected to urgent EGD duo to UGIB differ depending on weekend versus weekday admission, and whether any such differences are mediated by discrepancies in presence of risk factors.
AIMS&METHODS: We conducted retrospective-prospective study on patients submitted to urgent EGD in University Clinic ...Dr Dragisa Misovic-Dedinje", Belgrade, Serbia in period from 2002 to 2012. Data were collected on patient symptoms, possible risk factors, verified causes of bleeding, modality of treatment, complications and outcome. Patients were divided in two groups based on whether they were submitted to urgent EGD on weekend (Group I) or weekday (Group II). Proportions among the groups were compared in univariate analysis.
RESULTS: Study included 1150 patents (62% male). Among patients in Group I were significantly more those with severe symptoms, including melena or hematemesis (p=0.001). Esophageal varices and gastric ulcers were more common verified as cause of UGIB in Group I (p=0.007). Patients in Group I were more often submitted to endoscopic treatment aside from traditional one (p=0.000) and were associated with more complications (p=0.000). Nevertheless, there was no difference in mortality rate among the groups (Group I=3.6%; Group II=2.5%; p=0.348). Hospitalization length was significantly longer in Group I (p=0.009). Regarding risk factors, patients in Group I were more often associated with alcohol consumption (p=0.000).
CONCLUSION: Weekend admission of patients with upper gastrointestinal bleeding is not associated with increased mortality rate, although it is associated with more severe clinical picture, higher complication rate and longer hospitalization.
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Disclosure of Interest: None Declared
Keywords: esophagogastroduodenoscopy, upper gastrointestinal bleeding, weekend admission

P1581 ETHNIC DIFFERENCES IN UPPER GASTROINTESTINAL DISEASES IN SCOTLAND.

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INTRODUCTION: There is a paucity of data assessing ethnic variations in upper gastrointestinal (GI) diseases: we sought to study the incidence of upper GI diseases using adequate measure of ethnicity in Scotland.
AIMS&METHODS: Using the Scottish health and ethnicity linkage study (SHELS), linking NHS hospital admissions and mortality to the Scottish census 2001, we explored ethnic differences in incidence (2001-2010) of specific upper GI diseases (peptic ulcer disease, oesophagitis, gastritis, gallstones and pancreatitis) in Scotland. Risk ratios (RR) were calculated using Poisson regression with robust variance and multiplied by 100, by gender, adjusted for age and subsequently country of birth. The White Scottish population was the standard reference population (100). 95% confidence intervals (CI) were calculated to enable comparison and exclude 100 in the results below.
RESULTS: The total numbers of first events within the 9 years period of interest (over almost 29 million of Person-Year (PY) at risk) was 44,612 for peptic ulcer, 102,706 for oesophagitis, 141,235 for gastritis, 87,556 for gallstones and 17,177 for pancreatitis.
Looking at risk ratios for all specific upper GI diseases and compared to respectively White Scottish men and women, other White British and other White had a lower risk of upper GI diseases even after adjustment for country of birth. White Irish had an increased risk of upper GI diseases but not significant after adjustment for country of birth.
There were consistent ethnic variations in non–White minority ethnic group even after adjustment for country of birth. Chinese men and other South Asian (SA) men and women had a 1.5 to 1.7 fold increased risk of peptic ulcer disease. Pakistani and Bangladeshi had a 1.3 to 2 fold increased risk of esophagitis whereas Chinese had a lower risk (RR [CI] = 63.5 [50.2; 80.2] for men, 67.4 [51.6; 88.1] for women). South Asian had a 1.2 to 1.5 fold increased risk of gastritis whereas it was lower for men of African origin (RR [CI] = 65.6 [49.3; 87.3]). Gallstones was more incident in Chinese men (140.2 [117.5; 167.2]) and Pakistani women (131.3 [115.4; 149.4]), the latter also had an increased risk of pancreatitis (151.7 [123.3; 186.6]).
CONCLUSION: This unique data allowing the comparison of specific upper GI diseases incidences between ethnic groups has shown major differences. Further exploration on risk factors and understanding of differences is needed to promote health equality.
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Disclosure of Interest: None Declared
Keywords: ethnicity, gallstones, gastritis, oesophagitis, pancreatitis, peptic ulcer

P1582 A CLINICAL EXPERIENCE OF POEM FOR ACHALASIA AND ESOPHAGEAL DIFFUSE SPASM

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INTRODUCTION: Per-oral endoscopic myotomy (POEM) becomes widely accepted as a useful treatment for achalasia. We introduce the summary and present result of POEM in our institution.
AIMS&METHODS: Data on single-institution POEM were collected prospectively. Pre- and postoperative symptoms were quantified with Eckardt scores. Objective testing (manometry, endoscopy, barium swallow) was performed preoperatively and postoperatively.
RESULTS: Thirty achalasia patients and one diffuse esophageal spasm patient underwent POEM between September 2011 and December 2012. The mean age was 48.5 (26-79) years. Seven patients had prior balloon dilations or Botox inejection. Myotomy length was 14.2cm (7-26cm), and the median operating time was 154.7 minutes (80-345). No serious complications related to POEM were encountered.
All patients had relief of dysphagia and no patient had Eckardt scores greater than 2. The median hospital stay was 6.4 (5-10) days. During follow-up, medication was necessary in only one patients who developed reflux esophagitis (Los Angeles classification B); this was well controlled with regular intake of protein pump inhibitors (PPIs).
CONCLUSION: The outcome of POEM in out institution was excellent. All patients had dysphagia relief, There is significant though mild gastroesophageal reflux postoperatively in one patient but this was well controlled with regular intake of protein pump inhibitors (PPIs).
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Disclosure of Interest: None Declared
Keywords: Achalasia, Diffuse esophageal spasm, NOTES, Per oral endoscopic myotomy, POEM

P1583 ESOPHAGEAL PRESSURE RESPONSES TO A DRINK CHALLENGE TEST FOR EVALUATION OF OBSTRUCTION ACROSS THE ESOPHAGOGASTRIC JUNCTION

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INTRODUCTION: Impaired transit across the esophagogastric junction (EGJ) is a major determinant of the clinical outcome in patients with esophageal motility disorders.
AIMS&METHODS: The aim of the present study was to determine if pressure responses to a rapid drink challenge test measured by means of high resolution manometry (HRM) can discriminate patients with and without obstruction across the EGJ.
METHODS: In 20 patients with dysphagia and non-treated achalasia, 17 patients with treated achalasia, 37 patients with hypertensive esophagus and normal EGJ relaxation, and 20 healthy controls, a rapid drink challenge test, rapid drink of 200 ml water in sitting position, was performed at the end of the standard HRM protocol. Pressure responses of the esophagus were analysed and

pressure gradient across the EGJ was measured as intraesophageal minus intragastric pressure.
RESULTS: : The number of swallows performed and the time expended to drink 200 ml, was similar in all groups of patients (NS), and significantly larger than in healthy subjects (17±1 swallows during 38±2 sec, and 14±1 swallows during 24±2 sec. pooled data for patients and healthy subjects, respectively; $p<0.05$). The pressure gradient in healthy subjects was negative (-2±1 mmHg) whereas it was weakly positive in patients with hypertensive esophagus (6±2 mmHg; $p<0.05$). By contrast, patients with non-treated achalasia had a significantly greater pressure gradient across the EGJ (16±3 mmHg; $p<0.05$ vs all) that returned to levels similar to those of patients with non-obstructive hyperperistalsis after treatment (6±2 mmHg; $p< 0.05$ vs non-treated achalasia; NS vs hyperperistalsis). Overall, pressure gradient correlated with the degree of reported dysphagia (r=0.4; p=0.000). The pattern of esophageal pressures during water swallow was different among the studied groups: healthy subjects showed a complete inhibition of esophageal pressures (0±1presurizations) whereas patients with non-treated achalasia showed the largest number (8±2 vs. 3±1 presurizations, hypertensive peristalsis, $p<0.05$ for all) and the most prolonged pressure increments above 20 mmHg (mean duration 6±2 sec vs 1±0 sec, hypertensive peristalsis; $p<0.05$ for all). Patients with treated achalasia showed a trend to reduction of pressure activity (4±2 presurizations, 2±1 sec long; NS vs non-treated achalasia and hypertensive peristalsis)
CONCLUSION: Measurement of esophageal pressures during a rapid drink challenge test can be used to objectively assess functional obstruction across the EGJ in patients with esophageal motility disorders
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Disclosure of Interest: I. Marin: None Declared, C. Julia: None Declared, J. Serra Consultancy for: Reckitt Benckiser
Keywords: drink test, esophagogastric junction

P1584 ESOPHAGOGASTRIC JUNCTION OUTFLOW OBSTRUCTION: A NEW MANOMETRIC CONDITION UNDER INVESTIGATION.

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INTRODUCTION: Esophagogastric junction outflow obstruction (EGJOO) is a new disorder recently included under the Chicago Classification[1]. High Resolution Manometry (HRM) can overcome some of the limitations in the evaluation of the esophagogastric junction (EGJ) experienced with earlier technologies such as conventional manometry. The EGJOO is characterized by impaired EGJ relaxation (HRM revealing high Integrated Relaxation Pressure: IRP > 15 mmHg) and preserved esophageal peristalsis.
AIMS&METHODS: Description of manometric findings of patients with EGJOO diagnosed by HRM since the implementation of the Chicago Classification.
RESULTS: A total of 24 consecutive patients were included –average age 47.6 years old, 18 females (75%)-. One patient had undergone antirreflux surgery (Nissen fundoplication). Three patients suffered from hiatus hernia. The most common symptoms were epigastric pain and heartburn.
Manometric findings: The resting expiratory pressure of the lower esophageal sphincter (LES) was normal in 50% of the patients and elevated in the remaining 50% (mean 35.4 mmHg). As defined, all patients presented elevated IRP values (mean 17.4 mmHg). Mean distal contractile integral (1031 mmHg.s.cm) and contractile front velocity (4 cm/s) were normal. Mean distal latency was normal (7.8 s). Mean Upper esophageal sphincter resting pressure was 74 mmHg. Regarding esophageal peristalsis: 16 patients (66%) presented 'intact peristalsis', 1 (4%) 'weak peristalsis with small peristaltic defects', 3 (12%) 'weak peristalsis with large peristaltic defects' and 4 (16%) 'frequent failed peristalsis'.
Seven patients (29%) showed rapid increased in intrabolus pressure.
An incomplete esophageal transit was observed in 8 patients (33%) by Multichannel Intraluminal Impedance (MII) connected to manometry.
Using a 24-h esophageal pH monitoring, we detected pathological acid gastroesophageal reflux in 5 patients (20.8%).
EGJ structural stenosis or eosinophilic esophagitis were ruled out using complementary examinations (gastroscopy, biopsies, imaging test, etc).
CONCLUSION: EGJOO is a new manometric entity with a yet undefined meaning. In this series most patients presented intact peristalsis, although some unspecific esophageal motility alterations were found.
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EGJOO includes a heterogeneous group of patients with some individuals having an incomplete phenotype of achalasia (functional EGJOO) and others probably having an undetected mechanical cause of outflow obstruction such as hiatus hernia, structural esophageal stenosis (including post-surgical) or eosinophilic esophagitis.
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Disclosure of Interest: None Declared
Keywords: Chicago Classifications, esophagogastric junction, high resolution manometry, Outflow obstruction

P1585 PREVALENCE OF RELAXATION DISORDERS OF THE LOWER ESOPHAGEAL SPHINCTER IN PATIENTS UNDERGOING HIGH-RESOLUTION MANOMETRY

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INTRODUCTION: Esophageal manometry is indicated in patients with non-obstructive dysphagia and in patients scheduled for fundoplication. In both patient subsets, one of the main reasons for performance of this investigation is identification of patients with achalasia-like disturbances. However, the prevalence of LES-relaxation disorders in patients undergoing high-resolution esophageal manometry (HRM) is unknown.
AIMS&METHODS: In a prospective study, we determined the integrated relaxation pressure (IRP) according to the Chicago Classification in 787 subjects undergoing HRM at our institution between 09/2011 and 03/2013. Demographics and symptoms including PPI-responsiveness were evaluated in all subjects with relaxation disorders (IRP > 15 mmHg) and in 227 subjects without. Moreover, data on lower esophageal sphincter (LES) resting pressure and pH-metry data were analysed.
RESULTS: 28% of our pts came from the surgical department, 63% were female. Pts were 56.5±15.6 yrs old (mean±SD), mean BMI was 26.0±5.6 kg/m2. 65% of the pts reported heartburn, 60% regurgitation, 58% dysphagia, 56% retrosternal pain, 51% epigastric pain and 37% nausea. Of those who took PPI 20% responded completely, 53% partially and 17% did not respond. 24h-pH-metry (off PPI) was performed in 44% of the pts. In these, reflux time (pH < 4) was 8.0±10.3% of time. The resting pressure of the LES was 23.3±16.7 mmHg. Mean IRP was 11.3±9.8 mmHg. IRP exceeded 15 mmHg in 93 pts corresponding to 11.8% of the total cohort. IRP was significantly higher in pts with dysphagia than without (13.5±10.5 vs. 8.1±7.8 mmHg, $p<0.0001$). Moreover, we observed negative correlations between LES resting pressure and reflux time (p=0.005) and between IRP and reflux time (p=0.0009).
CONCLUSION: LES-relaxation occur in more than 10% of our pts undergoing HRM. Increased IRP is associated with dysphagia and reduced reflux time. However, symptoms are not specific for either GERD or LES-relaxation disorders.
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Disclosure of Interest: J. Keller Financial support for research from: Given Imaging, D. Menge: None Declared, V. Andresen: None Declared, S. Scherzberg: None Declared, K. Schmidt: None Declared, P. Layer: None Declared
Keywords: Achalasia, dysphagia, GERD, heartburn, high-resolution manometry

P1586 PREVALENCE OF AUTOIMMUNE COMORBIDITIES IN IDIOPATHIC ACHALASIA IS SIMILAR TO A MATCHED POPULATION OF PATIENTS SUFFERING FROM NON-ACHALASIA OESOPHAGEAL DISORDER

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INTRODUCTION: The pathogenesis of achalasia is multifactorial and genetic, infectious and autoimmune mechanisms have been all proposed. Recently an increased prevalence of autoimmune diseases has been reported in a Canadian un-matched cohort of achalasia patients. We aimed to compare the prevalence of autoimmune disease in patients with esophageal achalasia to a matched population of control patients.
AIMS&METHODS: The study population consisted of 180 patients (71 males, mean age 55 ± 16 years) with proven clinical and instrumental diagnosis of idiopathic achalasia. Gender and age matched consecutive subjects selected from the outpatient clinic and referring of esophageal disorders other than achalasia, served as controls. All patients were investigated for the presence of the following comorbidities: hematologic diseases and cardiopathies and neoplasms. Screened autoimmune diseases were I diabetes mellitus, hypothyroidism, Sjögren's syndrome, uveitis, systemic lupus erythematosus, rheumatoid arthritis.
RESULTS: The overall prevalence of comorbidities was similar in achalasia and control patients (62 vs 57%, respectively). Cardiopathies and hyperlipidemia were the most frequently observed comorbidities in achalasia and controls (30 vs 37% and 17 vs 31%, respectively p=NS). Similarly hematological disorders and type II diabetes were similarly prevalent in the two groups. As far as the overall prevalence of autoimmune disorders, there was a tendency, but not significant, to a higher prevalence in achalasia than in controls (8 vs 5%, p= NS), without any difference for each of the considered automimmune disease (data not shown). Most interestingly, presence of comorbidities, regardless of their autoimmune origin, did not significantly affect disease's phenotype as the age of disease onset was similar in achalasia patients with and without comorbidities (46±21 vs. 49±16 years, respectively, p=NS).
CONCLUSION: We showed that type and the frequency of comorbidities, either or not autoimmune, in a large series of achalasia patients and we showed that their prevalence is similar to that of a matched control population. Although larger epidemiological studies are needed to confirm our data, our results indicate that the putative mechanisms underlying the onset of achalasia are specific for this disease.
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Disclosure of Interest: None Declared
Keywords: Achalasia, autoimmune disease

P1587 LONG TERM OUTCOME OF PATIENTS WITH REFLUX SYMPTOMS AND SYMPTOMATIC ESOPHAGEAL DYSFUNCTION DURING AND AFTER A STANDARDIZED TEST MEAL : A HIGH-RESOLUTION MANOMETRY STUDY

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INTRODUCTION: Recently we presented novel methodology for the assessment of oesophageal function and symptoms not only with liquids but with solids and also during and after a standard test meal (Sweis DDW 2011, NGM 2012).
AIMS&METHODS: In the absence of a ''gold standard'' diagnosis, outcome data provides insight into the clinical impact of tests. 18 patients referred with reflux symptoms and 10 healthy controls underwent High Resolution Manometry(HRM) with 5ml water and a test meal followed by 10min postprandial observation of symptoms and events. 24hr pH studies were then performed. The number of Symptoms Associated with Dysfunction(SAD) was calculated. HRM findings and initial diagnosis were compared with the final diagnosis and outcome at 2 years
RESULTS: No symptoms occurred with 5ml water. 12/18(67%) patients had SAD (mean SAD 2 (0-7)) during/after the meal. Compared to 5ml water, manometric diagnosis was altered in 12/18(67%) after the test meal (most reclassified from hypotensive to normal motility). No healthy volunteers had SAD.
11/18 patients had GORD on pH studies. By 2 years, 5/11 that had dysmotility (e.g. hypotensive/failed peristalsis) during the meal with frequent symptomatic postprandial reflux events had anti-reflux surgery with excellent outcome. 6/11 with GORD did not have surgery, 2 with symptomatic reflux on HRM declined and remain symptomatic, 4 with symptomatic reflux were not offered surgery. 2 with severe hypotensive dysmotility and symptomatic reflux responded to optimal acid / reflux suppression. 1 with outlet obstruction (peptic stricture) and 1 with co-existing spasm did not respond to medication.
Of 7 with functional heartburn (negative pH results), 2 with normal HRM responded to diet. 2 with symptomatic reflux during HRM had good response to acid-suppression (suggests false neg pH study). The final 3 all had outflow obstruction identified only during the meal; 1 had good outcome after dilatation, 1 was too frail for therapy and remains symptomatic and the last was lost to follow-up
CONCLUSION: HRM studies which include a test meal and postprandial observation provide an objective explanation for symptoms in the majority of patients investgated for 'reflux' symptoms. Long-term follow-up suggests this information can guide management.
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Disclosure of Interest: None Declared
Keywords: dysphagia, manometry, pH monitoring, Reflux symptoms

P1588 PREDICTIVE VALUE OF ESOPHAGEAL MOTILITY TEST IN THE PROFICIENCY OF ESOPHAGEAL SPEECH

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INTRODUCTION: One of the speech rehabilitation methods following the total laryngectomy surgery is esophageal speech therapy. In this method where the success rates are rather low after the therapy, predetermining the patients to benefit from the therapy will be important to choose the appropriate method for speech rehabilitation and will also help in preventing the loss of cost, time and labour. In this study conducted in accordance with this purpose, the usability of manometric data, which was measured before the therapy with esophageal motility test, has been studied in order to predetermine the candidates suitable for esophageal speech.
AIMS&METHODS: This is a prospective clinical study performed multidisciplinarily in one center.51 male patients with total laryngectomy, mean age of 58.8±8.0, who haven't been exposed to any speech rehabilitation before are included in this study. Data is collected from 44 cases completing speech therapy which lasted for 6 months in total and consisted of 11 sessions. Manometric measures have been obtained through esophageal motility test and using water-perfusion system with Dent-Sleeve catheter on the patients before the therapy. In order to assess the level of esophageal speech Wepman used a scale for esophageal speech. Following the therapy, the patients were divided into two groups by considering the ones each of whose scores is 1, 2 or 3 are at the sufficient level and the ones each of whose scores is 4, 5, 6 or 7 are at the insufficient level according to this scale. Manometric correlation was studied between the 17 cases (Group I) which were able to reach esophageal speech at good level and 27 cases (Group II) which weren't.
RESULTS: The avarege manometric values of group 1 ve 2 are respectively; LES pressure 16.4 and 14.6 mmHg, peak amplitude 66.5 and 68 mmHg, contraction duration time 3.55 and 3.74 sn, onset velocity 3.40 and 3.43 cm/sn, UES pressure 17.2 ve 16.0 mmHg. There isn't any statistically significant difference between the groups could be observed in terms of age, period between the surgey and the beginning of speech therapy, type of neck dissection, having radiochemotherapy or not and manometric values of esophagus.
CONCLUSION: No predictive value of esophageal motility test was seen, which was carried out before the speech therapy given to the patients with total laryngectomy, on determining the esophagus speech level that the patient could reach.
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Disclosure of Interest: None Declared
Keywords: ESOPHAGEAL MOTILITY TEST, ESOPHAGEAL SPEECH

P1589 UPPER GASTROINTESTINAL SYMPTOMS ARE RISK FACTORS FOR LOW BMI AND POOR QUALITY OF LIFE REGARDLESS OF THEIR MEAL RELATION

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INTRODUCTION: The impact of functional gastrointestinal symptoms on body weight is questionable. Obesity is associated with GERD, but we know that upper GI symptoms may negatively affect body weight by limiting food intake and reducing BMI. This is the case of early satiation as a predominant symptoms of meal-related functional dyspepsia. Whether upper gastrointestinal symptoms, less strictly related to meal assumption, are able to impact body weight is not known. AIM: To examine the contribution of specific upper gastrointestinal symptoms on BMI and quality of life.
AIMS&METHODS: The subjects were 126 consecutive patients referring to the outpatients clinic for upper gastrointestinal symptoms (44 male, age 46±13 years). All subjects had a clinical and instrumental (upper GI endoscopy and 24h pH-impedance) diagnosis of GERD or FD. Subjects with underlying organic diseases or on a low calories dietary regimen were excluded (n=74). BMI was recorded and patients divided in under-, normal-, overweight or obese according to internationally accepted criteria. Also, UGI-tract symptoms were scored according to the PAGI standardized questionnaire, assessing the type, the severity (10 symptoms, scored 0-5) and the impact on quality of life (30 items, scored 0-5) of specific symptoms.
RESULTS: According to clinical and instrumental criteria 62 patients were diagnosed to have functional dyspepsia, 64 GERD, while 40 had overlapping symptoms. Averaged BMI values were 24±4 Kg/m^2, with 10, 56, and 8 % of patients being underweighted, overweighted and obese, respectively. In FD patients BMI values were similar than in GERD patients (25±4 vs. 26±4 Kg/m^2, respectively). Notwithstanding the underlying diagnosis, in underweighted patients, the pooled symptoms severity was significantly higher than in normal, overweighted or obese patients (92±40 vs. 45±34, p=0.002), and this was also associated with a worsen quality of life (85±31 vs.39±30, p=0.001). Most interestingly, this association was still significant when we excluded from the analysis items assessing meal-induced symptoms (early satiation and appettite loss) (80±38 vs.41±31 and 85±35 vs.39±31, for severity and quality of life repectively, p=0.004 and p=0.0001).
CONCLUSION: Here we show that more severe upper GI symptoms are risk factors for low BMI even in the absence of meal-related symptoms. The mechanisms underlying this association are still unclear and likely reflect the impact of the poor quality of life on patients daily life and food consumption. Larger studies are warrant to investigate how meal-unrelated GI symptoms affects BMI.
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Disclosure of Interest: None Declared
Keywords: BMI, Functional dyspepsia, GERD, quality of life

P1590 BENEFICIAL EFFECT OF BUSPIRONE, AN ORALLY AVAILABLE 5-HT1A RECEPTOR AGONIST, ON LOWER ESOPHAGEAL SPHINCTER FUNCTION IN PATIENTS WITH SYSTEMIC SCLEROSIS.

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INTRODUCTION: Domperidone is widely used for the management of symptoms in patients with Systemic Sclerosis (SSc) and esophageal involvement, but its efficacy is under question. Recently, buspirone, an orally available 5-HT_{1A} receptor agonist, was shown to enhance esophageal peristalsis and lower esophageal sphincter (LES) function in healthy volunteers.
AIMS&METHODS: Aim: To evaluate the efficacy of acute buspirone and domperidone administration in SSc patients with symptomatic esophageal involvement
Methods: Thirty consecutive SSc patients (aged 52.3±10.4 years, 26 women) underwent high resolution esophageal manometry (HRM) before and 30 minutes after administration of 10 mg buspirone (n=20) or 10 mg domperidone (n=10). We compared buspirone and domperidone effects, before and after drug administration, on: a) resting pressure of the LES; b) residual pressure of LES relaxation; c) amplitude, duration, and onset velocity of distal esophageal body contractions. Prior to HRM each patient completed a self-reported 0-10 visual analogue scale questionnaire for esophageal symptoms (ESQ). A paired t-test was performed for the comparisons.
RESULTS: There was no difference in terms of SSc characteristics, as well as of clinical severity (assessed by ESQ scores) and extent (assessed by HRM findings) of esophageal involvement between patients who received buspirone or domperidone. Buspirone significantly increased mean resting pressure of LES (11.53±3.4 vs. 9.42±2.6, $p < 0.001$), whereas domperidone has no effect on it (8.64±2.6 vs. 9.09±3, p=0.469). Comparison of the mean individual changes after administration of either drug revealed that buspirone was superior to domperidone in enhancing the resting pressure of LES (2.11±2.0 versus -0.45±2.3, p=0.006). None of the drugs has any effect on the other examined parameters.
CONCLUSION: Acute administration of buspirone, but not of domperidone, enhanced function of LES in patients with SSc, suggesting a putative role of 5-HT_{1A} receptor-mediated interactions in these patients. Prospective studies to examine whether buspirone exerts a long term beneficial effect in SSc-associated esophageal disease are warranted.
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Disclosure of Interest: None Declared
Keywords: buspirone, lower esophageal sphincter, systemic sclerosis

P1591 POTENTIAL VALUE OF ESOPHAGEAL BASELINE IMPEDANCE IN DIFFERENTIATING FUNCTIONAL HEARTBURN FROM NON-EROSIVE REFLUX DISEASE

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INTRODUCTION: : In clinical practice still lacking a simple and effective method to identify functional heartburn (FH) and non-erosive reflux disease (NERD). Esophageal baseline impedance appears to represent esophageal mucosal integrity, and dilated intercellular spaces were found existing in NERD but not in FH.
AIMS&METHODS: The aims of the study were to analyze the difference of esophageal intraluminal baseline impedance in FH and NERD patients.
Patients with heartburn and health volunteers (control) were included. All subjects underwent gastroscopy to exclude organic diseases and reflux esophagitis. Following the 24h impedance-pH monitoring and PPI test, patients were divided into two groups: NERD, with overload acid reflux; FH, with normal range of reflux parameters and negative PPI test. The controls presented normal results on gastroscopy and 24h impedance-pH monitoring. Baseline impedance values (BIV) were selected. Esophageal epithelial intercellular space (ICS) was quantitatively measured on H&E sections under light microscopy.
RESULTS: 36 NERD (f/m=20/16, 55.3±2.7 y), 40 FH (f/m=33/7, 53.1±2.1 y) and 33 controls (f/m=27/6, 42.7±2.7 y) were enrolled. The BIV of NERD (2407.7±206.6 Ω) was significantly lower than that of FH (3014.7±162.6Ω, p=0.025) and controls (3360±215.9Ω, p=0.001). NERD [1.25(1.15-1.60)μm, n=11] presented wider ICS than that of FH [0.98(0.90-1.05)μm, n=10, p=0.009] and control [1.01(0.94-1.06)μm, n=11, p=0.005]. There were no different both in BIV and ICS between FH and controls. Negative correlation was observed between BIV and ICS (r = -0.545, p=0.002).
CONCLUSION: FH patients presented significantly higher BIV and lower ICS than NERD, and the BIV which negatively correlated to ICS can represent esophageal mucosal integrity. The BIV might be a potential parameter to differentiate the FH from NERD when the heartburn patients underwent 24 hour impedance-pH monitoring.
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Disclosure of Interest: None Declared
Keywords: differentiate value, epithelial intercellular space, esophageal baseline impedance, functional heartburn, non-erosive reflux disease

P1592 OVERLAP OF FUNCTIONAL GASTROINTESTINAL DISORDERS WITH AUTOIMMUNE CONDITIONS

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INTRODUCTION: The functional gastrointestinal disorders (FGIDs) affect up to one-third of community members and arise from unknown etiology. Previous studies have suggested that intestinal permeability is increased in individuals with FGIDs, which may allow stimulation of the immune system by luminal gut bacteria, perhaps triggering autoimmune conditions.
AIMS&METHODS: We aimed to identify whether specific FGIDs are associated with autoimmune conditions.
Electronic medical records were obtained from the United Kingdom THIN database (n=23,471). FGIDs and autoimmune conditions (endocrine, psoriasis, rheumatologic, multi-system, liver and lung) were identified using Read codes. Four groups were defined, healthy control (n=14,490), IBS (n=4,080), functional dyspepsia (n=4,131), chronic constipation (n=1,874). There was some overlap between the three FGID groups. The sample was 66% female and the majority was born prior to 1950, enabling a prolonged medical record review.
RESULTS: While the prevalence of all autoimmune conditions was low, FGID groups were generally associated with higher prevalence than healthy controls (Table 1). IBS was associated with higher rates of psoriasis (OR=1.88) which was independent of control variables (Table 1). FD was associated with higher rates of psoriasis (OR=2.00) and rheumatologic conditions (OR=1.60) which was independent of control variables (Table 1). This was also true for constipation (psoriasis OR=1.55, rheumatologic OR=1.41) (Table 1). FGIDs were associated elevated prevalence of other conditions but these failed to maintain statistical significance after holding control variables constant.

Table 1. Odds ratios for selected autoimmune conditions

	Disease	OR[1]	Lower	Upper	p-value	OR[2]	Lower	Upper	p-value
IBS	Endocrine	0.73	0.60	0.89	0.0020	0.82	0.64	1.04	0.0990
	Psoriasis	1.88	1.59	2.22	<0.0001	1.28	1.04	1.58	0.0210
	Rheumatological	0.95	0.75	1.20	0.6770	1.00	0.75	1.32	0.9750
FD	Endocrine	1.21	1.03	1.43	0.0220	1.00	0.84	1.20	0.9680
	Psoriasis	2.00	1.70	2.35	<0.0001	1.52	1.27	1.81	<0.0001
	Rheumatological	1.60	1.31	1.94	<0.0001	1.52	1.23	1.88	<0.0001
Constipation	Endocrine	1.18	0.94	1.49	0.1590	0.93	0.73	1.17	0.5210
	Psoriasis	1.55	1.22	1.96	<0.0001	1.40	1.10	1.78	0.0070
	Rheumatological	1.41	1.07	1.86	0.0160	1.37	1.03	1.82	0.0320

[1]Unadjusted
[2]Adjusted for age, gender, anxiety and depression

CONCLUSION: Primary care medical records indicate FGIDs have a clear association with a number of autoimmune conditions. This supports the possibility of immune activation in these disorders leading to autoimmune disease at remote sites
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Disclosure of Interest: None Declared
Keywords: autoimmune disease, functional gastrointestinal disorders

P1593 THE FUNCTIONAL DYSPEPSIA TREATMENT TRIAL (FDTT): ANTIDEPRESSANT EFFECT ON GASTRIC SATIETY

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INTRODUCTION: Tricyclics and SSRIs are frequently used to treat functional dyspepsia (FD). However, their effect on meal tolerance is not clear.
AIMS&METHODS: To determine whether antidepressant use affects gastric volume in FD individuals. This study is a prospective, randomized, double-blind placebo-controlled trial at 8 sites. Inclusion criteria were: EGD within 5 years; no prior ulcers, esophagitis, abdominal surgery; no antidepressants; HADS <11. 292 subjects were randomized to 1 of 3 arms: 50mg amitriptyline(AMI), 10mg escitalopram(ESC), placebo(PLA). Balancing factors were gender, HADS, FD subtype, gastric emptying, satiety, BMI, race, and study site. A Nutrient Drink Test (NDT) for accommodation was performed by administering Ensure at 30mL/min. until participants were full. The Maximum Tolerated Volume (MTV) was reported as the primary outcome. An ITT analysis of covariance (baseline value and balancing factors) of the post NDT MTV was used to assess treatment effects.
RESULTS: The mean age of the 292 participants was 44 years, 219 (75%) were female, 250 (86%) were Caucasian, and 11 (4%) had an abnormal HADS score. Between the 3 arms, there were no differences in age or distribution of gender, race, FD subtype, or baseline gastric emptying or satiety results. After the 12 weeks of treatment, there was no differential treatment effect for the post-treatment NDT (mean MTV: PLA 839 v AMI 764 v ESC 823 ml, p=N. S.). There was a borderline significant interaction for treatment effect by FD subtype (p=0.09). Tests for interactions did not demonstrate differential treatment effect based on gender, age, BMI, baseline HADS, or baseline gastric emptying or NDT results.
CONCLUSION: The positive effects of amitriptyline and escitalopram on FD do not appear to affect gastric nutrient drink volume tolerated. Antidepressants may not help those patients with FD who have difficulty eating as their primary complaint.
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Disclosure of Interest: None Declared
Keywords: ANTIDEPRESSANT, FUNCTIONAL DYSPEPSIA, GASTRIC SATIETY

P1594 WHAT EXPLAINS LONG-TERM USE OF PPI? A POPULATION-BASED, CROSS-SECTIONAL ANALYSIS IN DENMARK

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INTRODUCTION: Long-term use of PPI has for the last decades continued to increase and is considered an important challenge in health care, influencing both the individual patient and the health care system in general. It is not fully understood what motivates long-term use in the general population.
AIMS&METHODS: The aim of the study was to describe variables associated with long-term use of PPI. An internet-based survey was conducted in September 2012 among members of a web-panel (n=18,427), representative of the Danish adult population. The survey included a total of 22 items on demographics, medication use, reasons for starting PPI therapy (*e.g.*heartburn/regurgitation, dyspepsia, ulcer prophylaxis), previous endoscopy, and ongoing acid-related symptoms. We defined long-term use as use of PPI in >1/3 of the last year. All variables were compared between long-term users and 'sporadic users' (use of PPI in <1/3 of last yr) by univariate analysis. Variables differing significantly between long-term users and sporadic users were included in a multivariate stepwise logistic regression model.
RESULTS: Total number of responders was 9,390 (mean age 48 yr, 49% males). Long-term use of PPI was reported by 584 (6%) and sporadic use by 693 (7%). Logistic regression identified six variables which significantly influenced the risk for long-term PPI use (table). Odds ratio for all six variables were adjusted for ongoing acid-related symptoms, which occurred at least monthly in 73% (95% CI: 71 – 75%) of long term-users and in 59% (56 – 62%) of sporadic users. Weekly or daily symptoms were reported by 58% (55 – 61%) of long-term users and by 28% (26 – 30%) of sporadic users.

Variable	Long-term users (N=584) N (%)	Sporadic users (N=693) N (%)	Odds ratio[α] (95% CI)

(continued)

Mean age [SD]	58 [14]	52 [17]	1.01 (1.00 – 1.02)$^{\beta}$
Male gender	314 (54)	319 (46)	1.5 (1.1 – 1.9)
Multiple (≥3) reasons for starting PPI therapy	136 (23)	95 (14)	1.7 (1.2 – 2.4)
PPI prescription renewal by telephone	443 (76)	260 (38)	4.5 (3.3 – 5.7)
Polypharmacy (≥4 types of medicine)	265 (45)	153 (22)	2.3 (1.7 – 3.1)
Previous endoscopy	388 (66)	291 (42)	1.6 (1.2 – 2.0)

α: All odds ratios were adjusted for ongoing symptoms. β: Odds ratio for age is per year.

CONCLUSION: Patients reporting multiple reasons for starting PPI therapy had an increased risk for long-term use, but no single specific reason, *e.g.* heartburn or ulcer prophylaxis, increased the risk significantly. Prescription renewal without seeing the doctor (by telephone), polypharmacy and male gender were important additional variables related to long-term use of PPIs.

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Keywords: PPI, questionnaire, Reflux

P1595 GASTRO-ESOPHAGEAL REFLUX AND FOOD CONSUMPTION FREQUENCY

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INTRODUCTION: Gastroesophageal reflux simptoms and disease(GERD) are common conditions, with multifactorial pathogenesis. Obesity and GERD are clearly related, both from a prevalence and causality association. But diet may be associated with symptomatic gastro-oesophageal reflux independent of nutritional status.

AIMS&METHODS: The aim of the study was to determine the presence of gastro-esophageal reflux symptoms and the prevalence of gastro-esophageal reflux disease (GERD) in general urban population and to evaluate the type of diet associated with this pathology.

A randomized sample of subjects (n=300), representative for general urban population, selected from the family doctors patient lists was invited for interview in the doctor's office. Selected subjects were evaluated for recent symptoms using Gastrointestinal Symptom Rating Scale (GSRS), for the diagnosis of GERD using Montreal criteria and for their diet using a food frequency questionnaire.

RESULTS: In the last 7 days preceding the survey, were present relevant symptoms for gastro-esophageal reflux in 26.4% of investigated subjects and GERD was diagnosed in 31.1% of subjects. People aged over 50 years experienced an increased prevalence of recent symptoms (36.4 %, $p<0.001$) and GERD (37.4%, $p>0.05$). Recent symptoms were more frequently present in obese and overweighed than normal weighted subjects (42.5% and 29.5% versus 10.5%, p=0.001), and GERD was present especially in overweighed people (41.1%, p=0.015). Using median as cut-off point, the GERD subjects are eating significantly more frequent the following foods: processed meat, canned food, milk, animal fat, pulses, cereals or grain bread /pasta, vegetables with 5% of carbohydrates cafeteria products, fruit compotes (canned or not) ($p<0.001$), poultry, fish, cheese, potatoes, corn powder, coffee, herb teas and alcoholic beverages ($p<0.05$). Between GERD and non-GERD subjects was not significantly different consumption for the following type of foods: red meat, eggs, vegetable oils, 10 % carbohydrates vegetables, fruits, white bread, sugar and sweets. Using a multivariate analysis to reduce the confounding factors, predictors for GERD were age, overweight and certain food (grain cereals, canned and fatty food).

CONCLUSION: Gastro-esophageal reflux is highly prevalent in adult urban population and is associated with age, nutritional status and diet.

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Disclosure of Interest: None Declared

Keywords: correlation, diet, gastro-esophageal reflux, prevalence

P1596 FACTORS ASSOCIATED WITH SYMPTOM MANIFESTATIONS IN EROSIVE ESOPHAGITIS

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INTRODUCTION: Some patients with erosive esophagitis (EE) suffer from symptoms associated with GERD, whereas others with an apparently similar esophagitis do not. Asymptomatic EE is found incidentally by screening endoscopy. The factors associated with symptom manifestations in EE are not clear.

AIMS&METHODS: We aimed to investigate the prevalence of symptomatic and asymptomatic EE in health check-up subjects and factors associated with symptom manifestations in EE.

Among consecutive 13342 adults who underwent EGD in health check-up programs from May 2010 to April 2011, 8840 subjects (5683 men, median age 45 years) were included in the analysis. They were asked to fill in the questionnaire including smoking and alcohol history, medication history, and the Hospital anxiety and depression scale. The presence and frequency of esophageal and dyspeptic symptoms were evaluated. The mucosal damage of the esophagus was assessed using the Los Angeles grading system.

RESULTS: Seven hundred and sixty-eight subjects were diagnosed as having GERD based on heartburn and/or acid regurgitation at least once per week. EE was observed in 675 out of 8840 subjects (7.6%). The prevalence of symptomatic and asymptomatic EE in the study subjects was 4.3% and 3.3%, respectively. Forty-three percent of individuals with EE had no esophageal symptoms. Male gender (OR, 1.71; 95% CI, 1.27-2.30, $P < 0.001$) and PDS (OR, 1.80; 95% CI, 1.15-2.82, $P = 0.010$) were independently associated with asymptomatic EE. Male gender (OR, 2.01; 95% CI, 1.52-2.66, $P < 0.001$), current smoking (OR, 1.32; 95% CI, 1.03-1.68, $P = 0.028$), anxiety (OR, 3.01; 95% CI, 1.72-5.28, $P < 0.001$), EPS (OR, 3.80; 95% CI, 2.88-5.01, $P < 0.001$), and PDS (OR, 1.93; 95% CI, 1.36-2.72, $P < 0.001$) were independently associated with symptomatic EE.

CONCLUSION: Asymptomatic EE is not uncommon in health check-up subjects. Current smoking, anxiety, and epigastric pain syndrome-like dyspepsia seem to be independent factors associated with symptom manifestations in EE.

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Disclosure of Interest: None Declared

Keywords: asymptomatic erosive esophagitis, Gastroesophageal reflux disease(GERD), symptomatic erosive esophagitis

P1597 IMPEDANCE–PHMETRY: RAPID AND ACCURATE ANALYSIS OF REFLUX SYMPTOM ASSOCIATION

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INTRODUCTION: Reflux-symptom association analysis (S.I. and S.A.P.) is an important tool to evaluate patients with reflux symptoms refractory to PPI treatment. An accurate calculation of S.I. and S.A.P. requires manual editing after automatic analysis of impedance-pHmetry tracings (MII-pH). Review of the whole tracing is time consuming and a shorter analysis confined to the time around symptomatic episodes is advocated in clinical practice, although its reliability has never been tested.

AIMS&METHODS: To assess if a ''short'' analysis provides similar results (i.e. identifies the same patients with positive reflux-symptom association) than a complete analysis and manual editing of the 24hs recording.

Forty consecutive patients underwent MII-pHrecordings (23 women, median age 55 years) to evaluate typical oesophageal symptoms (n=24) or cough (n=16) in two Italian Centers. After automatic analysis (MMS, Enschede, The Netherlands), tracings were anonymized and randomized. Three experienced observers trained in different centers independently performed a) review and editing of 24hs tracing and b)''short'' analysis confined to the 2 minutes-window period preceding each episode of the principal symptom. Both types of analysis were performed in different days and blinded to the results of each other. Values of Symptom Index (S.I.) and Symptom Association Probability (S.A.P.) for acid and non acid reflux were transformed into binary response (i.e. positive or negative). Percentage of concordance with confidence interval between 24hs analysis and ''short'' analysis was measured.

RESULTS: Concordance in classifying patients as S.I./S.A.P. positive or negative occurred in 37 (92.5%) to 40 (100%) out of the 40 patients (see table).

Percentage of concordance with confidence interval (in brackets) between 24hs analysis and "short" analysis.

	S.I.		S.A.P.	
	Acid	Non Acid	Acid	Non Acid
Observer 1	100 (91-100)	100 (91-100)	100 (91-100)	97.5 (85-100)
Observer 2	97.5 (85-100)	95 (82-99)	97.5 (85-100)	92.5 (78-98)
Observer 3	97.5 (85-100)	100 (91-100)	100 (91-100)	100 (91-100)

CONCLUSION: Positive/negative reflux symptom association determined after "short" analysis of MII-pH recordings was highly predictive of results after the complete 24hs analysis. A "short" analysis confined to the time around symptomatic episodes is quick and reliable and can be adopted in routine clinical practice.

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Disclosure of Interest: None Declared

Keywords: pH impedance monitoring, Reflux disease, Short Analysis

P1598 THE REAL PREVALENCE OF FUNCTIONAL HEARTBURN: THE LESSON OF PROLONGED WIRELESS PH MONITORING.

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INTRODUCTION: Functional heartburn (FH) is diagnosed in patients with heartburn refractory to PPIs when endoscopy, oesophageal acid exposure time (AET) and symptom index (SI) are negative (Rome III criteria). The diagnosis of FH is important for management, however it stands on fragile pH monitoring variables, i.e. symptoms are often absent or, when present, few, making symptom/reflux association indexes less reliable and AET is known to vary from day to day.

AIMS&METHODS: To assess consistency of diagnosis of FH during 48 to 96 hrs wireless oesophageal pH monitoring (BRAVO). 50 PPI refractory patients (11M, 48 yrs; 38-57) with heartburn as dominant complaint and a diagnosis of FH according to Rome III in the first 24-hr of monitoring were retrospectively analysed as part of an international collaboration study (Brazil, Italy and UK). pH variables were analysed in the following 24-hrs periods to determine if tracings were indicative of diagnosis of NERD (either AET > 5% or normal AET and SI > 50%, provided patients had at least 3 heartburn episodes/day). Only days with at least 22 hrs recordings were included. Patients were reclassified as FH or NERD at the end of the test. Non parametric statistics and chi-squared test were used when appropriate.

RESULTS: (median, IQR) 15 out of 50 patients had a pathological AET after the first day of monitoring (10 in the second day and 5 in subsequent days), which changed their diagnosis from FH to NERD. In one patient SI became positive after the first day, but this had no influence on patients classification as it occurred together with pathological AET. There was a trend toward a younger age in the 35 FH vs. the 15 newly diagnosed NERD (45 yrs; 38-55 vs 55 yrs; 46-59, p=0.086) whereas gender composition did not differ (F 77% vs 80%, p=ns). First day AET (0.9%; 0.5-2.7 vs 2%; 1.3-2.6, p=ns), number of HB episodes in the first day (1; 0-4 vs 1; 0-4, p=ns) or during the whole monitoring (3; 0-6 vs 4; 1-12, p=ns) were not different between FH and NERD.

CONCLUSION: One third of patients classified as FH at 24-hr pH-monitoring can be re-classified as NERD after a more prolonged pH recording period and needs to be adequately treated with PPIs before excluding a role of gastro oesophageal reflux in clinical presentation. Furthermore anti-reflux surgery becomes a therapeutic option in these patients. Our data suggest usefulness of 48-hr catheter or 48 to 96-hr wireless studies for diagnosis of FH.

Disclosure of Interest: None Declared

Keywords: functional heartburn, non erosive reflux disease, wireless pH-monitoring

P1599 ESOPHAGEAL WORK-UP PRIOR TO BARIATRIC SURGERY: WHO AND HOW TO INVESTIGATE

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INTRODUCTION: Gastroesophageal reflux disease (GERD) is more common in obese patients. Investigators advocate endoscopy and reflux monitoring prior to bariatric surgery as these operations influence GERD in different ways.

AIMS&METHODS: Our aim was to assess the prevalence of reflux symptoms and objective findings in a group of obese patients scheduled for bariatric surgery. The pre-operative work-up included quantification of esophageal symptoms (VAS-scores for intensity and frequency), upper GI endoscopy and 24-h impedance-pH (imp-pH) monitoring off PPI therapy. Esophagitis and/or Barrett's esophagus if present, were recorded according to Los Angeles respective Prague classification systems. Ambulatory imp-pH monitoring was classified as abnormal if either %time pH < 4 was abnormal (total > 4.2%, upright > 6.3%, recumbent > 1.2%), number of total (acid and non-acid) reflux episodes was > 73/24 hours or symptom index (SI) was > 50%.

RESULTS: The analysis included data from 100 consecutive patients (69f, age 40 ± 11y, BMI 44.9 ± 6.9 kg/m^2) investigated between Jan 2011 and Dec 2012. Overall 54% of patients reported typical reflux symptoms, 71% of patients had evidence of reflux disease (38% erosive esophagitis/Barrett's esophagus and 33% non-erosive reflux disease). A total of 11/38 (29%) patients with endoscopic visible lesion had normal imp-pH recordings whereas 27/60 (45%) patients with abnormal imp-pH recordings had erosive lesions. The sensitivity of endoscopy alone was inferior to imp-pH alone to identify GERD (54% vs. 85%, p < 0.01). Test accuracy for endoscopy and 24h imp-pH were 67% and 89% respectively.

Endoscopic visible lesions were present in 37% of symptomatic and 39% of asymptomatic patients (p=ns). Abnormal imp-pH findings were present in 68% of symptomatic and 50% of asymptomatic patients (p=ns). Typical GERD symptoms were not predictive of the presence of erosive or non-erosive reflux disease: 41/54 (76%) patients reporting heartburn/regurgitation had evidence of reflux disease as did 30/46 (65%) asymptomatic patients (p=ns).

CONCLUSION: Half of obese patients evaluated prior to bariatric surgery report typical GERD symptoms and more than two-thirds have objective evidence of GERD. Reflux monitoring is superior to endoscopy in detecting GERD, yet a substantial number of patients with erosive esophagitis have "normal" esophageal acid exposure. Since typical reflux symptoms do not predict the presence of esophagitis and abnormal acid exposure, endoscopy and reflux monitoring should be part of the pre-operative work-up prior to bariatric surgery.

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Disclosure of Interest: None Declared

Keywords: 24h-impedance-pH metry, Bariatric surgery, GERD, Obesity, Upper gastrointestinal endoscopy

P1600 QUANTIFICATION OF GASTROOESOPHAGEAL REFLUX BY MULTICHANNEL INTRALUMINAL IMPEDANCE AND PH-MONITORING IN PATIENTS WITH DENTAL EROSIONS

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INTRODUCTION: Silent, i.e. asymptomatic acidic distal gastrooesophageal reflux (GERD) has been shown to be common in patients with advanced dental erosions[1]. However, the prevalence of weakly acidic and of proximal oesophageal GERD in these patients is unknown, but is of crucial importance in the pathophysiology of reflux-associated dental erosions. The aim of this study was to for the first time quantify these reflux variables by multichannel intraluminal impedance and pH-monitoring (MII-pH).

AIMS&METHODS: All successive patients presenting to the University of Bern Dental Clinic 2010-2012 with at least medium dental erosions (Lussi erosion index > 1 or BEWE > 8), without symptoms of reflux (less than once per week) and without GERD treatment were referred for oesophageal 24-hour MII-pH after exclusion of extrinsic and non-reflux causes of dental erosions. The numbers of acidic (pH < 4) and weakly acidic (pH 4-7) reflux episodes, the % time with pH < 4 and < 5.5 and the percentage of proximal oesophageal reflux episodes below a pH-threshold of 4 are reported.

RESULTS: 95 successive patients (56 males, mean age (range) 34yr (9-67) with advanced dental erosions (mean (95%CI) BEWE 13 (12.4-13.7)) were studied. The mean DeMeester score was 48.6 (9.2-99.2) and in the distal oesophagus the mean % time with pH < 4 was 8.8 (5.5-12.1) and with pH < 5.5 was 40.0 (36.0-44.0). The mean numbers of acidic and weakly acidic reflux episodes were 78 (68-88)(normal upper limit < 50 episodes) and 31 (25-37)(normal upper limit < 33 episodes), respectively. 33% (29-37) of all acidic reflux episodes reached the proximal oesophagus.

CONCLUSION: In patients presenting to a tertiary care dental clinic with advanced dental erosions acidic reflux is markedly increased compared to normal values, is much more common than weakly acidic reflux and frequently reaches the proximal esophagus. The reason for the development of dental erosions in association with the paucity of symptoms despite the acidity of the reflux needs to be explored further.

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Disclosure of Interest: None Declared

Keywords: dental erosions, Gastroesophageal reflux disease(GERD), impedance-pH monitoring

P1601 DIFFERENT ACCURACY OF VARIOUS IMPEDANCE-PH NORMAL VALUES IN DIAGNOSING GERD IN PATIENTS WITH PROVEN OR HIGHLY SUSPECTED REFLUX DISEASE

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INTRODUCTION: Since the introduction of impedance-pH monitoring in clinical practice different normal values have been proposed in order to diagnose gastroesophageal reflux disease (GERD). The most common used [i.e. the United States (US), Belgian-French (BF) and Italian (ITA) normal values] have different

upper limit of normal for esophageal acid exposure time (AET) and total number of reflux episodes (NREs), the two main parameters used to distinguish normal from abnormal GER.
AIMS&METHODS: To evaluate whether using different normal values influences the final impedance-pH diagnosis of GERD. In this multicenter study, 40 consecutive patients reporting heartburn and regurgitation with proven reflux disease (n=20 with erosive esophagitis) or strong evidence of GERD (n=20 with positive PPI test) underwent 24-h impedance-pH testing off-therapy. Twenty patients ate a standardized Mediterranean diet, while 20 patients were asked to follow a free diet. We evaluated distal AET (% time pH < 4), NREs, symptom association analysis using both symptom association probability (SAP+ if ≥95%) and symptom index (SI+ if ≥50%). GERD was diagnosed in case of abnormal AET or increased NREs according to different normal values.
RESULTS: No differences were found regarding the frequency of patients with abnormal values of AET, NREs and positive symptom association analysis based on the type of diet (Table). Diagnosis of GERD was done in 15 (38%) patients using US values, in 17 (43%) using BF values and in 30 (75%) using ITA values (US vs. ITA p=0.001; US vs. BF p=0.820 and ITA vs. BF p=0.006).

Patients with Abnormal Values

	Whole Population (n=40)	Patients with Standardized Diet (n=20)	Patients with Free Diet (n=20)	p Value
ITA Normal Values (Am J Gastroenterol 2008;103:1–9)				
AET,% (n=4.2)	26 (65%)	13 (65%)	13 (65%)	1,0000
NREs, n (n=54)	21 (53%)	11 (55%)	10 (50%)	1,0000
BF Nomal Values (Aliment Pharmacol Ther 2005;22:1011–1021)				
AET,% (n=5.0)	10 (25%)	5 (25%)	5 (25%)	1,0000
NREs, n (n=75)	10 (25%)	6 (30%)	4 (20%)	0,7370
US Normal Values (Am J Gastroenterol 2004; 99:1037–43)				
AET,% (n=6.3)	7 (18%)	4 (10%)	3 (8%)	1,0000
NREs, n (n=73)	11 (28%)	7 (35%)	4 (20%)	0,5179
Symptom-Reflux Association				
SAP/SI+ for acid reflux	29 (73%)	15 (75%)	14 (70%)	1,0000
SAP/SI+ for non-acid reflux				
SAP/SI+ for acid/ non-acid reflux	7 (18%)	4 (10%)	3 (15%)	1,0000
	31 (78%)	17 (85%)	14 (70%)	0,6466

CONCLUSION: Our findings demonstrate that the use of US and BF normal values in Swiss/Italian patients with symptoms suggestive of reflux disease underestimate the presence of GERD, independently of the diet followed during the monitoring.
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Disclosure of Interest: None Declared
Keywords: GERD, impedance-pH monitoring, NERD

P1602 IMPEDANCE-PH EXPLORES WITH MORE ACCURACY THAN PH-METRY ALONE THE RELATIONSHIP BETWEEN ASPIRATION OF GASTRIC CONTENTS AND GASTROESOPHAGEAL REFLUX IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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INTRODUCTION: Previous studies demonstrated that patients with idiopathic pulmonary fibrosis (IPF) have risk of gastric aspiration [i.e. increased bile acids (BAs) and pepsin in saliva] or definite gastric aspiration [i.e. BAs or pepsin in broncho-alveolar lavage (BAL)]. However, these studies evaluated the association between gastroesophageal reflux (GER) and IPF by means of pH-metry, that has been recently overtaken by the novel impedance-pH monitoring (i.e. ability to detect acid re-reflux and non-acid reflux).
AIMS&METHODS: To assess in biopsy-proven IPF patients the relationship between the presence and concentration of BAs and pepsin in saliva/BAL and the severity of reflux disease expressed by esophageal acid exposure time (AET) and number of reflux episodes (NREs).
Saliva and BAL samples were collected in 38 and 21 IPF patients. All subjects underwent esophageal manometry and impedance-pH testing off therapy. BAs and pepsin were measured using two commercial assays. During manual analysis of impedance-pH testing, we measured AET (normal if <4.2%) and total number of acid and non-acid reflux episodes (normal if <54).
RESULTS: BAs and pepsin were found in saliva of 61% and 68% and in BAL of 62% and 67% IPF patients. Two out of 23 and 2/26 of IPF patients with BAs and pepsin in saliva had a normal AET, while only 1/23 and 1/26 had a total normal NREs, respectively. None out of 13 and 14 IPF patients with BAs and pepsin in BAL had a normal AET or a total normal NREs. Overall, all IPF with BAs or pepsin in saliva or BAL had an abnormal impedance-pH test (i.e. abnormal AET or NREs). Data on the relationship between presence/concentration of BAs and pepsin and severity of GER are found in the Table below. The higher value of correlation has been found between total NREs and presence of pepsin and BAs in saliva and BAL.

	AET	Total NREs
Presence of Pepsin in Saliva	r^2=0.2193 (p=0.003)	r^2=0.4007 (p<0.001)
Presence of BAs in Saliva	r^2=0.1493 (p=0.017)	r^2=0.5264 (p=0.001)
Concentration of BAs in Saliva	r^2=0.0129 (p=0.606)	r^2=0.0712 (p=0.218)
Presence of Pepsin in BAL	r^2=0.2344 (p=0.026)	r^2=0.2845 (p=0.013)
Presence of BAs in BAL	r^2=0.3660 (p=0.004)	r^2=0.4566 (p=0.001)
Concentration of BAs in BAL	r^2=0.0427 (p=0.498)	r^2=0.3558 (p=0.031)

CONCLUSION: Presence and concentration of BAs and pepsin in saliva and BAL correlate better with impedance-detected reflux episodes than with esophageal AET. Thus, impedance-pH is a more accurate tool to define the relationship between gastric aspiration and GER in this particular cohort of patients.
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Disclosure of Interest: None Declared
Keywords: GERD, Idiopathic Pulmonary Fibrosis, impedance-pH monitoring

P1603 PLASMA ADIPONECTIN LEVEL AND IT'S CLINICAL VALUE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE AND ARTERIAL HYPERTENSION

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INTRODUCTION: Adiponectin, an adipocyte-derived plasma protein, is considered to be an important modulator for metabolic and vascular diseases. The role of adiponectin in the context of cardiovascular risk assessment and stratification is currently receiving growing attention. The relations between adiponectin level and gastroesophageal reflux disease (GERD) remain unclear.
AIMS&METHODS: to investigate the plasma adiponectin level in hypertensive patients with different levels of blood pressure (BP) and different risk of cardiovascular events, to study adiponectin level in patients with different variants of GERD, and to examine whether the level of adiponectin could have an additive effect on subclinical target organ damage in these groups of patients. 40 patients with AH and 40 patients with GERD were enrolled into a study. Among patients with arteria hypertension (AH) 10 patients suffered from the 1st grade of hypertension and had low cardiovascular risk (CVR); 25 patients had moderate grade of hypertension, moderate (16 patients) and high (3 patients) CVR, and 5 patients had severe AH. The group of patients with GERD was performed by 29 patients without endoscopic signs of esophagitis, 8 patients with reflux-esophagitis, 2 patients with Barrett's esophagus, and 1 patient with esophageal adenocarcinoma. The group of comparison was performed by 20 healthy individuals. All patients were comparable with patients of the main group. Plasma adiponectin concentrations were measured with an enzyme-linked immunosorbent assay (ELISA) method. Differences between the groups at baseline and maximum changes from baseline were determined with a Mann-Whitney *U* test. Differences were considered significant with a $P < 0.05$.
RESULTS: Both men and women with AH when compared with patients with GERD exhibited significantly lower plasma adiponectin levels (9,45 vs. 15,46 mg/ml in women, 8,24 vs. 12 mg/ml in men, $P < 0.05$. Hypoadiponectinemia was significantly and independently correlated with cardiovascular risk in patients with AH. In patients with GERD increased circulating adiponectin levels were associated with erosive esophagitis ($p < 0,05$). Plasma adiponectin concentrations were negatively correlated with grade of AH and extent of erosive esophagitis. When counted in patients with both AH and GERD, the adiponectin plasma level was the same as in group of healthy individuals.
CONCLUSION: Our study demonstrates that adiponectin appears to serve as a biomarker for progressive course of AH in patients with high CVR. At the same time, plasma adiponectin level is closely connected with the extent of mucose damage in patients with GERD
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Disclosure of Interest: None Declared
Keywords: adiponectin, Arterial hypertension, Gastroesophageal reflux disease(GERD)

P1604 IMPAIRED OESOPHAGEAL MOTILITY IS MORE RELATED TO EROSIVE OESOPHAGITIS THAN REFLUX SYMPTOM GENERATION

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INTRODUCTION: Decreased oesophageal motility has been described in patients with GORD; however it is not clear if this impairment is consequence or cause of increased acid exposure. Since non-acid reflux is known to cause symptoms and may contain pancreatic enzymes and bile as well, it may be harmful to the oesophageal motility.
AIMS&METHODS: The aim of the study was to investigate the oesophageal motility in patients with symptomatic acidic and non-acidic reflux with or without erosive oesophagitis (EO).
Fifty-four patients (age: 44(18-73) years; male 21; female: 33) with suspected GORD or symptoms refractory to double dose PPI treatment were underwent upper gastrointestinal endoscopy, oesophageal manometry and Multichannel

intraluminal impedance and pH (MII-pH) monitoring. The presence of oesophagitis was graded according to the Los Angeles (LA) system. On manometry lower oesophageal sphincter (LOS) pressure, duration of relaxation, complete bolus transit, distal oesophageal amplitude and velocity were evaluated. During pH-MII acid refluxers were defined by abnormal DeMeester score, or either having positive acid reflux indices and/or positive symptom correlation with positive Symptom Association Probability (SAP) and/or positive Symptom Index (SI). Non-acid refluxers were defined by having positive symptom correlation to non-acid reflux events (SAP and/or SI) without positive acid reflux indices of abnormal % time pH <4, and normal DeMeester score.

RESULTS: Fifty-nine per cent (32/54) of the patients were predominantly acid refluxers and 41% (22/54) had primarily non-acidic reflux. EO was seen in 12 of the 32 acid refluxers (37.5%) but none in the group with non-acid reflux. The severity of EO ranged between LA-A and C with 4 patients in each category. No significant difference was observed between the groups with respect to LOS pressures, duration of LOS relaxation, complete bolus transit, distal oesophageal amplitude and velocity. In contrast, patients with EO and acid reflux had significantly lower LOS pressure, distal oesophageal amplitude and velocity compared either to non-acid relfuxers or to acid refluxers without EO. Furthermore, the number of acid reflux episodes in supine position was twice higher than in patients without EO.

CONCLUSION: While patients with acidic reflux and EO had commonly impaired oesophageal motility, subjects without erosions had mostly normal motility irrespectively to the acidic or non-acidic type of their reflux. These data suggest that oesophageal dysmotility is less important in the development of reflux symptoms than mucosal damage.

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Disclosure of Interest: None Declared

Keywords: erosive esophagitis, GERD symptoms, impedance-pH monitoring, manometry, Non-acid reflux, weakly acidic reflux

P1605 CAN 3-HOUR POST-PRANDIAL ANALYSIS PREDICT THE DIAGNOSIS OF GERD MADE ON 24-HOUR IMPEDANCE-PH TESTING?

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INTRODUCTION: Esophageal 24-hour Multichannel Intraluminal Impedance-pH (MII-pH) testing is the gold standard investigation to diagnose gastroesophageal reflux disease (GERD). Recently we applied this technique to evaluate post-prandial (PP) reflux patterns in GERD patients and controls observing that the majority of reflux events occur during the 1st PP hour. It is well known that manual analysis of MII-pH tracings is mandatory because of the well-known drawbacks of the current automated diagnostic software.

AIMS&METHODS: To assess whether the manual analysis of PP period alone may be used to diagnose GERD, using the 24-hour test as reference standard. We studied 30 patients with functional heartburn [FH; 21F; mean age 50y], 40 with pH-positive non-erosive reflux disease [pH-POS NERD; 28F; 49.5y] and 30 with erosive esophagitis [EE; 15F; 43.5y]. We also enrolled 25 healthy volunteers [HVs; 8F; 25y] for normal values. All patients underwent upper endoscopy, manometry and MII-pH studies off-therapy. During the 24-h study, patients and HVs ate three standard meals. Acid exposure time (AET) and total number of reflux events were assessed during the 24-h period and during the 1st hour after each meal. A test was considered abnormal/positive for GERD when AET was >4.2 and/or total number of refluxes were >54 in case of the 24h-analysis and when AET was >4.6 and/or total number of refluxes were >21 in case of the 3-h PP-analysis.

RESULTS: None of the HVs had abnormal PP- or 24h-analysis. Out of 30 patients with FH, 26 (87%) were negative for both evaluations, whereas 4/30 (13%) had a positive PP- and a negative 24h-analysis. Among pH-POS NERD patients, 32/40 (80%) had both positive PP- and 24h-analysis, whereas 8/40 (20%) had negative PP- but positive 24h-analysis. Patients with EE were positive for both analyses in 20/30 (67%) cases and both negative in 1/30 (3%) cases. Moreover, 4/30 (13%) had positive PP- but negative 24h-analysis, whereas 5/30 (17%) had negative PP- but positive 24h-analysis. Overall, compared to the 24-h manual analysis, the 3-h PP manual analysis showed an accuracy of 0.83 (IC95% 0.76-0.90), a sensitivity of 0.80 (0.70-0.90), a specificity of 0.87 (0.77-0.96), a positive predictive value of 0.87 (0.78-0.95) and a negative predictive value of 0.80 (0.70-0.90) in diagnosing GERD.

CONCLUSION: Our data show that MII-pH manual analysis of the 3-h PP period alone may be used to diagnose GERD. This finding is particularly relevant in case of failure of 24h MII-pH monitoring due to technical drawbacks or in case of limited time to manually analyze each tracing in clinical practice.

Disclosure of Interest: None Declared

Keywords: esophageal reflux, ph-impedence, post-prandial analysis

P1606 GASTRO-ESOPHAGEAL REFLUX DISEASE SYMPTOMS IN AGED PATIENTS

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INTRODUCTION: Aged patients may tend to have milder symptoms than younger patients, possibly resulting in delayed diagnosis. Because severe reflux esophagitis (RE) sometimes causes complications with bleeding or stenosis, quick diagnosis of severe RE is important. The difference of gastro-esophageal reflux disease (GERD) symptoms between aged and younger RE patients has not been fully studied so far.

AIMS&METHODS: The aim of this study is to examine if there is any difference in the degree of the GERD symptoms between aged and younger RE patients. The inclusion criteria of subjects were as follows: subjects who took an upper endoscopic examination in Juntendo university from April in 2008 to March in 2013, and were diagnosed as Los Angeles classification (LA) grade A, B, C, or D; subjects who did not take any proton pump inhibitors, H_2 receptor antagonists, non-steroidal anti-inflammatory drugs, and aspirin; subjects who did not suffer from organic diseases except RE; and subjects who answered the questionnaire of frequency scale for the symptoms of GERD (FSSG). Aged and younger subjects were defined as patients aged 65 or over and less than 65, respectively. Statistical analysis was performed using Student's t test. The level of statistical significance was set at 0.05.

RESULTS: 596 subjects were examined. 184 subjects (mean age 71.1 years; 114 males) were classified into the aged patient group, and 412 subjects (mean age 51.2 years; 307 males) were classified into the younger group. The average of the FSSG score in the aged patient group was 6.7, whereas the average of the FSSG score in the younger group was 8.4. Significant difference between the two groups was observed ($p=0.0024$). Similar results were also obtained in reflux symptoms of the FSSG questionnaire and dysmotility symptoms. Further analyses on the basis of gender indicated that all the scores examined in the aged patients were less than those in the younger patients. When esophagitis severity was examined, although the score of the aged group was less than that of the younger group in mild esophagitis of LA grade A and B (the scores of the aged and younger groups were 6.6 and 8.4, respectively; $p=0.002$), the score of the aged group was almost equal to that of the younger group in severe esophagitis of LA grade C and D (the scores of the aged and younger groups were 8.5 and 8.7, respectively; $p=0.47$).

CONCLUSION: The aged RE patients likely tend to have minor symptoms compared with the younger RE patients; however, no significant difference regarding severe esohagitis was observed between them. The findings suggest that there may be no significant, age-related differences in complaining of GERD symptoms in severe RE patients.

Disclosure of Interest: None Declared

Keywords: age-related differences, GERD symptoms, reflux esophagitis

P1607 HISTOLOGICAL DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE: INTER-ASSESSOR AGREEMENT

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INTRODUCTION: Definitions of standardized criteria for histological assessment of gastroesophageal reflux disease (GERD) have been developed and evaluated by an international working group.[1,2] Using these criteria, we showed previously that total epithelial thickness and papillary length measured at 0.5 cm and 2.0 cm above the Z-line are significant predictors of GERD.[3] Here, we report on inter-assessor agreement in these measurements.

AIMS&METHODS: Inter-assessor agreement in measurement of histological markers for GERD was assessed using biopsies from the Diamond study (NCT00291746).[4] The study included primary care patients who had not taken a proton pump inhibitor in the previous 2 months, and who had upper gastrointestinal symptoms of any severity on $\geq$2 days/week for $\geq$4 weeks and of at least mild severity on $\geq$3 days in the week before the study. GERD was diagnosed when at least one of the following was present: reflux esophagitis (Los Angeles grades A–D); pathological esophageal pH (<4 for $>5.5\%$ of the time); positive symptom association probability ($\geq$95%). Biopsies were collected at 0.5 cm and 2.0 cm above the Z-line (3 o'clock position) and were analysed independently in a single-blind manner by assessors at two pathology centres (MV; RF/LM). Variables assessed included total epithelial thickness, basal cell layer thickness and papillary length (all in μm), and dilated intercellular spaces (severity score: 0–2).

RESULTS: Our histology analyses included biopsies from 117 patients with and 78 without investigation-diagnosed GERD. The two independent readings were in agreement ($p>0.05$) for total epithelial thickness (error count rate from MV: 0.39, from RF/LM: 0.39; estimated difference in two independent readings: 16.78; standard error [SE]: 10.57; $p=0.11$) and for basal cell layer thickness (error count rate from MV: 0.52, from RF/LM: 0.35; estimated difference in two independent readings: –1.82; SE: 4.19; $p=0.66$) at 2.0 cm above the Z-line. Results were comparable at 0.5 cm above the Z-line. There was significant disagreement between readings for papillary length and dilated intercellular spaces, at both 0.5 cm and 2.0 cm above the Z-line.

CONCLUSION: These analyses further support the conclusion that total epithelial thickness is a robust histological marker for GERD.

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Keywords: basal cell layer thickness, dilated intercellular spaces, gastroesophageal reflux disease, histology, papillary length, total epithelial thickness

P1608 CAN APPEARANCE OF GASTROESOPHAGEAL FLAP VALVE BE A USEFUL PREDICTOR OF GASTROESOPHAGEAL AND ASSOCIATED LARYNGOPHARYNGEAL REFLUX STATUS?

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INTRODUCTION: Gastroesophageal flap valve (GEFV) is related as one of the common etiologic factors of reflux symptoms. We want to evaluate the effects of GEFV on laryngopharyngeal symptoms and signs in patients with gastroesophageal reflux (GER) and suspected laryngopharyngeal reflux (LPR).
AIMS&METHODS: Two hundred and fifty seven consecutive patients (151 men and 106 women; mean age 50,22 years) who underwent routine endoscopy were enrolled to our study. Symptoms of laryngopharygeal and upper gastrointestinal systems and endoscopic severity of esophageal and gastric mucosal injury were correlated to GEFV grades according to the Hill classification. GEFV was graded I through IV using Hill's classification. The GEFV was largely classified into two groups: Normal GEFV group (grades I) and the abnormal GEFV group (grades II-III and IV). The reflux symptom index (RSI) was used as the diagnostic method for LPR. The statistical analyses were made according to the changes in the severity and frequency of each symptom and sign.
RESULTS: The incidence of symptoms of laryngopharygeal and gastroesophageal reflux diseases were associated with abnormal GEFV grades. The frequency of abnormal valves (Hill grades II-III and IV) was 30,7%. Of these, 47,4% had erosive esophagitis (EE). The majority of patients with EE were classified as Los Angeles Classification Grades A and B (33,1 and 3,9%, respectively). Correlations and differentiation between the reflux symptom index with gastroesophageal flap valve grade and gastroesophageal reflux were investigated by the Spearman correlation test ($p<0,01$ and $p>0,05$ respectively).
CONCLUSION: Endoscopic grading of GEFV is simple and provides useful diagnosis on the status of laryngopharygeal and gastroesophageal reflux. But we did not find any correlation between reflux symptom index with gastroesophageal reflux as Los Angeles classification.
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Disclosure of Interest: None Declared
Keywords: Gastroesophageal flap valve, Hill classification, Reflux

P1609 ESOPHAGEAL IMPEDANCE BASAL VALUES IN PATIENTS WITH PATHOPHYSIOLOGICAL CHARACTERISTICS OF FUNCTIONAL HEARTBURN.

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INTRODUCTION: Proton pump inhibitors (PPIs) are considered the first line approach to gastroesophageal reflux disease (GERD) symptoms. On the other hand, patients with functional heartburn (FH) do not show any symptom improvement under PPI therapy. Sometimes, in clinical practice, patients with pathophysiological characteristics related to FH have a satisfactory response to PPIs. Recently, it has been suggested that low basal impedance may reflect impaired mucosal integrity and increased acid sensitivity.
AIMS&METHODS: The aim was to compare basal impedance values in patients with heartburn and pathophysiological characteristics related to FH divided into two groups on the basis of symptom relief after PPI therapy.
A group of patients with non-erosive reflux disease were treated with esomeprazole or pantoprazole 40 mg daily for 8 weeks. All patients performed two questionnaires (GIS and VAS) to evaluate the symptom relief during PPI therapy. All patients underwent manometry and impedance monitoring (MII-pH) previous wash-out from PPIs. We selected 50 patients with normal acid exposure time (AET), normal reflux number, and lack of association between symptoms and refluxes. For each patient, we evaluated the basal impedance value at channel 3, during the overnight rest, at three different times: 1, 2, 3 am. Patients who had a symptom relief higher than 50% during PPI therapy composed Group A, and patients who did not record any symptom relief composed Group B. The recorded values were compared in the two groups with a student paired t-test.
RESULTS: We evaluated 60 patients with GERD symptoms but without any pathophysiological characteristic of GERD. Group A was composed of 30 patients (7M, 23F) with mean age 49.7 (±12.3). Mean symptom relief during PPI therapy was 74.5 (±8.6). Mean AET 1.4 (±0.8), mean reflux number 30.4 (±8.7). Each patient had a mean of 3.7 symptoms during MII-pH. Group B was composed of 30 patients (10M, 20F) with mean age 50.3 (±11.5). Mean symptom relief during PPI therapy was 23.6 (±10.6). Mean AET 0.5 (±0.6), mean reflux number 24 (±6.9). Each patient had a mean of 3.4 symptoms during MII-pH. Basal impedance values were significantly lower in Group A (2338.3 ±725.9) than in Group B (4289 ±897.9) ($p<0.05$).
CONCLUSION: Patients with pathophysiological characteristics related to FH and a satisfactory response to PPIs showed lower basal impedance values. Consistently with the concept that low basal impedance may reflect impaired mucosal integrity, our result could partially explain the different response to PPI therapy in the two groups.
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Disclosure of Interest: None Declared
Keywords: functional heartburn, GERD, PPI

P1610 THE DIAGNOSTIC ACCURACY OF REFLUX SYMPTOMS IS IMPROVED BY ASSESSING EPIGASTRIC PAIN AND HISTOLOGY

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INTRODUCTION: International consensus guidelines characterize symptom-defined gastroesophageal reflux disease (sGERD) as: 1) ≥mild reflux symptoms on ≥2 days/week or ≥moderate reflux symptoms on ≥1 day/week (for research), or 2) troublesome reflux symptoms (for clinical practice).[1] Here, we report on further validation of sGERD diagnostic criteria (overall and without epigastric pain) against GERD defined by investigation (iGERD; with total epithelial thickness [TET] ≥430 μm as an additional, validated histological criterion[2]).
AIMS&METHODS: We assessed the specificity/sensitivity of sGERD, overall and without epigastric pain, against iGERD. Primary care patients were included if they had not taken a proton pump inhibitor in the past 2 months, and had upper gastrointestinal (GI) symptoms of any severity on ≥2 days/week for ≥4 weeks and of ≥mild severity on ≥3 days in the 7 days before the study (NCT00291746).[3] Patients completed the Reflux Disease Questionnaire (RDQ), were interviewed about a pre-specified list of 19 upper GI symptoms, and underwent upper GI endoscopy with esophageal biopsy (2.0 cm above the Z-line) and wireless pH-metry. iGERD was defined as ≥1 of: reflux esophagitis (Los Angeles grades A–D), pathological esophageal pH (<4 for >5.5% of the time), positive symptom association probability (SAP ≥95%). TET ≥430 μm was an additional criterion. sGERD was diagnosed if heartburn/regurgitation frequency/severity data from the RDQ met research definition criteria or if heartburn/regurgitation was reported as the most/second most bothersome symptom(s) at interview (clinical practice definition).
RESULTS: Of 231 biopsied patients, 55% had iGERD (30% RE, 37% pathological esophageal pH, 16% positive SAP and 39% TET ≥430 μm). Table 1 shows the specificity/sensitivity of sGERD research and clinical practice definitions, overall and without epigastric pain, for iGERD.
Table 1. Specificity/sensitivity (%) of sGERD definitions for iGERD

sGERD definition	iGERD with TET ≥430 μm	iGERD with TET <430 μm
For research		
Overall	32.9/87.7	12.3/67.1
No epigastric pain	78.9/41.3	58.7/21.1
For clinical practice		
Overall	71.1/52.3	47.7/28.9
No epigastric pain	86.8/31.0	69.0/13.2

CONCLUSION: Adding TET ≥430 μm as an iGERD criterion improves the specificity/sensitivity of sGERD definitions for iGERD. Absence of epigastric pain further increases the specificity, but with a decline in sensitivity. The sGERD research definition has higher sensitivity but lower specificity for iGERD than the sGERD clinical practice definition.
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Keywords: epigastric pain, Gastroesophageal reflux disease, histology, total epithelial thickness

P1611 THE RESTECH LARYNGOPHARYNGEAL PROBE MEASURES VAPORIZED ACID BUT DOES NOT UNIFORMLY CORRESPOND WITH THE BRAVO PH PROBE IN SIMULTANEOUS STUDIES

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INTRODUCTION: The Restech pH probe has been developed to measure vaporized acid in the laryngopharyngeal area
AIMS&METHODS: The aim of this study was (1) to determine if the Restech probe measures vaporized acid in vitro, (2) to determine the concordance of the

Restech probe placed in the pharynx with a Bravo pH probe placed in the distal esophagus. Methods: In vitro experiments: In a laboratory environment a water bath was set up set at 38 degrees Celsius. Multiple liquids that span the pH spectrum encountered in the upper GI tract and airways were studied. pH was recorded on the remote receiver by an investigator blinded to the substance being tested. Liquid pH was measured by dipping the catheter in the liquid medium. In random sequence the liquids were vaporized using an aerosol generator and the Restech probe was suspended in the vapour. The effect of drying the catheter was studied in vitro. In vivo studies: Simultaneous Restech and Bravo pH studies performed in 10 patients were analyzed.

RESULTS:

Substance	Published pH	Measured Liquid pH	Measured pH vapor	Difference Vaporized & liquid pH
0.1N HCl	1	1.1	1.1	0
Vinegar	2.4	2.4	2.4	0
Coca Cola	2.4	2.7	2.7	0
Diet Coke	3.1	3.2	3.4	0.2
Orange Juice	3.8	4.1	4.3	0.2
pH 4 buffer	4.0	4.2	4.1	-0.1
pH 7 buffer	7	7	7	0
pH 8 buffer	8	8.1	8	-0.1

CONCLUSION: Dehydration of the catheter resulted in activation of detection circuitry within 30 seconds and a pH of 15 was displayed. The Bravo probe showed reflux in 9/10 patients in the upright position and the Restech showed upright reflux in 6/10 patients. However, in the supine position, 7/10 Restech studies demonstrated reflux in the laryngo-pharynx with only 2 Bravo studies were positive in the supine period.Conclusions: 1. The Restech probe accurately measures the pH of liquids and the nebulized vapor of liquid. 2. The Restech probe records acidic events that are not recorded by the Bravo pH probe particularly in the supine position. 3. The supine events are not due to drying of the catheter as dessication of the probe is rapidly detected by inbuilt circuitry 4. Nocturnal acidification of the laryngo-pharynx may be important in extra-esophageal GERD.

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Keywords: GERD, Laryngopharyngeal reflux(LPR), pH-monitoring

P1612 CARDIAC MUCOSA AT THE GASTROESOPHAGEAL JUNCTION: INDICATOR OF GASTROESOPHAGEAL REFLUX DISEASE?

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INTRODUCTION: The native stratified squamous epithelium of the esophagus is unable to tolerate the acidic and/or proteolytic nature of persistent reflux, and it adapts to the damaging stimuli by converting into metaplastic columnar epithelium. Cardiac mucosa at the gastroesophageal junction is characterized by the presence of glands composed of mucous cells without parietal cells. The origin and significance of cardiac mucosa remains to be controversial.

AIMS&METHODS: Our study aimed to assess the prevalence of cardiac mucosa and to relate its presence to features related to gastroesophageal reflux disease (GERD). From the prospective Central European multicenter *histo*GERD trial we recruited 1,071 individuals (576 female, 495 males; median age 53 years) undergoing gastroscopy for various non-selected reasons. Biopsy material was systematically sampled from above and below the gastroesophageal junction and from the stomach.

RESULTS: Overall, cardiac mucosa was observed in 713 (66.6%) individuals. Its presence was associated with patients' symptoms and/or complaints, assessed by a questionnaire and clinical evaluation ($p=0.0025$), body mass index ($p<0.001$), histologic changes of the squamous epithelium indicating GERD (basal cell layer hyperplasia, papillary elongation, dilation of intercellular spaces, and presence of intraepithelial mononuclear cells; $p<0.001$, respectively), intestinal metaplasia ($p<0.001$), as well as the endoscopic diagnosis of esophagitis assessed according to the modified Los Angeles classification ($p<0.001$). No association with the endoscopic diagnosis of Barrett's esophagus and no association with gastric pathology, particularly *Helicobacter* infection was observed.

CONCLUSION: Cardiac mucosa is a common finding in biopsies sampled from the gastroesophageal junction. Its association with reflux symptoms, histologic changes of the squamous epithelium indicating GERD, as well as the endoscopic diagnosis of esophagitis suggests that injury and repair related to GERD contribute to its development and/or expansion.

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Disclosure of Interest: None Declared

Keywords: gastric cardia, gastroesophageal reflux disease, histological diagnosis, metaplasia, reflux esophagitis

P1613 THE ASSOCIATION BETWEEN GASTROESOPHAGEAL FLAP VALVE FUNCTION AND GASTROESOPHAGEAL REFLUX SYMPTOMS, ENDOSCOPIC FEATURES, HELICOBACTER PYLORI STATUS AND BODY MASS INDEX

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INTRODUCTION: Endoscopic investigation is usually preferred in patients with symptoms of gastroesophageal reflux disease (GERD) in clinical practice. It has been reported that grading of gastroesophageal flap valve (GEFV) function during endoscopy adds useful information in the evaluation of these patients. However, endoscopists frequently encounter patients with impaired GEFV function, but without symptoms of GERD. Therefore, primary aim of this study was to investigate relationship between GEFV appearance and reflux symptoms, secondary aims were to explore whether any association exists between GEFV and clinical diagnosis, *Helicobacter pylori* status, body mass index and other factors that might affect GEFV function.

AIMS&METHODS: 1070 consecutive patients (643 women) who had been referred for upper gastrointestinal endoscopy were enrolled into the study. Along with demographic characteristics, reflux symptoms including heartburn and regurgitation were gathered from each patient. The body mass index, smoking, alcohol, concomitant diseases, and proton pump inhibitors were also recorded. During endoscopic procedure, patients were assessed for the presence of esophagitis and hiatal hernia. Esophagogastric junction was inspected while endoscope in a retroflexed position and graded I to IV according to the Hill's classification. Grades I and II were classified as normal valves and grades III and IV as abnormal valves. Biopsy specimens were obtained from each patient in order to identify presence of *Helicobacter pylori* infection.

RESULTS: At endoscopic investigation, 348 patients had GEFV dysfunction considered as having Hill grade III&IV, 146 patients had esophagitis and 84 patients had hiatal hernia. 583 patients reported regurgitation while 507 patients had heartburn. Presence of hiatal hernia ($p=0.000$), esophagitis ($p=0.000$), regurgitation ($p=0.021$), and body mass index (>30 kg/m^2) ($p=0.015$) are independent risk factors that affect GEFV function. However, presence of heartburn ($p=0.438$), *Helicobacter pylori* infection ($p=0.855$), smoking ($p=0.446$) and alcohol ($p=0.833$) are not risk factors for GEFV function.

CONCLUSION: Although endoscopic grading of the GEFV appearance is useful as a prognostic factor, presence of hiatal hernia, esophagitis, regurgitaiton and body mass index >30 kg/m^2 are independent risk factors for GEVF appearence. Patients with abnormal valves (Hill grades III &IV) but without hiatal hernia, esophagitis and regurgitation should be evaluated individually by means of having or not having gastroesophageal reflux disease.

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Keywords: Endoscopy, Gastroesophageal flap valve, Gastroesophageal reflux disease(GERD), sypmtoms

P1614 THE ASSOCIATION OF BERNSTEIN TEST WITH PH-IMPEDANCE MONITORING AND DILATED INTERCELLULAR SPACE IN SUBTYPES OF GERD

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INTRODUCTION: Diagnostic tools in gastroesophageal reflux disease (GERD) has undergone significant evolution from Bernstein test to multichannel intraluminal impedance and pH (MII-pH) monitoring including the symptom association. Dilated intercellular space (DIS) may have a role in decreasing perception thresholds, particularly in NERD.

AIMS&METHODS: We aimed to investigate the relevance of Bernstein test in patients with different subtypes of GERD and to investigate the association of DIS with acid-induced heartburn. 81 GERD patients [mean age: 46±12, 41 F, 40 M] were prospectively divided into 3 subgroups by Roma III criteria. Bernstein test was performed and of the 33 who had distal esophagus biopsies; the severity, extent and level of DIS were evaluated. The definitions were as following: severity of DIS; mild if detected on X40 magnification, moderate if detected on X20 magnification and severe if detected on X10 magnification, extent of DIS; focal if detected on ≤ 4 high-powered fields, and diffuse if detected on >5 high-powered fields, level of DIS; 1/3 lower (basal and parabasal layer), 1/3 middle (spinocellular layer), 1/3 upper (granular cells). The severity, extent and level of DIS were compared between Bernstein(+) and Bernstein(-) patients.

RESULTS: Bernstein test was positive in 51.7%, 42.9% and 29.2% of ERD, NERD and functional heartburn, respectively. Bernstein positivity did not differ among GERD subtypes. Although total number of reflux episodes were higher in

Bernstein (+) group(p=0.03); acid refluxes, weak acid refluxes, pH < 4% and De Meester scores were similar. Age, sex, reflux symptom score, extraesophageal symptoms, PPI response, BMI, time for pH < 4%, number of acid refluxes, symptom index (SI) and symptom association probability (SAP) were not associated with Bernstein test significantly. Bernstein test was positive in 51% of patients examined for DIS. Severity of DIS was mild in 59%, moderate in 6%, severe in 35%; extent of DIS was focal in 53%, diffuse in 46%; level of DIS was 1/3 lower in 65%, 1/3 middle in 29% and 1/3 upper in 6% of Bernstein (+) patients. Severity, extent and level of DIS were not associated with Bernstein test.
CONCLUSION: Despite the higher level of total acid refluxes; the irrelevance of acid induced heartburn with mucosal inflammation, SI, SAP and PPI response denotes the role of sensitivity remote from the site of injury. Furthermore, the severity, extent and level of DIS were not associated with Bernstein test and GERD subtypes. Apart from the intraluminal acid stimuli, esophageal receptors, visceral afferent neurons and central perception may have a role in subtypes of GERD.
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Disclosure of Interest: None Declared
Keywords: Bernstein test, dilated intercellular spaces, Gastroesophageal reflux disease(GERD), pH-Impedance monitoring, subtypes of GERD

P1615 EDEMA OF THE INTERARYTENOID MUCOSA SEEN ON ENDOSCOPY IS RELATED TO BARRETT'S ESOPHAGUS AND IS AN INDEPENDENT PREDICTOR FOR NON-EROSIVE REFLUX DISEASE (NERD) IN JAPANESE POPULATION

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INTRODUCTION: Laryngopharyngeal reflux (LPR) is defined as the retrograde flow of gastric contents up through the esophagus to the larynx and hypopharynx; this is an extra-esophageal manifestation of gastroesophageal reflux disease (GERD). Non-erosive reflux disease (NERD) refers to a syndrome that is characterized by complaints of reflux symptoms such as heartburn without endoscopic evidence of mucosal injury. It accounts for more than half of gastroesophageal reflux disease (GERD) cases in Japan, as it does in Europe. NERD and erosive GERD cannot be distinguished by the severity of symptoms or their frequency, and they are equally characterized by compromised quality of life (QOL). Although both LPR and GERD are caused by reflux of stomach contents and the relationship between LPR and GERD are well understood, the relationship between LPR and NERD are still unknown.
AIMS&METHODS: In this study, we assessed esophago-gastroendoscopic findings related to GERD, specifically Barrett's esophagus, hiatal hernia, laryngopharyngeal findings, and GERD symptoms on the 12-question Frequency Scale for the Symptoms of Gastroesophageal Reflux Disease (FSSG). Then, independent predictors of Barrett's esophagus were analyzed, and the relationships among Barrett's esophagus, and hiatal hernia, laryngopharyngeal findings, and patients' symptoms and characteristics were investigated.
RESULTS: Among 652 NERD patients (307 females and 345 males) of the 704 patients who enrolled in this study were evaluated on univariate and multivariate analysis. Barrett's esophagus and hiatal hernia were present in 303 (46.4%) and 299 patients (45.9%), respectively. Barrett's esophagus was significantly related with male, aging, edema of the interarytenoid mucosa, redness of inferior portion of larynx and hiatal hernia on univariate analysis. However, patients' LPR and GERD symptoms had no significant relationship with Barrett's esophagus. Male (OR: 2.24; 95% CI: 1.58-3.19; p value < 0.001), aging (OR: 1.03; 95% CI: 1.02-1.04), edema of the interarytenoid mucosa (OR: 1.58; 95% CI: 1.06-2.37; p value =0.026) and hiatal hernia (OR: 4.04; 95% CI: 2.87-5.73; p value < 0.001) were independent predictors of Barrett's esophagus on multivariate analysis.
CONCLUSION: Although LPR and GERD symptoms had no significant relationship with the findings of Barrett's esophagus, edema of the interarytenoid mucosa and hiatal hernia were significantly related with Barrett's esophagus and they were considered to be clues for reflux of stomach contents involving gastric acid in Japanese NERD patients.
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Disclosure of Interest: None Declared
Keywords: Barrett's esophagus, Edema of the interarytenoid mucosa, Gastroesophageal reflux disease(GERD), Laryngopharyngeal reflux(LPR), Non-erosive reflux disease (NERD)

P1616 THE RESULTS OF THE OBSERVATIONAL STUDY ON THE USE OF GERDQ INTERNATIONAL QUESTIONNAIRE FOR DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE IN THE RUSSIAN POPULATION

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INTRODUCTION: Modern guidelines recommend symptom-based approach to gastroesophageal reflux disease (GERD) management. Brief, reliable and valid self-administered questionnaire could facilitate the diagnosis of GERD in primary care.
AIMS&METHODS: A prospective, multicenter, observational study was conducted to estimate the sensitivity and specificity of GerdQ international questionnaire for the diagnosis of GERD in routine practice in Russia. The study included 150 patients (aged ≥18) with upper gastrointestinal symptoms planned for endoscopy and pH-metry for diagnosis clarification. Patients completed GerdQ (6-question patient-centered self-assessment questionnaire). Gastroenterologists established GERD diagnosis based on clinical data followed by endoscopy and 24-hour pH-metry. The results of GerdQ questionnaire survey and gastroenterologist examination were compared with the results of instrumental methods (reflux esophagitis or pathological acid exposure to esophagus were used as diagnostic references for GERD).
RESULTS: 5 patients had short-term pH-metry, thus only 145 patients were included in PP analysis. According to PP-analysis GerdQ sensitivity for cut-off score ≥8 was 65,4%, specificity – 91,7%. ROC-analysis demonstrated high sensitivity and specificity of GerdQ, area under the curve (AUC) was 84,8% (95% CI 71,1-98,5; p < 0,001). Sensitivity of GERD diagnostics by gastroenterologist was 91%, specificity – 91,7%. The frequency of reflux-esophagitis revealed by endoscopy correlated with GerdQ total score: esophagitis presented in 72,2% patients with GerdQ score 3-7, 92,9% patients with GerdQ score 8-10 and 96,9% patients with GerdQ score 11-18. The frequency of pathological acid exposure to esophagus detected by 24-h pH-metry (esophageal pH < 4 during more than 5% of monitoring time) was 61,1%, 88,9% and 75,0%, respectively.
CONCLUSION: GerdQ is sufficiently sensitive and specific complementary tool for GERD diagnosis which allows reducing the need for upper endoscopy.
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Keywords: diagnosis, gastroesophageal reflux disease, questionnaire

P1617 FREQUENCY AND TIME TO ONSET OF RESPIRATORY TRACT INFECTIONS IN ESOMEPRAZOLE AND PLACEBO TREATED PATIENTS IN 24 RANDOMIZED CONTROLLED TRIALS

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INTRODUCTION: A causal association has been suggested between the use of potent gastric acid suppressive medication and occurrence of community-acquired respiratory tract infections (RTIs), particularly pneumonia, based on data from observational studies.
AIMS&METHODS: We aimed to compare the frequency and time to onset of community-acquired RTIs, including pneumonia, in patients receiving either the proton pump inhibitor esomeprazole or placebo in randomized, double-blind, controlled trials. The AstraZeneca ARIADNE safety database, which contains data on approximately 350 000 patients obtained from over 2 500 clinical trials, was searched for comparative, randomized, controlled, blinded clinical studies in which patients received either esomeprazole or placebo and that recorded all non-serious and serious adverse events (AE). The following categories of AE were analyzed: all RTIs (including signs and symptoms potentially indicating RTI); lower RTIs; and pneumonia. Events were analyzed in accordance with MedDRA v. 15.1 terminology. Patient data were pooled by treatment group, and AE frequencies and relative risks (RRs; with 95% confidence intervals [CIs], adjusted for time on treatment) were calculated. In addition, AE occurrence was analyzed according to patients' age, sex, treatment indication and time to onset of AE.
RESULTS: Twenty-four relevant placebo controlled-studies were identified, in which 9877 patients received esomeprazole and 5551 patients received placebo. The frequencies of occurrence of all three categories of AE were similar in patients receiving esomeprazole and patients receiving placebo (all RTIs: 10.8% versus 10.5%; lower RTIs: 1.9% versus 2.1%; and pneumonia: 0.2% versus 0.3%, respectively), and events were evenly distributed over patients' duration of treatment. The adjusted RR estimates for AEs in patients receiving esomeprazole relative to patients receiving placebo were as follows: all RTIs, 0.93 (95% CI: 0.84–1.02); lower RTIs, 0.81 (95% CI: 0.65–1.01); and pneumonia, 0.65 (95% CI: 0.35–1.20). The distribution of all three categories of AE showed similar age, sex, treatment indication and time to onset patterns in esomeprazole and placebo-treated patients.
CONCLUSION: This pooled analysis of data from randomized, double-blind, placebo-controlled clinical trials found no causal association between the use of potent acid suppressive therapy (esomeprazole) and occurrence of community-acquired RTIs, including pneumonia. The onset of events was evenly distributed over patients' duration of therapy, and presented similar age, sex, treatment indication and time to onset patterns in esomeprazole and placebo treated groups.
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Keywords: Esomeprazole, Placebo, pneumonia, randomized controlled trial, respiratory tract infection

P1618 TEMPORAL CHANGES IN THE GASTROINTESTINAL RISK PROFILE OF PATIENTS RECEIVING LOW-DOSE ACETYLSALICYLIC ACID FOR SECONDARY PREVENTION OF CARDIOVASCULAR EVENTS

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INTRODUCTION: The use of low-dose acetylsalicylic acid (ASA) is associated with an increased risk of gastrointestinal (GI) complications, which may lead to discontinuation of ASA treatment. For patients at high GI risk, concomitant

gastroprotective strategies are recommended (Bhatt *et al.* 2008). However, it is unclear how GI risk changes with time in new users of low-dose ASA.
AIMS&METHODS: This retrospective cohort study assessed the GI risk profile among new users of low-dose ASA. The Health Improvement Network (THIN) UK primary care database was used to identify patients who initiated low-dose ASA between 2000 and 2007 for secondary prevention of cardiovascular events. GI risk was assessed at baseline (the date of their first ASA prescription), and again after 1 year. Patients were considered to be at high GI risk if they met at least one criterion from a list of established GI risk factors (Bhatt *et al.* 2008). Patients were classified according to their initial indication for low-dose ASA treatment: secondary prevention of ischaemic heart disease (IHD), cerebrovascular disease (CD), unstable angina (UA), or myocardial infarction (MI).
RESULTS: Overall, 39% of ASA users at baseline were at high GI risk, and this proportion increased by calendar year (30% for patients initiating ASA in 2000, versus 52% in 2007). The proportion of patients at high GI risk at baseline was higher in individuals prescribed low-dose ASA for secondary prevention of MI (52%) than among those prescribed ASA for other indications (IHD, 35%; CD, 34%; UA, 43%). After 1 year, the proportion of patients at high GI risk was 36% overall, and was similar for all indications. Of patients who were at low GI risk at baseline, 16% were at high GI risk after 1 year. The proportions of patients whose risk increased were similar for all indications. Of patients who were at high GI risk at baseline, 67% continued to be at high GI risk after 1 year. The proportion of patients whose GI risk decreased the most was in patients prescribed ASA for secondary prevention of MI (62%) relative to other indications (IHD, 67%; CD, 73%; UA, 71%).
CONCLUSION: Results from this study show that the GI risk profile of users of low-dose ASA may change over time and vary by indication. Thus, physicians need to review regularly the GI risk of patients prescribed low-dose ASA, and tailor adequate gastroprotective strategies accordingly.
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Keywords: aspirin, cardiovascular diseases, risk factors

P1619 ARE PATIENTS ON ANTICOAGULANTS ADEQUATELY PROTECTED AGAINST UPPER GASTROINTESTINAL BLEEDING?

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INTRODUCTION: Due to the high prevalence of cardiovascular diseases anticoagulant medications (AC) are commonly prescribed. Treatment with AC is related to an increased incidence of acute upper gastrointestinal bleeding (AUGIB) especially in older patients and concomitant treatment with acetylsalicylic acid (ASA), clopidogrel, corticosteroids, nonsteroidal anti-inflammatory drugs (NSAID) and serotonin reuptake inhibitors (SRI). Proton pump inhibitors (PPI) are drugs with good protective effect against AUGIB.
AIMS&METHODS: A retrospective analysis of medical documentation of 440 consecutive patients with anticoagulant treatment was performed. We analyzed demographic features, indications for treatment with AC, history of AUGIB and the prescription of PPI.
RESULTS: There were 440 patiens (242 male and 196 female), mean age 75,8 ± 6,22 years (range 65-94). Indications for treatment with AC were: atrial fibrillation (AF) and stroke in 282 patients, valve replacement in 59 patients, pulmonary embolism in 52 patients and deep venous thrombosis in 47 patients. Warfarin was prescribed in 389 (88,4%) patients, acenocoumarol in 49 (11,1%) patients and dabigatran in 2 (0,5%) patients. ASA, NSAID, corticosteroids and SRI were concomitantly prescribed in 11 (2,5%), 7 (1,6%), 3 (0,7%) and 35 (8,0%) cases, respectively. Eight (1,8%) patients had history of AUGIB. PPI were prescribed in 97 (22,0%) patients with AC in monotherapy, in 26 (41,3%) patients with AC and concomitant therapy (17 with SRI, 7 with NSAR and 2 with corticosteroids) and in 2 patients (25%) with AC and history of AUGIB. There were 343 (78%) patients (all older than 65 years) without PPI despite the indication for use. In 57 (58,8%) patients PPI was prescribed in proper dose (standard), in 26 (26,8%) the prescribed dose of PPI was too high and in 14 (14,4%) the dose was unknown.
CONCLUSION: Gastric protection in patients on AC therapy is not satisfactory. All patients were older than 65 years which classifies them as a group of patients with higher risk of AUGIB. All patients with ACM therapy and concomitant NSAID or/and ASA therapy should be treated with PPI in standard dose, especially those older than 65 years and history of AUGIB. Gastric protection in patients with AC therapy without concomitant therapy (ASA, NSAR) and history of AUGIB should be exactly specified in national guidelines.
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Keywords: anticoagulants, upper gastrointestinal bleeding

P1620 CLINICAL COURSE AND GASTROINTESTINAL BLEEDING IN JAPANESE PATIENTS TAKING LOW-DOSE ASPIRIN - RETROSPECTIVE COHORT STUDY-

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INTRODUCTION: As a number of patients taking low-dose aspirin (LDA) increases for prophylaxis of atherothrombotic diseases, the adverse effect of gastrointestinal (GI) toxicity is also increasing. However, information regarding clinical course and the incidence of GI bleeding in Japanese patients taking LDA has not been fully elucidated.
AIMS&METHODS: We conducted this retrospective cohort study to clarify the incidence of GI bleeding in patients taking LDA. Among 5555 patients who underwent EGD in Teikyo University Hospital (Tokyo, Japan) from 2005 till 2006, 466 having received LDA continuously before and after EGD (>1 month) were included as the subjects. Those who had advanced malignant disesases were excluded. Age-, sex-, and examination month-matched controls were also selected to compare the difference. Based on the medical records, the patients' status (GI bleeding requiring hospitalization, death, discontinuation of aspirin, change of hospital) were investigated every month till the end of April, 2013.
RESULTS: The observation period ranged from 2 to 103 months (average 59 months, 2295 patient-year). The underlying diseases were ischemic heart diseases (71%), cerebrovascular diseases (31%), peripheral arterial disease (9%), and other thrombotic disease (5%). Of these, 57 patients died (12.2%, 24.8/1000 patient-year), which was comparable to the controls (50 patients, 10.7%). The major causes of death were infections, heart disease, neoplasms, and intracranial hemorrhage, and there was no death because of hemorrhage from the GI organs. GI bleeding occurred in 27 patients (5.8%, 11.8/1000 patient-year); 9 from the upper GI and 18 from the middle or lower GI. The majority of the patients were elderlies over 75 years old. The most common disease was colonic diverticular hemorrhage (11 patients, 41%). On the other hand, only 3 patients of the control developed the upper GI bleeding (0.6%), and there was no lower GI bleeding
CONCLUSION: In patients taking LDA, the rate of GI bleeding was almost half of the mortality rate. Gastrointestinal bleeding was much more common in aspirin users than in control, especially elderly patients. Over the half of the lesions responsible for bleeding in aspirin users was found in the middle or the lower portion of GI rather than the upper GI, and colonic diverticular hemorrhage were the most common disease.
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Disclosure of Interest: None Declared
Keywords: GI bleeding, low-dose aspirin, mortality rate

P1621 H2S-RELEASING NSAID ATB-346 POSSESSES THE REDUCED GASTROTOXICITY IN MUCOSA OF RATS WITH EXPERIMENTAL STRESS-INDUCED ULCERS

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INTRODUCTION: H_2S possesses strong anti-oxidative, anti-apoptic and anti-inflammatory activities in different tissues, including the gastric mucosa. However, NSAIDs reduce endogenous H_2S synthesis, while administration of H_2S donors can reduce the severity of NSAID-induced gastric damage. It is barely known what would happen to mechanisms of gastric defence and healing, including H_2S production, when the use of NSAIDs is accompanied by acute stress.
AIMS&METHODS: The purpose of our study was to explore effects of different NSAIDs (conventional – naproxen, selective cox-2 inhibitor – celecoxib, and H_2S-releasing – ATB-346) in experimental stress-related gastric lesions in rats, and to determine the role of lipoperoxidation and the nitric oxide (NO) system in ulcerogenesis and gastroprotection in rats. Two stress models of gastric ulceration were used: water-immersion restraint stress (WRS) and epinephrine-induced gastric damage. Naproxen, ATB-346 and celecoxib were examined in both models of gastric damage. In the gastric mucosa were determined: area and degree of destructive changes, alterations in malonic dialdehyde (MDA) concentration, activity of NO-synthases (inducible – iNOS and constitutive – cNOS) and arginase, the content of nitrite anion.
RESULTS: Oral administration of naproxen at the dose of 10 $mg \times kg^{-1}$ produced gastric mucosal lesions, whereas when ATB-346 and celecoxib were given at the same dose, gastric damage did not develop. In contrast, lipoperoxidation processes were enhanced in all groups as was the activity of NO-synthases. Both naproxen and ATB-346 increased the activity of NOS (total and iNOS) by the same rate. Pretreatment with naproxen in the WRS model in rats caused on the one hand an increase of area and severity of damage. On the other hand there was a decrease of NOS activity (both isoforms). ATB-346 displayed a cytoprotective effect, manifested by the decrease of total area of gastric damage, however parameters of lipoperoxidation and NO-syntase system did not differ substantially from those in the group treated with napoxen prior to WRS. In contrast, in the WRS model, none of the tested NSAIDs exacerbated gastric mucosal injury; indeed, they all reduced the extent of damage.
CONCLUSION: In our study we showed, that H_2S released from ATB-346 probably did not play the pivotal role in activation of iNOS, but it was certainly involved in other mechanisms (NOS-independent) of gastroprotection.

We hypothesize that the reduction of gastric damage with an H_2S-releasing NSAID in the both stress models of gastric ulceration is a result of its maintenance of gastric blood flow and inhibition of leukocytes adherence.
Disclosure of Interest: None Declared
Keywords: Hydrogen sulfide, NSAIDs-gastropathies, Stress ulcer

P1622 EFFECTS OF BENEXATE HYDROCHLORIDE BETADEX FOR GASTRIC ULCER: AN EXPERIMENTAL STUDY

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INTRODUCTION: Benexate hydrochloride betadex (BHB) is used as anti-ulcer agent, which is thought to increase blood flow in the gastric mucosa. However, the mechanism of pharmacological action that increases blood flow in a gastric mucosa by BHB is not certain. Also, BHB action of inflammation, which is closely related to tissue injury and ulcer healing, were not fully investigated. This study was performed to investigate BHB action of ulcer healing in rat by an enhancement of microcirculation mediated by nitric oxide (NO) and anti-inflammatory activity.
AIMS&METHODS: Benexate hydrochloride betadex (BHB) is used as anti-ulcer agent, which is thought to increase blood flow in the gastric mucosa. However, the mechanism of pharmacological action that increases blood flow in a gastric mucosa by BHB is not certain. Also, BHB action of inflammation, which is closely related to tissue injury and ulcer healing, were not fully investigated. This study was performed to investigate BHB action of ulcer healing in rat by an enhancement of microcirculation mediated by nitric oxide (NO) and anti-inflammatory activity.
Material and Methods: Gastric mucosal injury rat model was made by injecting 60% acetic acid solution into the stomach. After ulcer induction, rats were randomly allocated to one of the following 4 groups, water; BHB 1000 mg/kg; L-N-nitroarginine methyl ester (L-NAME); BHB and L-NAME. The rats were orogastrically gavaged with BHB or L-NAME for 5 days, and then sacrificed. We measured the area of gastric ulcers by planimetry and the expression of COX, cytokines, NO synthase (NOS) of stomach tissues by western blot analysis.
RESULTS: The size of ulcer lesions decreased in the group treated with BHB as compared with control group. The administration with L-NAME aggravated ethanol-induced mucosal injury. The iNOS and nNOS signals increased in gastric ulcerous mucosa treated with BHB. l-NAME administration significantly decreased the expressions of NOS compared to the control group. The degree of inhibited eNOS and nNOS levels increased after 70 mg/kg l-NAME + 1000 mg/kg BHB administration. The level of COX-2, IL-1β and TNF-α was significantly decreased in BHB-treated group.
CONCLUSION: These results suggest that BHB as anti-ulcer agent enhances microcirculation and reduces proinflammatory cytokines. BHB could be responsible for protection against acetic acid-induced gastric mucosal injury.
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Disclosure of Interest: None Declared
Keywords: anti-ulcer agent, Benexate, cyclooxygenase, Nitric oxide

P1623 N-3 POLYUNSATURATED FATTY ACID TO RESCUE FROM NSAID-ASSOCIATED GI DAMAGES THROUGH LIPID RAFT PRESERVATION

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INTRODUCTION: n-3-PUFAs had been applied in diverse clinical conditions including inflammatory diseases, anti-aging as well as cancer prevention supported with its anti-inflammatory and anti-oxidative actions. There is no clear result whether the n3-PUFAs rich in docosahexanoic acid and eicosapentanoic acid can be solving strategy against NSAID-damages.
AIMS&METHODS: Using *fat-1* transgenic mice, which can synthesize n-3-PUFA owing to over-expression of 3-*desaturase*, we investigated whether n-3-PUFA can attenuate NSAID-induced GI injury. Wild-type C57BL/6 and *fat-1* transgenic mice were deprived of food 24 h before indomethacin and treated with 20mg/kg indomethacin or vehicle by gavage and killed after 16 h for gastric injury and 2 days for duodenal injury.
RESULTS: Indomethacin induced erosive and ulcerative lesions in GI tract of wild-type C57BL/6 mice, whereas gross and pathologic scores were significantly decreased in *fat-1* transgenic mice. The expressions of inflammatory genes, adhesion molecules, apoptotic executors were significantly lower in the *fat*-1 mice compared to wild-type littermates. There was significant correlation between mucosal injury and n-3 PUFAs levels ($p<0.001$). Lipid raft was significantly disrupted after indomethacin, leading to increased apoptosis as well as autophagy, whereas n-3 PUFA preserved normal signaling of lipid raft to stabilize cell as well as attenuated apoptosis through receptor GPCR120.
CONCLUSION: All of our results can open healthy future to secure NSAID-induced GI damages as well as the development of safer NSAIDs such as n-3 PUFA formulated NSAIDs.
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Disclosure of Interest: None Declared
Keywords: GI damages, lipid raft, n-3 PUFA

P1624 TWO-WEEK TREATMENT WITH PROTON PUMP INHIBITOR IS ENOUGH FOR HEALING POST ESD ULCER COMPARED TO FOUR-WEEK: A PROSPECTIVE, RANDOMIZED STUDY

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INTRODUCTION: There has been no consensus regarding the optimal period of treatment in patients with post endoscopic submucosal dissection (ESD) ulcers. A previous study reported that the healing speed of post ESD ulcers was different from that of usual ulcers. Therefore we evaluated the optimal period of treatment for post ESD ulcers.
AIMS&METHODS: Patients who underwent ESD for gastric cancer without using antithrombotic drug were randomized to two groups. They were treated by esomeprazole 20 mg per day for 4 weeks (4W group) or 2 weeks (2W group). At 4 weeks after ESD, we measured the size of artificial ulcers by endoscopy and determined the ulcer healing rate and speed compared with the size of ESD specimens. All patients received rebapimide 300mg per day for 4 weeks. We got written informed consent from all study subjects. This randomized controlled trial study was approved by ethics committee and registered in the UMIN Clinical Trial Registry (UMIN000006951).
RESULTS: A total of 36 consecutive patients (age; 71.8±8.8 years) were included in this study Because the patient (2W group) showed re-bleeding within two weeks and received the additional endoscopic treatment, he was excluded for further analysis, but other patients could finish the treatment for 4 weeks without re-bleeding or any complications. The numbers of patients in healing / scar stage of ulcer in 2W and 4W group at 4 weeks after ESD were 12 / 3 and 16 / 4, respectively, which showed no significant difference (chi-square test). In patients with healing stage of ulcer at 4 weeks, we evaluated the ulcer healing rate and speed in 2W and 4W groups were 95.2±3.1 % vs. 95.8±4.5 % and 835.8±451.7 vs. 1262.3±835.1 cm^2 per 4 weeks, respectively, which showed no statistical difference (unpaired t-test).
CONCLUSION: Two-week treatment with proton pump inhibitor is as effective as four-week one for healing post ESD ulcer.
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Keywords: ESD (endoscopic submucosal dossection), proton pump inhibitor, RCT, ulcers

P1625 TWO WEEKS TREATMENT WITH ESOMEPRAZOLE IS USEFUL FOR THE ARTIFICIAL ULCERS INDUCED BY ESD

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INTRODUCTION: Endoscopic submucosal dissection (ESD) for gastric cancer is widely performed in worldwide, and the ulcers developed after ESD are usually treated with proton pump inhibitor (PPI).
Several studies have been reported regarding use period of PPI for these ulcers, however two weeks PPI administration has not been well studied yet.
Esomeprazole (EPZ) is enantiomer of omeprazole. The treatment effect of EPZ for artificial ulcer is unclear.
AIMS&METHODS: We aimed to clarify the effect of EPZ for the ulcer healing after ESD, and we compared healing effect between 2 weeks (w) and 4w EPZ treatment for the artificial ulcer.
Thirty three gastric cancer patients who were treated by ESD were prospectively enrolled and randomely assigned to treatment with EPZ 20mg/day for 2w + rebamipide 100mg tid /day for 8w or EPZ 20mg/day for 4w + rebamipide 100mg tid /day for 8w, and these groups were compared about the rate of ulcer healing after 8w.
Moreover, in order to check the validity to the ulcer healing of EPZ treatment group, comparison with other PPI (Lansoprazole: LPZ or Rabeprazole: RPZ) for 4w+ rebamipide 100mg tid /day for 8w groups used in the past was also examined.
RESULTS: Analyzed cases were total 156 cases, including 16 cases of EPZ 2w treatment group, 17 cases of EPZ 4w group, 79 cases of LPZ 4w group and 44 cases of RPZ 4w group. In these 4 groups, gender, age, lesion site, tumor size, macroscopic findings, depth of tumors, histopathology and procedure times were not different statisticaly. There was no difference in the frequency of perforation and bleeding rate. Postoperative ulcer reduction ratio after 1w was 23%/ 32%/

31%/ 20% in each of the four group (p = 0.039), LPZ 4w+ rebamipide group was significantly better than RPZ 4w+ rebamipide group, and EPZ 4w + rebamipide group showed better tendency compared to the RPZ 4w+ rebamipide group (p = 0.0689).
On the other hand, there was no difference in the reduction ratio of more than 99% in all groups 8w after ESD (p> 0.21).
About stage of ulcer healing, 75% cases in each group was at H2 stage or higher healing stage at the time of the 4w after ESD, and there was no difference of healing stage ratio among the four groups 4w, 8w after ESD (p = 0.48, p = 0.65).
CONCLUSION: Two weeks treatment with EPZ was useful for the artificial ulcers induced by ESD. This new combination therapy by EPZ 2 weeks + rebamipide 8 weeks is safe and cost-effective for ESD-induced artificial ulcer treatment.
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Disclosure of Interest: None Declared
Keywords: 2 weeks treatment, ESD (endoscopic submucosal dossection), Esomeprazole, gastric ulcer, gastric ulcer, Rebamipide

P1626 GASTRIC ULCER BLEEDING: IS THE NEOPLASTIC RISK FORGOTTEN?

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INTRODUCTION: Gastric ulcer has well-known malignant potential. For this reason even in benign looking ulcers, not only biopsies at the edges of the ulcer should be performed but also the proof of his complete healing. Gastric ulcer bleeding is potentially fatal, but should not minimize the risk of underlying malignancy. We intend to evaluate the handling of patients admitted with a diagnosis of gastric ulcer bleeding.
AIMS&METHODS: Retrospective study of patients admitted to a general hospital with a diagnosis of gastric ulcer bleeding (without initial diagnosis of neoplasia), during a period of two years. We collected demographic, analytical and endoscopic data. Follow-up after discharge and in consultation was assessed.
RESULTS: We identified 101 admissions for gastric ulcer, corresponding to 95 patients, mostly elderly (73.3% older than 65 years) and male (66.3%). The main reasons for admission to the emergency department were suspected gastrointestinal bleeding (melena, hematemesis), abdominal pain and syncope. Most lesions were located in the antrum (46.5%), followed by the body and incisura angularis. Eleven ulcers had endoscopic signs of malignancy. During hospitalization, biopsies were taken at the edge of the ulcer in 48.5% of patients diagnosed with two gastric adenocarcinomas. Only 8.9% of biopsies identified the presence of Helicobacter pylori. Endoscopic reassessment was held in the hospital after discharge in 34.7% of patients (biopsies in 73.5%), with the identification of two more gastric neoplasms. Twenty-one patients were lost in follow-up.
CONCLUSION: The prevalence of neoplasia in gastric ulcer bleeding is low, but not negligible, so there should be a correct clinical and endoscopic follow-up of these patients. This study highlighted a small number of endoscopic biopsies and reassessments.
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Disclosure of Interest: None Declared
Keywords: gastric ulcer, neoplastic risk

P1627 INCIDENCE OF GASTRIC ADENOCARCINOMA AMONG PATIENTS WITH INTESTINAL METAPLASIA

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INTRODUCTION: Gastric intestinal metaplasia (IM) has been known as a premalignant lesion, but how harmful is the presence of IM for the development of gastric cancer (GCA) is not fully determined.
AIMS&METHODS: We conducted a hospital-based cohort study based on 7,059 patients who were diagnosed for the first time between 1992 and 2010 with IM by endoscopic biopsy. The cumulative incidence and standardized incidence rate (SIR) were determined.
RESULTS: The total follow-up person-year was 42,325 and the median follow-up duration was 5.1 years. Eighty-one patients developed GCA during the follow-up period. The 5-year and 10-year cumulative incidences of GCA were 0.9% (95% confidence interval [CI], 0.6-1.1%) and 2.0% (95% CI, 1.5-2.6%), respectively. Compared with the general population, IM patients had significantly higher risk of GCA (SIR, 2.46; 95% CI, 1.96-3.06). The SIRs of GCA decreased steadily with increasing age (3.61, 3.82, 2.39, 2.01, for age <54, 55-64, 65-74, and >75 years, respectively). Compared with patients without dysplasia (SIR, 2.01; 95% CI, 1.54-2.57), patients with dysplasia had significantly higher risk of GCA (mild-to-moderate dysplasia, SIR, 7.82; 95% CI, 3.75-14.39; severe dysplasia, SIR, 35.23; 95% CI, 15.17-69.41).
CONCLUSION: IM is a risk factor for GCA with moderate increased risk, but the existence of dysplasia significantly increase the risk of GCA.
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Disclosure of Interest: None Declared
Keywords: Gastric cancer, incidence, intestinal metaplasia

P1628 LOW GRADE GASTRIC DYSPLASIA: THE LONG-TERM EVOLUTION

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INTRODUCTION: Although we recognize the importance of dysplasia as the penultimate stage of gastric carcinogenesis, its natural history is not clarified.
AIMS&METHODS: The aim of the present study is to evaluate the long - term evolution of the low grade gastric dysplasia, not submitted to endoscopic/surgical treatment.
RESULTS: Of the 51 patients, 46% belong to the male sex. 5/51 (9.8%) of the patients were less than 55 years of age and simultaneously had a family history of gastric cancer. 48/51 (94%) had extensive intestinal atrophy/metaplasia and 37 (72.5%) dysplasia only in the antrum. In regard to the endoscopic aspect, 27/51 (53%) showed dysplasia in flat mucosa, 20/51 (39.2%) in nodular mucosa and 4/51 (7.8%) in depressed mucosa. The histological degree regressed in 30/51 (58.8%) of the cases (average time: 9.1 months), maintained in 13/51 (25.5%) and developed in 8/51 (15.7%, average time 32 months). Of the lesions that regressed, 20/30 (66.7%) were initially detected in flat mucosa (p<0,008). The eight who had a histological evolution of the lesions initially showed low degree multifocal dysplasia, while none of the rest showed any signs of multifocality (p<0,001).
CONCLUSION: Almost all the patients showed regression of the lesions in the follow up. 15.4% of the cases had an evolution of histological degree. In this study the initial detection of the changes in the flat mucosa correlated significantly with its regression. The multifocality of the lesions was related with its progression in a significant statistical way.
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Disclosure of Interest: None Declared
Keywords: Gastric cancer, Low grade gastric dysplasia

P1629 ENDOSCOPY RESEARCH OPPORTUNITIES IN DIFFERENTIAL DIAGNOSIS OF MALIGNANT GASTRIC ULCER.

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INTRODUCTION: To study the endoscopy research opportunities in differential diagnosis of malignant gastric ulcer from chronic ulcer.
AIMS&METHODS: We have examined 79 patients with initial diagnosis of chronic gastric ulcer, who appealed in the consultative clinic of NCRC during the period from 2009 to 2012 years. All patients were checked with endoscopy with target biopsy (4-5 margins) Next examination was done in average in 12 months. During the time between examinations, patients received conservative treatments, herewith 25 of them (31,6%) got antiulcer eradication heatment Helicobacter pylori.
RESULTS: In our researches, gastric ulcers of 29 patients (36,7%) were becoming malignant in average in 12 months after first visit. Malignancy of gastric ulcer happened, generally, at the margings where gastric mucosa had prolonged non-healing defects. In some cases malignancy happened unicentric from one margin or multicentric up to malignancy of all the periphery of the ulcer, and later on distributed to the bottom. Endoscopically margings of gastric ulcer are high, rough, folds were converging to the edge of the ulcer. With malignancy of the ulcer from the margins of ulcerative defect, neither gastric mucosa itself, nor the scar in the area of the bottom of the ulcer don't become malignant completely. Efficiency of the targeted biopsy with multiply takes of pieces of tissue along the whole periphery of the ulcer reached 94-100%. In most of the cases we noticed malignancy of distal stomach - 19 patients (65,5%), less of proximal stomach (in subcardinal site on the greater curvature - 7 patients (24,1%), and of the body (at the border of the antral) - 3 patients (10,3%) (table#1). With examination of the biopsies of 4 patients (13,8%), with malignant ulcers also were discovered complexes of well formed cancer. In 3 cases (10,3%) depth of the invasion of cancer cells was limited by mucous layer, in 4 cases (13,8%) - by mucous and submucosal, in 7 cases (24,1%) - by mucous, submucosal and muscular layers, in 15 cases (51,7%) tumor elements were spreading at the entire thickness of the gastric wall. 7 patients from 29 with malignant ulcers, revealed metastasis in regional lymph nodes ligaments and along the main blood vessels.
CONCLUSION: Very high percentage of the malignancy of gastric ulcers leads to the need of constant oncological alertness for general practitioners at inspection and treatment of peptic ulcer patients. So, the prerequisite of the successful treatment of patients with malignant gastric ulcers is the prompt diagnostics of the nature of the pathological process, on which depends the choice of tactics of the surgery.
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Disclosure of Interest: None Declared
Keywords: endoscopic, endoscopic diagnosis

P1630 THE FACTORS ASSOCIATED WITH DEVELOPMENT OF INTESTINAL METAPLASIA: A NESTED CASE-CONTROL STUDY

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INTRODUCTION: Gastric cancer remains one of the leading causes of cancer mortality worldwide. Intestinal metaplasia, the key precancerous lesion of stomach, increases 6-times risk of gastric cancer and usually has no specific symptoms to detect.

AIMS&METHODS: We aim to investigate the factors associated the development of intestinal metaplasia in the general population and relatives of gastric cancer. We conducted a hospital-based nested case-control study based on gastric cancer family cohort and healthy control cohort. This is a hospital-based case control study with age- and gender-matching between 2007 and 2012 at Taichung Veterans General Hospital. Multivariate analyses were conducted to examine the independent factors associated with intestinal metaplasia.
RESULTS: Between 2007 and 2012, we identified 199 subjects with IM and 597 age- and gender-matched controls. Multivariate analyses found family history of gastric cancer (OR: 2.16, 95%CI: 1.38-3.37), *H. pylori* infection (OR: 1.60, 95%CI: 1.14-2.24), and gastric ulcer (OR: 1.78, 95%CI: 1.18-2.68) were independent risk factors for intestinal metaplasia development. Daily consumption of fruit was found to be inversely related with intestinal metaplasia (OR: 0.51, 95%CI: 0.36-0.74).
CONCLUSION: In conclusion, family history, *H. pylori* infection, and gastric ulcer were independent risk factors associated with intentional metaplasia. Daily fruit intake was a protective factor.
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Disclosure of Interest: None Declared
Keywords: case-control study, gastric cancer, intestinal metaplasia

P1631 CLINICAL OUTCOMES OF ENDOSCOPIC RESECTION IN GASTRIC NEUROENDOCRINE TUMOR IN KOREA :A NATIONWIDE MULTICENTER STUDY

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INTRODUCTION: Gastric neuroendocrine tumor (NET) less than 10 mm and limited to the sub mucosa has a low possibility of lymph node and distant metastasis. Therefore, the endoscopic resection (ER) has been used for these tumors. However, there were several reports about the clinical outcomes of ER in gastric NET.
AIMS&METHODS: We aimed to investigate the safety and efficacy of ER in gastric NET. From January 2002 to December 2011, 181 patients were diagnosed with gastric NET from 25 institutions, Korea. Among them, 80 patients (44%) were treated by ER. The clinicopathologic factor, therapeutic efficacy and follow up results were retrospectively evaluated.
RESULTS: The mean age of the patients was 52.8 ± 11.2 years. The 2 patients have carcinoid symptoms. The proportions of antrum, body, and fundus were 8.8%, 81.2%, and 10.0%. The mean size of the tumors 8 ± 5mm and the elevated lesions in endoscopic gross appearance was most prevalent (65/80). The endoscopic mucosal resection (EMR) was performed on 70 lesions and endoscopic submucosal resection was performed on 10 lesions. The complete resection rate was 89% and the lymphovascular invasion was 6.3%. The proportions of tumor negative lateral and vertical resection margin was 90%. During a mean follow up period of 28 months (range 1 – 106 months), the local recurrence occurred 5 patients and systemic recurrence occurred 1 patients. Among 5 patients with local recurrence, 4 patients underwent successful repeat EMR.
CONCLUSION: The ER may be considered for treatment of gastric NETs because the ER shows a high complete resection rate and provides accurate histopathologic evaluation. However, the appropriate selection criteria for ER in gastric NETs should be applied and the long term follow up data will be needed.
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Disclosure of Interest: None Declared
Keywords: clinical outcomes, endoscopic resection, gastric neuroendocrine tumor

P1632 RISK FACTORS OF RESIDUAL OR RECURRENT TUMOR IN PATIENTS WITH A LATERAL RESECTION MARGIN POSITIVE AFTER ENDOSCOPIC RESECTION OF EARLY GASTRIC CANCER.

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INTRODUCTION: Tumor-positive resection margins after endoscopic resection in early gastric cancer (EGC) patients pose a conflict in the outcome. Therefore, many treatment methods have been proposed such as close follow up with endoscopic exam, surgical resection, argon plasma coagulation (APC) and endoscopic resection (ER).
AIMS&METHODS: The aim of this study was to identify the associated risk factors in positive endoscopic lateral resection margin of EGC and therefore estimating the outcomes. A retrospective analysis of 602 patients (625 lesions) who underwent endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) of EGC at a single institute was performed. The patients with positive lateral resection margin after ER were divided into two groups, with and without residual/recurrent tumor. Clinicopathological characteristics and risk factors in lateral resection margin positive patients were analyzed.
RESULTS: A total of 91 patients with a positive lateral resection margin after EMR (n = 49) or ESD (n = 42) were enrolled. The residual/recurrent tumor rate was 35.4% (33 of 93 lesions). 19 had additional surgical gastrectomy, 25 had ER, 13 had argon plasma coagulation and 34 had close observation. Univariate analysis found that residual/recurrent tumor was associated with endoscopic resection type (EMR, ESD), gross type (elevated 37 lesions, flat or depressed 56 lesions), differentiation (differentiated 84 lesions, undifferentiated 9 lesions), and depth of invasion (mucosa 73 lesions, submucosa 20 lesions). Multivariate analysis found the independent risk factor of residual or recurrent tumors to be associated with the type of endoscopic resection (OR 2.885; 95 % CI 1.472–5.653, p = 0.002) and differentiation (OR 4.554; 95 % CI 1.045–19.846, p = 0.044).
CONCLUSION: Patients with EMR, undifferentiated in positive lateral resection margin after endoscopic resection of EGC are recommended to undergo additional endoscopic or surgical resection due to a high risk in residual/recurrent tumor.
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Disclosure of Interest: None Declared
Keywords: Early gastric cancer, Endoscopic resection, positive resection margin

P1633 VOLATILE COMPOUNDS IN BREATH TO DIFFERENTIATE BETWEEN GASTRIC CANCER AND BENIGN CONDITIONS

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INTRODUCTION: Most of the gastric cancers are diagnosed at advanced stages when the survival results are unsatisfactory. Therefore, there is a need for non-invasive markers to diagnose the disease at early stage. Here we report the initial results of volatile marker diagnostic development approach program.
AIMS&METHODS: The study aimed to identify potential volatile organic compounds (VOCs) present in exhaled breath characteristic to gastric adenocarcinoma.
Altogether 364 patients (148 men, 216 women; median age 62; range 22-87) were included to the study. Out of them 82 patients had morphologically confirmed gastric adenocarcinoma prior to surgery or chemotherapy; 45 patients had peptic ulcer disease (either active or a scar), 21 patients were diagnosed low-grade dysplasia in the gastric mucosa, while 216 patients were serving as group of control (all with documented stomach mucosa status according to Updated Sydney system; this group included also patients with atrophy and/or intestinal metaplasia).
Exhaled breath samples were collected in adsorbent tubes and stored until analyzed. The analysis was performed by using gas chromatography coupled with mass spectrometry (GC-MS) in order to identify the chemical composition of the samples.
Student t-test was used to judge the difference in VOCs between the groups; the significance level was set at 0.05.
RESULTS: Altogether 133 volatile components were identified; 17 of them revealed differences between some of the comparisons. Eleven VOCs were found in significantly higher concentrations in the cancer group when compared to the controls (see Table). Six compounds (2- methyl-1-propene; 2,4 dimethyl-Heptane; 4- methyl-Octane; 1,2,3 trimethyl-Benzene; 4- methyl-Decane; Naphtalene) were higher in cancer than in dysplasia cases. Four compounds (o-Xylene; alpha-Methylstyrene; 1,2,3 trimethyl-benzene; 1,2,3,4 tetramethyl-benzene) were higher in peptic ulcer than in controls. However, no difference was revealed between the dysplasia and control as well as between the cancer and peptic ulcer groups.
CONCLUSION: Specific volatile components in exhaled breath can discriminate between gastric cancer and benign conditions. This finding provides background for further new developments of volatile component applications in diagnostics, including for nanosensor based applications.
Disclosure of Interest: None Declared
Keywords: breath test, Gastric adenocarcinoma, volatile markers

P1634 CLINICAL UTILITY OF MOLECULAR CHARACTERIZATION OF GASTRIC CANCERS BASED ON SOMATIC MUTATIONS AND GENE AMPLIFICATIONS

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INTRODUCTION: According to the Czech national cancer register the prognosis of gastric cancer patients has remained unchanged over the course of the past 20 years. With a 5-year survival of just 30% (for all stages) it is the third most fatal malignancy of the gastrointestinal tract and sixth overall among solid cancers. The recent trends in discovery and use of biomarkers in other cancers have been mainly derived from detailed tumor profiling. Somatic mutations and gene amplifications are among the molecular aberations frequently studied.
AIMS&METHODS: It is the main purpose of this work to investigate frequency of somatic mutations and gene amplifications from FFPE sections as well as fresh biopsies in a group of 85 gastric cancer patients and to evaluate their potential utility in early diagnosis as well as therapy prediction and prognosis. We screened 7 genes frequently mutated in gastrointestinal cancers including APC, CTNNB1, KRAS, BRAF, EGFR, PIK3CA and TP53. In addition, we evaluated gene amplifications in a panel consisting of 70 genes often implicated in tumorogenesis.
RESULTS: The overall success rate of DNA extraction from the gastric FFPE samples was at a level of 85%. We have recorded fequencies of somatic mutations similar to the reports by Catalogue of Somatic Mutations in Cancer (COSMIC). The portion of mutated patients in the group was 24% (16/69) with TP53 as the most frequently mutated gene (12x), followed by PIK3CA (3x). When applying Lauren classificaion, most mutations were detected in samples of intestinal compared to the diffuse type, however, no effect of presence of somatic mutation on tumor localization, stage or survival was observed. The complex gene amplifications patterns were processed by hierarchical classification resulting in distinct clusters.

CONCLUSION: Somatic mutations are not associated with localization or stage and are likely not factors in prognosis of the disease. Molecular classification of gastric cancer based on gene amplification patterns results in distinct tumor similarities that may have clinical relevance for clinical management of gastric cancer.

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Disclosure of Interest: None Declared

Keywords: DNA mutations, gastric cancer, gene amplifications, HER2, molecular characterization, survival

P1635 RECURRENCE OF GASTRIC POLYPS AFTER ENDOSCOPIC REMOVAL WITH OR WITHOUT H. PYLORI ERADICATION

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INTRODUCTION: Gastric polyps are not rare finding during endoscopic examination. Evidence indicates that eradication of Helicobacter pylori (H. pylori) leads to disappearance of hyperplastic polyps in the stomach. However, little is known about the effect of the eradication of *H. pylori* on recurrence of hyperplastic or other gastric polyps following endoscopic removal.

AIMS&METHODS: The aim of the study was to evaluate the recurrence rate of gastric polyps after endoscopic removal and the association between the polyp recurrence and *H. pylori* eradication. The medical records of patients diagnosed with gastric polyps between January 2008 and December 2009 were reviewed. Gastric polyps were removed by biopsy or polypectomy according to the size or polyps. *H. pylori* infection and the success of eradication were assessed by endoscopic biopsy or urea breath test. At follow-up endoscopy, recurrence of gastric polyps was investigated.

RESULTS: Of the 248 patients with gastric polyps, 134 patients who underwent the follow-up endoscopy at least 2 months later after removal of polyps were analyzed. Thirty-three patients had hyperplastic polyps, 30 patients had fundic gland polyps and 71 patients had inflammatory polyps. Among 58 patients with *H. pylori* infection, 41 received the eradication therapy. During mean follow-up for 29.5 months, 2 patients showed the recurrence of gastric polyp after *H. pylori* eradication and no recurrence was observed in patients who did not receive the eradication therapy. There was no significant difference in recurrence rate of gastric polyps between patients with and without *H. pylori* eradication.

CONCLUSION: The eradication of *H. pylori* dose not reduce the recurrence of gastric polyp following endoscopic removal of gastric polyps.

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Disclosure of Interest: None Declared

Keywords: gastric polyp, Helicobacter pylori eradication, recurrence

P1636 THE ASSOCIATION OF MUCIN PHENOTYPIC EXPRESSION OF GASTRIC CANCER AND SURVIVAL RATE

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INTRODUCTION: So far, gastric cancers were classified into intestinal type and diffuse type based on Laurens criteria. Recently new immunohistochemical technique developed new classification criteria to gastric cancer. This classification is divided to gastric type and intestinal type. Moreover it has been gradually clarified that gastric type is often associated with poor prognosis and bad behavior.

AIMS&METHODS: In this study, we examined about mucin phenotype and analyzed about survival rate of gastric cancer patients.

Gastric cancer phenotype was classified by immunohistochemical method. We used anti-MUC2, MUC5AC, MUC6 and CD10 antibodies. Over 10% positive area in a specimen was considered positive phenotype. Along with the expression pattern of these mucin antibodies, we divided into gastric type, intestinal type, mixed type, and non-expression type. Gastric cancer patients were all received chemotherapy, and median survival time (MST) was calculated. The survival curve for each phenotype was showed by the Kaplan-Meyer method, and statistical analyses were applied by log-rank test.

RESULTS: Gastric type was defined as MUC5AC and MUC6 positive type and 12 patients were this phenotype. Intestinal type was defined as MUC2 or CD10 positive type and 6 patients were this phenotype. Mixed type was defined as these mucin positive type and 15 patients were this phenotype. Undifferentiated type was all mucin negative type and 8 patients were this phenotype. Survival curve after chemotherapy along with Kaplan-Meyer methods showed better prognosis in gastric phenotype patients, whereas intestinal phenotype patients showed poor prognosis (MST of gastric type vs. intestinal type, 1033 vs.191 days).

These survival rates were significantly different between these two groups by log-rank test (p=0.0062). Mixed type survival curve showed intermediate survival time (MST: 425 days).

CONCLUSION: Gastric phenotype by mucin expression patterns may be a predictive factor for the gastric cancer prognosis before chemotherapy. Further study is needed to clarify the mechanism of the association of these mucin phenotype and gastric cancer survival rate.

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Disclosure of Interest: None Declared

Keywords: chemotherapy, Gastric cancer, mucin phenotype

P1637 UTILITY OF EUS TO IDENTIFY THE EFFECTIVE RESPONDERS FROM PATIENTS WITH GASTRIC CARCINOMA WHO RECEIVE NEO-ADJUVANT CHEMOTHERAPY

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INTRODUCTION: EUS is an effective method to evaluate the preoperative stage of gastric cancer. But its clinical usage as an effective evaluator of chemotherapy response is not clear.

AIMS&METHODS: This study aimed to investigate if EUS can be chosen as an effective method to evaluate the treatment response and decide best time for operation of gastric cancer patients who receive neo-adjuvant chemotherapy.39 consecutive patients (Male: 23, median age : 50.5 +/-12.2) with histologically confirmed gastric carcinoma underwent EUS (Olympus-Eum2000-25R) and their EUS TN staging showed T3N0 or above stage and no distant metastasis. These patients were given a standard ECF neo-adjuvant chemotherapy. All these patients who receive neo-adjuvant chemotherapy were examined the TN stage by EUS again after 2 cycles, 3 cycles, 4 cycles till the results showed down-stage or 4 cycles were finished. After that, surgery were performed. All EUS examinations were performed at the day before next cycle. In addition to TN stage, the tumor size was recorded with 3 parameters—the maximum thickness, longitude of tumor and width by EUS. The surgical TN stage and pathological complete response (No residual carcinoma in the primary), pathological partial response (<10% residual carcinoma in the primary) were compared with EUS stage and tumor size change.

RESULTS: After neo-adjuvant chemotherapy, EUS correctly identified 53.8% (21/39) T stage and 46.1% (18/39) N stage of patients, respectively, in line with their histological staging. Whereas, 78.6% patients who EUS showed down-stage (11/14) were confirmed by pathology as partial response. In the same time, the tumor size changes were found correlated with pathological response.

CONCLUSION: Although EUS had relatively low accuracy of TN stage after neo-adjuvant chemotherapy comparing with preoperative EUS staging, the study showed a good correlation between down-stage or dramatic decreased tumor size checked by EUS and pathological response of tumor. So, EUS could be an effective method to evaluate the treatment response and decide best time for operation of gastric cancer patients who receive neo-adjuvant chemotherapy.

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Disclosure of Interest: None Declared

Keywords: EUS., Gastric adenocarcinoma, Neoadjuvant therapy

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00

***H. PYLORI* III – Poster Area**

P1638 PROSPECTIVE VALIDATION OF ENDOFASTER FOR A REAL-TIME DIAGNOSIS OF H. PYLORI INFECTION DURING UPPER ENDOSCOPY

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INTRODUCTION: EndoFaster is a new technology based on a real-time analysis of the gastric juice that can provide informations regarding Hp infection and pH value of the gastric contents. In a previous pilot study, the potential accuracy of EndoFaster in diagnosing *H. pylori* infection during upper GI-endoscopy has been shown.

AIMS&METHODS: Aim of this prospective multicenter study was to validate the efficacy of EndoFaster in a wide cohort of patients undergoing upper GI-endoscopy. Consecutive patients aged 40-75 years undergoing upper GI-endoscopy without either PPI or antibiotic therapies in the previous 4 weeks were prospectively enrolled. EndoFaster is an innovative device that is interposed between the endoscope and the suction system. After aspiration of 4-6 ml of gastric juice, EndoFaster performs an automatic analysis of the ammonium concentration of gastric juice within 2 minutes. Based on the previous pilot study, the test was considered positive for *H. pylori* infection when the ammonium concentration was >65 ppm/ml and negative when ≤55 ppm/ml, being indeterminate in the 56-65 ppm/ml interval. Histology with the addition of urea breath testing in discordant cases was considered as the reference standard for assessing *H. pylori* infection.

RESULTS: Overall, 209 patients were included in the study. However, 26 (12.4%) were excluded, because the aspirated gastric juice was insufficient for determining ammonium concentration. In the remaining 183 patients *H. pylori* infection was present in 71 (39%) patients at reference standard. The test with EndoFaster resulted to be positive in 77 (42%), negative in 86 (47%), and indeterminate in 20 (11%) cases, respectively. When excluding the patients with an indeterminate result, sensitivity, specificity, PPV and NPV of EndoFaster for *H. pylori* infection resulted to be 98.5%, 87.6%, 84.4% and 98.8 % respectively.

CONCLUSION: In this validation study, EndoFaster showed an overall feasibility of 78% and accuracy of 92% for a real-time determination of *H. pylori* status. The test appeared to confirm the high accuracy for *H. pylori* shown in the previous pilot study.

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Disclosure of Interest: None Declared

Keywords: Helicobacter pylori, Helicobacter pylori, Photodynamic therapy, Endoscope, Chitosan, Methylene blue.

P1639 DUODENAL HYPERPLASTIC ENTEROPATHY WITH INCREASED DENSITY OF ΓΔ INTRAEPITHELIAL LYMPHOCYTES IN HELICOBACTER PYLORI INFECTION

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INTRODUCTION: Not all duodenal biopsy specimens showing villous atrophy with crypt hyperplasia and increased intraepithelial lymphocytes (IELs) are explained by gluten sensitivity. In the present study we measured by morphometry the architectural and inflammatory changes in the duodenum seen in Helicobacter pylori (Hp.)
AIMS&METHODS: Altogether 25 untreated adults (N=25) and children (N=3) with dyspepsia positive for Hp. infection were included in the study. Multiple duodenal biopsies were obtained for the purpose of this study. All patients declared gluten-containing diet and were negative for serum endomysial antibodies. Further, they did not have duodenal IgA deposits targeting transglutaminase 2, a typical finding in coeliac disease. No chronic inflammatory bowel diseases were detected in these patients. Duodenal biopsy villous height : crypt depth ratio (VH:CrD) were measured from well oriented biopsy specimens. The densities of all T cells (CD3, cut off in frozen biopsy samples 37 cells/mm epithelium) as well as $\gamma\delta$ T cell receptor bearing IELs (cut off 4.3 cells/mm) were also measured. If patchy lesions were observed, the densities of IELs were counted in the biopsy specimen with most severe morphological lesions. The study was approved by the Ethical Committee of University of Medicine and Pharmacy "Carol Davila" Bucharest.
RESULTS: Shortened duodenal villi, less than 300 μm in length, were seen in 7/25 Hp.patients (28%). VH:CrD < 2, typical for untreated coeliac disease was observed in 16/25 individuals (64%) (range 0.5-4.0) together with crypt hyperplasia in 12/25 patients. All three of the Hp. infected children also had enteropathy with crypt hyperplasia. Duodenitis, expressed as increased density of CD3 positive IELs, was seen in 76% of the patients. Remarkably, 21/25 (84%) had an increased density of $\gamma\delta$ IELs ranging from 4.7 to 18.7 cells/mm epithelium, comparable to densities seen in coeliac disease.
CONCLUSION: We show for the first time small intestinal architectural changes, villus atrophy with crypt hyperplasia, to occur in acute Hp. infection. The duodenitis part is well known but also Hp. infected individuals react with an inflammation resulting in an increased density of $\gamma\delta$ T cells in the epithelial compartment. Acute Hp. infection, prevalent in many parts of the world, may result in a duodenal enteropathy mimicking coeliac disease, partial and subtotal villous atrophy together with mucosal inflammation. The finding of this kind of "coeliac-type" small intestinal mucosal behavior in Hp. infection should be repeated in larger patient cohorts.
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Disclosure of Interest: A. Popp : no conflict, J. Taavela : no conflict, M. Jinga : no conflict, V. Balaban : no conflict, K. Laurila : no conflict, I. Anca : no conflict, M. Maki : no conflict
Keywords: duodenal enteropathy, Helicobacter pylori infection

P1640 EFFICACY OF SEQUENTIAL THERAPY AND CVADRUPLE THERAPY AS FIRST-LINE REGIMENS IN HELICOBACTER PYLORI ERADICATION

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INTRODUCTION: *H. pylori* is an important pathological factor for gastritis, ulcer, gastric carcinoma and gastric MALT lymphoma. Eradication of infection depends of patient compliance and resistance of bacteria to antibiotics. In the regions with high resistance to clarithromicin, first treatment choices are sequential or cvadruple therapy.
AIMS&METHODS: AIM: To evaluate the efficacy of sequential and cvadruple therapy as first-line regimens for H. Pylori eradication in patients with actual documented infection, untreated previously. PATIENTS AND METHODS: We studied the efficacy and tolerance of two eradication regimens, administered to two groups of patients with actual infection (proven by respiratory test, fecal antigen or biopsy): A-sequential therapy with PPI double dose+Amoxicillin 1gx2/day 5 days followed by PPI double dose+Clarithromicin 0.5gx2/day+ Metronidazol 0.5gx2/day 5 days, B-cvadruple therapy with PPI double dose+Tetracyclin 0.5gx4/day+ De-Nol 120mgx4/day + Metronidazol 0.25gx4/day, 10 days. We analysed also the secondary effects by questionning the patients.
RESULTS: 48 patients were treated. In group A (26 patients), eradication was tested in 22 patients and was obtained in 18 patients (ITT 69%, PP 84%). In group B (22 patients), eradication was tested in 19 patients and was obtained in 18 patients (ITT 72%, PP 86%). Adverse events appeared in A - 15% cases, B-18% cases, with no influence on finalizing the treatment.
CONCLUSION: The efficacy of both eradication treatments proposed as first-line regimens is high. The eradication rate was superior to triple therapy (70-80% in studies) but lower that similar regimens metaanalysis.
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Disclosure of Interest: None Declared
Keywords: Cvadruple therapy, Helicobacter pylori eradication, Sequential therapy

P1641 IS THE ERADICATION OF HELICOBACTER PYLORI POSSIBLE WITH HIGH-DOSE PPI IN EXTENSIVE METABOLISERS WITH RESPECT TO CYP2C19 GENOTYPE POLYMORPHISM?

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INTRODUCTION: CYP2C19 genotype polymorphism is a significant factor on the treatment success of *H. pylori* eradication. In terms of genotype polymorphism in CYP2C19, the eradication of *H. Pylori* has been found unsuccessful in consequence of the insufficient rise of intragastric pH and the low level of antibiotic bioavailability in extensive metabolisers.
AIMS&METHODS: It is our aim to determine whether the eradication rate increases with the treatment of high-dose PPI in extensive metaboliers in which the eradication ended unsuccessfully with the previous treatment of standard dose PPI. H. Pylori eradication could not be achieved with standard eradication treatment in extensive metabolisers were included in the study. In our previous study in addition to a standard dose of antibiotics, an eradication treatment with rabeprazole and pantoprazole were performed for the patients (n156) with extensive metabolisers during 14 days. Among this group, 25 patients who did not respond to the eradication treatment were administered a high dose of PPI for the 2nd eradication treatment. As in the first eradication treatment, clarithromycin 2x500 mg and amoxicilline 2x1 gr were given. The dose of rabeprazole for PPI was increased to 3x20 mg and for the group given 3x40 mg pantoprazole in the second treatment.
RESULTS: The eradication rate with normal dose of PPI is 64.7% (n:101) for the 156 extensive metabolisers. The usage of rabeprazole or pantoprazole on the eradication rate was not found. The eradication was not achieved in 55 of 156 patients with extensive metabolisers. Among this group the 25 patients whose eradication treatments were unsuccessful were administered the second eradication treatment with high-dose PPI. 68% (n:17) of them were female. 48% (n:12) of the patients were given rabeprazole. The eradication rate in high dose of PPI (n:25) group was 80% (n:20). The eradication rate was higher for the patients eradicated with high dose of PPI treatment (standart dose 64.7% vs. high dose 80%). In the extensive metaboliser, the impact of different PPI usages on the success of eradication was not been determined (p=0.54).
CONCLUSION: In *H. pylori* eradication, in terms of antibiotic bioavailability the intragastric pH should be 5 or over for 24 hours. In extensive metabolisers, in case of a failure of the eradication treatment before applying to different treatment protocols, the treatment may become successful with the increase of PPI on condition that the antibiotic and the duration are reserved.
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Disclosure of Interest: None Declared
Keywords: extensive metaboliser, h.pylori, high dose PPI

P1642 HELICOBACTER PYLORI ERRADICATION WITH STANDARD TRIPLE THERAPY - FORGET OR USE?

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INTRODUCTION: The most popular first line Helicobacter pylori eradication scheme is the called triple standard (STT): PPI bid and clarithromycin (500mg bid) associated with amoxicillin (1g bid) 7 to 14 days. The Maastricht IV consensus recommended based mainly in Italian studies, a novel first-line quadruple therapy (sequential or concomitant) in countries with high clarythromycin resistance. This scheme adds complexity and costs to the eradication schemes. Also, some recent studies have not demonstrated differences between the effectiveness of STT and the sequential therapy.
AIMS&METHODS: AIM: Evaluate the efficacy of HP eradication with STT (14 days) in a cohort of patients treated in the period of between January 2005 and December 2012 in a tertiary center in Northern Portugal. METHODS: Retrospective cohort study. Inclusion criteria: 1) proven HP infection; 2) eradication treatment with STT 14 days ; 3) HP eradication confirmed by urease breath (UBT) test 6-8 weeks after treatment. Exclusion criteria: 1) previous treatment with HP; 2) age inferior to 18 years; 3) previous gastric surgery; 4) PPI, antacid or misoprostol 4 weeks before UBT.
RESULTS: RESULTS: 1073 patients were included in this study. 44.7% (n=480) of male sex. Average age: 50.6 years old. HP was successful eradicated in 67.1% of the patients treated with IAC 14 days. We found a relation statistically significant between: 1) age and the therapy result (p=0,029) with younger patients showing lower eradication rates and 2) the year of eradication and therapy result (p=0.039) with athe lowest eradication success with STT in 2012 (53%)
CONCLUSION: CONCLUSION: This study is consistent with the most recent literature which reports the eradication levels with STT inferior to 70% much less than desirable. This study supports that this eradication scheme shoul be abandoned in our area.
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Disclosure of Interest: None Declared
Keywords: Helicobacter pylori eradication, STANDARD TRIPLE THERAPY

P1643 SEQUENTIAL THERAPY VERSUS STANDARD TRIPLE-DRUG THERAPY FOR HELICOBACTER PYLORI ERADICATION: A PROSPECTIVE RANDOMIZED STUDY.

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INTRODUCTION: Eradication rates following standard triple therapy for *Helicobacter pylori* infection are declining. Recent studies, conducted in some countries, have shown that sequential therapy for *H. pylori* infection yields high cure rates.
AIMS&METHODS: Aim: To compare the efficacy and tolerability of a sequential regimen as a first-line treatment of *H. pylori* infection with a standard triple regime in Morocco.
Methods: A total of 281 naive *H. pylori* infected patients, confirmed by histological examination, were assigned randomly to either standard triple therapy (omeprazole (20 mg) bid plus amoxicillin (1g) bid and clarithromycin (500 mg) bid for 7 days) or sequential therapy groups (omeprazole (20 mg) twice daily (bid) plus amoxicillin (1g) bid for 5 days, followed by omeprazole (20 mg) bid plus tinidazole (500 mg) bid and clarithromycin (500 mg) bid for a further 5 days. *H pylori* eradication was checked four to six weeks after treatment by using a 13C-urea breath test. Compliance and adverse events were assessed.
RESULTS: The two groups did not differ significantly in gender, age, previous disease history, endoscopic and histological features and smoking. The intention-to-treat and per-protocol eradication rates were 65.9% and 71% in the standard triple group, and 82.8% and 89.9% in the sequential group, respectively. The eradication rate was significantly higher in the sequential group compared with the standard triple group ($p < 0.001$), There was no statistically significant difference in compliance (97.5% vs. 96.3%) and incidence of side-effects (27.5% vs 27.9%) between the two groups.
CONCLUSION: for eradication of *H. pylori*infection, the ten-day sequential therapy is more effective than the standard triple therapy and it is equally tolerated compared with.
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Disclosure of Interest: None Declared
Keywords: Helicobacter pylori, Sequential therapy, standard triple-drug

P1644 ENHANCING BACTERICIDAL EFFECT (IN VITRO) AGAINST HELICOBACTER PYLORI AND AMELIORATING TOXIC EFFECT BY PRE-TREATMENT OF CHITOSAN IN PHOTODYNAMIC THERAPY USING ENDOSCOPIC LIGHT SOURCE AND METHYLENE BLUE.

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INTRODUCTION: Photodynamic therapy (PDT) is a method for inactivating cells (viral, bacterial and cancer cells) using photosensitizers (PS) and light of various wavelengths. Recently, we have reported the killing effects against *Helicobacter pylori* (Hp) by PDT using endoscopic light (*J Photochem Photobiol B 2010;101:206, J Photochem Photobiol B 2012;117:55*). Methylene blue (MB) has been used commonly as standard PS but it has also genotoxic effects to DNA of human cells. To decrease these cytotoxic effects, the authors investigated the study to minimize the dose of MB in PDT by pretreatment of chitosan.
AIMS&METHODS: The standard strain of *H. pylori*, 26695, was purchased from the Korean Culture Type Collection (KCTC, Taejeon, Korea) for use as a test strain. Hp was cultured at 37 °C in a standard microaerobic (5% O_2, 10% CO_2 and 85% N_2 gas) atmosphere. After pre-incubation for 15min with or without low molecular chitosan (50 KDa, Sigma Chemical Co, St. Louis, MO, USA) along with various kinds of concentration of MB (Sigma Chemical Co, St. Louis, MO, USA). Endoscopic white light source from endoscopy (Olympus Co. Japan) were irradiated for 5, 10 and 15 min. For detection of DNA injury by irradiation, alkaline gel electrophoresis was done with DNA from harvested Hp after treatment with Endonuclease III (NEB, Ipswich, MA, USA).
RESULTS: The bactericidal effects were measured by counting viable cells after PDT. In the control group, the number of viable cells was maintained constantly during the experiment. In the groups treated with either 0.02 mg/ml MB alone for 15 min, bacteria decreased approximately a tenfold. The group that treated with 0.02mg/ml MB with 0.005% chitosan showed 100 fold reductions. In the group treated with 0.04 mg/ml of MB alone for 15 min, bacteria decreased about 100,000 fold. The group treated with 0.04 mg/ml MB with 0.005% chitosan, showed 1,000,000 fold reductions. The bacterial killing effects of PDT using MB substantially increased by the treatment of 0.005% chitosan.
CONCLUSION: Bacterial killing by using methylene blue with pre-treatment of chitosan under endoscopic light might be more effective than by only methylene blue. Furthermore, it might ameliorate the genotoxic injury by decreasing the dose of methylene blue.
Disclosure of Interest: None Declared
Keywords: Chitosan, Endoscope, Helicobacter pylori, Methylene blue, Photodynamic therapy

P1645 EVALUATION OF CHANGES IN SERUM PEPSINOGEN AND GASTRIN LEVELS IN RESPONSE TO THE ERADICATION OF HELICOBACTER PYLORI INFECTION

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INTRODUCTION: Gastric *H. pylori* infection is the leading cause of gastritis, peptic ulcer disease, gastric adenocarcinoma and lymphoma (MALT). Evaluation of the infection eradication after treatment is important. Chronic *H. pylori* infection is associated with gastric gland atrophy and dysfunction, causing increased serum levels of gastrin and pepsinogen. In recent years measurement of serum gastrin and pepsinogen subtypes has been considered to evaluate the eradication of *H. pylori* eradication and as a marker of gastric mucosal health.
AIMS&METHODS: Eighty patients with positive *H. pylori* infection were enrolled. All of the patients were endoscopied and had been scheduled for eradication therapy. We evaluated the changes of serum gastrin and pepsinogen type 1 and 2 in these patients before and after eradication therapy in two weeks intervals until eight weeks after the initiation of treatment. The results were classified according to the success rate of eradication.
RESULTS: Pepsinogen type 1 and 2 and gastrin serum levels significantly decreased after successful eradication in comparison with failed eradication. All three markers decreased after 8 weeks of therapy significantly. Pepsinogen 1 decreased by 41.1% after 8 weeks of eradication (p value < 0.001). These rates were 64.1% for pepsinogen 2 and 31% for gastrin levels (p values < 0.001 for both). Even after two weeks of initiation of the successful eradication therapy significant decreases in these markers have been recorded ($p < 0.001$ for all biomarkers).
CONCLUSION: According to the findings of this study, changes in the type1 and 2 pepsinogen and gastrin serum levels can be a reliable indicator of successful eradication of *H.pylori* infection. These results can even be used as early as two weeks after prescription of the eradication regimens.
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Disclosure of Interest: None Declared
Keywords: Gastrin, Helicobacter pylori eradication, pepsinogens, Serum concentration

P1646 COMPARISON OF QUADRUPLE AND TRIPLE DRUG REGIMENS CONTAINING FURAZOLIDONE ON ERADICATION OF HELICOBACTER PYLORI

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INTRODUCTION: The effectiveness of most commonly recommended eradication regimens of *Helicobacter pylori* has decreased to unacceptably low levels, largely related to development of resistance to metronidazole and clarithromycin and successful eradication of H pylori infections remains a challenge. Alternative treatments with superior efficacy and safety should be designed and appropriately tested in all areas depending on their native resistance patterns. Furazolidone has been used successfully in eradication regimens previously.
AIMS&METHODS: *Helicobacter pylori* infected patients with proven peptic ulcer, duodenal and /or gastric erosions were randomly allocated into three groups: group A (OABF) with furazolidone (F) (200 mg b.i.d.), group B (OABM-F) metronidazole (M) (500 mg b.i.d.) for the first five days, followed by furazolidone (F) (200 mg b.i.d.) for the second five days and group C (OAF) with furazolidone (F) (200 mg t.i.d.). Omeprazole (O) (20 mg b.i.d.) and amoxicillin (A) (1000 mg b.i.d.) were given in all groups; bismuth (B) (240 mg b.i.d.) was prescribed in groups A & B. Duration of all eradication regimens were ten days. Two months after treatment, a C14-urea breath test was performed.
RESULTS: Three hundred and seventy two patients were enrolled (124 patients in each group). One hundred and twenty patients in group A (OABF), 120 patients in group B (OABM-F) and 116 patients in group C (OAF) completed the study.
The intention-to-treat eradication rates were 83.7% (95% CI = 77.3–90.4), 79.8% (95% CI =72.6–87), and 84.6% (95% CI = 78.2–91.1) and per-protocol eradication rates were 86.6% (95% CI = 80.5–92.8), 82.5% (95% CI = 75.6–89.4), and 90.5% (95% CI = 85.1–95.9) for groups OABF, OABM-F, and OAF, respectively. No statistical significant differences were found in severe drug adverse effects between the above mentioned three groups. The most common deleterious effect, nausea and fever, occurred in all groups, but more frequently in group C (OAF) with $p < 0.05$.
CONCLUSION: In developing countries, furazolidone-based regimens can substitute clarithromycin-based regimens for *Helicobacter pylori* eradication because of a very low level of resistance and low cost. Considering per-protocol eradication rate of ten days OAF regimen, and the acceptable limit of ninety percent, we recommend this regimen in developing countries like Iran. In order to minimize rare serious adverse effects, one week high dose OAF regimen should be taken into consideration in later studies.
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Disclosure of Interest: None Declared
Keywords: Furazolidone, Helicobacter pylori eradication, quadruple therapy, triple therapy

P1647 MAASTRICHT IV: IS IT THE END FOR THE EMPIRICAL TRIPLE THERAPY OF HELICOBACTER PYLORI IN A SOUTH-EUROPEAN COUNTRY?

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INTRODUCTION: The most widely used empirical eradication treatment for *Helicobacter pylori* (Hp) involves the association of a proton pump inhibitor

(PPI) with clarithromycin and amoxicillin or metronidazole. The Maastricht IV consensus report recommends that this treatment protocol should not be prescribed if the clarithromycin resistance rate in a specific population exceed 15 to 20%.

AIMS&METHODS: This prospective unicentric study, involving adult patients with positive ^{13}C Urea Breath Test (UBT), was performed to evaluate the success rate of the standard triple therapy for Hp eradication in a south-european country, the corresponding clarithromycin resistance rate and possible factors associated with treatment failure (age, sex, urban/rural residence, personal and family history of gastric pathology, consumption of olive oil/alcohol/tobacco, Body Mass Index, frequent infections requiring antibiotherapy, genetic profiles of Hp, therapy compliance and adverse events). All patients were submitted to upper digestive endoscopy with gastric biopsies for histological and microbiological characterization (genotyping with determination of cagA, babA, vacA and IceA status, and minimum inhibitory concentration determination against metronidazole, clarithromycin, levofloxacin, amoxicillin and tetracycline). They were then treated with standard, triple-therapy protocol (Pantoprazol+ Amoxicillin+Clarithromycin, 14 days). Hp eradication rate was assessed with UBT after 8 to 12 weeks. Statistical analysis with SPSS v20.0.

RESULTS: Eighty patients were enrolled in the protocol (males sex – 23; mean age – 41±13 years) and 75% completed the 14 day therapy. There were adverse effects in 46.3%. Hp eradication was sucessful in 68.8%. Clarithromycin resistance rate was 20% and mutation A2143G was the most commonly identified (18.8%). The factors associated with treatment failure (Hp+ vs Hp-) were: frequent infections (32% vs 10.9%), active smoking (20% vs 3.6%); vacAs2 gene (72% vs 47.3 %); vacAm2 gene (96% versus 74.5%).

CONCLUSION: In this south-european country Hp eradication rate with empirical triple-therapy is very low. Clarithromycin resistance rates are high and, following the Maastricht IV recommendations, the traditional triple treatment should not be used as first choice in this country, especially in patients with a history of smoking or frequent infections.

Disclosure of Interest: None Declared

Keywords: Antibiotics, Helicobacter pylori eradication, resistance

P1648 THE EFFECT OF AMALGAM FILLING ON HELICOBACTER PYLORI ERADICATION

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INTRODUCTION: Mercury is a toxic and non-essential metal in the human body.

AIMS&METHODS: We aimed to evaluate whether amalgam filling including mercury is an efficient factor on the treatment of H. Pylori (Hp) eradication. A total of 189 dyspeptic cases including 96 patients who have at least one amalgam filling and 93 patients with normal dental examination were enrolled into the study. All the patients were examined by single dentist. The dentist performed the patients' mouth examination in terms of rotting teeth, dental amalgam filling, damaged dental filling, the number of dental filling, and recorded the duration of having dental amalgam filling. The Hp diagnosis was made based on the histology. The patients received the standart triple therapy consisting of lansoprazole, 30 mg b.d., clarithromycin, 500 mg b.d., amoxicillin, 1gr b.d., for 14 days for Hp eradication. Carbon-13 urea breath test was used to determine Hp after drug treatment.

RESULTS: Hp infection in the filling group (74%) was significantly higher than non-filling group (59%) (p:0.031). But there was no significant correlation between Hp colonization severity and both the numbers of amalgam filling and the duration of filling. There was no significant difference regarding endoscopic lesions in both groups. In histopathological examination, atrophy and intestinal metaplasia were similar in both groups. But inflammation and activiation (91.7%, 68.8 %, respectively) were signifancantly higher in the filling group than non-filling group (78,5%, 54.8% ; p:0.011, p:0.049, respectively). Hp infection was detected in 126 (66,67%) subjects in all group. We suggested eradication treatment for Hp infection to the patients. But, 50 patients came after treatment follow-up. The eradication rate following the treatment was 68 % (34/50). Higher eradication rate was seen in the non-filling group (92%, 23/25) compared to filling group (44%, 11/25) (p:0.001). In filling group, there are 11 patients who have filling deformation. The eradication rate in patients with damaged filling were lower (36%, 4/11) than in the patients with undamaged filling (58,3%, 7/12) (p:0.292). Logistic regression analysis of risk factors including age, gender, fillings, endoscopic lesions, and gastric histological findings showed existence of amalgam filling is an independent predictor for *H. pylori* eradication (p:0.001).

CONCLUSION: Hp colonization rate is higher in patients with amalgam filling than unfilling ones and the presence of dental amalgam filling is an independent predictor for insufficent Hp eradication.

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Disclosure of Interest: None Declared

Keywords: amalgam, Helicobacter pylori eradication

P1649 SYSTEMATIC CHARACTERIZATION OF MIR-21 EXPRESSION IN GASTRIC MUCOSA

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INTRODUCTION: Gastric cancer (GCA) is a complex, *H.pylori*-triggered malignant disease. Global and specific deregulation of microRNA (miRNA) expression patterns are frequently detected in patients with gastric cancer. The aim of our study was to characterize miR-21 expression, the most highly-upregulated miRNA in GCA, in regard to various conditions such as *H. pylori* infection and its preneoplastic precursors in gastric mucosa.

AIMS&METHODS: The aim of our study was to characterize miR-21 expression, the most highly-upregulated miRNA in GCA, in regard to various conditions such as *H. pylori* infection and its preneoplastic precursors in gastric mucosa. In a prospective study, patients were systematically characterized for the presence of *H. pylori* infection, inflammatory, atrophic or malignant changes in gastric mucosa. MiR-21 expression was analyzed using total RNA from biopsies (corpus, antrum and/or primary tumor) of 80 patients (20 normal mucosa (N), 24 chronic gastritis (CG), 20 atrophic gastritis / intestinal metaplasia (AG) and 16 with gastric cancer (GCA) by qRT-PCR. RNU6b has been used for normalization.

RESULTS: As expected, biopsies from the GCA showed higher expression levels of miR-21 ($p = 0.0004$ and 0.0002 for Corpus und Antrum, respectively) in comparison to normal tissue. In the assessment of regional differences in miR-21 expression, we found significantly higher expression in antrum compared to the corpus ($p = 0.016$). Especially in the antrum, presence of *H. pylori* was associated with significantly higher miR-21 expression (mean ± SD for N 0.22 ± 0.08 vs. 0.32 ± 0.12, $p < 0.002$). In confirmation of the histopathological changes, a gradual increase in miR-21 expression was detected in the gastric mucosa from normal mucosa to chronic and atrophic gastritis (N 0.22 ± 0.08, CG 0.33 ± 0.18, AG 0.39 ± 0.11, p=0.0009). Interestingly, not only tumor tissue, but also adjusted normal tissue from GCA patients showed significantly higher miR-21 expression levels (1.2 ± 1.69, $p < 0.02$) as compared to N and CG/AG/IM.

CONCLUSION: Increased expression of miR-21 is characteristic not only for tumors, but also for surrounding mucosa and for antrum and corpus of patients with gastric cancer. *H. pylori* and preneoplastic conditions, such as chronic gastritis and intestinal metaplasia, are also associated with miR-21 upregulation. These findings provide valuable information for the clinical implementation of miRNAs.

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Disclosure of Interest: None Declared

Keywords: biomarker, gastric cancer, Gastritis, *H. pylori*, microRNA

P1650 ASSESSMENT OF DISEASE DISSEMINATION IN GASTRIC MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA USING EXTENSIVE STAGING: A SINGLE-CENTER EXPERIENCE.

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INTRODUCTION: Endoscopic ultrasonography (eUS) is considered as the best tool for locoregional staging of patients with gastric mucosa-associated lymphoid tissue (MALT) lymphoma. Diagnostic yield of computed tomography (CT) and (18)F-fluorodeoxyglucose positron emission tomography/computed tomography ((18)FDG-PET) needs to be evaluated in a large cohort.

AIMS&METHODS: Between 1995 and 2013, a total of 218 consecutive patients with gastric MALT lymphoma underwent 328 staging procedures (age 60 (22-86) yrs, 162 males). The standardized staging protocol included gastroscopy with multiple biopsies, eUS, colonoscopy, CT of thorax and abdomen, otorhinolaryngologic assessment and bone marrow biopsy. (18)FDG-PET was also performed in 43 pts. The diagnosis of MALT lymphoma was ascertained on histologic analysis of gastric biopsies in all patients. Performance of CT-scan and (18)FDG-PET were evaluated. The AUROC curves for gastric wall thickness and nodal involvement were calculated.

RESULTS: According to eUS, 145 (51%) out of 287 patients had increased (>5 mm) gastric wall thickness. Ninety-three (32%) out of 287 pts had perigastric lymph node involvement. Both CT and (18)FDG-PET were less efficient than eUS to assess gastric wall thickness and perigastric lymph node involvement.

Increased gastric wall thickness	Se	Sp	AUROC	*p*
Computed tomography	54%	87%	0.70 ± 0.03 (0.64-0.77)	<0.001
(18)FDG-PET	94%	42%	0.70 ± 0.08 (0.54-0.86)	0.03
Lymph node involvement assessment	Se	Sp	AUROC	*p*
Computed tomography	34%	95%	0.65 ± 0.04 (0.58-0.72)	<0.001
(18)FDG-PET	58%	96%	0. 77 ± 0.08 (0.61-0.92)	0.003

However, CT also showed lung and/or liver involvement and superior diaphragmatic lymph nodes in 19 and 2 cases, respectively. (18)FDG-PET showed lung and/or liver involvement in 3 more pts and concomittant neoplasia in 3 cases. Colonoscopy showed colonic involvement in only 2 (0.6%) cases but also permitted to detect adenomas in 29 (9%) pts. Twenty-five (8%) pts had bone marrow involvement. Otorhinolaryngologic assessment showed 3 (1%) pts with dissemination of MALT lymphoma.

CONCLUSION: eUS has an higher diagnostic yield for locoregional staging of pts with MALT lymphoma, compared to CT and (18)FDG-PET. However, dissemination to another MALT organ is frequent (12.5%) and needs to be assess with bone marrow biopsy, otorhinolaryngologic assessment and (18)FDG-PET.

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Disclosure of Interest: None Declared
Keywords: Lymphoma, ultrasonography

P1651 POTENTIAL ROLE OF THE IQGAP1 PROTEIN DURING HELICOBACTER PYLORI INFECTION AND GASTRIC ADENOCARCINOMA

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INTRODUCTION: IQGAP1 is a member of the IQGAP family of scaffold proteins, it is a component of pathways via which Cdc42 or Rac1 modulates cadherin-based cell adhesion. This protein plays a crucial role in the cell adhesion. The gastric adenocarcinomas are classified in 2 different types, the intestinal type which is the more frequent one and the diffuse type. Almost 30% of the diffuse gastric cancer is associated to a mutation of the *cdh*1 coding for the E-cadherin, but the origin of the other 70% is not elucidated. Mutations of IQGAP1 have been detected only in diffuse gastric cancer and not in the intestinal type.
AIMS&METHODS: Our aim was to identify the role of IQGAP1 in *Helicobacter pylori* infection and gastric adenocarcinoma.
Eighty mice, wild type or mutant IQGAP1+/-, were infected with different *Helicobacter* sp. strains (*Helicobacter felis*, *Helicobacter pylori* SS1 and HPARE). Stomachs were recovered 6 months and 1 year after infection. A histologic analysis was performed to evaluate inflammation, hyperplasia, atrophy, metaplasia, and dysplasia.
RESULTS: Six months post-infection, IQGAP1+/- mice had developed more mucous metaplasia than the wild type mice, but no difference was shown between wild type and IQGAP1+/- mice for the other items. Globally, all of the mice infected by Helicobacter strains had developed more inflammation, hyperplasia, atrophy and dysplasia than the non-infected mice. One year post-infection, differences between wild type mice and IQGAP1+/- mice were more important. Finally, IQGAP1+/- mice infected with *H. pylori* HPARE showed significantly more hyperplasia, atrophy, mucous metaplasia, pseudo-intestinal metaplasia and dysplasia.
CONCLUSION: These results suggest than IQGAP1 is a crucial protein in gastric adenocarcinoma linked to *H. pylori* infection.
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Disclosure of Interest: None Declared
Keywords: mouse model, precancerous lesions

P1652 PSCA, MUC1, PLCE1 GENE POLYMORPHISMS IN GASTRIC CANCER AND HIGH RISK ATROPHIC GASTRITIS

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INTRODUCTION: Gastric cancer (GC) is one of the major malignant diseases worldwide with very high mortality rates. Intestinal type GC is linked with *H. pylori* infection, while the pathogenesis of diffuse type GC is less understood. Recent genome-wide association studies (GWAS) revieled a link between GC and single nucleotide polymorphisms (SNPs) of the genes encoding prostate stem cell antigen (PSCA), phospholipase C epsilon 1 (PLCE1) and mucin 1 (MUC1) genes. Most of the replication studies of these GWAS results so far have been conducted in Asian populations, while data in Caucasian subjects with GC and premalignant gastric conditions are higly lacking.
AIMS&METHODS: The aim of the study was to evaluate the relationship between SNPs of the genes encoding PSCA (rs2976392, rs2294008), MUC1 (rs4072037) and PLCE1 (rs2274223) with the risk of developing GC or high risk atrophic gastritis (HRAG) in individuals of Caucasian ethnicity.
Gene polymorphisms were analyzed in 634 subjects (GC: n=252; HRAG: n=136, controls: n=246) of Caucasian origin. DNA was extracted from peripheral blood leukocytes using salting out method. PSCA A>G (rs2976392), PSCA C>T (rs2294008), MUC1 G>A (rs4072037) and PLCE1 A>G (rs2274223) SNPs were genotyped by real-time PCR (RT-PCR), using predesigned Taqman primers.
RESULTS: Frequencies of genotypes in our study are similar to the data reported on subjects of Caucasian ethnicity. Analysis of data revealed that the frequencies of all SNP genotypes are in line with Hardy-Weinberg equilibrium. MUC1 A allele (rs4072037) was associated with higher incidence of GC (53.2%, OR – 1.57; p=0.00064) and HRAG (51.5%, OR-1.47, p=0.0136) when compared to controls (42.0%). PSCA T/T genotype of rs2294008 was linked with higher risk of GC (26.3%, OR – 2.41, p=0.00021) and HRAG (17.2%, OR – 1.72, p = 0.04303) when comparing to the control group (12.9%). There was a higher frequency of PSCA rs2976392 A/A genotype in GC group (41.2%, OR-2.35, p=0.00032) and HRAG group (34.8%, OR – 1.82, p=0.0285) than in control group (23.3%). No significant differences were determined between the frequencies of genotypes for PLCE1 rs2274223 with similar distribution of A/A, A/G, G/G genotypes between controls (37.8%, 48.1%, 14.1%), GC (38.5%, 49.8%, 11.7%) and HRAG (41.5%, 42.2%, 16.3%) groups.
CONCLUSION: SNPs of PSCA (rs2976392, rs2294008) and MUC1 (rs4072037) genes are linked with the presence of GC and HRAG and appear as potential biomarkers to identify the risk of these conditions. No significant association was determined between PLCE1 rs2274223 and the risk of GC or HRAG.
Disclosure of Interest: None Declared
Keywords: Atrophic gastritis, Gastric cancer, Gene polymorphism, MUC1, PLCE1, PSCA

P1653 A PILOT STUDY OF CONFOCAL LASER ENDOMICROSOPY FOR STAGING AND FOLLOW-UP OF GASTROINTESTINAL MALT-LYMPHOMA

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INTRODUCTION: The extranodal marginal zone B-cell lymphoma of the mucosa associated lymphoid tissue (MALT-lymphoma) requires lifelong follow-up due to the risk of relapse or transformation into high-grade lymphoma.
AIMS&METHODS: To improve the diagnostic yield for gastrointestinal (GI) MALT-lymphoma during staging and follow-up, we investigated the diagnostic role of confocal laser endomicroscopy (CLE) in the context of a prospective clinical pilot trial (NCT01583699). Patients with suspect of upper-GI MALT-lymphoma underwent endosonography (EUS) followed by upper-GI endoscopy using a CLE-colonoscope (Pentax EC-3870CIFK, working length 150cm, Pentax, Tokyo, Japan and Optiscan Pty Ltd, Notting Hill, Victoria, Australia). After i.v.-administration of 5 ml of 10% flourescein 4-quadrant CLE-pictures and conventional biopsies were taken randomly every 10 centimeters during withdrawal from the deep small bowel to the pylorus, then from the antrum, body and, if technically feasible, the fundus of the stomach, and from the esophagus. Additional CLE-pictures and biopsies were taken from distinct looking areas. At the end of each examination, a preliminary diagnosis based on the CLE-pictures was set. This was later compared to the histological result.
RESULTS: Between January 2012 and April 2013 a total of 22 patients (12 male, 10 female, median age 69 years, range 35 to 80 years) had been studied. Initial MALT-onset included the stomach in 18 cases, the small bowel in 6 cases, the lungs in 2 cases and the colon in 1 case. Histological assessment of conventional biopsies taken during the study revealed MALT-lymphoma of the stomach and duodenum in 13 and 4 patients, respectively. In 7 patients no MALT-lymphoma was found. Compared to histology, the sensitivity of EUS, white light endoscopy and CLE for MALT-lymphoma was 60%, 93% and 87%, the specificity was 71%, 43% and 100%, respectively. In those cases where MALT-lymphoma presence was missed by CLE, infiltration of lymphoma cells was limited to deeper wall layers that could not be assessed by CLE.
CONCLUSION: The results of this first prospective study on the diagnostic role of confocal laser endomicroscopy in GI MALT-lymphoma showed a promising clinical value of this new endoscopic method. Current drawbacks like the limited tissue penetration might be overcome by future technical improvements to make endomicroscopy a reliable tool for a safe and biopsy-sparing surveillance of gastrointestinal MALT-lymphoma.
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Disclosure of Interest: None Declared
Keywords: endomicroscopy, MALToma

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00
SMALL INTESTINAL III – Poster Area

P1654 AUTOLOGOUS STEM CELL TRANSPLANTATION FOR REFRACTORY COELIAC DISEASE TYPE II: A PROMISING THERAPEUTIC OPTION - THE IRISH EXPERIENCE

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INTRODUCTION: Refractory Coeliac disease (RCD II) is serious complication of celiac disease. The risk of progression from RCD II to enteropathy-associated T-cell lymphoma (EATL) is estimated at 60-80% and has poor survival. Therapeutic options for RCD II are limited. To date, the use of a novel therapeutic approach of high-dose chemotherapy followed by autologous stem cell transplant (ASCT) in a small cohort of patients with RCD II has stimulated great interest world wide with promising results.
AIMS&METHODS: We describe two patients with RCD II who received ASCT.
RESULTS: CASE 1: 36-year-old female with an 8 year history of CD who presented with a weight loss, bdominal pain, bloating, and diarrhoea. She was compliant with GFD and negative anti-tTG. Panendoscopy revealed severe ulcerative jejunitus. Duodenal biopsies revealed loss of CD8-positive cells and T cell clonality consistent with RCD type II. Abdominal CT showed abnormal thickening of her jejunum with mesenteric lymphadenopathy. Investigation for overt lymphoma were negative. She required total parenteral nutrition as she was not able to maintain nutrition. Cladribine was commenced as she failed to respond to steroid. Despite that, she was still severely malnourished and she proceeded to ASCT in July 2012. Post-transplant, she is well clinically with resolution of her symptoms. CASE 2: 67-year-old female with a one year history of celiac disease presented with weight loss despite strict GFD. At presentation she weighed 37kg and has progressive ataxia. Panendoscopy showed severe villous atrophy with ulcerative jejunitis. Duodenal biopsies revealed abnormal phenotypic expression of T-lymphocytes with loss of CD8-positive cells with T-cell clonality consistent with RCD type II. Investigations for lymphoma were

negative. She failed to respond to steroid and azathioprine and proceeded to ASCT in December 2011. Post transplant she has maintained her weight and her ataxia has remained stable.
CONCLUSION: RCD II remains very difficult to treat. In the absence of published randomized clinical trials, evidence is growing for the safety and feasibility of ASCT in this disease. 24 patients worldwide (including the 2 described here) have received ASCT for this condition and only one patient to date has developed lymphoma (4 years post ASCT). Our 2 patients are the first and only patients in Ireland and the UK to receive an ASCT for RCD II. Multicentre randomized trials or trials with historical control groups will be needed to consolidate ASCT for patients with RCD II.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, refractory coeliac disease, Stem Cells

P1655 MOLECULAR BASIS FOR THE MYOCARDIUM INVOLVEMENT IN COELIAC DISEASE

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INTRODUCTION: Coeliac disease (CD) is characterized by autoantibodies against endomysium (EMA), a connective tissue sheet around muscle cells. These antibodies target tissue transglutaminase (TG2). It has earlier been reported that CD prevalence is higher among patients with end-stage heart failure or cardiomyopathy.
AIMS&METHODS: Aim of this study was to characterise the myocardial lesions and assess if anti-TG2 antibodies play a role in the cardiac manifestations of CD. Myocardium and mediastinal lymph node biopsy samples were analysed by immunohistochemistry in two adolescent patients (18 and 20 years old) with known CD who presented with severe myocarditis after stopping the gluten-free diet. Consecutive childhood myocarditis cases treated at the intensive care unit were prospectively followed up and investigated for coeliac disease antibodies (anti-TG2 and EMA) and HLA-DQ. Human umbilical cord cells prepared from high-risk newborn first degree relatives of CD patients or cells prepared from the intestinal biopsy specimens of CD patients were differentiated into striated muscle cells and investigated in vitro in the presence of tissueeluted or cloned coeliac antibodies.
RESULTS: Both coeliac adolescents were critically ill and required balloon pump-assisted cardiac support, one of them died. Ultrasound and MRI studies revealed low ejection fraction and signs consistent with myocardial oedema and inflammation, but no viral agent could be identified. Frozen samples of the affected myocardium specimens contained high amounts of in vivo EMA deposition bound to TG2, but no cellular infiltrate of inflammatory cells. Severe myocarditis was diagnosed in 8 children of whom 3 died, 2 were diagnosed with CD by anti-TG2 and EMA serum antibody positivity and jejunal biopsy, both DQ2 positive. The other 3 survivors had neither anti-TG2/EMA antibodies nor DQ2 or DQ8 at the screening for CD, one was later diagnosed with cystic fibrosis and one other with Alström syndrome. During prospective follow up of the risk cohort two children developed CD. In vitro experiments with normal, risk and coeliac muscle cells revealed high susceptibility of affected persons to TG2-specific antibody action.
CONCLUSION: Severe myocarditis could be a sentinel sign of other chronic childhood diseases and HLA-DQ2 or DQ8 carriers should be screened for CD. Anti-TG2 antibodies deposited around myocardial fibres can play a role in the severe clinical presentation upon an otherwise benign (perhaps viral) precipitating illness.
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Disclosure of Interest: None Declared
Keywords: Coeliac disease, myocarditis

P1656 SIGNIFICANCE OF ANTI A-ENOLASE ANTIBODIES IN CELIAC DISEASE PATIENTS

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INTRODUCTION: Celiac disease (CD) is an autoimmune gluten sensitive enteropathy occuring in genetically predisposed individuals. It is accompanied by presence of multiple antibodies, typically anti endomysium (EMA) or anti transglutaminase (tTG) antibodies (Ab). Some recent studies showed that α-enolase, a multifunctional glycolytic enzyme described as glycolytic pathway component, heat shock protein and plasminogen binding protein might be a possible novel autoantigen in CD. Anti α-enolase Ab were reported in several autoimmunological disorders but data about its presence and role in CD has not been explained so far.
AIMS&METHODS: The aim of this study was to determine the frequency of anti α-enolase Ab, its correlation with the presence of IgA tTG Ab and the intensity of duodenal mucosa lesions in CD patients, depending on the adherence to gluten free diet (GFD).
Methods: We examined 43 CD patients (aged from 18-72 years, mean age 40), including patients newly diagnosed CD (n=9), CD patients non adhering to gluten free diet (n=10), adhering gluten free diet (n=14) and 10 healthy volunteers, the control group. *Clinical investigation* included disease history, gastroscopy with biopsies from the distal part of duodenum. Biopsies for *histology* were stained with H-E and evaluated according to Marsh scale. *Serologic investigation* of blood serum collected from patients included anti α-enolase Ab titer, evaluated with αENOL ELISA Kit (ElAb company, China) and IgA tTG Ab evaluated with ELISA (Demeditec diagnostic GmbH, Germany).
RESULTS: Mean anti α-enolase Ab titer was higher in all CD patients in comparison with control group (1,1 ng/mL and 0,795 ng/mL respectively, p=0,8). In newly diagnosed CD mean titer of anti α-enolase Ab was lower compared to CD patients non adhering to gluten free diet (0,556 ng/mL and 1,4 ng/mL respectively). The highest mean titer of α-enolase Ab in that last group corresponded with grade III intensity of duodenal mucosa lesions, according to Marsh scale. No statistical differences were found between titer of IgA tTG Ab and anti α-enolase Ab in examined groups.
CONCLUSION: 1/Increased anti α-enolase Ab titer is observed in CD patients in comparison with healthy people. 2/ Anti α-enolase Ab may be considered as an indicator of inflammation of small intestinal mucosa in CD patients exposed to gluten. 3/Further investigation on the usefulness of anti α-enolase Ab in clinical control of CD is needed.
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Disclosure of Interest: None Declared
Keywords: anti α-enolase antibodies, celiac disease

P1657 SMALL INTESTINAL BACTERIAL OVERGROWTH AND GASTROINTESTINAL SYMPTOMS IN CELIAC DISEASE PATIENTS AND IN PATIENTS RECEIVING PROTON POMP INHIBITORS.

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INTRODUCTION: Small intestinal bacterial overgrowth (SIBO) is a heterogeneous syndrome characterized by quantitative and/or qualitative changes of the small intestinal bacterial microflora. In the clinical setting, the most useful diagnostic method of SIBO is the Hydrogen Breath Test. SIBO is observed in some anatomical or motility disorders. Recently other diseases, such as irritable bowel syndrome, Crohn's disease, or prolonged proton pomp inhibitor (PPI) treatment are supposed to be SIBO risk factors. But still the prevalence of bacterial overgrowth and its influence on the course of gastrointestinal disorders such as celiac disease (CD) is not fully explored.
AIMS&METHODS: Aims We determined the SIBO prevalence in CD and in patients on prolonged PPI treatment. Furthermore we evaluated the symptoms experienced by each group of patients presenting SIBO.**Methods** We examined 50 patients (aged from 23-72 years, mean age 42), including 20 patients with CD disease, 20 treated with PPI for at least 2 months and 10 healthy volunteers (control group). *Clinical investigation*. A medical history was obtained, including information pertaining to current symptoms, medicine taken and duration of its use. *Diagnosis of SIBO*. The patients underwent a Hydrogen Breath Test. Lactulose was used as a substrate (10g in 100ml of water). Four samples of exhaled breath were analyzed. SIBO was diagnosed when there was a rise in exhaled hydrogen by 12 ppm above the baseline.
RESULTS: Bacterial overgrowth was found in 87% of CD patients and in 90% of patients on the prolonged PPI therapy in comparison with 50% cases in the control group. Such symptoms as flatulence, dyspepsia and abdominal pain were significantly more frequent in celiac patients with SIBO (96%, 28% and 21% respectively) compared with CD without bacterial overgrowth. In patients treated with PPI, such symptoms as flatulence (60%), dyspepsia (45%) and diarrhea (35%) were coexisting with positive result of Hydrogen Breath Test.
CONCLUSION: Celiac disease and the use of PPI may predispose to SIBO. SIBO may contribute to development of such symptoms as abdominal pain, heartburn, flatulence, and diarrhea in the course of CD or PPI treatment. Non-invasive SIBO screening should be recommended in patients presenting the above symptoms or risk factors of bacterial intestinal overgrowth. Concomitant probiotics administration or antibiotics, such as rifaximin could decrease the level of symptoms in this group of patient.
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Disclosure of Interest: None Declared
Keywords: celiac disease, proton pomp inhibitor, small intestinal bacterial overgrowth (SIBO)

P1658 THE SEROPREVALENCE OF POSITIVE CELIAC DISEASE TESTS SUBSTANTIALLY DIFFERS DEPENDING UPON THE CRITERIA SET FOR A POSITIVE TEST RESULT

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INTRODUCTION: Serology is frequently used to access the prevalence of celiac disease in a population; several tests are being used for the purpose. In individuals who are HLA DQ2.5 and DQ8 negative the disease practically can be excluded.
AIMS&METHODS: We aimed to detect the prevalence of celiac disease based on serological tests and HLA typing in Latvia. : In 1444 subjects being selected for a population cross-sectional study in Latvia were enrolled. Samples were screened by FDA-cleared ELISAs (QUANTA Lite®, INOVA) for antibodies to human tissue transglutaminase IgA(h-tTG-IgA), deamidated gliadin IgA and IgG (DGP IgA,DGP IgG), and combined h-tTG/DGP IgG/IgA. All cases that were positive with any of the serological tests were HLA sequenced. HLA DQ2.5 or DQ8 positive cases were considered at genetic risk for celiac disease.

RESULTS:

Tests considered	Cut-off	Serology positive	Serology and HLA positive
Any test positive	>20 Units	7.34%	2.84%
Any individual test positive*	>20 Units	2.98%	1.25%
Any individual test positive*	>30 Units	1.39%	0.69%
Two individual tests positive*	>20 Units	0.55%	**0.49%**
Two individual tests positive*	>30 Unit	0.42%	**0.42%**
h-tTG-IgA positive	>20 Units	1.66%	**0.69%**
h-tTG-IgA positive	>30 Units	0.76%	**0.49%**

*tTG/DGP IgG/IgA screen excluded

Altogether 104 samples gave a positive result to at least one of the tests. The positivity rates are given in the Table.

CONCLUSION: The seroprevalence is depends substantially upon the test used and the selected cut-off value. Addition of HLA typing to analyze patients with a positive serology is changing the prevalence figures substantially. The prevalence of celiac disease in Latvia could be lower than previously thought and lower than in Europe in average based on presence HLA DQ2.5 or DQ8 and serological markers. The real prevalence of celiac disease should not exceed the proportion of HLA positive cases that are double-test positive or at least h-tTG-IgA positive (i.e. is below 0.69% or even below 0.42%>0.49%).

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Disclosure of Interest: None Declared

Keywords: celiac disease diagnosis, genetic testing, prevalence, Serology

P1659 COELIAC DISEASE: DOES DIETICIAN FOLLOW UP IMPROVE OVERALL OUTCOME

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INTRODUCTION: Coeliac disease is a chronic, permanent potentially life-threatening condition. Regular follow-up is an opportunity to provide patient-centered care that is sensitive to the individual's circumstances. The annual assessment should involve assessment of, and motivation towards, strict adherence to a gluten-free diet. Assessment of these patients should also involve measurement of their TTG, B12, folate, ferritin, Hb, calcium and vitamin D levels to prevent any complications and provide supplementation if required and role of dieticians is very important in this regards.

AIMS&METHODS: Aim of this audit was to compare compliance and nutritional assessment in diagnosed CD patients in dietician followed up patients against the patients who were not followed up by dieticians. We looked at results of 173, biopsy proven CD patients over the last 10 years. We reviewed their TTG, B12, folate, calcium, vitamin D, Hb. and ferritin.

RESULTS: 87 patients were followed up in dietician clinic and 86 were not followed up. 53 male patients (31 followed up, 22 non-follow up). 120 females (56 follow up and 64 non follow up patients) TTG performed in follow up vs. non-follow group up was 89.7% and 57% respectively, $\chi 2$ 23.661 and $p < 0.001$. B12, folate and calcium 94.3% and 76.7% in follow up vs non-follow up respectively. $\chi 2$ 0.724 And p.001. Vitamin D was checked in 90.8% in followed up and 38.4% in non- followed up patients with a $\chi 2$ 52.086. All the patients followed up had their ferritin and Hb checked. 18/87 in the non-follow up group did not have ferritin checked. 8/87, not followed up did not have their Hb monitored.

CONCLUSION: The results clearly demonstrate that assessment of compliance and supplement monitoring is much better in the follow up group of patients. Measurement of vitamin D level was particularly poor in the non-follow up group. The benefits may not be immediately obvious but definitely helps in the long term in preventing any coeliac disease related complications eg osteoporosis, refractory anaemia, malnutrition and lymphoma.

Previous studies have shown that adherence to gluten-free diet can be poor; ranging from 45-87%. Coeliac disease is not simply a malabsorptive gastrointestinal disorder. It is a multisystem, autoimmune disease that carries a significant health burden and risk of complications. Treatment of coeliac disease is primarily nutritional and the dietician's role is therefore of paramount importance. These micronutrient deficiencies require monitoring which is best provided by a dietician.

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Disclosure of Interest: None Declared

Keywords: Coeliac disease CD, haemoglobin Hb

P1660 ROUTINE DUODENAL BIOPSIES IN THOSE WITH POTENTIAL COELIAC DISEASE- IS IT WORTHWHILE ?

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INTRODUCTION: Coeliac disease (CD) is a common condition affecting as many as 1% of the UK adult population. It has increasingly been understood that patients may present with subtle or atypical symptoms, consequently the time to diagnosis may be protracted. With this in mind the threshold for investigation has lowered, with an anti-tissue transglutaminase (tTG) level usually used as the first line of investigation.

The British Society of Gastroenterology guidelines suggest that if there is a possibility of CD, taking a duodenal biopsy at the time of endoscopy is a worthwhile practice. The aim of this study is to determine the diagnostic yield of a histological diagnosis of CD in those with low clinical suspicion.

AIMS&METHODS: We retrospectively reviewed all duodenal biopsies performed in order to investigate a potential diagnosis of CD over a 16 month period, excluding biopsies taken to investigate other conditions or as part of the monitoring of known CD. 730 cases were identified using our histopathology computer-database, which were then analysed with respect to indication, histological features and correlation with anti-tTG levels.

RESULTS: The population which underwent gastroscopy with duodenal biopsies was predominantly female (66%), with an average age of 60 years old. Of the biopsies performed 41 were taken to prove a serological diagnosis of CD, of which 59% confirmed this diagnosis.

Of the remaining 689 patients the most common indication for taking a duodenal biopsy was anaemia accounting for 52%, followed by weight loss (9%), diarrhoea (9%), abdominal pain (3%), endoscopic features of CD (2%) with the remainder made up of patients with non-specific symptoms. Only 54% of patients had an anti-tTG level taken prior to obtaining histology. The diagnostic yield for a tissue diagnosis of CD when clinical suspicion was low was 11%, with anaemia being the most likely indication to engender this diagnosis. 38 patients who had histological evidence of CD did not have an anti-tTG prior to endoscopy.

There were 20 patients who had histological evidence of CD in the presence of negative serology and normal IgGA levels, accounting for 5.8% of this study group.

CONCLUSION: Our data shows that when the clinical suspicion of CD is low and anti tTG negative, histology is usually normal, with a number needed to test of 17.

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When analysing the 20 patients who had histology positive, serology negative CD there were no features in their history to suggest that they would be particularly high risk for having CD. A low threshold for performing duodenal biopsy would therefore be the only way to identify this cohort of patients.

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Disclosure of Interest: None Declared

Keywords: coeliac, duodenal histology

P1661 DUODENAL BULB BIOPSY MORPHOMETRY AND IGA DEPOSITS IN THE DIAGNOSIS OF COELIAC DISEASE

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INTRODUCTION: It has been recently shown that celiac disease (CD) can be diagnosed solely on duodenal bulb biopsies. We wanted to re-evaluate this by morphometric measurements as in the duodenal bulb, villi may be stumpy and distorted next to Brunner's glands. Also other diseases may result in villous atrophy and further, the quality of bulb biopsies is a concern. We also hypothesized that bulb IgA deposits targeting transglutaminase 2 (TG2) could be a specific indicator of CD.

AIMS&METHODS: 70 consecutive patients, 30 adults and 40 children went to endoscopy because of gastrointestinal symptoms or suspicion of CD. Bulb and duodenal villous height to crypt depth ratio (VH:CrD) was evaluated by two independent observers and TG2-specific IgA deposits were examined by double color immunofluorescence in frozen biopsy samples.

RESULTS: 25 patients (3 adults and 22 children) received CD diagnosis, duodenal VH:CrD was in all <2 and they all had typical IgA deposits targeting TG2, especially around the Brunner glands. The remaining 45 patients received other diagnoses and were excluded for CD. The final diagnoses were Helicobacter pylori (n=18), Giardia (n=5), IBD (n=7), chronic diarheea (n=2), dyspepsia (n=6), recurrent abdominal pain (n=5), Entamoeba hystolitica (n=1), malnutrition (n=1). Also duodenal IgA deposits were negative in these patients. However, we found in the non-CD bulb specimens histological lesions mimicking CD (VH:CrD<2) in 12/27 adults and 7/8 children. Altogether 37 bulb biopsies were not qualified for accurate morphometric evaluations even after recuttings. None of the non-CD patients had bulb mucosal TG2-specific IgA deposits.

CONCLUSION: In our series the bulb specimens were often of poor quality and difficult to interpret in morphometric analyses. Further, other conditions may cause bulb injury, when morphometrically analyzed, similar to CD. These results indicate that bulb biopsies alone should be evaluated with caution in the diagnosis of CD. Measurement of TG2-specific IgA deposits might prove to be a strong tool to prove or exclude CD in bulb specimens.

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Keywords: bulb morphometry, celiac disease diagnosis

P1662 PUSH ENTEROSCOPY: A NOVEL METHOD TO ASCERT DIFFICULT TO DIAGNOSE COELIAC DISEASE IN PAEDIATRICS

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INTRODUCTION: New ESPGHAN guidelines on the diagnosis of coeliac disease (CD) suggest a move away from upper GI endoscopy (UGE) for symptomatic patients with tissue transglutaminase (tTG) >10 times normal and positive HLA typing (1). CD is a patchy disease and tTG may be more sensitive than

UGE in such cases. However guidelines do not cover patients with moderatley raised tTG or asymptomatic 'at risk patients' who have inconclusive histopathology on UGE. Push enteroscopy (PE) can achieve biopsies more distally in the small bowel and may characterise patchy disease in such 'difficult to diagnose CD'. To our knowledge PE has not been described in the diagnosis of paediatric CD.

AIMS&METHODS: We aim to describe the novel use of PE in a tertiary paediatric CD service. All patients screened with tTG are prospectively logged on the department dietetic CD database. We identified patients from July 2009- July 2012 who had a positive tTG but negative/inconclusive UGE histopathology and were referred for PE. Details on demographics, symptomatology, screening investigations, were extracted. Initial UGE biopsies were assesed as to whether biopsy site and number complied with ESPGHAN guidelines (1) and graded according modified Marsh criteria. Details on repeat screening, timing of PE, location of repeat biospies were also taken.

RESULTS: From 163 patients screened with tTGs, 8 patients (5F) were referred for PE due to initial positive screening but negative/inconclusive UGE biopsies (Table). All patients were EMA positive. 6/8 patients had a diagnosis of CD confirmed on PE, although only 4/8 were from the distal sites alone. 1/8 patients could have potentially been given a dx of CD on serology and HLA typing alone if ESPGHAN guidelines had been followed (1).

Age (yrs)	Symptoms	TTG	UGE ESPGHAN compliant?	UGEPath	HLA DQ2/DQ8	PE Path	Dx Sites
6.1	Pain	3.2	Yes	Normal	Pos	3b	Proximal + distal
6.9	Pain	4.6	Yes	Normal	NK	1a	Distal
13.7	Pain	128	Yes	Normal	Pos	3b	Distal
12.4	Diabetic	73	Yes	Normal	Pos	3a	Proximal+Distal
9.4	Diabetic	>128	No	1	Pos	3b	Distal
13.4	Hypocalcaemic	39	Yes	Normal	Pos	3a	Distal
3	Diabetic	>128	No	Normal	Pos	3a	Proximal +Distal
4.5	Diarrhoea	25	Yes	1	NK	1	Proximal

CONCLUSION: PE may have a role in the diagnosis of CD in children where serology is inadequately high to obviate need for UGE and initial pathology is inconclusive. The relative increased diagnostic yield of PE in comparison to performing a repeat UGE is not yet well characterised and the authors note that compliance to ESPGHAN guidelines in terms of initial UGE biospy site and numbers is important. However further study into the use of PE in difficult diagnose CD in children is warranted.

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Disclosure of Interest: None Declared

Keywords: ESPGHAN guidelines, push enteroscopy

P1663 EVOLUTION AND HLA-ASSOCIATION OF THE EARLY INFANTILE GLIADIN ANTIBODY RESPONSE IN A HIGH-RISK COHORT FOR COELIAC DISEASE

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INTRODUCTION: Antibodies against gliadin (AGA) and deamidated gliadin peptides (DGP) are regarded as early signs of developing coeliac disease in young children, but their predictive value is still uncertain.

AIMS&METHODS: To characterize the outcome of serum AGA and DGP antibody positivity observed in infancy. During 2007-2010, 1324 infants with a 1st degree relative with coeliac disease (CD) were recruited in 8 countries shortly after birth (EU-PreventCD project www.preventcd.com) and 931 HLA DQ2 and/or DQ8 positives were randomised double-blind to 100 mg of gluten suspension/day or placebo from 4 months of age. From 6 months all children consumed gluten-containing foods and serum samples were collected at 4,6,9,12,18,24 and 36 months Small bowel biopsies were performed based on symptoms suggestive of CD and/or anti-tissuetransglutaminase (TG2A) or AGA antibodies.

RESULTS: As of 5/2013, 814 children have been followed till 3 years and CD diagnosis was obtained in 56. At least 5-fold transient increase over baseline in AGA-IgA without TG2A occurred in 134 infants at 6 months, median 16.7 U/ml (range 6-100); the antibodies equally recognised native and deamidated peptides. This early response was associated with the duration of exclusive breast feeding. A smaller AGA peak was observed in 35 children ($p<0.0001$) at 9 months who were stationary at 6 months, median 8.2 U/ml (range 6-100, $p<0.001$). Both these groups had in 41% HLA DQ2.2 (with or without DQ2.5) compared to 14.4% in children without an AGA or DGP peak. Evaluating the children with complete sets of follow-up samples, the outcome was:

	At 2 years of age (n=723)			At 3 years of age (n=588)		
	N	CD (%)	TG2A (%)	N	CD (%)	TG2A (%)
AGA >5x baseline at 6 months	115	3.4*	5.2	97	6.2*	7.2
AGA >5x baseline at 9 months	21	9.5**	9.5	17	23.5***	23.5
AGA not >5x baseline during first year of life	524	5.5	7.1	416	9.6	13.7
Other pattern	63	4.7	7.9	58	10.3	12.07

Odds ratios: *0.62, **1.80, ***2.79

CONCLUSION: Both AGA and DGP had low predictive value for CD in these children. An early IgA AGA response at 6 months of age or earlier seems to be beneficial while at 9 months or later is associated with higher CD risk.

Disclosure of Interest: None Declared

Keywords: Coeliac disease, deamidated gliadin antibody

P1664 COELIAC DISEASE MANIFESTATION IN EARLY AGE IN A PROSPECTIVELY FOLLOWED CONTEMPORARY NATURAL HISTORY COHORT OF FIRST DEGREE RELATIVES

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INTRODUCTION: The manifestation of coeliac disease (CD) in genetically predisposed subjects may be dependent on the way of gluten introduction in infancy, but also on other environmental factors (e.g. seasonal infections, vaccinations, baby food items and local food preferences) that vary from one time period to the other. A multinational study, EU-PreventCD project (www.preventcd.com) is underway, where children born between September 2006 – July 2010 and having a first-degree relative with CD were recruited shortly after birth and received in double-blind placebo-controlled way 100 mg/day gluten from 4 months of age followed by gradual introduction scheme of 250-1000 mg gluten after 6 months of age in all. By the time the outcome of the PreventCD study will be known, it will be of interest to establish the baseline prevalence of CD in a similar cohort living in the same environment without the intentional modification of the diet.

AIMS&METHODS: The aim of this study was to collect a natural history cohort similar to the Hungarian PreventCD participants (n=186) and follow them prospectively with active screening for anti-transglutaminase (anti-TG2) and endomysial antibodies. Consecutively presented children born in the same time period as PreventCD participants were enrolled with the similar inclusion criteria and typed for HLA-DQ alleles. Gluten introduction and consumption were allowed according to the parents' wish. Gluten intake was recorded by a food frequency questionnaire. A small bowel biopsy was offered to children who developed seropositivity.

RESULTS: Altogether 303 children met the inclusion criteria and were enrolled. The median follow up time was 3.6 years (range 0.4.-6.4). The index coeliac patient was a sib in 115 cases (38%), the mother in 153 cases (50%) and the father in 35 cases (12%) and 84% of the children had DQ2 or DQ8. The median time of gluten introduction was 9 months, but there was no significant difference in gluten consumption at the age of 1.5, 2 or 3 years as compared to the Hungarian PreventCD participants. Anti-TG2 antibodies appeared in 43 subjects (14.2%) in the natural history cohort and frequency of CD confirmed by histology was 12.2%. The majority of these children (92%) was asymptomatic at the time when seropositivity was detected.

CONCLUSION: Prospective follow up and screening was able to detect a high prevalence of coeliac disease already in young age in this genetically predisposed cohort. Similar cohort composition and food preferences make this cohort suitable for a future comparison with the PreventCD study.

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Disclosure of Interest: None Declared

Keywords: coeliac disease, transglutaminase antibodies

P1665 COMPARATIVE STUDY OF ANTIGLIADIN ANTIBODIES IN BREAST MILK OF CELIAC AND NON CELIAC MOTHERS

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INTRODUCTION: Results on the influence of diet on food antibodies production, including antigliadin antibodies (AGA), in breast milk (BM) and colostrum are contradictory[1,2]. Moreover, there is scarce information on AGA in BM of general population and coeliac mothers.

AIMS&METHODS: Objectives: To study the presence of antibodies against gliadin in BM and their relationship with maternal diet.

Methods: samples of mature milk were obtained at different months of lactation (1-32) from 23 mothers: 12 on a normal diet (ND) and 11 on a gluten free diet

(GFD) (coeliac mothers) and were analyzed for Secretory AGA-IgA (S-AGA) and AGA-IgA by indirect homemade ELISA. Total IgA (g/L) was measured in human milk whey using an ELISA kit from Bethyl Laboratories.
RESULTS: AGA levels vary from one mother to another, but are stable in each mother from the first month of lactation onwards. S-AGA and AGA-IgA were detected in BM, both in mothers on a GFD and mothers on a normal gluten containing diet.
The comparison of the estimated kernel density curves for S-AGA showed a difference between both groups, with slightly lower values for mothers on GFD. Similar results were obtained for AGA-IgA. However differences between the 2 groups of mothers did not reach statistical significance (repeated measures ANOVA, S-AGA p-value = 0.12, AGA-IgA p-value=0.16); analysis of these results suggests however this was related to the low sample size: 106 observations but only 23 different individuals.
Total IgA values varied between 0.1 and 1 g/L in most individuals, the median IgA value being 0.66 g/L and the interquartile range [0.44; 0.94]. We observed a great variability among mothers, some cases showing unusually high values.
To assess the relationship between IgA and the other variables, a linear mixed model approach was used. The model including S-AGA instead of AGA-IgA had a considerably higher AICC (Corrected Akaike Information Criterion) (229.2 vs. 235.7), indicating that a positive association exists between levels of AGA and total IgA. This association is higher between levels of AGA-IgA and total IgA than for S-AGA and total IgA
CONCLUSION: AGA was present in all BM samples, independently of mother's diet. Thus breastfeeding is a way of transferring antibodies to the baby, so this practice could be relevant for CD prevention in breastfed infants.
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Disclosure of Interest: None Declared
Keywords: antigliadin antibodies, breast milk, celiac disease

P1666 TOWARDS NON-INVASIVE DIAGNOSIS AND MONITORING OF CELIAC DISEASE: A PROSPECTIVE STUDY TO THE USEFULNESS OF I-FABP

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INTRODUCTION: Our retrospective studies showed the differentiating potential of intestinal fatty acid binding protein (I-FABP), a sensitive marker for enterocyte damage, for celiac disease (CD) in patients with positive CD autoantibodies (IgA-tTG). This study evaluates the usefulness of plasma I-FABP in diagnosing CD in children with positive IgA-tTG titers, and for monitoring disease activity in patients on a gluten-free diet (GFD) and during gluten challenge (GC).
AIMS&METHODS: In a prospective, multicentre study 80 children presenting with positive CD autoantibodies were included. Patients fulfilling the ESPGHAN criteria for CD (villous atrophy and/or IgA-tTG >10x cut-off level) started a GFD. Plasma I-FABP and IgA-tTG were determined at presentation and after 3, 6, 12 and 26 weeks of GFD. The control group consisted of 90 children with a clinical suspicion of CD but normal CD autoantibody titers. Moreover, 20 adult CD patients in clinical remission underwent a two-week GC. Study visits occurred at -14, 0, 3, 14 and 28 days after starting GC.
RESULTS: Plasma I-FABP levels were significantly elevated at presentation in children with CD (775 pg/ml [438-1354]) compared with the controls (207 pg/ml [123-288], $p<0.001$) and correlated with Marsh grade (R=0.37, $p<0.05$, n=61). The positive and negatie predictive values of I-FABP for CD were 95.2% and 77.0%, respectively. I-FABP levels decreased significantly to 444 (n=18), 378 (n=57), 258 (n=50) en 221 (n=52) pg/ml after 3, 6, 12 and 26 weeks GFD, respectively. Median IgA-tTG titers did not normalize within 6 months of GFD. Adult CD patients on a GC showed a significant increase in I-FABP levels from baseline to day 14, and a decrease after gluten withdrawal, while autoantibody titers increased slightly from baseline to day 14 but markedly by day 28, when gluten was already eliminated. I-FABP levels correlated significantly with intraepithelial lymphocyte count, while no correlation with autoantibodies, villous atrophy or symptoms was found.
CONCLUSION: An elevated I-FABP level confirms the diagnosis of CD in 91.7% of children with positive autoantibody titers. I-FABP analysis could reduce the need for a duodenal biopsy with almost 75%. I-FABP levels increase and decrease faster after gluten introduction and gluten withdrawal in CD patients, respectively, as compared with the currently used CD autoantibodies. Plasma I-FABP is a reliable additional marker for CD diagnosis and might provide insight in intestinal damage in CD children on a GFD and adults on a GC.
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Disclosure of Interest: None Declared
Keywords: celiac disease, diagnosis, follow-up, I-FABP, non-invasive

P1667 PREVALENCE AND CLINICAL PICTURES OF THE DISEASE IN ITALY: RESULTS OF THE SALIVARY SCREENING.

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INTRODUCTION: Coeliac disease (CD) is a common, autoimmune pathology, caused by a permanent intolerance to gluten contained in wheat and to similar prolamines present in barley and rye. There are several patterns of MC: symptomatic CD, and silent CD, both characterized by typical histological lesions in the duodenum mucosa. The typical manifestation is distinguished by gastrointestinal symptoms such as diarrhoea, vomiting, abdominal distension and failure to thrive. On the other hand atypical forms are characterized by extraintestinal symptoms (anaemia, low height, delayed puberty, headaches).
AIMS&METHODS: The aim of our study was to perform a CD screening in school-age children in order to obtain a timely diagnosis of the disease that might permit a propter growth and to compare clinical appearance of the disease in three different cohorts: a big metropolis (Rome), a small mountain city (L'Aquila) and a small seaside city (Civitavecchia).
Salivary samples were collected and tested for anti-transglutaminase antibodies (tTGAb) using a fluid-phase radioimmunoprecipitation method. Subjects salivary tTGAb-positive were subsequently tested for serum CD-specific antibodies (RIA tTGAb and ELISA tTGAb). Confirmed positive children underwent endoscopy with multiple duodenal biopsies, and at CD diagnosis, started a gluten-free diet. The study was performed on: Group 1: 5733 out of 7377 school-children who were invited to participate in the city of Rome; Group 2: 751 out of 954 school-children who were invited to participate in the city of L'Aquila; Group 3: 816 out of 1004 school-children who were invited to participate in the city of Civitavecchia.
RESULTS: The coeliac children were: Group 1: 68 (45 newly diagnosed and 23 already coeliacs), Group 2: 13 (7 newly diagnosed and 6 already coeliacs), Group 3: 11 (8 newly diagnosed and 3 already coeliacs). The CD prevalence in the three groups investigated were: Group 1: 1.2%, Group 2: 1.7% Group 3: 1.3%. The clinical pictures of the three groups showed that under the water level the iceberg depht were different: Group 1: 66% of CD children; Group 2: 54% of CD children; Group 3: 73% of CD children.
CONCLUSION: CD prevalence is higher than expected, particularly in group 2 children, with a modified clinical spectrum. Our study demonstrates the high compliance of the parents and of the children to the salivary test. CD iceberg is still deep, hence, the salivary tTGAb, that is a non-invasive, simple, reproducible and sensitive screening method has proved to be a powerful tool in identifying celiac children.
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Disclosure of Interest: None Declared
Keywords: children, Coeliac disease, saliva, Screening, transglutaminase antibodies

P1668 THE 'SUSPECTED BLOOD INDICATOR' (SBI) IN SMALL BOWEL BLEEDING FOR DETECTION OF BLEEDING LESIONS BY CAPSULE ENDOSCOPY: NO ACTIVE BLEEDING IN CASE OF NEGATIVE SBI

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INTRODUCTION: Capsule endoscopy is the gold standard to diagnose small bowel bleeding. The latest generation of the suspected blood indicator (SBI) algorithm offers a technical feature that might easily and quickly detect the bleeding site in the small bowel but validity of this feature has not been evaluated yet.
AIMS&METHODS: All patients who presented at our clinic for suspected bleeding of the small bowel between 2010 and 2012 were retrospectively analyzed. Intestinal bleeding remained obscure after gastroscopy and colonoscopy, and small bowel capsule endoscopy (CE) was performed. The second-generation PillCam SB 2 capsule endoscope (Given Imaging, Yonkheam, Israel) and Rapid Access 6 software were used to detect (1) luminal blood content and (2) small bowel lesions responsible for bleeding. The findings of an independent and experienced investigator were correlated to the results of the SBI.
RESULTS: A total of 188 patients (126 m, 62f, mean age 59.6 years) were investigated. Red blood cell transfusion was necessary in 56 cases (29%). The SBI showed positive findings in 169 patients whereas the investigator detected active bleeding in 42 cases. None of the active bleedings as diagnosed by the investigator was SBI negative (sensitivity 100%, specificity of 13%). Small bowel lesions were described by the investigator in 46 cases, of which SBI was positive in 45 (97.8%). One angiectasia was missed by the SBI.
CONCLUSION: The new SBI software is a reliable tool to exclude active bleeding and relevant lesions and the patient might be dismissed from the hospital in case of negative SBI. Nevertheless analysis of capsule videos by an investigator remains important for the detection and differentiation of polyps, tumors and other type of lesions.
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Keywords: capsule endoscopy, Endoscopy, small bowel capsule endoscopy, small bowel diseases, Small intestinal bleeding, Upper GI and small intestinal bleeding

P1669 DIABETES, ATRIAL FIBRILATION AND LARGE BOWEL DIVERTICULOSIS: RISK FACTORS FOR SMALL BOWEL ANGIODYSPLASIAS

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INTRODUCTION: Small bowel angiodysplasias is one of the main causes of small bowel bleeding.
AIMS&METHODS: Aim: To identify risk factors for small bowel angiodysplasias.
Methods: 984 patients (mean age 60±18 years, 543 men, 256 smokers) undergone small bowel capsule endoscopy, gastroscopy and colonoscopy were evaluated. 490 were evaluated for iron deficiency anemia, 311 for diarrhea, 60 for unexplained abdominal pain and for 123 other causes. Stat: X2, logistic regression analysis.
RESULTS: 451 (42%) patients presented small bowel angiodysplasias, 308 (78%) anemic and 107 (22%) non-anemics ($p<0.0001$). Mean age of patients with small bowel angiodysplasias was 68±14 years versus 55±19 years in those without angiodysplasias ($p<0.0001$) and mean BMI 26.5±4 versus 25.7±5.3 respectively ($p=0.01$). Small bowel angiodysplasias were found in: 255 (61%) men and 90 (22%) smokers; while they were not present in 289 (51%) men ($p=0.0009$) and 165 (29%) smokers ($p=0.01$). Small bowel angiodysplasias were found in: 119 (64%) diabetics versus 296 (37%) non-diabetics ($p<0.0001$), 81 (67%) patients with chronic renal failure versus 361 (40%) without ($p<0.0001$), 90 (64%) patients with large bowel diverticula versus 278 (36%) without ($p<0.0001$), 23 (48%) with heart valve disease versus 392 (42%) without ($p=0.41$), 147 (35%) patients with ischemic heart disease versus 110 (19%) without ($p<0.0001$), 52 (13%) with atrial fibrillation versus 24 (4%) without ($p<0.0001$), 38 (9%) with COPD versus 29 (5%) without ($p=0.01$), 26 (6%) with stroke versus 12 (2%) without ($p=0.0008$), 9 (1%) with parkinsons disease versus 26 (5%) without ($p=0.04$). In logistic regression analysis for all the above mentioned risk factors: age ($p<0.0001$), male gender ($p=0.02$), presence of diabetes ($p=0.002$), atrial fibrillation ($p=0.02$) and large bowel diverticulosis ($p=0.02$), as well as absence of parkinsons disease ($p=0.05$) were significant risk factors for the presence of small bowel angiodysplasias.
CONCLUSION: Small bowel angiodysplasias were more frequent among patients with small bowel related anemia. Old age, male gender, presence of diabetes, atrial fibrillation and large bowel diverticulosis, as well as absence of parkinsons disease were significant risk factors for the presence of small bowel angiodysplasias.
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Disclosure of Interest: None Declared
Keywords: capsule endoscopy, small bowel angiodysplasias

P1670 FACTORS ASSOCIATED WITH POSITIVE CAPSULE ENDOSCOPY FINDINGS IN PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING

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INTRODUCTION: Capsule endoscopy (CE) is the first line examination to evaluate obscure gastrointestinal bleeding (OGIB). The identification of factors associated with the detection of lesions by CE could improve resource utilization and thereby improve patient selection for CE examination.
AIMS&METHODS: To identify factors associated with positive CE findings in patients with OGIB.
Retrospective study of 214 CE procedures (208 patients) performed between 2005-2013, in the setting of OGIB. Demographic variables, type of OGIB (occult versus overt), number of transfusions, type of positive finding, number of endoscopies (EGD) and colonoscopies performed prior to CE, hemoglobin value, comorbidities and medication; and Charlson comorbidity index was evaluated. Overt bleeding was subdivided into ongoing and previous. Only lesions with high hemorrhagic potential (P2-ulcers, vascular lesions, tumors / masses, multiple erosions and blood) were classified as positive findings.
Statistical tests: t-student; $\chi 2$.
RESULTS: 59% - female, mean age-62years. Occult bleeding-64.5% (88.4%-microcytic anemia, 11.6% positive fecal occult blood test). Overt bleeding-35.5% (previous-63.2% ongoing-36.8%). Positive finding-43% (angiodysplasia-31.9%; ulcers-28.6%; blood-25.3%, tumor/mass-6.6%).
The identification of positive findings was significantly higher in those with ongoing-overt bleeding ($p<0.001$). Increasing number of pre-capsule EGD ($p<0.001$) and colonoscopies ($p<0.001$), increasing transfusion requirements ($p<0.001$), moderate/severe renal disease ($p=0.009$) and NSAID intake ($p=0.005$) were all significantly associated with the identification of positive findings in CE.
CONCLUSION: Our study suggests that CE should be used early in OGIB. Ongoing-overt bleeding, increasing number of endoscopies and transfusion requirements, a more severe renal disease and NSAIDs intake, were associated with more positive findings on CE.
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Disclosure of Interest: None Declared
Keywords: capsule endoscopy, obscure gastrointestinal bleeding

P1671 THE BLOOD UREA NITROGEN/CREATININE RATIO IS USEFUL FOR DISTINGUISHING THE COLONIC BLEEDING FROM THE SMALL BOWEL BLEEDING IN OBSCURE GASTROINTESTINAL BLEEDING.

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INTRODUCTION: The diagnosis of a bleeding source is still challenging in obscure gastrointestinal bleedings (OGIBs). Capsule endoscopy and device assisted enteroscopy are useful for the small bowel exploration. However, in about 10% of OGIB cases, the bleeding source is extra-small bowel area and hemorrhagic diverticulum of the colon is one of the common extra-small bowel sources. To increase the probability of the small bowel bleeding before endoscopy is important for an accurate diagnosis.
AIMS&METHODS: We conducted a retrospective case series study to evaluate the blood urea nitrogen (BUN)/creatinine (Cre) ratio for distinguishing the colonic bleeding from other sites in OGIB.
198 consecutive OGIB patients who had undergone the double balloon endoscopy (DBE) from June 2003 to Dec. 2012 at Nippon Medical School Hospital were enrolled. The clinical characteristics (such as gender and age), bleeding types (such as occult and overt), blood transfusions, initial blood tests (such as hemoglobin(Hb), mean corpuscular volume (MCV), total protein(TP), BUN, Cre and BUN/Cre ratio) were assessed.
We divided OGIB patients who could be identified the source of bleeding by DBE into two groups. One group is a colonic bleeding, and the other group is the source above the ileocecal valve (ICV). We analyze the differences of each clinical parameter among two groups. Fisher's exact test was used for categorical variables, and Mann-Whitney test was used for continuous variables. A p value of <0.05 was considered significant.
RESULTS: 138 (69.7%) of 198 OGIB patients were diagnosed. There were 53 females (38.4%) and 85 (62.6%) males. The mean age was 62.9 (SD 14.8 range 19-87) years old. The bleeding types were occult and overt in 22 (15.9%) and 116 (84.1%) patients, respectively. The colonic bleedings were in 17 patients (12.3%). 111 patients (80.4%) were small bowel bleedings and 10 patient (7.2%) were upper GI bleedings.
The colonic bleeding group was a lower BUN/Cre ratio than other group with a statistically significance ($p = 0.04$, 17.4±4.2 in colonic bleeding group, and 24.2±15.1 in above ICV group). Gender, age, bleeding types, blood transfusions, Hb, MCV, TP, BUN, and Cre were not statistically significant.
CONCLUSION: The BUN/Cre ratio is helpful to distinguish the colonic bleeding from small bowel bleeding in OGIB. When the higher probability of the small bowel bleeding is confirmed, diagnostic rate will be improved. The higher BUN/Cre ratio may suggest a small bowel bleeding and lower BUN/Cre ratio patients may need a repeat colonoscopy for the detection of a source.
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Disclosure of Interest: K. Mitsui: None Declared, M. Suzuki: None Declared, S. Fujimori Financial support for research from: Given imaging, A. Ehara: None Declared, T. Kobayashi: None Declared, S. Tanaka: None Declared, A. Tatsuguchi: None Declared, C. Sakamoto Financial support for research from: Pfizer,Astellas, Otsuka, Zeria
Keywords: double balloon endoscopy, GI bleeding, obscure gastrointestinal bleeding, Small Bowel

P1672 LUBIPROSTONE, A STIMULATOR OF CLC-2, PREVENTS NSAID-INDUCED SMALL INTESTINAL DAMAGE IN RATS THROUGH EP4 RECEPTOR-DEPENDENT MECHANISM

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INTRODUCTION: Lubiprostone, a bicyclic fatty acid of the prostone group, is used for the treatment of chronic constipation, and this action is due to stimulation of intestinal fluid secretion through the activation of ClC-2-type Cl^- channels. Other studies showed that lubiprostone modulated gastrointestinal motility, via different prostaglandin (PG) EP receptor subtypes, and increased duodenal HCO_3^- secretion through the activation of EP4 receptors. Recently, NSAID-induced enteropathy has become an important topic to gastroenterologists. However, it remains unknown whether lubiprostone has any effect on these lesions.
AIMS&METHODS: We examined the effect of lubiprostone on the intestinal ulcerogenic response to indomethacin in rats and investigated the underlying mechanisms of the protective action.
Male SD rats were used without fasting. The animals were given indomethacin (10 mg/kg) SC and killed 24 h later to examine the hemorrhagic lesions developed in the small intestine. Lubiprostone (0.01-1 mg/kg) was given once PO 30 min before the administration of indomethacin. Various EP antagonists were given PO 30 min before lubiprostone. Enterobacterial count was determined by a culture method, mucus secretion was examined by PAS staining, and the protein expression of iNOS was examined by Western blotting. Furthermore, intestinal fluid (Cl^-) secretion was measured electrically by short circuit current (Isc) using a Ussing chamber.
RESULTS: Indomethacin caused hemorrhagic lesions in the small intestine, accompanied by increases in bacterial invasion and iNOS expression as well as myeloperoxidase (MPO) activity in the mucosa. Lubiprostone dose-dependently reduced the severity of these lesions, with the concomitant suppression of bacterial invasion, iNOS expression and MPO activity. The amelioration effects of lubiprostone on the indomethacin-induced intestinal lesions and accompanying inflammatory changes were significantly abrogated by pretreatment of the animals with the EP4 antagonist AE3-208 but not the EP1 (ONO-8711) or the EP3

(AE5-599) antagonists. In addition, lubiprostone dose-depdently increased mucus secretion as well as the Isc of the small intestine, and these responses were also attenuated by prior administration of the EP4 antagonist.
CONCLUSION: Lubiprostone prevents the indomethacin-induced small intestinal lesions via the EP4 receptor-dependent mechanism, and this effect may be functionally associated with the increase of mucus and fluid (Cl^-) secretions that are known to be important for suppression of bacterial invasion and iNOS expression, the major pathogenic factors in NSAID-induced small intestinal lesions.
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Disclosure of Interest: None Declared
Keywords: ClC-2-type Cl- channels, NSAID-induced enteropathy, prostaglandins E

P1673 ANGIODYSPLASIAS OF THE JEJUNUM ARE THE MOST FREQUENT CAUSE OF OBSCURE GASTROINTESTINAL BLEEDING: OUR EXPERIENCE FROM 3050 PATIENTS SUBJECTED TO SMALL BOWEL CAPSULE ENDOSCOPY

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INTRODUCTION: Angiodysplasias of the small intestine are a common cause of obscure gastrointestinal bleeding. We aimed to determine the yield and distribution of angiodysplasias in different age groups in patients subjected to small bowel capsule endoscopy.
AIMS&METHODS: From March 2003 till March 2013, 3050 patients (males/females: 1492/1558, mean age ± SD: 60.8±18.4) have been subjected to small bowel capsule endoscopy (Given imaging, Yoqneam, Israel) in our Department. Among them, there were 2017 patients (66.13%) who had a history of gastrointestinal bleeding (melena or blood per rectum) or a positive fecal occult blood test result and/or iron-deficiency anemia, with a negative gastroscopy and colonoscopy and were categorized as having obscure gastrointestinal bleeding.
RESULTS: In patients with obscure gastrointestinal bleeding subjects to small bowel capsule endoscopy, positive findings were noted in 1146 (56.81%); precisely, angiodysplasias (n=661, 57.67%), apthoid ulcerations (n=186, 16.23%), ulcers (n=127, 11.08%), polyps (n=119, 10.38%) and tumors (n=53, 4.62%). In patients with angiodysplasias, those were more frequently seen in the first half of the capsule recording (jejunum) as opposed to the second half (ileum) (72% versus 54%, $p<0.01$). Angiodysplasias were more commonly seen in patients $\geq$ 65 years old, as opposed to those $<$ 65 years old (61% versus 39%, $p<0.01$).
CONCLUSION: Most patients are subjected to small bowel capsule endoscopy because of obscure gastrointestinal bleeding and among them angiodysplasias are the commonest findings. When present, angiodysplasias are more frequently seen in the jejunum and in patients $\geq$ 65 years old.
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Disclosure of Interest: None Declared
Keywords: angiodysplasia, small bowel capsule endoscopy

P1674 REPEAT ENDOTHERAPY FOR SMALL INTESTINE VASCULAR LESIONS BY DOUBLE-BALLOON ENDOSCOPY IS ASSOCIATED WITH FAVOURABLE OUTCOMES

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INTRODUCTION: Gastrointestinal bleeding secondary to small intestine vascular lesions (SIVL) is associated with rebleeding despite initial haemostasis by double-balloon endoscopy (DBE).
AIMS&METHODS: Our study evaluated the long-term outcomes of DBE endotherapy of SIVL (as described by the Yano-Yamamoto classification); impact of repeat DBE endotherapy for recurrent bleeding was also assessed. Retrospective cohort study of 43 patients (male 24, female 19, age (±SD) 63.9 ± 14.9), who underwent 69 sessions of DBE endotherapy of SIVL. Each patient underwent 1.6 sessions of DBE haemostasis on average (range, 1-6). The mean (±SD) follow-up period was 4.9 ± 1.7 years (range: 2.4 to 9.1 years).
RESULTS: Overt rebleeding occurred in 16/43 patients (37%). Patients with multiple SIVL showed a significantly higher rate of overt rebleeding than those with solitary SIVL (12/23 (52%) vs. 4/20 (20%) P = 0.017). The trend for frequency of rebleeding after first DBE haemostasis, appeared to be higher for patients with type 1a SIVL than those with type 1b or type 2 lesions; type 1a 8/16 (50%) vs. type 1b 5/19 (26%) (P = 0.12) and type 1a 8/16 (50%) vs. type 2 2/7 (29%) (P = 0.31), respectively. While 12 of the 16 patients (group A) underwent repeat DBE haemostasis at every episode of overt bleeding, the remaining 4 patients (group B), did not undergo repeat DBE haemostasis during every episode of overt rebleeding. We assessed the frequency of overt rebleeding/year/patient during 2 phases after initial DBE endotherapy. Phase 1 included the 1st year of follow up, while phase 2 included follow up during the 2nd year and later. In group A, the frequency of overt rebleeding during phase 1 was significantly higher than during phase 2; 1.58 ± 0.90 vs. 0.12 ± 0.19 times/year/patient, respectively (P < 0.001). In group B, the frequency of overt bleeding was almost the same between 2 phases; phase 1: 0.50 ± 0.57 times/year/patient vs. phase 2: 0.50 ± 0.29 (P = 0.495). With focus on phase 2, patients in group B showed a significantly higher rate of overt rebleeding than those in group A; group A 0.12 ± 0.19 vs. group B 0.50 ± 0.29 times/year/patient (P = 0.007).
CONCLUSION: While the presence of multiple SIVL was associated with rebleeding, repeat DBE endotherapy resulted in an improved long-term outcome in patients with refractory SIVL bleeding.
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Keywords: Double-balloon endoscopy, Endoscopic haemostasis, Small intestine vascular lesions, Therapeutic endoscopy

P1675 A PRELIMINARY REPORT OF SEARCHING GENOTYPE ASSOCIATED WITH NSAID-INDUCED SMALL INTESTINAL INJURY

S. Fujimori[1,*], T. Mushiroda[2], K. Mitsui[1], Y. Takahashi[1], M. Yonezawa[1], S. Tanaka[1], A. Tatsuguchi[1], C. Sakamoto[1]. [1]*Depertment of Gastroenterology, NIPPON MEDICAL SCHOOL, Graduate School of Medicine, Tokyo,* [2]*Reserach Group for Pharmacogenomics, RIKEN Center for Integrative, Yokohama, Japan*

INTRODUCTION: We previously reported finding individual variability in NSAID-induced small intestinal injury in two RCTs administering diclofenac sodium to healthy volunteers (1,2). Recent upper gastrointestinal studies show the possibility that genetic polymorphisms of NSAID-metabolizing enzymes (CYP2C9, CYP3A4) and cyclooxygenase (COX-1) are associated with NSAID-induced gastroduodenal injuries (3,4).
AIMS&METHODS: The aim of the study was to investigate the association of genetic polymorphisms for traditional NSAID-induced small intestinal injury among 17 genes which are reported to possibly be associated with NSAID-induced gastroduodenal injuries. Subjects were 55 healthy volunteers and 8 patients who were clear on NSAIDs-induced small intestinal injury by the aforementioned studies and clinical course. Subjects were divided into three groups based on the number of small intestinal mucosal breaks after NSAID treatment as evaluated by capsule endoscopy. The severe group was defined as the detection of five or more mucosal breaks; the mild group was defined as detecting one to four mucosal brakes, and the control group was defined as no mucosal breaks being detected. 45 SNPs on 17 genes (CDKN2BAS, COX-1, COX-2, CRP, CYP2C9, CYP2C19, three types of CYP3A4, CYSLTR1, ITGB3, IL-1β, IL-1RN, IL-6, PLA2G4A, PON1, TNF-α) were genotyped by multiplex PCR-based invader assay. The frequency of genotype in 45 SNPs was compared among the three groups in various combinations.
RESULTS: As a result of capsule endoscopy evaluation, there were 16 subjects categorized in the severe group, 15 in the mild group, and 32 in the control group, respectively. When comparing the severe and mild groups with the control group, there was a significant tendency of SNP (rs1330344) on the COX-1 gene (P=0.060) and SNP (rs1205) on the CRP gene (P=0.077). In comparing the severe group to the mild and control groups, there was also a significant tendency of SNP (rs12721627) on the CYP3A4*16 gene (P=0.061) for which genotype C/G was detected only in subjects with severe small intestinal mucosal breaks.
CONCLUSION: COX-1, CRP, and CYP3A4*16 are candidate genotypes for identification of patients with a high risk of NSAID-induced small intestinal injury.
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Disclosure of Interest: S. Fujimori Other: Given Imaging, T. Mushiroda: None Declared, K. Mitsui: None Declared, Y. Takahashi: None Declared, M. Yonezawa: None Declared, S. Tanaka: None Declared, A. Tatsuguchi: None Declared, C. Sakamoto Other: Pfizer, Otsuka, Astellas, Zeria
Keywords: capsule endoscopy, genotype, NSAID ENTEROPATHY

WEDNESDAY, OCTOBER 16, 2013 9:00–14:00
NUTRITION III – Poster Area

P1676 HOW USEFUL IS PATIENTS OWN ASSESSMENT OF THEIR NUTRITIONAL STATUS?

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INTRODUCTION: Many patients admitted to acute surgical specialties are at risk of malnutrition, and there are many screening tools in use, including the MUST screening. This has recently been added to NICE guidelines. Certain assessments use patients' own perceptions of their nutrition, such as SGA.
AIMS&METHODS: The aim of this study is to see if patient's subjective assessment is predictive of and possible to use in place of their MUST score.
An adapted form of the Subjective Global Assessment (SGA) was used, basing the questionnaire for patients own assessment, looking at the domains of weight's perception of their weight loss in the past month, food intake over a month, medical barriers to stopping them eating (such as nausea, vomiting, unable to tolerate foods) and activity levels.
Data was collected over a 2 month period, with patients completing the nutrition questionnaire and the project time collecting data for MUST.

RESULTS: 108 patients admitted between November and December 2012 was included. 21 were elective and 87 were acute admissions. 59 were managed conservatively, 32 had open abdominal surgery, 14 laparoscopic and 3 soft tissue or breast surgery. The patients MUST score was calculated, and the duration of patients stay was calculated. 4 patients died within 28 days of admission

MUST score vs patients subjective assessment of weight loss

	High risk (39 patients) %	Moderate risk (12 patients) %	Low risk (57 patients) %
No recent weight loss	38.5	33.4	77.2
Recent weight loss in past month	61.5	66.6	22.8

CONCLUSION: Patient's interpretation of their recent nutrition does not reflect on their BMI on admission

There seems to an association with increasing MUST score with subjective weight loss, decreased appetite, increased symptoms preventing adequate nutrition, and decreased patient activity.

There is significant statistical difference for patients' subjective weight loss and subjective decrease in food intake with increased hospital stay. There is no difference between their interpretations of symptoms preventing eat nor their activity status with increased hospital stay.

This shows that patient's subjective assessment of their nutrition is predictive of their MUST score and weight loss and type and amount of food is associated with increased length of stay.

Subjective views could well be used in future as part of nutrition risk scoring.

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Disclosure of Interest: None Declared

Keywords: MUST score, nutritional status assessment, subjective health assessment

P1677 LONG-TERM TAUROLIDINE LOCK THERAPY IS MORE EFFECTIVE IN PREVENTING CATHETER RELATED BLOODSTREAM INFECTIONS IN ADULT HOME PARENTERAL NUTRITION PATIENTS THAN HEPARIN: A FOLLOW-UP OF 212 PATIENTS

E. D. Olthof[1,*], G. J. Huisman- de Waal[1], M. W. Versleijen[1], W. Kievit[2], G. J. Wanten[1]. [1]*Department of Gastroenterology and Hepatology,* [2]*Department of Health Evidence, RADBOUD UNIVERSITY NIJMEGEN MEDICAL CENTRE, Nijmegen, Netherlands*

INTRODUCTION: Home parenteral nutrition (HPN) patients are at risk for developing catheter-related bloodstream infections (CRBSI). In a previous prospective open-label randomized controlled trial in 30 HPN patients presenting with CRBSI we showed that catheter locking with 2% taurolidine (TauroSept®) dramatically (90%) reduced re-infections compared with low-dose (150 U/ml) heparin. Our complete HPN population therefore switched to taurolidine in 2008.

AIMS&METHODS: Aim of the present retrospective study was to compare taurolidine with heparin catheter lock therapy for their efficacy regarding the prevention of CRBSI in HPN patients. Data of positive peripheral blood cultures, which were related to the patients venous access, were retrospectively collected from 212 patients that received HPN between January 2000 and November 2011, comprising 175 and 761 central venous catheter (CVC) access years during catheter lock therapy with taurolidine and heparin, respectively.

RESULTS: Thirty-two peripheral positive blood cultures were found in 194 taurolidine locked CVCs of 86 patients in total, while 276 peripheral positive blood cultures were detected in 699 heparin locked CVCs of 187 patients in total. Therefore, bloodstream infection incidence rates of CVC were 0.5/year and 0.99/year for taurolidine and heparin, respectively. Since 66 taurolidine locked CVCs are still *in situ*, the number of bloodstream infections per catheter will probably decrease even more.

CONCLUSION: Long-term use of the lock solution taurolidine is more effective in preventing CRBSI in HPN patients than heparin.

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Disclosure of Interest: None Declared

Keywords: bloodstream infection, catheter lock solution, heparin, parenteral nutrition, taurolidine

P1678 LEUKOCYTE ACTIVATION BY MEDIUM-CHAIN TRIGLYCERIDES IS NOT MODULATED BY FISH OIL OR OLIVE OIL-BASED LIPIDS

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INTRODUCTION: Medium-chain triglycerides (MCTs) as part of parenteral nutrition formulations activate leukocytes *in vitro*. Novel parenteral lipid emulsions have been developed that contain mixed lipids: MCTs, long-chain triglycerides (LCTs), fish oil (FO) and/or olive oil (OO).

AIMS&METHODS: Aim of this study was to investigated whether leukocyte activation by MCTs involves shared signaling pathways with fish oil and olive oil, which have anti-inflammatory and immune neutral characteristics. *In vitro* effects of various mixed lipids, and effects of addition of n-3 fatty acids (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) to LCT/MCT, on the expression of surface activation markers and reactive oxygen species (ROS) production of leukocytes was studied.

RESULTS: We found that MCT-containing lipids (LCT/MCT, LCT/MCT/FO, LCT/MCT/FO/OO) activated immune cells, with decreased L-selectin expression (30, 36, 24%, respectively), increased degranulation (71, 83, 62%, respectively) and adhesion (46, 48, 37%, respectively) in granulocytes compared to lipid-free medium. Immune cells exposed to MCT-free lipids (LCT, FO, SO/OO) had a similar immune status compared to immune cells not exposed to lipids. Stimulus-induced ROS production decreased in MCT-containing lipids by 6 to 25%, and remained unchanged in MCT-free lipid emulsions, except for a 13% decrease in ROS production after incubation with FO. Incubation with LCT/MCT and micelles of EPA slightly activated granulocytes (12% decrease in L-selectin, 15% increase of degranulation) and monocytes (9% increase in adhesion), whereas addition of micelles of DHA did not alter the immune status, compared to LCT/MCT alone. Addition of EPA or DHA micelles to LCT/MCT did not alter ROS production.

CONCLUSION: Leukocyte activation by MCTs is not modulated by fish oil or olive oil-based lipids, suggesting that MCTs exert their effects via different signaling pathways.

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Disclosure of Interest: None Declared

Keywords: fish oil, immune activation, medium chain triglyceride, olive oil, parenteral nutrition

P1679 MICROBIOCIDAL EFFECTS OF VARIOUS TAUROLIDINE CONTAINING CATHETER LOCK-SOLUTIONS

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INTRODUCTION: We have recently shown that use of a catheter lock solution containing taurolidine dramatically decreased catheter related bloodstream infections in patients on home parenteral nutrition (HPN) when compared to heparin. Several taurolidine containing solutions are commercially available, some in combination with citrate or heparin.

AIMS&METHODS: Aim of this study was to investigate the effect of these different lock solutions on growth and biofilm formation of Gram negative, Gram positive and fungal pathogens (*Escherichias coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*) and *Candida glabrata* (*C. glabrata*), respectively). To this end, clinical isolates obtained during CRBSI episodes of HPN patients were grown in the presence of 10x, 20x, 33x and 100x diluted lock solutions (2%taurolidine, 1.3%taurolidine-citrate, 1.3%taurolidine-heparin and heparin) or PBS (control) in LB-medium and RMPI medium for bacteria and yeasts, respectively. Crystal violet was used for biofilm staining. Biofilm formation and growth of clinical isolates was determined by optical density measurement at 595 and 660 nm, respectively.

RESULTS: Preliminary results show that 10x diluted solutions of all taurolidine lock solutions completely prevented growth of *E. coli*, *S. aureus* and *C. glabrata* over a three day experiment. Growth of *S. aureus* and *E. coli* was detected about 10 hours earlier in 33x diluted 1.3%taurolidine-citrate and 1.3%taurolidine-heparin compared with 2%taurolidine lock solution, while heparin did not inhibit growth of clinical isolates compared to PBS. Effects of lock solutions on biofilm formation were in line with the effects on microbial growth.

CONCLUSION: Taurolidine containing lock solutions have a potent microbiocidal effect on fungal, Gram positive and Gram negative pathogens. While 2%taurolidine appears to be the most potent in this respect, the relevance of this finding for clinical practice remains to be established.

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Keywords: catheter lock solution, heparin, microbiocidal, pathogens, taurolidine

P1681 PERCUTANEOUS ENDOSCOPIC GASTROSTOMY: CLINICAL INDICATION AND PATIENT TOLERABILITY.

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INTRODUCTION: Percutaneous endoscopic gastrostomy (PEG) is an effective long-term alternative to parenteral feeding for patients with functioning gastrointestinal tract. It has been established that mortality following PEG depends on the underlying condition, and patients with oropharngeal cancer and cerebrovascular accidents generally have a poor prognosis. However, there have been no studies analysing the patient tolerability of PEG based on underlying condition.

AIMS&METHODS: A retrospective analysis of all patients who had undergone a PEG insertion at Milton Keynes hospital between 2008 to 2012 was performed. Patients were identified form the endoscopy unit database.

RESULTS: 118 patients were included in this study with a median age of 75 years and 49.8% were male. 21% had PEG for cancer, 38% for cerebrovascular accidents, 34.7% for progressive neurological disorders and 6% for dementia. Rates of moderate/severe patient discomfort during the procedure were 24% for patients with cancer, 8.9% for patients with cerebrovascular accidents, 19.5% for patients with progressive neurological disorders and 57.1% for patients with dementia.

	Cancer (n=25)	Cerebrovascular accidents (n=45)	Neurological conditions (n=41)	Dementia (n=7)
Moderate/severe discomfort	24%	8.9%	19.5%	57.1%
Duration of procedure	18 minutes	17 minutes	18 minutes	21 minutes
Mean amount of midazolam	2.0mg	1.5mg	1.8mg	2.0mg

CONCLUSION: Patient tolerability of PEG is known to depend on endoscopist skill and amount of sedation used. However, it is clear that different patient cohorts have different experiences of the procedure. Patients with dementia experience significant discomfort, require more sedation and the procedure is longer. Patients with cerebrovascular accidents tolerate the procedure far better, experiencing less discomfort ($p<0.001$) and require less sedation compared to the other cohorts. We theorise that the underlying reasons may be a result of oropharngeal paresthesia and strongly supports its continuing use for this indication. Patients who have PEGs performed for other indications may warrant higher doses of sedation to improve patient tolerability.

Disclosure of Interest: None Declared
Keywords: Discomfort, Percutaneous endoscopic cecostomy

P1682 PREDICTIVE FACTORS FOR ENTERAL NUTRITION IN PATIENTS RECEIVING NEOADJUVANT CHEMORADIOTHERAPY FOR LOCALLY ADVANCED OESOPHAGEAL CARCINOMA.

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INTRODUCTION: Dysphagia and weight loss are the two major symptoms of oesophageal cancer. Neoadjuvant treatment with chemoradiotherapy (CRT) for locally advanced oesophageal cancer could further aggravate these symptoms and potentially jeopardize nutritional status. As poor nutritional status is associated with an increased risk for peroperative morbidity and mortality, early nutritional support is warranted. The aim of this study is to identify predictive factors for starting enteral nutrition in these patients.

AIMS&METHODS: Data were retrospectively collected from medical records of all consecutive patients who were treated with the same course of neoadjuvant CRT for locally advanced oesophageal cancer in our hospital between April 2009 and October 2012. Univariate and multivariate logistic regression analysis were performed to determine significant associations between patient parameters and the overall use of enteral nutrition as well as the use of enteral nutrition after the start of CRT ('reactive enteral nutrition'). Tested parameters were age, gender, ASA-score, dysphagia, smoking, alcohol use, tumour histology, tumour location, cTNM stage, tumour stricture diameter of <10mm. Only parameters with a p-value of <0.1 in the univariate analysis were used in the multivariate model.

RESULTS: A total of 255 patients (mean age 63 ± 8.9, 193 males [76%], 197 adenocarcinoma [77%], 57 squamous cell carcinoma [22%]) were included, of which 76 (29.8%) received enteral nutrition. For the overall use of enteral nutrition, univariate analysis showed significant associations ($p<0.1$) for dysphagia, squamous cell carcinoma, tumour length and a tumour stricture diameter of <10mm. After multivariate analysis, a tumour stricture diameter of <10mm appeared to be the only significant predictor (OR 4.96 [95% CI 2.49-9.87]) for the overall use of enteral nutrition. Cigarette smoking was the only parameter significantly associated with the start of 'reactive enteral nutrition' in univariate analysis (OR 1.93 [95% CI 1.02-3.648]). Therefore no multivariate analysis was performed for 'reactive enteral nutrition'.

CONCLUSION: This study demonstrates that a tumour stricture diameter of <10mm is the only objective predictor for the need of enteral nutrition in patients with locally advanced oesophageal cancer during neoadjuvant CRT. This predictor may be helpful in avoiding a delay in the start of enteral nutrition in high risk patients.

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Disclosure of Interest: None Declared
Keywords: Enteral Nutrition, Neoadjuvant chemoradiation, Oesophageal carcinoma, Predictive factors

P1683 ENDOSCOPIC OR RADIOLOGICALLY PLACED GASTROJEJUNOSTOMIES IN HIGH-RISK PATIENTS: A RANDOMISED STUDY

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INTRODUCTION: In patients at risk of aspiration pneumonia due to gastro-oesophageal reflux who require gastrojejunostomy feeding tubes, the tubes are placed either radiologically (RIGJ) or endoscopicaly (PEGJ). There is little published evidence to inform which is superior.

AIMS&METHODS: Consecutive patients referred for long-term jejunal feeding because of high risk of aspiration pneumonia (proven GORD or pneumonia whilst being NG fed) were randomly allocated to have a RIGJ or PEGJ inserted. A Tc^{99m} colloid study was done to determine the presence of gastro-oesophageal reflux and jejunal gastric reflux after feeding tube placement. We recorded pneumonia, death, feeding tube displacement, blockage and replacement to 90 days post placement.

RESULTS: 65 patients were randomised, 31 RIGJ and 34 PEGJ. Baseline characteristics including Barthell index were similar between groups. GORD was demonstrated by Tc99m tracer injected intragastrically in 52% but in no patient when injected jejunally.

Jejunal feeding tube and clinical complications (number)

	RIGJ n=31			PEGJ n=34		
*p<0.05	**30days**	**30-90days**	**Total**	**30days**	**30-90days**	**Total**
Jejunal tube fallen out of position	0	0	**0**	7	2	**9***
Jejunal tube irreversibly blocked	3	0	**3**	3	2	**5**
Jejunal tube replaced	2	0	**2**	5	3	**8**
Blockage cleared by patient/carer	8	4	**12**	22	12	**34***
Blockage cleared by community H/C	2	2	**4**	8	3	**11**
Blockage cleared in hospital	3	0	**3**	10	5	**15***
Further Pneumonia	2	1	**3**	2	3	**5**
Death	2	2	**4**	2	1	**3**

CONCLUSION: There was little difference in clinical outcomes between RIGJ *vs* PEGJ tubes for feeding patients at high risk of pneumonia. However, RIGJ tubes were considerably less prone to blockage and displacement than PEGJ tubes. Tube blockage was a major cause of frustration for patients and resource use for health care services. Replacing enteral tubes in frail patients was distressing and a significant use of health care resource. Consideration should be given to placing RIGJ in preference to PEGJ tubes.

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Disclosure of Interest: None Declared
Keywords: Enteral, Gastrojejunostomy, pneumonia

P1684 FOOD PREFERENCE AND TASTE CHANGES AFTER GASTROINTESTINAL SURGERY

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INTRODUCTION: Early postoperative nutrition is of clinical benefit. However, patients are often initially reluctant to eat after surgery. Dysguesia and alterations in food preference are often reported. We conducted a study to describe perioperative changes in taste and food preference with a view to being able to optimise food choices and thus improve intake.

AIMS&METHODS: Consecutive patients undergoing colorectal surgery were recruited. Three sets of tests were conducted, pre-operatively and on post-operative days (POD) 1, 2 and 3. In Test 1, patients were asked to rate the palatability (Horrible-Nice, using Likert scales (0-100%)) of a neutral flavoured nutritional supplement flavoured with 'standard' concentrations of the 6 core tastes (sweet, sour, salt, bitter, spicy and savoury). In Test 2, patients were shown photos of foods representative of the core tastes and asked to rate them in terms of appeal as in Test 1. Test 3 comprised provision of a snack box containing representative foods of the core tastes which patients were asked to rate as before. Differences from baseline were assessed using t-tests.

RESULTS: 31 patients completed the study, M:F=21:10, median age of 72 (33-82). Test 1, enhanced taste from baseline was seen on POD1 ($p<0.01$) for salty, sweat & spicy taste.

....Day.of.test....	Taste Test				Photographs			
	Salty	Sweat	Spicy	Savoury	Salty	Sweat	Spicy	Savoury
Baseline reading	27	48	48	47	29	34	40	54
% change POD 1	+58%*	+18%*	+20%*	+8%	+33%*	+3%	-30%	-30%
% change POD 2	+53%*	+14%*	+4%	+7%	+4%	-1%	-32%	-28%
% change POD 3	+48%*	+11%	-3%	0	-1%	-1%	-21%	-12%

POD=Post Operative Day, Increased score from baseline $p<0.01$

Test 2, only salty food (popcorn) scored higher ($p<0.01$) than baseline (figure 2) all other foods scored lower. Foods representing bitter and sour exhibited the greatest decline (40.4% for gherkins, 38.7% for grapefruit). Test 3, patients rated sweat (fudge) 63%, salty (crackers) 50% best at POD 1 ($p<0.01$) and sour (gherkins) 22%, spicy (Bombay mix) 16% worst. With all 3 Tests, scores reverted to baseline by POD 3.

CONCLUSION: After surgery patients rated sweat and salty snack foods greatest. This was confirmed by tests of palatability and appeal. Though while spicy and savoury palability tests scored highly patients did not find the snakes particularly desirable. Further work is required to explore patients food preferences post surgery.

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Keywords: Colorectal surgery, Taste

P1685 SAFETY OF GASTROSTOMY FEEDING TUBE PLACEMENT IN PATIENTS WITH VENTRICULO-PERITONEAL SHUNTS INSITU

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INTRODUCTION: Gastrotomy feeding tubes placed in patients with ventriculo-peritoneal (VP) shunts are thought to be more susceptible to infection of the ventriculo-peritoneal shunt, At the Royal free hospital we have placed 7 gastrostomy feeding tubes over a 3 year period in patients with VP shunts.
AIMS&METHODS: We carried out a retrospective chart review of all patients in the Royal Free hospital with VP shunts having Percutaneous Endoscopic Gastrostomy (PEG) tubes placemented between 2010 and 2012. We assessed timing of PEG insertion in relation to VP shunt placement, the use of prophylactic antibiotics, general complications, specific complication of shunt infection/meningitis and 30 day mortality.
RESULTS: Between 2010 and 2012 we identified 7 patients in our institution with VP shunts who attended for PEG insertion. No PEG tubes were inserted within 1 month of VP shunt placement.
In one case the endoscopist was unable to site the tube endoscopically and the procedure was converted to a surgical gastrostomy. There were no complications associated with any of the procedures and specifically there were no episodes of shunt infection or meningitis. 30 day mortality was 0%. All patients received prophylactic antibiotics.
CONCLUSION: In our series of PEG insertions in patients with VP shunts in situ there was no increased risk in complications and no episodes of shunt infection/meningitis. In this small series this is compatible with the published rate of VP shunt infection of around 5% and suggests that in patients requiring long term enteral nutritional support the presence of a VP shunt should not be considered a contraindication to PEG insertion.
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Keywords: Gastrostomy, percutaneous endoscopic gastrostomy, SHUNT, VENTRICULO-PERITONEAL SHUNT

P1686 PREDICTIVE LABORATORY FACTORS OF EARLY DEATH AFTER PERCUTANEOUS ENDSCOPIC GASTROSTOMY

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INTRODUCTION: Percutaneous endoscopic gastrostomy (PEG) is an accepted method to enable enteral feeding in patients with swallowing difficulties. However, complications and early death are considerably prevalent after PEG. To decrease early mortality after PEG, it is very important to definite risk factors of this procedure.
AIMS&METHODS: The aim of our study was to clarify laboratory factors that could predict early death within 30 days following the PEG procedure. A retrospective analysis of all patients who underwent PEG at Kure Medical Center and Chugoku Cancer Center from April 2008 to January 2012 were performed. We examined clinical date and preoperative laboratory date and extracted predictive factors of early death after PEG using univariate and multivariate analyses.
RESULTS: A total of 544 patients [253 female (46.5%) and 291 male (53.5%); mean age 78 y.o.] were assessed. Cerebral vascular disorder was the most common primary disease (176 of 544, 32%). The 30-day mortality rate following the PEG procedure was 5.3% (29 of 544), and pneumonia was the most common cause of death (10 of 29, 34%). Multivariate analysis on predictive laboratory factors of early death revealed a significant correlation between values of C-reactive protein and blood urea nitrogen and early death.
CONCLUSION: The values of C-reactive protein and blood urea nitrogen may be useful predictive laboratory factors for early death after PEG. To avoid early death after PEG, it is necessary to assess these factors and provide some treatment against inflammation and dehydration before PEG.
Disclosure of Interest: None Declared
Keywords: mortality, Percutaneous endoscopic gastrostomy