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Abstracts

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Abstracts

22nd National Congress of Digestive Diseases, Italian Federation of Societies of Digestive Diseases – FISMAD Naples, 24–27 February 2016

Plenary sessions

PC.01 Plenary Session

PC.01.1

MANAGEMENT OF BILIARY ANASTOMOTIC STRICTURE AFTER LIVER TRANSPLANTATION (BASALT STUDY): RESULTS OF A NATIONAL SURVEY IN ITALY

Cantù P.^{*21}, Parzanese I.²¹, Balassone V.¹, Di Sario A.², Soggiu F.³, Lombardi G.⁴, Barbaro F.⁶, Pisani A.⁷, Baldan A.⁸, Cariani G.⁹, Boarino V.¹⁰, Fasoli A.¹¹, Bertani H.¹², Forti E.¹³, Bulajic M.¹⁴, Ghinolfi D.¹⁵, Nadal E.¹⁶, Cerofolini A.¹⁷, Barresi L.¹⁸, Stroppa I.¹, Mazzaferro V.³, Cipolletta L.⁴, Tringali A.⁶, Costamagna G.⁵, Ravelli P.¹⁹, Bazzoli F.⁹, Merighi A.¹⁰, Parodi M.C.¹¹, Conigliaro R.¹², Mutignani M.¹³, Zilli M.¹⁴, Filipponi F.¹⁵, Fantin A.¹⁶, Rodella L.¹⁷, Traina M.¹⁸, Rotondano G.²⁰, Rosa R.²¹, Malinverno F.²², Donato F.²², Colombo M.²², Conte D.²¹, Rossi G.²³, Penagini R.²¹

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Background and aim: An International Consensus on management of biliary anastomotic stricture (AS) after liver transplantation (LT) still lacks. Aim was to retrospectively report the overall workload and to give a picture of the management of AS after LT in Italy.

Material and methods: A questionnaire was sent to the Endoscopy Units working with the 21 Italian Liver Transplantation Centers. The questionnaire was composed of 5 topics including: 1. annual workload (year 2013), 2. selection criteria (clinical, biochemical, radiological) for endotherapy, 3. criteria to confirm the presence of AS, 4. type of endotherapy, 5. treatment of recurrent AS.

Results: Eighteen of the 21 Units returned the questionnaire.

1. Twelve out seventeen are high volume (> 250 ERCPs/year) Units. During 2013, 170 of 705 (23%) liver transplanted pts underwent endotherapy for AS. 319 (5.4%) out of a total of 5886 ERCPs (median/Centre 13, range 5-60) were performed. Interventional radiology or surgery was used in 3.5% and 2.4% of patients after unsuccessful ERCP. In 5.6% of cases interventional radiology was preferred as first-line treatment. In seven out of seventeen Units biliary complications after hepatico-jejunal anastomosis were approached by enteroscopy. 2. In 83% of the Units selection criteria for ERCP included alteration of liver tests associated with AS documented at non-invasive imagings; biliary obstructive symptoms were additionally required in the others. Trend of liver tests was considered in 83%; Magnetic Resonance (MR) or T-tube cholangiography was used in 89%. 3. There was no consensus on operative criteria to confirm AS during ERCP.

4. AS was treated by fully covered metal stent (SEMS) or plastic multistenting (PM) in 6 Centers, PM only in 9 and single plastic stenting in one. Use of fully covered SEMS was independent of the overall ERCP workload of the Units. Fully covered SEMS were used only transpapillary, being removed after three (25%) or six

(75%) months. PM was planned at three months interval or at stent dysfunction in 94% of the Units. During PM, removal of all stents at each procedure and progressive increase of stents was the preferred option, using short guidewire technique in 35% of Centers. Duration of endotherapy was planned until radiological resolution of the stricture in the majority of the Centers. During follow-up MR cholangiography at three or six months was generally used.

5. Recurrent AS was treated endoscopically in 83% of Centers, by PM in 44% or crossing-over endotherapies in 28%, i.e. PM if fully covered SEMS failed as first line treatment or viceversa.

Conclusions: In Italy, most Endoscopic Units which Liver Transplantation Centers refer to are high volume ones and the workload dedicated to AS is substantial. Selection criteria for endotherapy are homogeneous among Centers. Progressive plastic multistenting is the preferred option for first and second line endoscopic treatment although use of fully covered SEMS is not negligible.

PC.01.2

PREDICTIVE VALUE OF THE “DICA” ENDOSCOPIC CLASSIFICATION ON THE OUTCOME OF THE DIVERTICULAR DISEASE OF THE COLON: AN INTERNATIONAL STUDY

Tursi A.^{*1}, Brandimarte G.², Di Mario F.³, Annunziata M.L.⁴, Bafutto M.⁵, Bianco M.A.⁶, Colucci R.⁷, Conigliaro R.⁸, Danese S.⁹, De Bastiani R.¹⁰, Elisei W.¹¹, Escalante R.¹², Faggiani R.¹³, Ferrini L.¹⁴, Forti G.¹⁵, Latella G.¹⁶, Graziani M.G.¹⁷, Oliveira E.¹⁸, Papa A.¹⁹, Penna A.²⁰, Portincasa P.²¹, Søreide K.²², Spadaccini A.²³, Usai P.²⁴, Zampalenta C.¹³, Cassieri C.², Desserud K.F.²², Di Cesare L.², Fiorella S.²³, Landi R.¹⁹, Lecca P.G.², Goni E.³, Lai M.A.²⁴, Pigò F.⁸, Rotondano G.⁶, Schiaccianocce G.²¹, Scarpignato C.²⁵, Picchio M.²⁶

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Background and aim: The endoscopic classification DICA (Diverticular Inflammation and Complication Assessment) has been recently developed for patients suffering from diverticulosis and

diverticular disease. The aim of this study was to assess its predictive value on the outcome of the disease.

Material and methods: We reassessed retrospectively patients in whom endoscopic videos and/or photos and clinical follow-up were available. For each patient, we recorded: age at the time of disease occurrence; severity of DICA (grade 1, 2 or 3) at the time of diagnosis; months of follow-up; therapy taken during the follow-up; occurrence/recurrence (in months) of diverticulitis.

Results: The study enrolled 1651 patients (793 M, 858 F, mean age 66.6 ± 11.1 years): 939 (56.9%) patients were classified as DICA 1, 501 (30.3%) as DICA 2 and 211 (12.8%) as DICA 3. The mean follow-up was 29.5 ± 28.7 months. Acute diverticulitis (AD) occurred/recurred in 263 (15.95) patients; surgery was necessary in 57 (21.7%) of those cases.

DICA was the only factor significantly associated to the occurrence of diverticulitis (p < 0.0001) and surgery (p < 0.0001) either at univariate or multivariate analysis. At each level of DICA classification a significant increase of diverticulitis occurrence was detected (hazard ratio (95% CI): DICA 1 vs DICA 3: 18.992 (12.267 to 29.406); p < 0.0001) (figure).

Therapy with various regimens was taken by 869 (52.6%) patients during the follow-up. With respect to prevention of occurrence/recurrence of diverticulitis, assumption of therapy was effective only in DICA 2 patients with HR (95% CI) of 1.796 (p = 0.002). In those patients, therapeutic regimens including mesalazine were the only effective therapies to reduce diverticulitis occurrence/recurrence compared to no therapy (HR (95% CI) vs no therapy: 0.2103 (0.122 to 0.364), p < 0.0001).

Conclusions: DICA classification is a valid parameter to predict the risk of diverticulitis occurrence/recurrence in patients suffering from diverticular disease of the colon.

PC.01.3

KNOCKDOWN OF SMAD7 WITH MONGERSEN ATTENUATES COLITIS AND COLITIS-DRIVEN FIBROSIS IN MICE

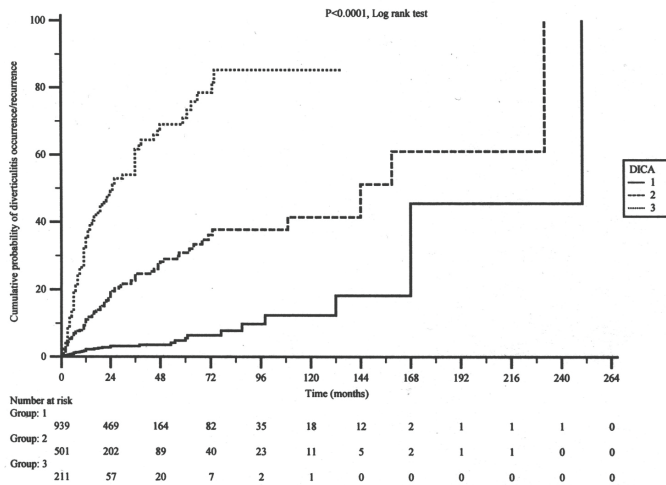
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Background and aim: In Crohn’s disease (CD), tissue-damaging immune response is associated with high Smad7, an inhibitor of TGF-β1 signaling. Smad7 inhibition with Mongersen, a specific antisense oligonucleotide, restores endogenous TGF-β1 activity leading to inhibition of inflammatory signals and associates with clinical benefit in CD patients. Since TGF-β1 is pro-fibrogenic, it remains unclear whether Mongersen-induced Smad7 inhibition increases risk of intestinal fibrosis.

Aim: To assess the impact of Smad7 inhibition by Mongersen on the course of colitis-driven intestinal fibrosis in mice.

Material and methods: Chronic colitis-driven fibrosis was induced in BALB/c female mice by rectal administration of increasing doses of trinitrobenzene sulfonic acid (TNBS). Mice were given TNBS once a week for 7 weeks. At week 4, a time-point in which mucosal inflammation stimulates collagen deposition, Mongersen or control oligonucleotide were administered to mice by oral gavage every 48 hours until week 7. At the end, colonic samples were taken for histologic examination, total RNA and protein extraction.

Results: TNBS-induced chronic colitis was associated with enhanced expression Smad7, diminished TGF-β1-associated Smad2/3 phosphorylation (p) and elevated levels of TGF-β1 RNA transcripts. As expected mice treated with TNBS exhibited colonic deposition of collagen I and fibrosis. Knockdown of Smad7 with Mongersen reduced colitis, deposition of collagen and attenuated fibrosis development. Interestingly, these findings were associated with diminished expression of both TGF-β1 RNA and p-Smad2/3.



Conclusions: Data indicate that Mongersen ameliorates chronic colitis and limits the occurrence of intestinal fibrosis.

PC.01.4

PERIBILIARY GLANDS AS A NICHE OF EXTRA-PANCREATIC INSULIN-PRODUCING AND GLUCOSE-SENSITIVE CELLS

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Background and aim: Peribiliary glands contain a niche of heterogeneous endodermal stem/progenitor cells that can differentiate, in vitro and in vivo, towards pancreatic islets. Whether these cells play a role in insulin production in diabetes is unknown. The aim of this study was to evaluate, in experimental diabetes, proliferation of peribiliary glands and differentiation of biliary tree stem/progenitor cells towards insulin-producing cells.

Material and methods: Diabetes was generated in mice by intraperitoneal injection of a single dose of 200 mg/kg (N=12) or 120 mg/kg (N=12) of streptozotocin. Liver, pancreas and extrahepatic biliary trees were en bloc dissected and examined by Light Microscopy and Immunohistochemistry, and RT-PCR analysis. Moreover human biliary tree stem/progenitor cells (hBTSCs) isolated from peribiliary glands of liver donors (N=5) have been challenged in culture with high glucose concentration for 14 days and thereafter analyzed by RT-PCR and immunofluorescence.

Results: Peribiliary glands proliferated in experimental induced diabetes. Their proliferation was greatest at the hepato-pancreatic ampulla and inversely correlated with pancreatic islet area. Peribiliary glands proliferation was characterized by the expansion of Sox9-positive stem/progenitor cells that gave rise to insulin-producing cells. Insulin producing cells were mostly located in the portion of the biliary tree closest to the duodenum, and their appearance was associated with the up-regulation of MafA and Gli1 gene expression.

The culturing of hBTSCs under high glucose concentration for 14 days, determined the increase of the gene expression of Ngn3, MafA and Insulin, and the appearance of islet-like structures composed of densely packed insulin-positive cells.

Conclusions: Peribiliary glands and associated stem/progenitor cells respond to diabetes with proliferation and differentiation towards insulin-producing cells. Peribiliary gland niche may rescue the pancreatic islet impairment in diabetes with important implications for the patho-physiology and complications of this disease.

PC.01.5

A NEW SUB-CLASSIFICATION OF ESOPHAGO-GASTRIC JUNCTION MORPHOLOGY TYPE I HELPS TO BETTER RECOGNIZE PATIENTS WITH A POSITIVE IMPEDANCE-PH MONITORING

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Background and aim: High-resolution manometry (HRM) provides information on esophagogastric junction (EGJ) morphology, being able to distinguish whether the lower esophageal sphincter (LES) and crural diaphragm (CD) are superimposed or separated. Actually, three different subtypes can be described by means of HRM, and it was recently demonstrated that increasing separation between LES and CD could cause a gradual and significant increase of reflux. Type I morphology is the group with the lowest incidence of a positive impedance-pH test. We aimed to verify if a new sub-classification of the EGJ Type I could better correlate with a positive impedance-pH test in patients with reflux symptoms.

Material and methods: Consecutive patients with suspected GERD were enrolled. All patients underwent HRM and impedance-pH testing off-therapy. EGJ was classified as: Type I, no separation between the LES and CD; Type II, minimal separation (>1 and <2 cm); Type III, ≥2 cm separation. Only patients with EGJ Type I were enrolled in the study. EGJ Type I was further divided into Type IA, a complete overlap of LES and CD (with a minimum presence of intra-abdominal LES segment), and Type IB, a minimal separation, with LES located from the upper border of CD (in correspondence of pressure inversion point, 0.0 cm) to 1 cm above. We measured esophageal acid exposure time (AET), number of total reflux episodes and symptom association analysis by means of impedance pH monitoring.

Results: We enrolled 130 consecutive patients and identified 60 (46.2%) patients with Type I EGJ. Overall, Type I subjects showed a positive MII-pH in 50% of cases, with 25 median number of reflux episodes, a 1.5% mean AET and a 43.3% of positive symptom association. Using the sub-classification, we identified 23 (38.3%) Type IA and 37 (61.7%) Type IB subjects. Type IB had a higher number of reflux episodes (38 vs. 18, p<0.03), a greater mean AET (3.2 vs. 0.9, p<0.05) and a greater positive symptom association (54% vs. 26%, p<0.02) compared to Type IA. Type IB morphology had a more frequent probability to show a positive MII-pH than Type IA (62.1% vs. 30%, p<0.001).

Conclusions: This simple new sub-classification of EGJ Type I can be useful to better estimate an abnormal impedance-pH testing in GERD patients and it supports the role of the intra-abdominal LES segment in preventing reflux.

PC.01.6**RISK FACTORS FOR THE OCCURRENCE OF SPORADIC PANCREATIC NEUROENDOCRINE TUMOURS: A MULTICENTER EUROPEAN STUDY (EPINET)**

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Background and aim: Pancreatic neuroendocrine tumors (PNETs) are rare neoplasms, but their incidence is rising and the prevalence, due to long survival, is much higher. Few, unicentre, small studies investigated potential demographic-environmental risk factors; none of those the role of obesity (BMI>30). Diabetes, smoking and alcohol have been suggested as risk factors. **Aim:** To determine risk factors for the development of sporadic PNETs.

Material and methods: Prospective case-control study performed in five European countries. Histologically proved sporadic PNETs and sex-age matched controls (3:1 ratio, based on a power calculation) were interviewed about demographics, environmental and familial risk factors using a pre-definite questionnaire. Cases and controls were compared by Fisher's test or Chi square tests, risk factors analyzed by logistic regression analysis.

Results: 196 cases and 570 controls were collected. 1st degree family history of any cancer (51% vs 46%; $p=0.2$) nor cancer site specific family history, smoking (56% vs 50% $p=0.18$) and alcohol drinking (76.5% vs 70% $p=0.09$) were not associated with risk of PNETs. Obesity (26% vs 19%; $p=0.04$) and diabetes (18% vs 12%; $p=0.05$) were the only factors significantly more frequent in cases than in controls. In a logistic regression analysis, obesity (OR 1.5; 95% CI 1-2.2) and diabetes (OR 1.5; 95% CI 1-2.4), were both associated with a significantly increased risk. Previous medical history, the use of drugs and for women reproductive factors were also not associated with PNET risk.

Conclusions: This is the first prospective multicentre study investigating risk factors for the occurrence of PNETs. Among previously reported risk factors, only diabetes was confirmed in this study, while the role of obesity is suggested for the first time.

PC.01.7**EUROPEAN COLONOSCOPY QUALITY INVESTIGATION GROUP: IMPROVING STANDARDS IN COLONOSCOPY THROUGH A PRACTICE LEVEL AUDIT TOOL**

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Background and aim: Colorectal cancer is a major cause of morbidity and mortality. Colonoscopy remains the investigation of choice for diagnosis and screening. Many countries have implemented screening programmes to allow for early detection.

The ESGE quality in colonoscopy position statement highlights key quality indicators in colonoscopy and concluded that the success of screening programmes is related to the prompt provision of high quality, patient centred colonoscopy service. The European Colonoscopy Quality Investigation (ECQI) group of leading European clinicians developed a practical tool to enable audit of current clinical practice across Europe to assess whether quality standards are being achieved and to identify, test, and implement practical ways of improving quality in colonoscopy. The aim was to understand how quality is evaluated in current clinical practice via the development and implementation of an online tool to audit colonoscopy practice.

Material and methods: At the inaugural meeting in 2013, the ECQI group recommended a clinical practice level audit tool to be developed to enable colonoscopists to audit their own practice. The audit tool was designed to encourage improvement in outcomes (e.g. adenoma detection rate), and to ensure consistency and high standards across clinical practice, within countries and across Europe, and was validated by the group in September 2014. A phase 1 pilot to test this tool was performed in November 2014, with early outputs discussed by the group in December 2014. The audit tool was further revised to improve usability via a collaborative iteration process.

Results: The online audit tool was piloted at centres across 10 European countries with 313 patient visits recorded on the initial questionnaire during a 1 week period. Questions included: patient demographics, the status and experience of the practitioner performing the endoscopy, details of the bowel preparation procedure used and the quality of bowel cleansing achieved, colonoscopic findings, and follow up arrangements. Following the review of the phase 1 pilot, consensus from the ECQI group resulted in the refinement of the tool to create an updated version which included three separate sections: Practitioner, Centre and Patient level questionnaires to improve efficiency of use. This will form part of a second phase pilot planned for 2015.

Conclusions: ECQI Group enabled the development of a validated, practice level audit tool to enable clinicians to audit their own practice. This tool will be tested in a second pilot phase, and its value will be further evaluated by the Group in order to make recommendations for its use across Europe. The range of experience and geographical spread of the participants allows for quality evaluation to be compared across practices and countries. The longer term aim of this project is to enhance the quality of colonoscopy at a practice level by enabling clinicians to be involved in improving their own practice.

PC.01.8**SERUM DETERMINATION OF SQUAMOUS CELLULAR CARCINOMA ANTIGEN AS A BIOMARKER OF BARRETT'S ESOPHAGUS AND ESOPHAGEAL CANCER: A PHASE III STUDY**

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Background and aim: The cost/effectiveness of surveillance in patients with Barrett's esophagus (BE) is still debated and the use of biomarkers in screening and surveillance not recommended. Squamous Cell Carcinoma Antigen is expressed in several epithelial tumors but no information is available regarding SCCA-IgM determination in BE. The study aimed at evaluating the potential role of the determination of the immunocomplexed Squamous Cell Carcinoma Antigen (SCCA-IgM) in screening for BE and in surveillance for esophageal adenocarcinoma (EAC).

Material and methods: SCCA-IgM levels were determined (ELISA, Hepa-Ic, Xeptagen, Marghera, Venezia, Italy) in 213 patients prospectively recruited in our Department among whom 53 with

BE, 53 with EAC and 107 controls, including 42 blood donors and 65 patients with gastroesophageal reflux but with no endoscopic/histologic diagnosis of BE (GERD). The cut-off levels for the determination of SCCA-IgM for BE/EAC versus controls and for Barrett “at risk” (long and/or dysplastic BE) versus BE “at low risk” (short non-dysplastic BE) were calculated by ROC curves. Statistics also included Kolmogorov-Smirnov, Kruskal-Wallis, Mann-Whitney and chi square tests. Immuno-staining for SCCA-IgM was obtained in a subgroup of 75 patients (Hepa-Ab, Xeptagen).

Results: Median SCCA-IgM values were significantly higher in BE and EAC patients than in GERD ($p < 0.0001$). Patients with SCCA-IgM levels higher than the cut-off calculated on the basis of a ROC curve (56.6 AU/mL, 91.5% sensitivity, 75.4% specificity, positive predictive value [PPV] 85.8%, negative predictive value [NPV] 84.4%, AUC of

0.799) had a 33 times higher Relative Risk (RR) of harboring BE or EAC ($p = 0.0001$). BE patients “at risk” (long and/or dysplastic BE) had SCCA-IgM levels significantly higher than those with short non-dysplastic BE ($p = 0.035$) and patients with SCCA-IgM above the calculated cut-off (78.5 AU/mL, sensitivity 85%, specificity 54%, PPV=68%, NPV=76%, AUC=0.67) had a 15 times higher RR of having Barrett “at risk”. SCCA was expressed in the proliferative compartment of BE mucosa in 66% of the cases and in cardiac-type gastric metaplasia only in 15% ($p = 0.003$).

Conclusions: Serum SCCA-IgM determination allows the identification of patients at risk for Barrett’s esophagus and esophageal adenocarcinoma and the stratification of Barrett patients in subgroups with increasing cancer risk. Large, prospective studies are required to confirm this evidence in stage IV biomarker studies.

Oral Communications

OC.01 Endoscopy 1

OC.01.1

THE VALUE OF CONTRAST ENHANCED ENDOSCOPIC ULTRASOUND IN THE FINE NEEDLE ASPIRATION

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Background and aim: *Background:* The diagnosis of pancreatic neoplasia can be reached with endoscopic ultrasound-fine needle aspiration (EUS-FNA) that allows pancreatic tissue sampling. However EUS-FNA is associated with a high risk of false-negative or nondiagnostic results mainly due to inadequate biopsy specimens. Contrast-enhanced harmonic endoscopic ultrasound (CH-EUS) consists of an ultrasound scan performed after the infusion of microbubbles of sulfur hexafluoride stabilized by a lipid monolayer membrane (Sonovue®, Bracco, Italy) about one third of a Red Blood Cell in size that produce a Doppler signal in the microvasculature and are not absorbed by the parenchymal cell. With Sonovue an accurate image of the vascular pattern of the pancreatic parenchyma may be achieved without the artifacts of the classical Doppler EUS and small lesions may be better identified.

Aims: To evaluate whether the use of CH-EUS allows an improvement in the identification of pancreatic masses in order to increase the diagnostic yield of the EUS-FNA.

Material and methods: A total of 29 patients with pancreatic solid lesions were enrolled in the study. Nineteen patients underwent to EUS-FNA and 10 were studied with the same procedure preceded by of intravenous infusion Sonovue. All masses were punctured with a minimum number of 4 passes. The adequacy of biopsy specimens obtained by FNA was compared between the two groups.

Results: Of the 19 patients undergoing EUS-FNA, in 4 cases (21%) a non diagnostic cytology was obtained, while in 15 cases (79%) a definitive diagnosis could be defined. Eight patients (53%) has a cytologic diagnosis of malignancy and 7 (47%) of benign lesion. None of the 10 patients who underwent to FNA preceded by CH-EUS had an inadequate cytology for a definitive diagnosis. In all cases the biopsy sampling was adequate to allow a definitive diagnosis. In 6 patients (60%) a benign lesions was identified and in 4 (40%) a malignant mass diagnosed.

Conclusions: This study shows that a better view of the pancreatic lesions vascularity by means of CH-EUS allows locate the proper area for biopsy sampling improving the results of conventional EUS-FNA and the probability to reach definitive diagnosis.

OC.01.2

PRELIMINARY RESULTS OF MACROSCOPIC VISUAL ADEQUACY EVALUATION OF EUS-FNA SAMPLES

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Background and aim: The evaluation on site (ROSE) appears to have a significant impact on EUS-FNA success rate, but the presence of a cytopathologist during the procedure is not guaranteed in all the endoscopic centers. Macroscopic on-site evaluation (MOSE) was efficacy to estimate the adequacy of a core specimen for histologic diagnosis during EUS-FNA using a 19-G needle. Recently, increased adequacy of EUS-FNA was reported even when ROSE was performed

by an expert endosonographer (79% vs 97%). Aim of this study was to assess the relation of macroscopic visual adequacy (MVA) in the FNA specimens and the diagnostic yields.

Material and methods: A total of 17 patients, who underwent to EUS-FNA, were prospectively enrolled. Macroscopic visual adequacy (MVA) was performed evaluating each FNA pass in Cytorich®Red Preservative Fluid prepared for cell block study. MVA was assessed in terms of presence of blood (much, scant, absent or red, absent) or presence of clots), frustule >3 mm (short, long, whitish or red, absent) and fragments <3mm (representative, little representative, absent). EUS-FNA was performed with 22-or 25-G needle.

Results: There were 12 men and 5 women, 66±8.34 years old. Thirteen were pancreatic solid lesions and four lymphadenopathy. Median of needle passes was 3.7±0.85. When frustules or fragments were absent, sample was not adequate. Among 17 EUS-FNA, 63 needle passes were performed: 11 passes (18%) with 22-G and 52 passes (83%) with 25-G needle. 17.5% samples were inadequate on MVA and 14% were inadequate to the cytological diagnosis. 89% samples were adequate on MVA and to cytological diagnosis.

Conclusions: MVA can be an indicator of specimen adequacy and could help to reduce number of EUS-FNA passes.

OC.01.3

ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION, CELL-BLOCK APPROACH: EXPERIENCE IN A SINGLE CENTER

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Background and aim: Endoscopic ultrasound guided fine needle aspiration (EUS-FNA) represents a pivotal diagnostic adjunct for diagnosis of tumors of the gastrointestinal tract and of adjacent structures.

EUS-FNA achieves a correct diagnosis in the majority of cases, nevertheless cytological diagnosis may be missing due to the presence of necrotic tissue, inflammation, tissue contamination by mucosal cells or poor samples. European Society of Gastrointestinal Endoscopy published the guidelines for EUS guided sampling, which relies on factors involving the endoscopist and the cytopathologist (expertise, training and reciprocal interaction) as well as the lesion (size, site and echo-pattern).

It is reported in the literature that cell-block may increase the diagnostic yield of the procedure by preserving the tissue. In particular, it offers the possibility of multiple sections allowing, besides H&E staining, immunohistochemistry or molecular analysis. Our aim is to evaluate the diagnostic sensibility and specificity of EUS-FNA with cell-block tissue processing.

Material and methods: We included all consecutive patients undergoing EUS-FNA with cell-block procedure Between September 2014 and September 2015 in the Maggiore della Carità Hospital-Novara (Italy).

Standard EUS FNA needles (19-22-25 G) were used, without on site cytological evaluation.

Needle content was washed in lysing solution and centrifuged at 1,800g to prepare cell blocks; the pellet was congealed using human plasma and thrombin with buffered formalin fixation. Subsequently, paraffin-embedded cell blocks were prepared and sections obtained by cutting cell blocks. Transferred to glass slides sections were stained with H&E and investigated with immunohistochemical analysis when required to define the histotype. DNA extraction and appropriate molecular analysis were performed.

Adequacy and correct diagnosis were calculated on the base of surgical specimens, clinical and radiological follow-up.

The sensitivity, specificity and predictive values (PPV, NPV) were evaluated.

Results: 100 patients were enrolled (M: 49), 90 affected by primitive pancreatic tumour and 10 by non primitive lesions. Among the 90 primitive tumours 72 were ductal adenocarcinoma, 13 mass forming pancreatitis, 3 IPMN, 1 neuroendocrine carcinoma and one serous cystadenoma.

The H&E staining resulted inadequate in 26 cases (28.9%). After KRAS mutational analysis among 20/26 cytologic inadequate cases, the finding of a KRAS gene point mutation in 10 cases improved the cytological diagnosis in suspected lesions and the sensitivity of the procedure (PPV: 93.3%, NPV: 62.5%).

Conclusions: EUS-FNA procedure with cell-block approach allowed a correct diagnosis in most of the described cases. Cell-block method with adjunctive use of ancillary tests such as biomolecular analysis and immunohistochemical tests provides significant improvement to the diagnosis in uncertain cytological evaluations.

OC.01.4

EUS PREDICTIVE FACTORS OF RECURRENCE IN PATIENTS WITH LOCAL ADVANCED RECTAL CANCER

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Background and aim: Locally advanced rectal cancer (LARC) remains a poor outcome disease due to an high rate of pelvic and systemic recurrence with a negative impact on survival and quality of life of patients. Several pre-operative prognostic factors have been studied to select patients with more aggressive disease and high risk of recurrence. Few data are available regarding the rectal-endoscopic ultrasound (R-EUS) factors possible related to recurrence. The aim of this study was to identify R-EUS features of recurrence in patients with LARC treated with rectal excision after neoadjuvant therapy.

Material and methods: Consecutive patients with LARC who underwent neoadjuvant chemotherapy (NACT_RT) and rectal surgery were studied. Pre and postoperative clinical data were collected in an electronic database. Computer tomography (CT) and R-EUS were performed in all patients to stage the disease before (pre R-EUS) and after (post R-EUS) NACT_RT. Follow-up data on oncological outcome were retrieved from patient records. Several clinical and tumor related data were considered such as age, gender, morphology, distance from anal verge, pre and post-treatment stage, histological final stage, mucinous phenotype and grading tumor. During pre e post therapy R-EUS, we assessed: the morphology, the circumferential rectal wall involvement, the intraluminal tumor reduction and the residual circumferential rectal wall involvement. Factors related to recurrence were evaluated by univariate and multivariate analysis. Disease free survival was estimated using Kaplan-Meier curve.

Results: Seventy-four patients were evaluated, 52 male, median age 65,8 years (range 42-82 years). Recurrence was diagnosed in 18 of 74 patients, 7 of which had a local recurrence (9%) and 11 a systemic recurrence (14%). The one-year recurrence occurred in 6/74 patients (8%) whereas the remain 12/74 patients (16%) developed recurrence within the third year. Factors significantly related to recurrence on univariate analysis were the circumferential involvement evaluated both in the pre R-EUS than in the post R-EUS (respectively $p=0,0418$ and $p=0,0006$), the intraluminal reduction of the tumor after NACT_RT ($p=0,0075$), the post R-EUS staging according to TNM ($p=0,0237$ for N-parameter and $p=0,0329$ for T-parameter). As expected the final histological stage and the grading tumor proven to be related with high risk of recurrence (respectively $p=0,0032$ and $p=0,027$).

Conclusions: Our data suggest a possible role of restaging R-EUS in patients with LARC to identify a subgroup of subjects with a major risk of recurrence and may be used to plan different therapeutic and follow-up strategy to reduce the recurrence rate.

OC.01.5

ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) OF LARGE SUPERFICIAL COLORECTAL NEOPLASMS AT THE DENTATE LINE OR ILEOCECAL VALVE

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Background and aim: Conventional endoscopic snare resection of neoplasms at the low rectum is difficult due to the narrowness of the anal canal, pain sensibility, presence of hemorrhoids; whereas that of lesions at the ileocecal valve (ICV) due to the ICV itself, difficult delineation of the tumor border at the ileal mucosa, abundant fat tissue in the submucosa. Limited data exist for the endoscopic submucosal dissection (ESD) of these lesions.

Aim: To assess the efficacy and outcomes of ESD of superficial neoplasms in the low rectum and ICV.

Material and methods: Retrospective analysis of prospectively collected database in a single non academic Western center. From 1.2010 to 7.2015, all consecutive patients underwent ESD for a superficial neoplasm in the low rectum (within 10 mm from the dentate line) and over the ICV, and no deep SM invasion (defined by the Kudo pit pattern V and/or the Sano microcapillary pattern 3B) were included. ESD was performed with the standard technique. Follow-up was scheduled every 3 or 6 months after piecemeal or en bloc resection with negative lateral and vertical margins (R0), respectively. Biopsies were taken regardless the presence of residual tissue at chromoscopy.

Results: A total of 7 ICV neoplasms and 21 neoplasms in the low rectum underwent ESD (Table). Neoplasms in the low rectum involved the squamous epithelium of the anal canal for at least 50% of the circumference in 9 (43%) cases. A full involvement of the ICV lip was observed in 4 (57%) cases, and an extension into the distal ileum for a median length of 15 mm in 2 (29%) cases. Rectal ESDs were complicated by a delayed bleeding in 1 case. A curative resection (also comprising en bloc resections with positive lateral margins for adenoma without residues at follow-up) was achieved in 6 (86%) ICV and 14 (67%) rectal lesions. During the follow-up (median 12 months, range 12-32), a minute area of residual adenomatous tissue was resected in one (5%) patient underwent rectal ESD. An asymptomatic substenosis of the anal canal was observed at digital rectal examination in 2 cases.

	ICV (n.7)	Low rectum (n.21)
Size, mm (median, range)	44 (20-85)	48 (23-180)
Morphology, LST-G / NG	6 / 1	19 / 2
Scar presence	0	6 (29%)
ESD en bloc	6 (86%)	16 (76%)
ESD R0	3 (43%)	11 (52%)

Conclusions: ESD allows en bloc resection of large neoplasms of the ICV and the low rectum involving the squamous epithelium of the anal canal. However, the ESD en bloc R0 resection rate is low due to challenging technical and anatomical aspects that prevent to perform the mucosal incision far from tumor margins.

OC.01.6
UNDERWATER ENDOSCOPIC MUCOSAL RESECTION: THE THIRD WAY FOR EN BLOC RESECTION OF COLONIC LESIONS?

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Background and aim: Underwater endoscopic mucosal resection, without submucosal injection has been described for removing large flat colorectal lesions.
Aim of the study was to evaluate the reproducibility of this technique in terms of ease of implementation, safety and efficacy.
Material and methods: A prospective observational study of consecutive underwater endoscopic mucosal resection in a community hospital was performed.
Results: From September 2014 to April 2015, twenty-five flat or sessile colorectal lesions (median size 22.8 mm, range 10-50mm; 18 placed in the right colon) were removed in 25 patients. Two of the lesions were adenomatous recurrences on scar of prior resection and one was a recurrence on a surgical anastomosis. The resection was performed en bloc in 76% of the cases. At the pathological examination, 14 lesions (56%) had advanced histology and 7 (28%) were sessile serrated adenomas (two with high-grade dysplasia). Complete resection was observed in all the lesions removed en bloc. Intra-procedural bleeding was observed in two cases; both were managed endoscopically and were uneventful. No major adverse events occurred.
Conclusions: Underwater endoscopic mucosal resection appears to be an easy, safe and effective technique in a community setting. Further studies tacking the early and late recurrence of this technique as well as comparing it to traditional mucosal resection are warranted.

OC.01.7
ENDOSCOPIC MANAGEMENT OF PATIENTS WITH POST-SURGICAL LEAKS INVOLVING THE GASTROINTESTINAL TRACT. A LARGE CASE SERIES

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Background and aim: Post-surgical anastomotic leaks often require a reintervention, are associated with a definite morbidity and mortality, and with relevant costs. We described the endoscopic management in a large series of patients with different post-surgical leaks involving the GI tract.
Material and methods: This was a retrospective analysis of prospectively collected cases with anastomotic leaks managed with different endoscopic approaches in two endoscopic centres during 5 years. Interventions included: 1) overthe-scope clip (OTCS) positioning; 2) placement of a covered selfexpanding metal stent (SEMS); 3) fibrin glue injection (Tissucol); and 4) endo-sponge application, according to both the endoscopic feature and patient's status.
Results: A total of 76 patients underwent endoscopic treatment for an leak either in the upper (47 cases) or lower (29 cases) gastrointestinal tract, and the approach was successful in 39 (83%) and 22 (75.9%) patients, respectively, accounting for an overall 80.3% success rate. Fistula closure was achieved in 84.9% and 78.3% of patients managed by using a single or a combination of endoscopic

devices. Overall, leak closure failed in 15 (19.7%) patients, and the surgical approach was successful in all 14 patients who underwent re-intervention, whilst 1 patient died due to sepsis a 7 days.

Table 1
Outcome of fistula treatment according to devices used

Device used	Patients treated	Fistula closure (%)
OTSC	39	33 (84.6)
SEMS	7	5 (71.4)
Endo-sponge	7	7 (100)
OTSC + SEMS	21	17 (80.9)
OTSC + Tissucol	1	0
SEMS + Tissucol	1	1

Conclusions: Our data suggests that an endoscopic approach is successful and safe in the majority of patients with anastomotic GI leaks. Therefore, an endoscopic treatment could be attempted before resorting in more invasive, costly and risky re-intervention.

OC.01.8
SPLIT VS SAME-DAY REGIMES FOR BOWEL PREPARATION BEFORE COLONOSCOPY: A META-ANALYSIS OF PUBLISHED STUDIES

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Background and aim: An adequate colon cleansing is essential for a good quality colonoscopy and the split regimens (S) are actually considered the standard of care. However, 15-20% of patients still have an inadequate bowel cleansing after a split preparation. Recently a new regimen (same-day, SD) in which the purge is assumed the morning before the colonoscopy has been introduced, but published studies are underpowered and report controversial results. Therefore, our aim was to assess the colon cleansing rate of split vs. same-day regimens.
Material and methods: Published randomized clinical trials (1960-2015) comparing S vs. SD preparations in adults undergoing colonoscopy were selected using MEDLINE, the Cochrane Central Register of Controlled Trials, clinical trial.gov, ISI Web of Science. Search terms included bowel, preparation, colon, cleaning, colonoscopy, same-day and split. Rate difference (RD) of the degree of colon cleaning between split and same-day was the primary measure of treatment effect. Compliance (defined as the completion of at least > 75% of both doses of the purge) and presence of adverse events (nausea, vomiting, abdominal pain and abdominal discomfort) were

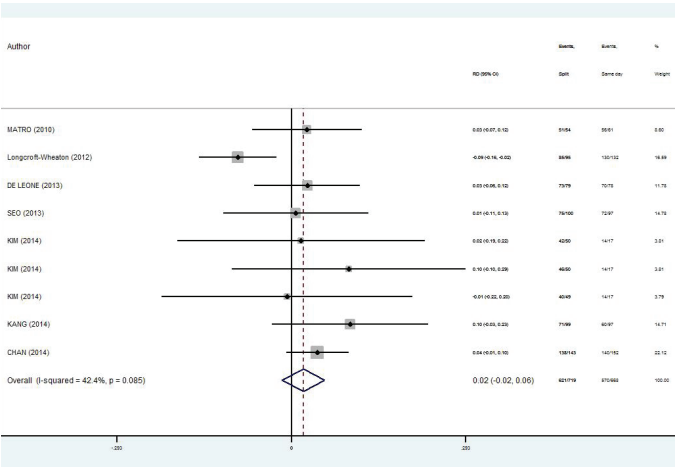


Fig. 1. Good or excellent grade of colon preparation prior colonoscopy pooled rate difference between split and same day regimen

secondary outcomes. Statistics: the meta-analyses were performed by computing RD using random-effects model, if heterogeneity was present. Egger's-Hardbord regression test was pre-defined statistical tests for publication bias assessment.

Results: From 122 initially screened abstracts, 11 full text studies were retrieved and a total of 12 treatment arms were analysed (1837 patients). Seven studies compared PEG vs. PEG, 1 sodium picosulfate vs sodium picosulfate, 1 sodium picosulfate vs. PEG and 3 PEG vs. sodium picosulfate. Overall, 88% (621/719) patients in the S group vs. 86% (570/688) in the SD group had an adequate bowel cleansing. Pooled RD was 2% [C.I.95% -1.6 to 5.6], heterogeneity chi-squared=13.88 (d.f.= 8) $p = 0.085$; I-squared (variation in RD attributable to heterogeneity)= 42.4%, $p = 0.280$, Fig.1]. In all but one studies, split preparation was more effective than SD. Also, patients were more compliant and had slightly less adverse events with the split preparations but significant heterogeneity was present.

Conclusions: Data shows that split preparations give a similar adequate colon preparation compared with same-day preparations and with a better compliance and less adverse events.

OC.01.9

OLGA-BASED STAGING AND DYSPLASIA RELEVANCE IN 50-70 YEARS OLD PATIENTS IN A PRIMARY OPEN ACCESS ENDOSCOPY: PRELIMINARY RESULTS

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Background and aim: Patients with gastric atrophy and intestinal metaplasia may have a greater than 10-fold increased risk of gastric cancer than the general population. A recent European consensus statement suggested that biopsies of the proximal and distal stomach are needed for adequate assessment of premalignant gastric conditions, and that systems for histopathological staging may be useful for identifying subgroups of patients with different risks of progression to gastric cancer (1). Operative link on gastritis assessment (OLGA) staging system was proposed for clinical purposes to simplify the assessment of gastric cancer. If low-grade dysplasia is detected a repeat surveillance gastroscopy with a topographic mapping biopsy strategy should be performed within 1 year.

Material and methods: Patients (age 50-70 years) undergoing upper endoscopy from September 2013 to September 2015 in our open access Endoscopy Service were enrolled. Biopsies from antrum (2), angulus (1), and corpus (2) were obtained in patients with normal endoscopy. Histological assessment according to OLGA and OLGIM staging was performed by two experienced gastrointestinal pathologists, who also evaluated *Helicobacter pylori* status. OLGA III/IV and pts with dysplasia were considered eligible for surveillance of these lesions.

Results: 2026 upper endoscopy were performed (female 61.3%). Biopsies were obtained from 1470 patients (F 1073 = 72.9% and M 397 = 27.1%). Eight patients presented with OLGA III stage (0.5%) and 5 with OLGA IV stage (0.34%). Furthermore, 2/8 pts with OLGA III stage and 1/5 with OLGA IV stage had low grade dysplasia without an endoscopic defined lesion; 1 patient with OLGA IV had low grade dysplasia with an endoscopic lesion represented by erosions and areas of scarring. *Helicobacter pylori* has been found in 5/13 pts with OLGA III/IV stage. One patient undergoing the endoscopic follow-up one year later presented the same OLGA IV stage without dysplasia.

Conclusions: In our population with dyspepsia and epigastric pain without significant lesions at upper endoscopy 0.84% of patients presented with an OLGA III/IV stage. Four of these patients had low grade dysplasia, one with a visible lesion. Follow-up of these lesions and cost-effectiveness of this strategy are ongoing.

Reference:

1. Dinis-Ribeiro M, Areia M, de Vries AC, et al. Management of precancerous conditions and lesions in the stomach (MAPS). Endoscopy 2012; 44: 74-94.

OC.02 IBD 1

OC.02.1

HIGH EXPRESSION OF DUBA, A REGULATOR OF T CELL ACTIVATION, IN INFLAMMATORY BOWEL DISEASE

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Background and aim: The Ubiquitinase DUBA belongs to a family of proteolytic enzymes whose function is to remove ubiquitin from target proteins or polyubiquitin chains, resulting in altered signaling or changes in protein stability. Control of ubiquitination is involved in many important biological processes as well as in cancer and inflammatory diseases. Since recent studies have shown the involvement of DUBA in T cell activation, we aimed at investigating the expression of DUBA in inflammatory bowel disease (IBD).

Material and methods: DUBA was silenced in normal peripheral blood mononuclear cell (PBMC) with a specific small interference RNA (siRNA) and transfected T-cells were then activated with anti-CD3/CD28 beads for further 24h. Pro-inflammatory cytokines (i.e. IL-17A, INF- γ) were evaluated by real-time PCR. DUBA expression was evaluated in inflamed biopsy samples of patients with ulcerative colitis (UC) and patients with Crohn's disease (CD), as well as in control biopsy samples and in the colons of mice with dextran-sulfate sodium (DSS)-induced colitis by real-time PCR, western blotting and immunohistochemistry.

Results: In vitro silencing of DUBA with a specific siRNA diminished production of IL-17A and INF- γ from anti-CD3/CD28-activated T cells, thus indicating a prominent role for DUBA in the positive control of pathogenic cytokine responses. High DUBA was seen in inflamed intestine of patients with UC and patients with CD as compared to normal controls. Consistently, induction of DSS-colitis in mice was accompanied by increased expression of DUBA at the protein but not RNA level. Immunohistochemical analysis revealed that both epithelial cells and lamina propria mononuclear cells expressed elevated levels of DUBA during colitis.

Conclusions: To the best of our knowledge this is the first to show a deregulated expression of DUBA during colitis. The DUBA-mediated positive control of effectors cytokine production suggests the involvement of DUBA in the progression of IBD.

OC.02.2

HUMAN NEUTROPHIL ELASTASE CONTRIBUTES TO LOSS OF FUNCTION OF INFLIXIMAB IN ULCERATIVE COLITIS

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Background and aim: Up to a third of patients with ulcerative colitis (UC) are primary non-responders to anti-tumor necrosis factor- α agents, which act in the UC protease-rich inflamed mucosa. Human neutrophil elastase (HNE) is a protease highly expressed in UC, whose main target in extracellular matrix is elastin, but the balance between HNE and its inhibitor elafin remains unclear. Our aims were to investigate the elastolytic activity in UC, and

determine if HNE degrades infliximab, rendering it ineffective, and if elafin can prevent these effects.

Material and methods: Perendoscopic intestinal biopsies were collected from the inflamed mucosa of 35 patients with UC, 29 patients with Crohn's disease (CD) and 30 control subjects. Elastolytic activity was determined by elastase activity assay, whereas elastin was assessed by van Gieson staining and ELISA. Elafin expression was evaluated by ELISA, immunoblotting and immunofluorescence. The effect of elafin on elastolytic activity of UC biopsies was investigated in vitro. After co-incubation with HNE, the integrity and the TNF-alpha neutralizing function of infliximab were studied by immunoblotting or using a nuclear factor-kB reporter cell line, respectively.

Results: Mucosal samples from inflamed areas of UC patients displayed significantly ($p < 0.05$) higher elastolytic activity and reduced elastin expression (mean 17.3 ng/mg, SEM 2.8) compared to CD (37.6 ng/mg, SEM 5.8) and control subjects (44.4 ng/mg, SEM 6.5). Levels of elafin were paradoxically increased in UC in comparison to control subjects and, to a lesser extent, to CD. However, addition of elafin restored elastolytic activity to normal levels. HNE degraded infliximab and this cleavage was inhibited by elafin. Infliximab largely lost its ability to neutralize TNF-alpha after co-incubation with HNE.

Conclusions: The increased activity of HNE in UC may affect therapeutic efficacy of infliximab agents in these patients, thus providing an explanation for the unresponsiveness to infliximab in UC patients.

OC.02.3

SMAD7 KNOCKDOWN RESTORES ARL HYDROCARBON RECEPTOR EXPRESSION AND PROTECTIVE SIGNALS IN INFLAMMATORY BOWEL DISEASE

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Background and aim: Excessive T cells mediated immune response promotes pathogenic inflammation in the gut. Such abnormal T-cell response is in part due to a defective activity of counter-regulatory mechanisms. Aryl hydrocarbon receptor (AhR), a cytosolic transcription factor known for mediating the toxicity of xenobiotic molecules as dioxin, delivers protective and anti-inflammatory signals in the gut. Expression of AhR is markedly reduced in Crohn's disease (CD), and this defect contributes to amplify inflammatory signals. Since CD lamina propria (LP) T cells are resistant to TGF-beta1-mediated immunosuppression due to high Smad7, an inhibitor of TGF-beta1 activity, we examined whether the reduced AhR expression in CD relies on high Smad7.

Material and methods: AhR and IL-22 were evaluated in normal LPMC stimulated with TGF-beta1 and 6-formylindolo[3,2-b]carbazole (Ficz), a high-affinity ligand of AhR, and in CD LPMC incubated with a specific antisense oligonucleotides for Smad7 and then stimulated with Ficz in presence or absence of TGF-beta1. AhR expression was also evaluated in LP T cells isolated from transgenic mice over-expressing Smad7 in T cells and the Smad7-dependent down-regulation of AhR was studied in the trinitrobenzene-sulfonic-acid (TNBS) model of colitis.

Results: In normal LPMC, TGF-beta1 induced AhR and this event associated with increased production of IL-22 following stimulation with FICZ. Inhibition of Smad7 in CD LPMC restored TGF-beta1 signaling and enabled TGF-beta1 to boost AhR expression. Consistently, AhR expression and consequently Ficz-mediated IL-22 production were markedly reduced in T cells isolated from Smad7 transgenic

mice. Moreover, Smad7 transgenic mice injected with Ficz were not protected against TNBS induced colitis.

Conclusions: Smad7 sustains the defective expression of AhR thus contributing to amplify and maintain pathological process in the gut.

OC.02.4

OXIDATIVE STRESS AND THROMBOXANE-DEPENDENT PLATELET ACTIVATION IN INFLAMMATORY BOWEL DISEASE (IBD): EFFECTS OF ANTI-TNF-ALFA TREATMENT

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Background and aim: Patients with IBD, namely Crohn's disease (CD) and ulcerative colitis (UC), have a higher risk of coronary artery disease (CAD) despite having a lower burden of traditional risk factors. We previously reported that several inflammatory diseases are associated with enhanced lipid peroxidation and persistent platelet activation. Platelets from patients with CD release more soluble CD40L than control subjects and this might be responsible for the platelet hyperactivation observed in CD. Thus, we tested the hypothesis that the urinary levels of F2-isoprostane 8-iso-prostaglandin (PG) 2 α , marker of oxidative stress, and urinary 11-dehydro-thromboxane (TX) B2 and plasma CD40L, markers of platelet activation, are enhanced in IBD patients.

Material and methods: Urinary samples were taken from 129 IBD patients (59 CD, 70 UC, mean age 45 \pm 15 yrs, 81 males) and 37 healthy subjects (mean age 38 \pm 17 yrs, 8 males). Among CD patients, 51 had ileo-colonic disease, and 8 had ileal disease. Among UC patients, 34 had a left-sided colitis and 36 had a pancolitis. Urinary levels of 8-iso-PGF2 α and 11-dehydro-TXB2, as well as plasma CD40L levels, were measured in IBD patients and control subjects and a cross-sectional comparison was performed. Among all subjects, 13 patients on chronic treatment with biologic agents were followed up for up to 6 months.

Results: IBD patients had significantly higher urinary 8-iso-PGF2 α and 11-dehydro-TXB2 as well as plasma CD40L than control subjects. Interestingly, those with the urinary excretion of both 8-iso-PGF2 α and 11-dehydro-TXB2 in excess of 2000 pg/mg creatinine had higher disease activity scores. In both IBD patients and control subjects, a significant direct correlation was found between urinary 8-iso-PGF2 α and 11-dehydro-TXB2 (Rho=0.639, $p < 0.0001$). Plasma CD40L was also significantly related to both 8-iso-PGF2 α and 11-dehydro-TXB2 (Rho=0.604, $p < 0.0001$, and Rho=0.895 and $p < 0.0001$, respectively). These associations remained highly significant when considering the whole group of patients, without controls, or the single diseases (UC or CD). In particular, in UC patients, both CD40L and 11-dehydro-TXB2 were also directly correlated with the clinical activity index (CAI) (Rho=0.544, $p < 0.0001$; Rho=0.665, $p < 0.0001$). Initiation of biologic agents in 13 patients was associated with a significant reduction of the urinary excretion of both 8-iso-PGF2 α and 11-dehydro-TXB2 after 2 months ($p = 0.008$ for both) and 6 months ($p = 0.008$ for both) of follow-up, concurrent with improvement in clinical activity indices.

Conclusions: This study supports the presence of enhanced TX-dependent platelet activation in IBD patients. Further studies are underway in order to establish whether urinary and blood levels

of markers of platelets activation correlate with the incidence of CAD in IBD. Our results may also provide the rationale for targeting platelet activation to improve both IBD activity and cardiovascular risk.

OC.02.5

EXPERIMENTAL COMPARISON BETWEEN TWO MARKERS OF INTESTINAL INFLAMMATION, HMGB1 AND FECAL CALPROTECTIN, IN INFLAMMATORY BOWEL DISEASES

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Background and aim: In inflammatory bowel diseases (IBD), the fecal marker currently mostly used is calprotectin. Recently, HMGB1 has been proposed as a new surrogate marker of intestinal inflammation. This is a non-histone chromatin protein with an architectural function, which, after proinflammatory stimuli (TNF α , IL-1, IFN- γ), is secreted by immune cells. We evaluated the correlation between fecal levels of HMGB1 and disease severity (as assessed by endoscopic indexes), and compared the results with those obtained with the measurement of fecal calprotectin. Moreover, we assessed the specificity of this marker for IBD by analyzing samples of non-IBD patients.

Material and methods: We recruited three groups of patients: IBD patients (of which 20 with Crohn's Disease and 25 with Ulcerative Colitis); a control group consisting of 15 irritable bowel disease (IBS) patients; a control group consisting of 7 patients with intestinal inflammation of non-IBD type (3 infectious colitis and 4 diverticulitis). We collected two fecal samples for each subject: calprotectin was analyzed by ELISA, HMGB1 by the Western blot technique.

Results: Both calprotectin and HMGB1 were significantly increased in IBD compared to IBS patients. In non-IBD patients, calprotectin was statistically more elevated than in IBS controls. Calprotectin more effectively than HMGB1 correlated with endoscopic indices of Crohn's Disease with significant discrimination between mild IBD vs IBS ($p < 0.01$), and mild vs moderate IBD ($p < 0.05$).

In Ulcerative Colitis, HMGB1 discriminated mild disease from IBS controls ($p < 0.01$), and moderate vs severe disease activity ($p < 0.01$). Both markers showed satisfactory sensitivity and specificity by the ROC curves: calprotectin showed sensitivity of 85% and specificity of 86.7% in Crohn's disease, while in Ulcerative Colitis sensitivity was 68% and specificity 87.6%; on the other hand, HMGB1 had 75% sensitivity and 73.3% specificity in Crohn's disease, and 80% sensitivity and 73% specificity in Ulcerative Colitis. In IBD calprotectin had 75.5% sensitivity and 86.7% specificity, while HMGB1 showed 77.7% sensitivity and 73.4% specificity.

In non-IBD patients, calprotectin showed high sensitivity and specificity (85.7% and 93.7% respectively), while HMGB1 had 57.14% sensitivity and 73.3% specificity.

Conclusions: HMGB1 is as useful as fecal calprotectin in assessing intestinal inflammation in IBD with a significant correlation with disease severity. HMGB1 performs better in UC while fecal calprotectin in CD.

OC.02.6

IDENTIFICATION OF A CUT-OFF FOR PERSISTENT ANTI-INFLIXIMAB ANTIBODIES AS A PREDICTOR OF RESPONSE TO INFLIXIMAB MONOTHERAPY

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Background and aim: The clinical and predictive role of anti-Infliximab antibodies (AIA) presence and concentration are still debated, both in Crohn's disease (CD) and ulcerative colitis (UC) patients. However, there is increasing evidence of their usefulness in order to improve the management of patients on biological treatment who experience a loss of response (LOR). AIA can be subdivided into 2 types, persistent and transient, on the basis of their occurrence on multiple samples and capability of interfering with infliximab trough levels (TL), and therefore persistent AIA seem to play a major role on treatment outcome.

The aim of our retrospective study was to evaluate the clinical relevance of persistent AIA in a single-center cohort of inflammatory bowel disease (IBD) patients.

Material and methods: We selected from our cohort of 56 IBD patients treated with IFX mono-therapy who achieved clinical and biochemical remission after induction (IFX schedule: 5 mg/kg at week 0, week 2, and week 6), 18 patients (32.1%) who developed persistent AIA during 48 weeks follow-up. Blood samples were drawn at standardized time points (i.e., baseline, 2 weeks, 6 weeks, and every 8 weeks) before IFX infusion. TL and AIA were measured using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). Clinical disease activity was assessed both at week 14 (i.e. after induction) and week 48 by the Harvey-Bradshaw Index (HBI, remission defined by HBI <5) in CD patients and by the Mayo score for UC patients (remission defined by Mayo score <2). Also, protein-C reactive and erythrocyte sedimentation rate (ESR) were measured.

Results: Eighteen patients (11 CD and 7 UC, 10M/8F, median age 39.5 years, range 18–69) developed persistent AIA at a median of 2 weeks (range 2–22) during 48 weeks follow-up. Among these patients, 12 (66.7%) experienced LOR during the follow-up period. Median AIA were significantly higher in patients who showed LOR as compared to patients who maintained remission (8.29 U/ml, range 0.62–30.52 U/ml, versus 1.41 U/ml, range 0.77–9.94 U/ml; $P=0.04$). ROC curve identified a persistent AIA cut-off of 3.91 U/mL as the threshold with the highest accuracy for the identification of relapsers (AUROC=0.799, specificity=75.0%, sensitivity=83.3%).

Conclusions: The early occurrence of elevated persistent AIA serum concentrations during IFX mono-therapy treatment is associated with high risk of LOR. Furthermore, the use of an AIA concentration cut-off of 3.91 U/mL can be useful to accurately identify patients with LOR, although these results need to be confirmed in larger series.

OC.02.7

ADALIMUMAB TROUGH LEVELS AT WEEK EIGHT AS PREDICTIVE FACTOR OF LONG TERM CLINICAL REMISSION

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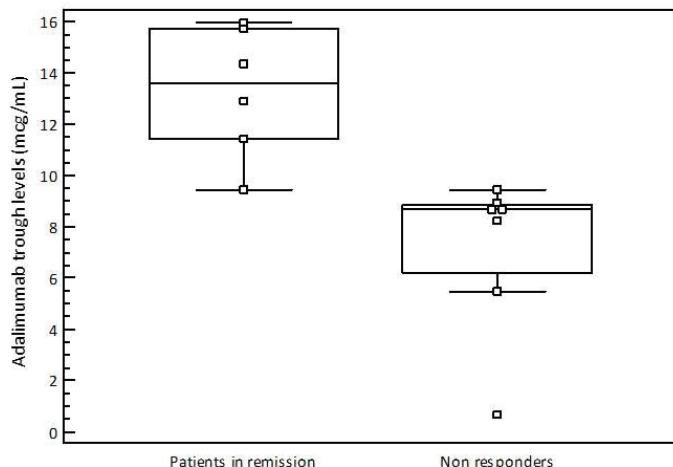
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Background and aim: Adalimumab (ADA) has been approved for the treatment of Crohn's disease refractory to standard medications.

Loss of response (LOR) during the first year of treatment with ADA is relatively frequent and the main factor associated with this phenomenon is the reduction of drug serum concentration to subtherapeutic levels due to the development of neutralizing antidrug antibodies. As a consequence, dosing ADA trough levels has been proposed as a useful tool in the therapeutic management of patients who experience LOR and in the identification of patients at risk of anti-TNF therapy failure.

Material and methods: The aim of our prospective study was to evaluate whether ADA TL at week 8 may predict long term clinical remission in a single-center cohort of Crohn's Disease patients. In order to carry this study out, we included 13 patients with Crohn's disease (8 males, median age 41 years, range 21-66) who underwent ADA therapy and achieved clinical remission after induction. Blood samples were drawn at standardized time points (0, 2, 8 and 48 week) before ADA administration. ADA TL were measured using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). Disease activity was assessed both at week 8 and week 48 by the Harvey-Bradshaw Index (HBI, remission defined by HBI<5).

Results: Among these 13 patients, 7 (53.8%) experienced LOR during follow-up. We found significantly lower ADA TL at week 8 in patients who experienced LOR as compared to patients who maintained remission during the follow-up (8.66 mcg/mL, range 0.68-9.46 mcg/mL versus 13.63 mcg/mL, range 9.45-15.97 mcg/mL; $P=0.0023$). Receiver Operating Characteristic curve identified an ADA TL cut-off of 8.93 mcg/mL as the threshold with the highest accuracy for identification of patients who maintained remission (AUROC 0.976, 95% confidence interval 0.715-1; specificity 85.71%, sensitivity 100%).



Conclusions: Patients who experienced LOR to ADA during long-term follow-up (48 weeks) have significantly lower ADA TL at week 8 as compared to patients in remission. Furthermore, an ADA TL concentration cut-off of 8.93 mcg/mL can be used to accurately identify patients who maintain long term clinical remission. We suggest that the assessment of ADA TL at week 8 can be used as a predictive tool for long term clinical response, although these preliminary results need to be confirmed in larger series.

OC.02.8

A PROSPECTIVE "REAL LIFE" STUDY ON ADALIMUMAB EFFICACY IN STEROID-DEPENDENT CROHN'S DISEASE PATIENTS: RESULTS FROM A LONG TERM FOLLOW-UP

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Background and aim: Adalimumab (ADA) is effective in the induction and maintenance 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 of ADA (80/40 or 160/80 mg every other week followed by 40 mg every other week) in 110 steroid-dependent pts. At week 6, 91% of pts have had a clinical benefit (remission: 45.5%, response: 45.5%). At the end of the follow-up (mean 14.6 months), 80.9% of responders have maintained the clinical benefit (remission: 64.5%, response: 16.4%). 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. Up to now no data are available on long term efficacy of ADA in the setting of steroid-dependent pts.

Material and methods: All the 110 pts treated in the previous study were followed up until April 2015 and the following variables were evaluated at the end of the follow up: maintenance of clinical benefit, ADA discontinuation, dose escalation, switch to another biologic, surgical treatment and side effects.

Results: At the end of the follow up (mean 74.16 ± 10.3 months) only 5 pts resulted lost during the follow-up. Concerning the remaining 105 pts, 42 pts (40%) obtained the clinical benefit: 1) 37/42 (88%) were still in maintaining treatment with ADA at the dosage of 40 mg sc (of these pts 13/37 [35%] received a weekly maintaining treatment); 2) 5/37 (12%) discontinued ADA due to mucosal healing. Sixty-three pts (60%) discontinued ADA: 1) 50/63 (79%) for lost of clinical benefit (20 of these 50 pts were operated on [40%]); 2) 6/63 (10%) for side effects; 3) 5/63 (8%) for severe endoscopic activity despite clinical response; 4) 2/63 (3%) died for reason non related to ADA treatment. Among pts who discontinued ADA 24/63 (38%) were then effectively switched to another biologic (infliximab or golimumab). At univariable analysis we did not find variables related to the treatment outcomes. ADA was well tolerated. Only one pts developed an acute leukaemia after 2 years of ADA discontinuation.

Conclusions: This long term "real life" prospective study showed that ADA is a good maintaining treatment in steroid dependent CD but 1/3 of them needed dose escalation to maintain clinical benefit. The rate of long term side effects that needed treatment discontinuation is quite low. In pts intolerant to or with lost of response to ADA a switch to another biologic is an effective opportunity.

OC.02.9

CROSS-SECTIONAL EVALUATION OF TRANSMURAL HEALING IN PATIENTS WITH CROHN'S DISEASE ON MAINTENANCE TREATMENT WITH BIOLOGICS

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Background and aim: Transmural healing (TH) of Crohn's disease (CD) is a new underexplored and interesting outcome of the concept

of deep remission. The aim of this study was to assess the rate of TH evaluated by bowel sonography (BS) and magnetic resonance enterography (MRE) in CD patients treated with biologics, directly comparing the two cross-sectional procedures.

Material and methods: We performed a 2-year observational longitudinal prospective study evaluating steroid-free clinical remission (CR), mucosal healing (MH), and TH in all patients with CD who would complete a 2 years period of maintenance treatment with biologics. All patients underwent endoscopy, BS and MRE before starting biologics and 2 years later. Furthermore, the Crohn's Disease Activity Index (CDAI) score was calculated before treatment and 2 years later.

Results: The study included 40 CD patients biologics (38% infliximab and 62% adalimumab). TH was evident in 10 patients (25%) at BS and in 9 patients (23%) at MRE ($k=0.84$; $P < 0.01$). No significant differences were noted about TH in relation to the type of biologic used ($P = NS$). MH was obtained in 14 subjects (35%). A good agreement was observed between MH and TH at BS ($k = 0.63$; $P < 0.001$) and TH at MRE ($k = 0.64$; $P < 0.001$). CR was achieved in 24 patients (60%). A poor agreement was found between CR and TH, both at BS and MRE ($k = 0.27$ and 0.29 , respectively; $P < 0.01$).

Conclusions: TH can be reached in about 25% of CD patients treated with biologic with high agreement between BS and MRE on defining this outcome. After considering the advantages of BS (high diagnostic accuracy, low costs, high patient compliance, high availability) and the limitations of MRE (high costs, low availability), we suggest the use of BS as first cross-sectional procedure in defining TH in patients with CD.

OC.02.10

ADHERENCE OF ITALIAN GASTROENTEROLOGISTS TO GUIDELINES FOR THE MANAGEMENT OF ULCERATIVE COLITIS: A MULTICENTRE PROSPECTIVE OBSERVATIONAL ITALIAN AIGO STUDY

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Background and aim: Several guidelines and consensus are available for the therapeutic management of patients with ulcerative colitis (UC). Only few studies evaluated the use of evidence-based therapy by physicians in their clinical practice. The aim of this study was to assess the extent of physicians' adherence to prescribing guidelines in the management of UC.

Material and methods: A multicentre observational prospective study on the adherence to guidelines in UC was conducted in 28 gastroenterology (GI) unit across Italy. Consecutive outpatients with a flare of UC were enrolled in the study. A questionnaire was administered to the attending physicians consisting of two sections, the first (A) included questions about the GI unit, personal experience in IBD, number of IBD/UC patients followed by the unit, the second (B) included questions on the extension and severity of UC, on the specific medical treatment undertaken and on the adherence to guidelines.

Results: 546 patients were enrolled. An interim analysis of the first 446 patients, enrolled by high (27%), medium (47%) and low (26%)

IBD volume unit, included 39% extensive, 49% left-distal colitis, 12% proctitis. The extension did not differ by hospital volume; severe flares were less frequent in patients enrolled by medium volume IBD units (8% vs 21% high and 19% low volume unit). In 88.8% of flares, the management was based on guidelines regardless of the physician's experience in IBD and size of the IBD population followed by the unit. Physicians referred mainly to ECCO guidelines, to a greater extent physicians from high volume if compared to low volume IBD units (89.3% vs 63%).

Conclusions: The adherence of Italian gastroenterologists to guidelines for the management of ulcerative colitis is high. In the clinical practice, the compliance with guidelines is not affected by the size of the IBD unit and the physicians experience in IBD.

OC.03 Liver

OC.03.1

QUANTIFICATION OF SERUM HBSAG IS A USEFUL PARAMETER TO OPTIMIZE ANTIVIRAL NUC THERAPY IN CHRONIC HBV INFECTION

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Background and aim: Serum HBsAg loss is the recommended stopping rule in nucleoside-analogues (NUC) responders, yet this event occurs rarely. Decreasing serum HBsAg levels, preceding HBsAg seroclearance (HBsAg <20 UI/ml), has not been sufficiently investigated and the predictive value of baseline and on-treatment quantitative serum HBsAg levels in the therapeutic response to NUC in chronic hepatitis B patients remains unclear. We aimed to investigate the kinetics of HBsAg levels during NUC therapy to evaluate the treatment period to achieve HBsAg seroclearance.

Material and methods: Patients with chronic HBV infection, receiving NUC antiviral therapy with stable viral suppression (HBV-DNA < 20 IU/ml), were recruited at the Gastroenterology Unit of the University of Naples "Federico II". Sequential serum samples from these patients were tested for quantification of HBsAg with the "HBsAg II quantitative immunoassay" (Roche). HBsAg levels were determined at baseline, where possible, and on-treatment every 12 months.

Results: A total of 95 HBsAg-positive, HBeAg-negative patients (male/female: 73/22, median age 58 yrs, range 35-79 yrs, 33% cirrhotic) virally suppressed with different NUCs, were enrolled. Precisely 56 patients were in therapy with Tenofovir (TDF), 22 with Entecavir (ETV) and 17 with Lamivudine (LAM).

The median treatment duration was 110 months, range 48-183 months.

There was a significant decrease of the HBsAg levels during NUC therapy (p value <0.001); in particular, at time of enrollment, the HBsAg baseline mean value was 3471 UI/ml (450-28948 IU/ml), while the mean value at the last determination of HBsAg was 1758 IU/ml (20-21905 IU/ml). Only 2/95 patients (1.9%) didn't show a substantial decrease in HbsAg levels.

The statistically significant decrease of HBsAg levels was also maintained when the patients were clustered according to antiviral therapy, presence of cirrhosis and previous treatment with interferon (table 1).

Table 1
HBsAg levels in different subgroups of patients

	HBsAg pre-therapy (mean value \pm SD)	HBsAg last determination (mean value \pm SD)	p value
NUC therapy (no. of patients)			
Tenofovir (56)	3295 \pm 4506	1863 \pm 3511	0.07
Entecavir (22)	4701 \pm 6966	1874 \pm 2984	<0.05
Lamivudine (17)	2458 \pm 3427	1261 \pm 3146	0.7
Liver disease (no. of patients)			
Chronic Hepatitis B (64)	3590 \pm 5254	1510 \pm 2437	<0.05
Cirrhosis (31)	3224 \pm 4599	2271 \pm 4627	0.9
IFN therapy (no. of patients)			
Previous IFN (34)	4820 \pm 6781	2311 \pm 244	<0.05
No IFN (61)	2719 \pm 5026	1450 \pm 2753	0.06
Overall (95 patients)	3471 \pm 5028	1758 \pm 3308	<0.001

Of particular interest, HBsAg seroclearance occurred in 19% of patients (18/95 patients). Moreover, HBsAg seroconversion to HBsAb occurred in 3/18 patients, in which undetectable HBsAg value was evidenced at least two years before the seroconversion. In these 3 patients NUC therapy was stopped, and until now none relapsed.

Conclusions: The results of this study suggest a role of on-treatment HBsAg quantification in the management of NUC-treated patients. If validated, prospectively in a larger patient cohort, HBsAg measurement would be a useful parameter to optimize antiviral treatment schedule.

OC.03.2

THE PRESENCE OF WHITE MATTER LESIONS IS ASSOCIATED WITH THE HISTOLOGICAL SEVERITY OF NON-ALCOHOLIC FATTY LIVER DISEASE

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Background and aim: Nonalcoholic fatty liver disease (NAFLD) has been associated with increased cardiovascular risk, including coronary artery disease and cerebrovascular events. No studies however assessed the potential relationship between NAFLD and subclinical cerebrovascular alterations. We tested the correlation between NAFLD and its histological severity with vascular white matter lesions (WML) in patients with biopsy-proven NAFLD and in non steatotic controls.

Material and methods: Data were recorded in 79 consecutive biopsy-proven NAFLD, and in 82 controls with normal ALT and no history of chronic liver diseases, without ultrasonographic evidence of steatosis and liver stiffness value <6 KPa. All subjects underwent magnetic resonance assessment and WML were classified according to the Fazekas score as absent (0/III), or present (mild I/III; moderate II/III, and severe I/III). For the purpose of analyses, all controls were considered without NASH and without F2-F4 liver fibrosis.

Results: WML were found in 26.7% of the entire cohort (43/161). The prevalence was similar in NAFLD vs. no-NAFLD (29.1% VS 24.3%; $p=0.49$), but higher in NASH vs. no-NASH (37.7% vs 21.2%, $p=0.02$) and F2-F4 vs. F0-F1 fibrosis (47.3% vs 20.3%, $p=0.001$). In both the entire cohort and in NAFLD, only female gender (OR 4.37, 95%CI 1.79–10.6, $p=0.001$; and OR 5.21, 95%CI 1.39–19.6, $p=0.01$), age >45 years (OR 3.09, 95%CI 1.06–9.06, $p=0.03$; and OR 11.1, 95%CI 1.14–108.7, $p=0.03$), and F2-F4 fibrosis (OR 3.36, 95%CI 1.29–8.73, $p=0.01$; and OR 5.34, 95%CI 1.40–20.3, $p=0.01$) were independently associated with WML by multivariate analysis. Among NAFLD, the prevalence of WML progressively increased from patients without (1/18; 5.5%), or with one (1/17, 5.8%), to those with two (9/30; 30%) and further to those with three (12/14; 85.7%) risk factors.

Conclusions: The presence of WML is not associated with NAFLD, but with metabolic diseases in general, and histological severity of NAFLD. Clinical implications of this issue need to be assessed by longitudinal studies.

OC.03.3

NUNA NUTRITIONAL NAVIGATOR SMARTPHONE FREE APPLICATION FOR IMPROVING ADHERENCE TO MEDITERRANEAN DIET AND REDUCING BODY WEIGHT IN NON-ALCOHOLIC FATTY LIVER DISEASE PATIENTS: A PILOT STUDY

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Background and aim: Non-alcoholic fatty liver disease (NAFLD) represents the most common chronic liver disease in Western countries and diet and obesity play a key role in its development. An inverse association between NAFLD severity and greater adherence to Mediterranean Diet (MD) has been reported, indicating this dietary pattern as a new therapeutic option.

Unfortunately environmental factors often encourage impulse purchases which in turn worsen the quality of patient's grocery shopping, home stored food and, finally, dietary habits.

NUNA Nutritional Navigator smartphone free application is the tool for applying a new environmental educational method assuming that patients can get a better diet by improving the quality of grocery shopping choices and home stored food.

The aim of this study was to investigate whether NUNA free was able to improve adherence to the MD in NAFLD patients.

Material and methods: NUNA is able to recognize foods, record items and calculate nutrients and MD adherence score. A pantry pyramidal graphic is provided: green and yellow colored for higher scores, red colored for low ones. NUNA is also able to help in choosing foods. Once a food item is selected, a dynamic and smart traffic light advice is provided: green and yellow mean "purchase"; red means "do not purchase". Colors are managed by an algorithm and change in relationship to the user's nutritional needs, the nutritional composition of the selected item and the overall pantry quality.

We conducted a cohort trial involving 8 NAFLD patients who had a body-mass index (BMI) of at least 25. Patients received counseling on lifestyle modification and were invited to download NUNA and to use it for 8 weeks. Adherence to the MD was assessed using a recently posteriori adaptation of the Mediterranean diet score of Sofi et al (Sofi-MDS). The coprimary end points were the change in Sofi-MDS and in body weight.

Results: Half of the patients were women. At baseline, the mean age of the patients was 55 (r: 21–73) years, the mean weight was 83,2 \pm 14,6 (range: 61–101,6) kg, the mean BMI was 30,7 \pm 6,6 (range: 23,4–44); the mean Sofi-MDS was 11,2 \pm 1,3 (range: 10–13). At week 8, Sofi-MDS increased of 2,8 points ($p=0,001$) and patients had lost a mean of 2,5 kg of body weight ($p=0,005$) and 1,1 points of their BMI ($p=0,008$).

Conclusions: In this study NUNA Nutritional Navigator as an adjunct to lifestyle advices, was associated with improved Sofi-MDS and reduced body weight.

OC.03.4

EFFICACY AND SAFETY OF OBETICHOIC ACID IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS: AN ANALYSIS OF THE ITALIAN PATIENTS FROM A PHASE 3, RANDOMIZED, PLACEBO-CONTROLLED STUDY

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Background and aim: Obeticholic acid (OCA) is a potent, selective farnesoid X receptor (FXR) agonist currently under investigation for the treatment of primary biliary cirrhosis (PBC). This study evaluated the efficacy and safety of OCA for the treatment of PBC.

Material and methods: This is a subgroup analysis of Italian patients who participated in an international Phase 3, 12 month, double-blind, placebo-controlled trial. Eligible patients with PBC who had an alkaline phosphatase (ALP) > 1.67X ULN and/or bilirubin > ULN but <2X ULN were randomized to receive OCA 5 mg with the ability to up-titrate to 10 mg after 6 months (Titration OCA), OCA 10 mg or placebo. Patients were permitted to remain on stable doses ursodeoxycholic acid (UDCA). The primary composite endpoint was the proportion of patients with an ALP <1.67X ULN and a >15% reduction in ALP and a total bilirubin <ULN.

Results: Thirty-two out of 216 intent-to-treat patients were at Italian sites. In the Italian patient group the mean age was 52.3 years, 84% were female, and 94% were on a UDCA. The majority of patients (91%) completed the double-blind portion of the study. The percentage of patients at the Italian sites achieving the primary composite endpoint at 52 weeks was consistent with the total study population. The baseline values for the placebo, Titration OCA and OCA 10 mg for: ALP (U/L): 314.6, 302.2, 312.6, respectively; total bilirubin (μmol/L): 14.4, 12.0, 13.4, respectively; AST (U/L): 56.7, 49.8, 46.5, respectively; ALT (U/L): 60.5, 58.0, 45.4, respectively; GGT (U/L): 325.4, 287.9, 223.6, respectively. The 12 month values for the placebo, Titration OCA and OCA 10 mg for: ALP (U/L): 365.9, 188.2, 188.3, respectively; total bilirubin (μmol/L): 16.8, 11.4, 10.8, respectively; AST (U/L): 62.2, 35.0, 35.7, respectively; ALT (U/L): 61.1, 29.7, 28.8, respectively; GGT (U/L): 298.1, 84.1, and 57.7, respectively. The laboratory results for the Italian patients were consistent with the overall population. Mild to moderate pruritus was the most common treatment emergent adverse event (TEAE) and occurred in 45%, 64% and 50% of patients in the placebo, Titration OCA, 10 mg OCA groups respectively. There were no differences between the groups for any other TEAE.

		ALP (U/L)	Total Bilirubin (μmol/L)	AST (U/L)	ALT (U/L)	GGT (U/L)
Placebo						
Italian Patients	Baseline	314.6 (132.4)	14.4 (7.1)	56.7 (39.3)	60.5 (34.4)	325.4 (387.2)
N=11	12 months	365.9 (196.8)	16.8 (7.3)	62.2 (58.9)	61.1 (39.6)	298.1 (378.5)
Titration OCA						
Italian Patients	Baseline	302.2 (89.8)	12.0 (4.4)	49.8 (14.8)	58.0 (27.6)	287.9 (206.1)
N=11	12 months	188.2 (40.4)**	11.4 (3.9)*	35.0 (7.5)*	29.7 (11.7)**	84.1 (49.6)**
OCA 10 mg						
Italian Patients	Baseline	312.6 (87.7)	13.4 (4.7)	46.5 (28.5)	45.4 (30.2)	223.6 (191.0)
N=10	12 months	188.3 (61.0)**	10.8 (3.7)*	35.7 (27.3)	28.8 (24.4)	57.7 (42.8)*

Data are Mean (SD). *p<0.05, **p<0.01. P-value for comparing active treatments to Placebo is obtained using an ANCOVA model with baseline value as a covariate and fixed effects for treatment and randomization strata factor. P-values based on LS Mean change from baseline values.

Conclusions: In this study, OCA (± UDCA) given to patients with PBC at the Italian sites produced clinically meaningful improvements in liver biochemistry. The results were consistent with the overall study population.

OC.03.5

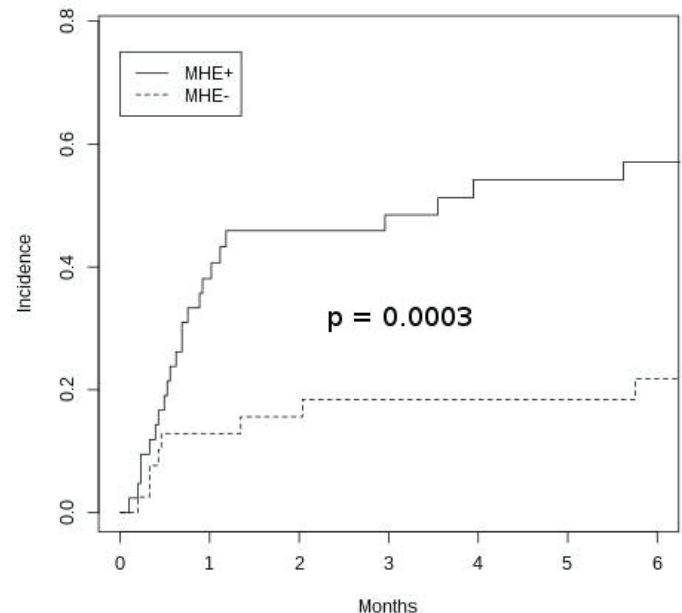
COGNITIVE IMPAIRMENT PREDICTS THE OCCURRENCE OF HEPATIC ENCEPHALOPATHY AFTER TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT

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Background and aim: Hepatic encephalopathy is a major problem in patients treated with TIPS. The aim of the study was to establish whether pre-TIPS covert HE is an independent risk factors for the development of HE after TIPS.

Material and methods: 82 consecutive cirrhotic patients submitted to TIPS were included (Gender 57 M; Age 57.9 ± 10.1 yrs; MELD 11.2 ± 3.6; CPT class A 17, B 53, C 12; TIPS indication: 37 bleeding, 45 refractory ascites). All patients underwent the PHES to identify those affected by covert HE before TIPS. The incidence of the first episode of HE taking into account the competing risk nature of the data (death or liver transplantation) was estimated.

Results: Thirty-five (43%) patients developed overt HE. The difference of post TIPS HE was highly significant (p=0.0003) between the patients with or without covert HE before TIPS. Seventy-seven % of the patients with post TIPS HE were classified as affected by covert HE before TIPS. Age: (sHR 1.05, CI 1.02-1.08, p=0.002); C-PSCORE: (sHR 1.29, CI 1.06-1.56, p=0.01) and covert HE: (sHR 3.16 CI: 1.43-6.99 p=0.004) were associated to post TIPS HE. Taking into consideration only the results of PHES evaluation, the negative predicting value was 0.80 for all patients and 0.88 for the patients submitted to TIPS because of refractory ascites. Thus, a patient with refractory ascites, without covert HE before TIPS, has almost 90% probability to be free of HE after TIPS.



Conclusions: Psychometric evaluation before TIPS is able to identify the large majority of the patients who will develop HE after TIPS and can be used to select the patients in order to have the lowest incidence of this important complication.

OC.03.6

ANTICOAGULATION THERAPY FOR NON MALIGNANT PORTAL VEIN THROMBOSIS IN CIRRHOTIC PATIENTS: A SAFE TREATMENT?

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Background and aim: Non-neoplastic portal vein thrombosis (PVT) is a frequent event in cirrhotic patients but its natural history is poorly understood. It can be treated with anticoagulants, however the safety and efficacy of this therapeutic approach are still unknown. We performed a retrospective study evaluating the effect of anticoagulants in a series of cirrhotic patients with non-neoplastic PVT.

Material and methods: A retrospective ultrasound chart review of cirrhotic patients seen in our Liver Unit between February 2008 and March 2015 was performed. Subjects with non-neoplastic PVT (defined as the absence of invasion or infiltration of the portal vein by neoplasia) were identified by reviewing US and TC reports. Partial vs complete PVT was considered as the absence or presence of power-Doppler signal at the ultrasound. Demographic, clinical, laboratory, endoscopic parameters and thrombophilia screening were analyzed. Dose, duration, efficacy and side effects of anticoagulant therapy were also evaluated.

Results: Charts of 375 cirrhotic patients of any etiology were evaluated. Non-neoplastic PVT was identified in 28 cases (7.5%) and it was mostly partial. Low platelet count, high MELD score (13±4), Child-Pugh class B or C and esophageal varices were the most frequent characteristics of these patients. Thrombophilic disorders (antithrombin deficiency, protein C deficiency, protein S deficiency, presence of Lupus Anticoagulant antibodies) were observed in 9 patients; 16 patients received anticoagulation therapy (low-weight heparin or warfarin) for 3-6 months and 12 patients received no treatment. Partial or complete recanalization was achieved in 12 anticoagulated patients (75%), while in 3 patients (25%) spontaneous improvement of PVT (p=0.025) was observed. The recurrence of thrombosis was seen in 43% patients after stopping anticoagulation therapy. Five anticoagulated patients developed bleeding complications but no deaths were observed. Ten patients without treatment developed liver-related events (portal hypertension-related bleeding, ascites, hepatic encephalopathy) and 4 patients died.

Conclusions: In our study, anticoagulation therapy is a safe treatment for PVT, leading to recanalization of the portal vein in 75% of patients. It seems to be reasonable to maintain indefinitely the anticoagulation therapy to prevent thrombosis recurrence.

OC.03.7

CIRCULATING MICROPARTICLES AND RISK OF PORTAL VEIN THROMBOSIS IN PATIENTS WITH LIVER CIRRHOSIS AND HEPATOCELLULAR CARCINOMA

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Background and aim: studies which explore the hypercoagulable state associated with this hepatocellular carcinoma (HCC) and its correlation with the risk of portal vein thrombosis (PVT) are lacking. We investigated the presence and cellular origins of circulating microparticles (MP) of different cellular origins in plasma from patients with cirrhosis with and without HCC evaluated the possible contribution of MP to PVT occurrence in HCC patients.

Material and methods: Plasma levels of annexin V MP, endothelial-, platelet- and leukocyte-derived MP, tissue factor-bearing MP and thrombomodulin-bearing MP were measured by cytoflowimetry in 65 adult cirrhotic patients, 33 with and 32 without HCC. PVT occurred in 12 (18%) cirrhotic patients, 8 with HCC and 4 without HCC. Fifty healthy subjects used as controls.

Results: Patients with cirrhosis and HCC had significantly higher median plasma levels of MP than patients with cirrhosis without HCC and healthy controls. Patients with HCC and cirrhosis who developed PVT showed significantly higher median plasma levels of annexin V MP and endothelial-derived MP than patients with cirrhosis and HCC who did not developed PVT. MP were associated with a higher but not statistically significant RR for PVT. Cirrhotic patients without HCC showed significantly higher median levels of MP compared to healthy controls.

Conclusions: Hypercoagulability as assessed by circulating plasma MP levels is clearly present in cirrhotic with HCC patients and may contribute to the PVT occurrence. The “degree” of hypercoagulability increases from cirrhosis alone to cirrhosis with HCC.

OC.03.8

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

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Background and aim: Despite the promising results of earlier studies, a clear superiority of drug-eluting beads transarterial chemoembolization over conventional chemoembolization has not been established yet. Aim of this meta-analysis is to evaluate the efficacy and safety of the two treatments in hepatocellular carcinoma patients.

Material and methods: Computerized bibliographic search on the main databases was performed. One-year, two-year, three-year survival rates were analyzed. Hazard ratios from Kaplan-Meier curves were extracted in order to perform an unbiased comparison of survival estimates. Objective response and severe adverse event rate were analyzed too. Comparisons between the two treatments were performed by using Mantel-Haenszel test in case of low heterogeneity or DerSimonian and Laird test in case of high heterogeneity. The results were expressed as odds ratio and 95% confidence interval.

Study	Arm	Drug	Sample size	Recruitment period	Study design	Region	CP (A/B/C)	BCLC (A/B/C)	Quality
PRECISION V 2010	DEB-TACE	Doxorubicin	93	2005-2007	RCT	Europe	77/16/0	24/69/0	M
Song et al 2012	cTACE	Doxorubicin	108	2007	R	Korea	89/19/0	29/79/0	H
	DEB-TACE	Doxorubicin	60	2008-2011			56/4/0	27/33/0	
	cTACE	Doxorubicin or Epirubicin/Cisplatin	69				62/6/0	28/41/0	
Sacco et al 2011	DEB-TACE	Doxorubicin	33	2006-2009	RCT	Italy	29/4/0	22/11/0	M
Van Malenstein et al 2011	cTACE	Doxorubicin	34	2009	RCT	Belgium	25/9/0	22/12/0	M
	DEB-TACE	Doxorubicin	16	2006-2009			14/2/0	2/9/5	
Golfieri et al 2014	DEB-TACE	Doxorubicin	14	2009	RCT	Italy	14/0/0	1/10/3	H
Ferrer et al 2011	cTACE	Epirubicin	89	2008-2010	P	Spain	75/14/0	41/26/22	M
	DEB-TACE	Doxorubicin	47	1999-2009			NA	NA	
Dhanasekaran et al 2010	cTACE	Doxorubicin	25	2009	R	USA	22/11/12	NA	H
	DEB-TACE	Doxorubicin/Cisplatin/Mytomicin-C	26	2008			11/11/4	NA	
Wiggermann et al 2011	DEB-TACE	Epirubicin	22	2003-2008	R	Germany	22/0/0	1/17/3	H
Recchia et al 2012	cTACE	Cisplatin	22	2008	P	Italy	22/0/0	4/15/2	L
	DEB-TACE	Doxorubicin	35	2008-2010			NA	NA	
Facciorusso et al 2015	cTACE	Doxorubicin	70	2010	R	Italy	129/16/0	58/81/6	H
	DEB-TACE	Doxorubicin	145	2007-2011			93/11/0	41/63/0	
Arabi et al 2015	cTACE	Doxorubicin	104	2007-2011	R	Saudi Arabia	24/11/0	NA	M
	DEB-TACE	Cisplatin	35	2006-2014			17/2/0	NA	
Klocekner et al 2015	cTACE	Mytomicin-C	19	2014	R	Germany	51/2/3	8/34/34	M
	DEB-TACE	Mytomicin-C	76	2002-2013			103/64/7	30/59/85	

DEB, Drug-eluting beads; R, Retrospective; RCT, Randomized-controlled trial; P, prospective; CP, Child-Pugh; BCLC, Barcelona clinic liver cancer; H, High; M, Moderate; L, Low; NA, Not assessed.

Table 1. Characteristics of the included studies.

Results: Four randomized-controlled trials and 8 observational studies with 1449 patients were included in the meta-analysis (Table 1). Non-significant trends in favor of drug-eluting beads chemoembolization were observed as for 1-year (odds ratio: 0.76, 0.48-1.21, p=0.25), 2-year (odds ratio: 0.68, 0.42-1.12, p=0.13) and

3-year survival (odds ratio: 0.57, 0.32–1.01, $p=0.06$). Meta-analysis of plotted hazard ratios confirmed this trend (hazard ratio: 0.86, 0.71–1.03, $p=0.10$). Pooled data of objective response showed no significant difference between the two treatments (odds ratio: 1.21, 0.69–2.12, $p=0.51$). Meta-regression analysis identified response criteria as significant contributor to the high heterogeneity observed. No statistically significant difference in adverse events was registered (odds ratio: 0.85, 0.60–1.20, $p=0.36$).

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

OC.03.9

SPONTANEOUS BACTERIAL PERITONITIS (SBP) IS NOT ASSOCIATED WITH HIGHER MORTALITY IF COMPARED WITH OTHER INFECTIONS IN PATIENTS AWAITING LIVER TRANSPLANTATION (LT)

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Background and aim: Background: Infection represents the main cause of decompensation or worsening of liver function in cirrhotic patients; Spontaneous bacterial peritonitis (SBP) is considered a life threatening cause of Systemic inflammation (SIRS) or sepsis, especially amongst patients listed for LT. The present study aimed to evaluate the prevalence of SBP amongst patients listed at Padua LT Center from 2006 to 2014, and to compare the outcome between the patients who did experience SBP to patients who experienced non-SBP infections.

Material and methods: All consecutive patient who had a first episode of SBP in the waiting list (WL) were included. Re-LT, and pediatrics were excluded. For each patient, MELD score before, at the time of infection, and 30 days after SBP (MELD30) were calculated. A control group of patients who experienced non-SBP infection while on the WL was retrieved. All continuous variables are expressed as mean \pm SD. Statistical analysis was performed using T-student test and Fisher's exact test. Data from intra-individual variables were obtained using Wilcoxon signed rank test.

Results: Forty two out of 940 (4.4%) patients (59% male; mean age 57.2 \pm 7.3) developed SBP, 274 \pm 551 days after admission in the WL. MELD score at infection was significantly higher than at admission (17.8 \pm 5.89 vs 21.9 \pm 5.19; $p=0.0001$). For 33.3% SBP was the cause of death and for those who survived, relapse of SBP was not uncommon (11.9%). Patients who resolved infection presented MELD30 significantly lower than during infection ($p=.016$), but not different than MELD at admission ($p=0.12$). Control group consisted of 78 patients who experienced non-SBP infections in the WL, with similar MELD score at admission (19.1 \pm 5.5 vs 17.8 \pm 5.89; $p=0.12$). Non-SBP infections produced a significant increase of MELD ($p=0.000024$), and MELD30 significantly lower in those who resolved infection ($p=0.02$). Mortality due to infection between two groups was not significantly different (14/42 vs 22/78; $p=.67$).

Conclusions: SBP is not an uncommon event in patients awaiting LT, but its presence does not significantly worsen the prognosis if compared with other infections.

OC.04 Colon Cancer

OC.04.1

SMAD7 KNOCKDOWN IN COLON CANCER CELLS ACTIVATES PROTEIN KINASE RNA-ASSOCIATED EIF2-ALPHA PATHWAY THEREBY LEADING TO CELL DEATH

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Background and aim: Background: Up-regulation of Smad7, an inhibitor of TGF- β 1, occurs in sporadic colorectal cancer (CRC). Knockdown of Smad7 with a specific antisense oligonucleotide (AS) leads to activation of eIF2 α , an attenuator of protein synthesis, and arrest of CRC cells in the S phase of the cell cycle with the downstream effect of inducing cell death.

Aim: To investigate the mechanisms by which Smad7 knockdown activates eIF2 α .

Material and methods: Phosphorylation of eIF2 α was evaluated in CRC cell lines (i.e. HCT116 and DLD-1) either untreated or treated with Smad7 sense (S) or AS by Western blotting (WB) and immunofluorescence (IF). Expression of ATF4 and CHOP, two downstream targets of eIF2 α , were evaluated by IF and activation of PKR, GCN2 and PERK, up-stream kinases that induce eIF2 α phosphorylation, was assessed by WB. Wild type or PKR-deficient CRC cells treated with Smad7 AS were monitored for eIF2 α activation and induction of death. Finally, we assessed whether enhanced phosphorylation of eIF2 α seen in cells treated with Smad7 AS was also associated with reduced interaction between eIF2 α and PP1, a phosphatase that normally dephosphorylates eIF2 α .

Results: Smad7 knockdown increased ATF4 and CHOP expression thus confirming previous data showing activation of eIF2 α phosphorylation in CRC cells treated with Smad7 AS. Among kinases that induce eIF2 α phosphorylation, only PKR was activated by Smad7 knockdown. Consistently, silencing of PKR reduced but did not abolish Smad7 AS-induced eIF2 α phosphorylation and cell death, thus suggesting the existence of further mechanisms that control eIF2 α phosphorylation in Smad7-deficient cells. Indeed, in CRC cells, Smad7 interacted with PP1 and Smad7 knockdown reduced association of PP1 with eIF2 α .

Conclusions: Data show that Smad7 is involved in CRC cell survival and suggest that Smad7 is a valid target for therapeutic intervention in CRC.

OC.04.2

GENETIC DIVERSITY OF THE KIR/HLA SYSTEM AND OUTCOME OF PATIENTS WITH METASTATIC COLORECTAL CANCER TREATED WITH CHEMOTHERAPY

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Background and aim: To explore genes of the killer-cell immunoglobulin-like receptor (KIR) and of the Human Leukocyte Antigen (HLA) ligand and their relationship with the outcome of metastatic colorectal cancer (mCRC) patients treated with first-line 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI).

Material and methods: A total of 224 mCRC patients were screened for KIR/HLA typing and they were compared with 222 normal control subjects. The determination of the KIR/HLA combinations was based upon the gene content and variants. Genetic associations with complete response (CR), time to progression (TTP) and overall survival (OS) were evaluated by calculating odds and hazard

ratios. Multivariate modeling with prognostic covariates was also performed.

Results: For CR, the presence of KIR2DL5A, 2DS5, 2DS1, 3DS1, and KIR3DS1/HLA-Bw4-I80 was associated with increased CR rates, with median ORs ranging from 2.1 to 4.3, while the absence of KIR2DS4 and 3DL1 was associated with increased CR rates (OR 3.1). After univariate analysis, patients that underwent resective surgery of tumor, absence of KIR2DS5, and presence of KIR3DL1/HLA-Bw4-I80 showed a significant better OS (HR 1.5 to 2.8). Multivariate analysis identified as parameters independently related to OS the type of treatment (surgery; HR 2.0) and KIR3DL1/HLA-Bw4-I80 genotype (HR for T-I80 2.7 and for no functional KIR/HLA interaction 1.8). For TTP, no association with KIR/HLA genes was observed. Instead, no significant differences were noted between KIR gene frequencies in RC patients compared with normal subjects, but when combinations of KIR genes and their HLA ligands were considered on the survival of patients, there were significant increases in frequencies of KIR2DL1 (inhibitory KIR) and A-Bw4 (ligand for inhibitory KIR3DL1) in recurrence, while KIR3DS1/HLA-Bw4-I80 and KIR2DS3 reduced the risk of recurrence.

Conclusions: This study, for the first time, evidences that the genotyping for KIR-HLA pairs are found predictive markers associated with complete response and improves overall survival prediction of FOLFIRI treatment response in metastatic colorectal cancer. These results suggest a role of the KIR/HLA system in patient outcome, and guide new research on the immunogenetics of mCRC through mechanistic studies and clinical validation.

OC.04.3

EXPRESSION OF TBET AND RORγ-T IN REGULATORY T CELLS INFLUENCE THE INCIDENCE AND SIZE OF TUMOR MASSES IN A CAC MODEL

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Background and aim: Mucosal inflammation drives colon carcinogenesis is not fully understood. Although accumulation of FoxP3-expressing T regulatory cells (Tregs) in sporadic colorectal cancer tissue represents a positive prognostic factor, co-expression of the Th17-related transcription factor ROR-γ-t and IL17A in these cells promotes tumor growth. Tregs can also co-express Tbet and RORγ-t during chronic inflammation but their role in the development of colitis-associated colorectal cancer (CAC) is unknown. In this study, we investigated the functional role of Tbet and/or ROR-γ-t-expressing Tregs in CAC murine model.

Material and methods: Treg specific Tbet and RORγ-t conditional knockout (ko) mice were used in a CAC model based on the initial intraperitoneal injection of AOM followed by 3 cycles of 7 days administration of oral 2% DSS each separated by 14 days in which mice were kept on water. Colitis severity and tumor onset were assessed by endoscopy and mice were killed at day 80. Expression of pro and anti-inflammatory proteins was assessed in the tumoral and peritumoral tissue of mice by RT-PCR and IHC. The expression of TF and cytokines Th1 and Th-17-related were analyzed in the Tregs and conventional non-Treg (ConvT) cells by flow cytometry.

Results: At the end of the AOM/DSS protocol, wt mice developed multiple polyps in the context of the inflamed mucosa. Although Tbet ko mice showed milder colitis during the first DSS cycle as compared to the Wt, this difference was lost at end of the experiment where tumor incidence and mean size resulted similar between the groups. In contrast, the colon of RORγ-t ko mice resulted more inflamed as compared to Wt but characterized by fewer and smaller tumors. The accumulation of FoxP3-expressing Tregs and ConvT cells did not differ in the peritumoral and tumoral areas among the groups. However, depletion RORγ-t in Tregs caused a reduced expression of IL-6 and STAT3 phosphorylation in epithelial cells.

Conclusions: In a CAC model RORγ-t but not Tbet expression by Tregs promotes severe colitis characterized by low expression of IL6. At the same time these mice develop a reduced number of tumors of small size characterized by a low expression of p-STAT3 thus implying that the expression of ROR-γ-t in Tregs is required to sustain the IL-6-STAT3 carcinogenic axis operating in the CAC.

OC.04.4

FROM INFLAMMATORY BOWEL DISEASE TO COLON CANCER: WHAT IS THE ROLE OF INFILTRATING IMMUNE CELLS?

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Background and aim: Patients with ulcerative colitis and Crohn's disease have an increased risk of developing colorectal cancer (CRC) but the underlying mechanisms are unknown. Several studies have demonstrated that colitis-associated CRC (CAC) is more aggressive compared to sporadic CRC, suggesting a role for the host inflammatory response. The aim of our study is to understand if and how chronic inflammation contributes to the development of CRC.

Material and methods: Immune cells were isolated from fresh intestinal biopsy tissues. This pilot study collected 30 samples of which IBD at onset (n=8), IBD after therapy (n=7), CRC (n=9), CAC (n=2) and healthy donors (n=4). The samples were digested and after were stained with fluorochrome conjugated monoclonal antibodies against intracellular and surface markers to identify specific lymphocyte subsets. Acquisition was performed on a FACS Canto II flow cytometer and data were analysed with FlowJo.

Results: IBD patients both at onset and after therapy, showed a different pattern of infiltrating immune cells compared to CRC and CAC, not only in terms of frequency but also of cytokine production. Accordingly, the frequency of type-1 innate lymphoid cells (ILC1) was higher in IBD (mean around 20%), compared to CAC and sporadic CRC; moreover, these infiltrating ILC1 produced high amounts of TNF-α in beginning IBD patients at onset, compared to treated IBD and sporadic CRC. We also observed higher frequencies of infiltrating Vδ1 in CRC

compared to IBD at onset, while Vδ2 cells had an opposite pattern. The cytokine production analysis revealed that Vδ1 T cells produced IL-17 in sporadic CRC and IFN-γ in IBD, while Vδ2 T cells produce IL-17 only in treated IBD patients and did not show any differences for IFN-γ production. TNF-α was produced exclusively by Vδ2 T cells without significative differences in all tested group.

Conclusions: Our preliminary results suggest an appreciated and unexpected role for distinct subsets of innate lymphoid cells in the progression from colitis to colon cancer and provides a tool to evaluate their contribution to the development of cancer-associated chronic inflammation.

OC.04.5

RECURRENCE AFTER ENDOSCOPIC RESECTION OF ADVANCED COLORECTAL ADENOMA: A RECURSIVE PARTITIONING ANALYSIS OF PREDICTIVE FACTORS

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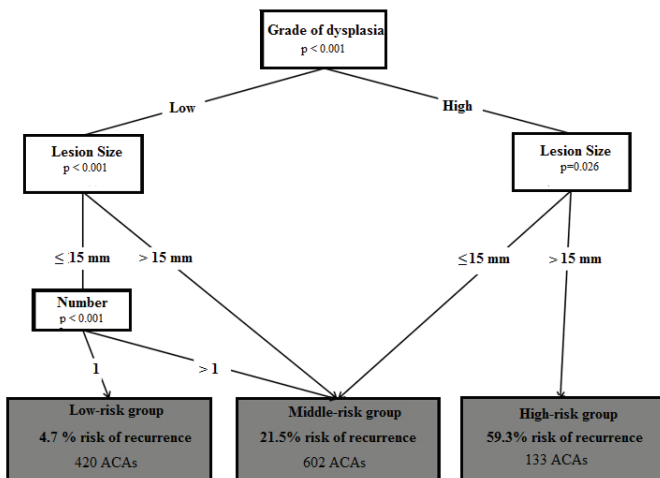
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Background and aim: Several studies have pointed out different risk factors for advanced colorectal adenoma (ACA) recurrence

after polypectomy, but the interaction between these factors is still unclear. We aimed to generate a prognostic model for post-polypectomy ACA recurrence by defining different prognostic groups.

Material and methods: Out of 3360 patients who underwent colon polypectomy at University of Foggia between 2004 and 2008, data of 843 patients with 1155 ACAs was retrospectively reviewed. Recursive partitioning analysis of predictors for 3-year post-polypectomy recurrence was performed.

Results: Median ACA size was 16 mm (interquartile range 12–23) while their median number was 1.5 (1–2). Pedunculated, sessile and non-polypoid lesions were 40.9%, 39.6% and 19.5% of ACAs detected, respectively. Independent predictors of 3-year recurrence were lesion size [odds ratio (OR): 3.96, 95% confidence interval: 1.87–7.55, $p < 0.001$], number (OR: 3.22, 2.19–5.39; $p < 0.001$) and grade of dysplasia (OR: 4.25, 2.11–7.50; $p < 0.001$), as confirmed both in logistic regression and in random forest analysis. Recursive partitioning analysis identified three risk groups: low-risk in presence of single ACA ≤ 15 mm with low-grade dysplasia (LGD), medium-risk in case of high-grade dysplasia (HGD) ≤ 15 mm, LGD > 15 mm or multiple LGDs ≤ 15 mm, and high-risk if HGD > 15 mm (Figure 1). Three-year recurrence rate was 4.7%, 21.5% and 59.3%, respectively ($p < 0.001$).



Conclusions: ACAs ≥ 15 mm presenting HGD are at higher risk of recurrence and might benefit from more intensive surveillance, while single LGD ≤ 15 mm could be considered for longer follow-up intervals.

OC.04.6

EARLY DETECTION OF METACHRONOUS COLORECTAL CANCER: THE ROLE OF FATTY ACID SYNTHASE (FASN)

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Background and aim: Patients undergoing curative resection of colorectal cancer have an increasing risk (from 0.6 up 9%) to develop a metachronous tumor, being this risk higher in the first 3 years following the diagnosis. Therefore, it would be desirable that non invasive investigations such as those based on the analysis of markers can detect, after a therapeutic resection of a CRC, the patients who have an increased risk of developing a second tumor, in order to restrict the most frequent controls only to these cases. In this study, the following markers will be evaluated with immunohistochemistry: ki-67, a nuclear protein

which is used as an index of cell proliferation; bcl-2 an oncoprotein, whose overexpression plays a role in the early stages of colorectal carcinogenesis; p-53, "the guardian of the genome", and FASN, an enzyme that catalyzes the synthesis of long-chain fatty acids, which are considered as a late marker of tumor progression.

The aim is to evaluate whether the expression of biological markers such as p53, bcl-2, Ki-67 and FASN on healthy colon mucosa is predictive of onset, presence or absence of metachronous cancer.

Material and methods: In a prospective study consecutive outpatients or inpatients diagnosed with CRC stage I–III were recruited. Patients with HNPCC or IBD were excluded. All patients underwent periodic colonoscopies during which biopsies were performed on healthy mucosa in pre-defined colic sections. The biological markers were assessed with immunohistochemistry on biopsy samples.

Results: In three year observation time a total of 16 patients (age: 53–83 years old, M:F 8:8) were examined. Three patients were diagnosed with synchronous lesions, four patients with metachronous lesions and one patient experienced recurrence of the disease. A patient, whose FASN was already positive on a healthy colon mucosa, developed a metachronous lesion on the same site of the positive biopsy, while in case of patients with synchronous lesions or recurrent disease, the FASN became positive at the same time such lesions were detected. None of the others markers investigated were detected during the study period.

Conclusions: The expression of FASN on healthy colon mucosa suggests that colon cells can transiently modify their metabolism in order to gain a greater input of energy. Therefore, the finding of its positivity, as reported in this study, may indicated an increased risk to develop a metachronous lesion and the need to submit such patients to a more intensive follow-up.

OC.04.7

IDENTIFICATION OF PROTEOMIC PROFILES ASSOCIATED WITH TUMOR REGRESSION GRADING IN RECTAL CANCER

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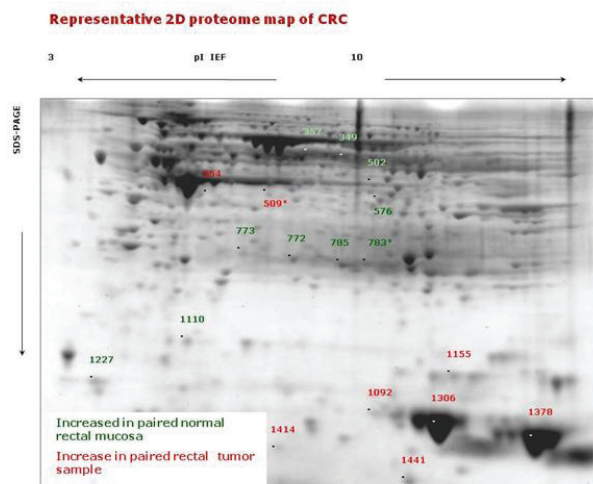
Background and aim: Rectal cancer response to neoadjuvant chemoradiotherapy (CRT) is variable. Identifying markers of response will help select patients more likely to benefit from therapy. Objective of the study is to identify at diagnosis proteomic profiles associated with tumor regression grading (TRG) in rectal cancer.

Material and methods: This study includes 40 patients with rectal cancer treated with CRT followed by surgery. Proteins from pre-treatment tumor biopsies and control from paired normal biopsies were screened for comparative proteomic approach by using 2D difference gel electrophoresis (2D-DIGE). Differential spots found with Decyder were identified by MALDI-TOF and peptide fingerprinting with Mascot search engine. Interactions among identified proteins were analyzed with STRING 9.1 search tool. Pathological TRG was assessed on surgical specimens.

Results: A total of 30 proteins were identified as discriminators between tumor samples and controls by principal component analysis and hierarchical clustering ($p < 0.01$; spot map $> 50\%$). These proteins were already described as involved in rectal metabolic cell pathways and angiogenesis. Possible correlations between these proteins and TRG are under evaluation.

Conclusions: Comparative proteomics approach based on 2D-DIGE and MALDI-TOF identification succeeded in differentiating rectal tumor samples from paired normal rectal mucosa. Further analyses will unravel possible correlations between distinct protein profiles

and TRG response to CRT treatment that could be used to select optimal therapy in rectal cancer patients.



OC.04.8

PROGNOSTIC ROLE OF 25-HYDROXYVITAMIN D IN PATIENTS WITH LIVER METASTASES FROM COLORECTAL CANCER TREATED WITH RADIOFREQUENCY ABLATION

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Background and aim: Vitamin D is implicated in the etiology of several neoplastic diseases but its relationship with colorectal cancer survival is still unclear. Aim of this study was to determine whether vitamin D levels influence survival outcomes in colorectal cancer liver metastases (CLM) patients treated with percutaneous radiofrequency ablation (RFA).

Material and methods: We measured 25(OH)D3 levels in 143 patients with 215 CLMs who underwent RFA between 1999 and 2011 at our Institution. The influence of 25(OH)D3 levels on overall survival (OS) and time to recurrence (TTR) was evaluated in univariate and multivariate Cox analyses.

Results: Median age was 68 years (range 41–85) and median number of nodules was 2 (1–3) with a median maximum diameter of 26 mm (10–48). Median OS was 44 months (36–62) and survival rate (SR) was 91.4%, 46.5% and 42.2% at 1, 4 and 5 years in the whole cohort. Median OS was 65 months (52–74) if 25(OH)D3 > 20 ng/mL and 34 months (24–41) if ≤ 20 ng/mL, (p<0.001). In the whole cohort, median TTR was 34 months (26–47) with a recurrence-free survival (RFS) rate of 79.4%, 37.7% and 27.4% at 1, 4 and 5 years. TTR was 50 months (36–62) in the case of 25(OH)D3 > 20 ng/mL and 24 months (20–32) if ≤ 20 ng/mL (p<0.001). Nodule size and 25(OH)D3 resulted as significant predictors of both OS and TTR in multivariate analysis.

Conclusions: Our study provides support for the use of 25(OH)D3 as a new predictor of outcome for CLM patients.

OC.04.9

SURVEILLANCE PROTOCOL FOR ABDOMINAL DESMOID TUMOURS IN FAMILIAL ADENOMATOUS POLYPOSIS (FAP): EXPERIENCE OF A REGIONAL REFERRAL CENTRE

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Background and aim: Desmoid tumours (DTs) are benign proliferations of stromal cells, rare in the general population and common

in patients with Familial Adenomatous Polyposis (FAP) who have undergone prophylactic colectomy. In 10% of the cases DTs show a locally aggressive and rapid growth and are a main cause of death after prophylactic colectomy in FAP patients. Nevertheless International Guidelines have not defined a surveillance protocol yet.

Aims of the present study were: to define a surveillance protocol and to evaluate the best diagnostic tool between MRI and CT; to identify DTs with aggressive behaviour.

Material and methods: From January 2010 to September 2015 patients who referred to the “Regional Referral Centre for FAP of Lazio Region” with a proven diagnosis of FAP were enrolled in the study. All patients underwent contrast-enhanced (CE) abdominal CT and MRI at least 1 year after prophylactic colectomy. Patients with DTs and without intestinal obstruction and ureteral compression received follow up examination after 6–12 months or alternatively after 2–3 months. Patients without DTs underwent follow up examination after 3 years. DTs growth assessment was performed by using RECIST criteria 1.1. The “average monthly growth rate” was also evaluated.

Results: 75 patients (40M/35F) were enrolled in the study. DTs were detected in 13/75 (17.3%) cases (7M/6F): 3 abdominal wall DTs (AWD) and 10 intrabdominal DTs (IAD). The average age at diagnosis was 31.6 years (range 19–53), the average time of onset after colectomy was 19.8 months (range 9–34). In 4/13 cases (30.7%) the IAD showed an aggressive behaviour (asymptomatic intestinal obstruction and ureteral compression seen at imaging in 3 cases and symptomatic intestinal perforation in one case). The “average monthly growth rate” was 0.58 cm (range 0.47 cm–0.75 cm) for an average follow up of 11 months (range 4–20 months). The highest value was detected in the unique symptomatic case. CT was better than MRI for imaging IAD in 13 vs 9 cases.

Conclusions: The proposed surveillance protocol allowed to detect early asymptomatic intestinal obstruction and ureteral compression in 3 cases improving clinical management. CT had a better diagnostic output than MRI and could play an important role for the first diagnosis of DTs. The evaluation of the “average monthly growth rate” could allow the identification of IAD with aggressive behaviour, improving, thus, the clinical management.

OC.05 Esophagus

OC.05.1

PROLONGED INTRA-ESOPHAGEAL PH PROFILE AND ESOPHAGEAL MOTILITY IN CHILDREN WITH EOSINOPHILIC ESOPHAGITIS

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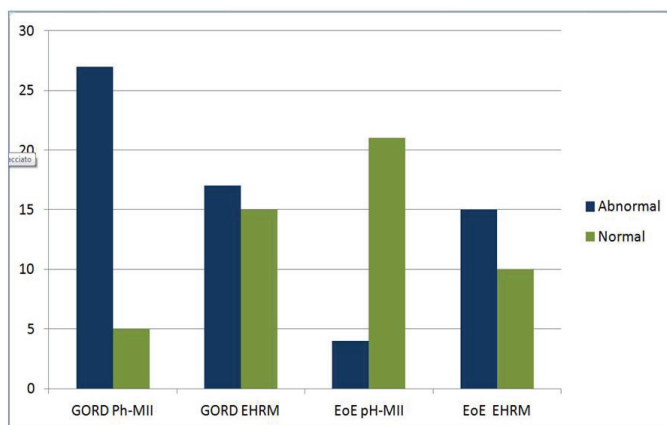
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Background and aim: Patients (pts) with eosinophilic esophagitis (EoE), a chronic immune-mediated disorder, may exhibit symptoms of disturbed food transit (i.e. dysphagia, impaction) or mimicking gastro-oesophageal reflux (GOR). We aimed at characterizing in EoE pts the intra-esophageal pH pattern with 24-h multichannel intraluminal impedance (MII-pH) as well as the esophageal motility with high-resolution manometry (EHRM).

Material and methods: during a 30 month period we studied 57 patients (pts), median age 11 years (range: 7–16): 25 with EoE, diagnosed according to widely agreed criteria (JPGN 2014;58:107–18; ESPGHAN guidelines) and 32 with GOR disease (GORD). All underwent esophagogastro-duodenoscopy, MII-pH and EHRM. The pH-MII and data analysis were done according to ESPGHAN EURO-

PIG protocol (JPGN 2012;55:230-4); variables analysed: reflux index, symptom index, number and type of liquid reflux, number of long lasting reflux episodes, correlation symptom-reflux. The test was diagnostic of GORD if at least ≥ 2 of the previous variables were positive. The EHRM was performed with water perfused catheters and swallow contractile patterns categorized using criteria recently reported by a paediatric group (Am J Gastroenterol 2010;105:460-7). Several motility variables were analysed: esophago-gastric junction (EGJ) morphology, end-expiratory and end-inspiratory EGJ pressure, distal contractile integral (DCI), pressurization front velocity (cm/s), peristaltic propagation pattern.

Results: An abnormal MII-pH profile was markedly more common in GORD pts (27; 84.37%) than in EoE pts (4; 16%; $p<0.001$). On the contrary, EHRM irregularities were detected more commonly in EoE than the GORD pts: in particular, when motility tracing were analysed no significant difference for EGJ pressure and deglutitive EGJ relaxation was detected between the 2 groups; however, abnormalities such as peristaltic dysfunction (i.e. failed peristalsis, aperistalsis, and esophageal spasm features) and lower distal contractile integral adjusted for esophageal body length (DCIa) were more common in EoE (17; 68%) than in GORD pts (15; 46.8%) ($p<0.05$).



Conclusions: The great majority of EoE pts have a normal MII-pH profile that doesn't support the use of proton pump inhibitory therapy. EoE pts exhibit higher prevalence of esophageal motility abnormalities than GORD: this feature is likely sustained by the inflammatory infiltrate that characterizes the esophageal wall in EoE and accounts for the esophageal dysmotility complaints often detected in EoE pts.

OC.05.2

HIGH RESOLUTION MANOMETRY AND CLINICAL CHARACTERISTICS OF PATIENTS WITH OUTFLOW OBSTRUCTION: IS THIS A TRULY RELEVANT NOVEL MANOMETRIC DIAGNOSIS?

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Background and aim: Recently the Chicago Classification (CC) introduced a novel diagnosis to define the presence of impaired relaxation of the lower esophageal sphincter and normal peristalsis: the outflow obstruction (OO). However, limited high resolution manometry (HRM) and clinical data are available on the characteristics of patients presenting this manometric feature. This study aimed to compare the characteristics of consecutive

patients with a manometric diagnosis of OO with those of a group of patients with GERD. Secondary aim was to evaluate their reserve of esophageal peristalsis by means of multiple rapid swallows (MRS).

Material and methods: We included 21 patients with an HRM diagnosis of OO, characterized by impaired EGJ relaxation (Integrated Relaxation Pressure; IRP >15 mmHg) but preserved peristalsis and 21 consecutive patients with GERD, as control group (CG). All patients underwent HRM off-therapy. We evaluated esophagogastric junction (EGJ) basal and maximal pressure, prevalence of compartmentalized waves (pressurization of >30 mmHg extending from the contractile front to the EGJ) and intra-bolus pressure (IBP) in both groups. All patients underwent a provocative MRS (3 mL x 5 times consecutively). IRP and distal contractile integral (DCI) during MRS were evaluated in both groups. The MRS/wet swallow ratio was also calculated.

Results: Mean age (58 ± 14.4 vs 56.6 ± 17.4), female (15 vs 12) and BMI (24.2 ± 3.2 vs 22.7 ± 2.7) were similar in both groups ($p=ns$). Dysphagia (100%) and regurgitation (59%) were prevalent symptoms in OO group. Heartburn (100%) was the prevalent symptom in CG, whereas dysphagia was absent and regurgitation (28.6%) was less frequent. EGJ basal (32.6 ± 11.6 vs 19.5 ± 11.6) and maximal pressure (48.4 ± 13.7 vs 30.4 ± 13.3) were higher in OO group ($p<0.001$). Compartmentalized waves were found in 71.4% of OO patients. As shown in Table 1, IBP was higher in OO group ($p<0.005$). DCI-MRS was two times higher in CG than in OO group. IRP during MRS decreased under 15 mmHg in 9/22 (40.9%) of patients with OO. DCI MRS/wet swallow ratio was >1 in 20/21 patients from CG but only in 3/21 in OO group.

Table 1: Main HRM findings in patients with OO and CG.

	OO mean (sd)	CG mean (sd)	P
IRP (mmHg)	21.3 (5.3)	9.7 (3.9)	<0.0001
DCI (mmHg*s*cm)	1864.4 (1085.7)	1352.1 (911.2)	0.106
DL (s)	6.9 (1.3)	6.7 (1)	0.770
Intra bolus pressure (mmHg)	20.6 (13.5)	11.2 (5.5)	0.005
DCI MRS (mmHg*s*cm)	949.9 (620.4)	1884.6 (1493)	0.011
MRS-IRP (mmHg)	16.7 (9.2)	6 (3.4)	0.001
DCI MRS/wet swallow ratio	0.6 (0.4)	1.4 (0.8)	<0.0001

Control Group, CG; Distal Contractile Integral, DCI; Distal Latency, DL; High Resolution Manometry, HRM; Integrated Relaxation Pressure, IRP; Multiple Rapid Swallows, MRS; Outflow Obstruction, OO; Standard Deviation, SD.

Conclusions: In our cohort, the diagnosis of OO was associated with the presence of obstructive symptoms (dysphagia±regurgitation) as major complain supporting the relevance of this manometric diagnosis which can be achieved by HRM. Moreover, the reserve of esophageal function evaluated with MRS and MRS/wet swallow ratio showed a reduction in OO group.

OC.05.3

NERD AND PH CYCLICAL FLUCTUATION: PROPOSED OF THE IDEAL DIAGNOSTIC ALGORITHM

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Background and aim: Non-Erosive Reflux Disease (NERD) is the most common phenotypic manifestation of Gastroesophageal Reflux Disease (GERD) and includes patients who have typical symptoms without mucosal alterations at endoscopy. These patients are pathophysiological extremely heterogeneous and must be properly classified.

Aim of our study is to demonstrate the cyclical fluctuation of pH in patients with NERD and therefore the need to investigate them through prolonged ambulatory pH monitoring and only negative patients by pH impedance.

Material and methods: From September 2013 to September 2015 300 patients with NERD (excluded esophageal injury by endoscopy) were included in our prospective study. Prolonged ambulatory pH monitoring (72/96 h) by Bravo system were performed in all of 300

patients, while pH impedance was performed only in patients with normal values.

Results: In 120 patients we have been identified pathological acid refluxes already in the first day, so pH monitoring was suspended and the patients were excluded from the study; in the remaining 180 patients the pH monitoring was prolonged for further 2-3 days (total of 72/96 h) identifying 144 patients with pathological acid refluxes (96 patients positive only in a day, 48 patients in all days of registration) and 36 patients with normal values. PH-impedance was performed only in the latter patients with evidence of 22 patients with alkaline reflux, 13 patients with weakly acidic or alkaline refluxes and 1 negative for any kind of reflux.

Conclusions: Patients with NERD are markedly heterogeneous so becomes important clearly distinguish these patients, taking into account the physiological pH fluctuations during the same day and “day by day”. This is possible by the pH monitoring Bravo system (highly tolerable and able to monitor pH for prolonged time, in respect of normal physiology) which is also able to evaluate the response to antisecretory therapy.

pH-impedance is able to detect any type of chemical reflux and allow to distinguish different types of patients suffering from NERD but not respect normal physiology and not allow a prolonged pH monitoring (not considering “day by day” pH fluctuations). Our data show that most of examined patients (88%), do not need to run a pH-impedance. To correctly classify patients with NERD and to optimizing the available resources we find useful to use first pH monitoring BRAVO system, subjecting only negative patients to pH-impedance.

OC.05.4

YIELD OF PROLONGED WIRELESS PH MONITORING IN 24 TREATED ACHALASIA PATIENTS: RETROSPECTIVE ANALYSIS

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Background and aim: Gastro-oesophageal reflux disease (GORD) is a long-term complication of achalasia treatments. 24 hr pH monitoring is often used to detect GORD in these patients. Sensitivity of the test could be influenced by day to day variability of oesophageal acid exposure time (AET) and by low incidence/absence of symptoms. Aim of our study was to evaluate the yield of prolonged wireless pH monitoring in patients with achalasia successfully treated.

Material and methods: 24 patients with achalasia (10 M; 50 years; 34-75) who underwent prolonged wireless pH monitoring after a successful treatment with single or multiple pneumatic dilation or with Heller myotomy (22 and 2 respectively) were reviewed from our cohort of patient and included in the study. pH variables were analysed in the first 24 hrs of monitoring to determine if tracings were indicative of GORD (AET>4.7% and/or positive SI/SAP for symptoms, i.e. heartburn, chest pain and regurgitation); the same variables were analysed in the following 24 hrs periods in order to obtain a worst-day diagnosis of GORD. Furthermore SI and SAP were measured on the whole period. Endoscopic findings during pH wireless capsule positioning were acquired; basal tone of the lower oesophageal sphincter was obtained during oesophageal manometry performed before the endoscopy. PPI therapy was evaluated before and after the test, and at the follow up time.

Results: All patients had at least 48 hrs of monitoring; in nine patients pH monitoring lasted 96 hrs. Descriptive data are shown in the table. Three out of 24 patients had GORD diagnosis during the first day of monitoring; all of them had oesophagitis at endoscopy. During the following days of monitoring four more patients had a worst-day diagnosis of GORD (two with oesophagitis). Patients reporting symptoms during the test (8/24) had negative SI and

SAP both during each 24 hrs and the whole period. In 3/17 patients without oesophagitis (normal AET and negative SI and SAP for heartburn) prescription of PPIs was stopped without detrimental effect on symptoms, whereas in three asymptomatic patients with both oesophagitis and pathological wireless pH monitoring PPIs were started after the test and continued until the last follow up.

Table

Data from 24 treated achalasia patients divided according to worst day GORD diagnosis at prolonged wireless pH monitoring. Median; IQR

	GORD positive (7)	GORD negative (17)	p value
Age	41; 35-46	58; 40-67	0.10
Patients with oesophagitis	5	1	0.0007
n° of pneumatic dilation before pH monitoring	2; 1-2	2; 1-2	0.88
Interval between treatment and pH monitoring (mos)	15; 12-16	15; 13-27	0.56
Basal LOS pressure (mmHg)	6; 3-11	4; 3-6	0.32
Follow up time after pH monitoring (mos)	22; 6-36	43; 29-55	0.08

LOS, lower oesophageal sphincter.

Conclusions: In achalasia patients after successful treatment GORD like symptoms may not be due to reflux. Prolonged wireless pH monitoring is a useful test together with endoscopy for evaluation of GORD and effective management of these patients.

OC.05.5

ROLE OF HIGH RESOLUTION MANOMETRY FINDINGS AND OF GASTRO-ESOPHAGEAL REFLUX DISEASE IN PATIENTS WITH NON OBSTRUCTIVE DYSPHAGIA

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Background and aim: Background: Non-obstructive dysphagia (NOD) is a real challenge in the clinical management. Esophageal high resolution manometry (HRM) is a novel method, used to analyze patients with NOD. The role of gastro-esophageal reflux disease (GERD) in eliciting NOD is not yet fully elucidated. Moreover, it is still not clear how findings on HRM relate to bolus transport through the esophagus.

Aim: To assess the role of HRM findings and of the presence of GERD in NOD pathogenesis and perception.

Material and methods: 47 consecutive patients with dysphagia underwent HRM followed by 24h impedance-pH monitoring (MII-pH). All patients performed upper endoscopy within 3 months before the study. Patients were analyzed in the semi-recumbent position, with a catheter incorporating 36 solid state pressure sensors, located at 1 cm intervals, and 9 impedance measuring segments (MMS, Enschede, The Netherlands). A total of 10 saline (5 ml) swallows, at 30-sec intervals were analyzed in each subject. High resolution manometry tracings were analyzed according to the Chicago classification v3.0. Acid exposure time (AET) and/or SAP at MII-pH were considered for GERD diagnosis. Data were compared with those obtained from 44 typical symptoms GERD patients, without dysphagia (Group 2).

Results: Seven patients presenting evidence of esophageal spasm and 3 of achalasia, and were therefore excluded from the study. The remaining 37 NOD patients were considered for the data analysis (Group 1). Mean (\pm SD) values of IRP, CFV and DCI did not differ between Group 1 and 2 patients (Table). Seventeen out of the 37 patients (46%) belonging to Group 1 presented positive AET and 19/44 (43%) Group 2 patients presented positive AET/SAP ($p < 0.05$).

Conclusions: In NOD patients, in the absence of esophageal motor abnormalities, high resolution manometry findings are comparable

to those observed in patients with GERD. In a relevant percentage of NOD patients, a pathological acid exposure in the distal esophagus might sensitize esophageal mucosa to an increased perception of esophageal bolus passage, and, therefore might explain dysphagia occurrence.

Table: Mean (\pm SD) IRP, DL, CFV and DCI values in Group 1 and 2.

	Group 1	Group 2
IRP 4sec (mmHg)	9.3 \pm 1.4	8.9 \pm 2.1
DL (sec.)	4.8 \pm 1.1	5.2 \pm 1.1
CFV (cm/sec.)	4.2 \pm 0.9	4.6 \pm 1.2
DCI (mmHg-s-cm)	1987 \pm 201	1689 \pm 457

OC.05.6

CLINICAL CHARACTERISTICS AND OUTCOMES OF POEM ACCORDING TO ACHALASIA MANOMETRIC PATTERN. DO THE OUTCOMES OF TREATMENT DEPEND ON MANOMETRIC SUBTYPE?

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Background and aim: According to High Resolution Manometry (HRM), achalasia can be classified into 3 types. Previous studies on pneumatic dilation and surgical myotomy demonstrated that worst outcomes are associated with the type III. One of the theoretical benefits of Per-Oral Endoscopy Myotomy (POEM) is that the length of myotomy can be customized according to the HRM findings. Aim of this study is to investigate characteristics and POEM outcomes of 3 achalasia types in a large series of patients.

Material and methods: A total of 290 patients with achalasia treated with POEM between 2011 and October 2015, were retrospectively identified on a prospective database. Patients who underwent HRM during preoperative work-up, and with a minimal 6 months follow-up were enrolled.

POEM was performed according to the Inoue's technique. In case of type I and type II achalasia an 8-12 cm myotomy was performed. In case of type III achalasia myotomy was usually longer (>12cm). ANOVA and Pearson Chi-square test were used to find associations between achalasia types with baseline characteristic (age, gender, Eckardt score, symptoms duration, previous treatments, esophageal shape, diameter and LES pressure), procedure time and POEM outcomes (ECK<4). If there was a statistically significant difference a post hoc analysis was performed using LSD method.

Results: A total of 182 patients were enrolled (mean age 46.4 years, mean follow-up 12.8 months, range 6–48 months). Fifty-two patients (29%) had Type I achalasia, 112 (61%) Type II and 18 (10%) type III.

At univariate analysis significant differences were found among patients with type I, type II and type III achalasia with regards to basal LES pressure (33.3 mmHg, 47.9 mmHg and 57.3mmHg, respectively. $p<0.005$), 4sIRP (26.7mmHg, 32.6mmHg and 33.2 mmHg, respectively. $p<0.005$) and esophageal diameter (5.2cm, 4.7cm and 3.6 cm, respectively. $p<0.005$).

No differences were found regarding age, gender, preoperative symptoms, symptoms duration, previous treatments and esophageal shape. At post-hoc analysis myotomy was significantly longer in patients with type III achalasia (14.3 \pm 2.8cm) compared to type I (10.9 \pm 2.3cm) or type II (11.4 \pm 2.2cm) ($p<0.0001$)

Success rate was similar in all patients, 96.2% for type I, 96.4% for type II and 94.4% for type III achalasia (p ns).

Conclusions: When myotomy is customized on HRM findings, POEM outcomes do not significant differ in patients with type I, II and III achalasia.

OC.05.7

LARYNGOPHARYNGEAL SYMPTOMS IN PRIMARY CARE: USEFULNESS OF SALIVARY PEPSIN MEASUREMENT IN PREDICTING GERD

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Background and aim: Incidence of chronic laryngeal symptoms in primary care is 2%/year and, gastroesophageal reflux disease (GERD) is considered by far the main factor associated to them, leading to a specific syndrome called Laryngopharyngeal Reflux (LPR). Several studies documented that pepsin measurement in saliva can be adopted as surrogate marker of GERD in these patients. Recently, a low cost, non-invasive salivary pepsin test (PeptestTM, RD Biomed Limited, UK) has been shown to be able to measure pepsin in the saliva/sputum and to discriminate with good sensitivity and specificity between patients with typical GERD (i.e. with heartburn and regurgitation) from those without and could be used to diagnose LPR without pH monitoring, in primary care setting. We aimed to investigate the usefulness of PeptestTM in primary care patients presenting with chronic laryngeal symptoms suggestive of LPR.

Material and methods: In a prospective multicenter, controlled, pilot study, consecutive patients presenting with chronic laryngeal symptoms were enrolled by primary care physicians. Uninvestigated individuals with no gastrointestinal symptoms or disease (including GERD) or history of surgery served as healthy controls (HCs). All subjects completed RSI questionnaire and in case of a score >13 a symptom-based diagnosis of LPR was made and GIS questionnaire was completed to investigate reflux symptoms and QoL. All individuals were asked to provide 2 samples of sputum collected one hour after the two main meal. A positive PeptestTM was considered in case of a concentration of pepsin higher than 25mg/mL.

Results: Between February and April 2014 and during August 2015, n=86 patients with LPR (37 Male/49 Female, age 54 \pm 14; RSI \geq 13, mean RSI 22 \pm 6, mean GSI 22 \pm 6.4) and 59 healthy controls (30M/29F, mean age 41 \pm 15; RSI<5, mean RSI 0.5 \pm 1, mean GSI 33 \pm 5.6) were tested. In total 256 samples were examined, whereas 34 samples were discarded because of technical problems (i.e. unclear storage, poor/excessive quantity). At least one positive result was found in 64/86 (74%) LPR patients and in 54/59 (92%) HCs ($p<0.0095$), whereas two positive results were observed in 34/70 (49%) LPR patients and 26/46 (57%) HCs ($p=0.4505$). One (in case of a single test) or two negative tests were registered in 22/86 (26%) LPR patients vs 4/59 (7%) of HCs ($p<0.0039$). PeptestTM had an accuracy of 47% (IC95 39%-55%) a sensitivity of 74% (IC95 65%-84%), a specificity of 7% (IC95 0%-13%), a positive predictive value of 54% (IC95 45%-63%) and a negative predictive value of 2% (IC95 0%-8%) in identifying LPR as diagnosed by RSI.

Conclusions: In this pilot study, PeptestTM was not able to discriminate among primary care patients with LPR from those without and therefore cannot be suggested as preliminary tool to select patients requiring pH monitoring. Further studies including investigated healthy controls are mandatory to elucidate the diagnostic utility of salivary pepsin measurement in primary care setting.

OC.05.8

ESOPHAGO-GASTRIC JUNCTION MORPHOLOGY VARIABILITY DURING STANDARD MANOMETRIC PROTOCOL AND AFTER ESOPHAGEAL STIMULATION AND BODY CHANGE POSITION – PRELIMINARY RESULTS

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Background and aim: High-resolution manometry (HRM) provides a better representation of the esophagogastric junction (EGJ) isolating the crural diaphragm (CD) from the lower esophageal sphincter (LES). According to the Chicago Classification (CC), three different EGJ morphologic subtypes can be detected based on the separation between the LES and the CD. However, few concerns have been raised about the possibility to describe a dynamic structure like the EGJ by a single snapshot taken at the beginning of the test. Thus, we aimed to assess whether EGJ morphology may vary during the standard manometric protocol and after esophageal stimulation and body change position.

Material and methods: Consecutive patients with esophageal symptoms presenting to different motility laboratories in Italy were enrolled. Patients underwent a solid state HRM with the following protocol: 5-min baseline recording after probe introduction, 10 single water swallows (WS, 5mL), 2 multiple rapid swallows (MRS, five 2mL water swallows 2–3 s apart), change of body position (seated) and multiple water swallow (MWS, 200mL of water using 'multiple, rapid swallows' without stopping). Tracings were analyzed based on the CC and EGJ morphology was assessed after each step as: Type I, no separation between the LES and the CD; Type II, minimal separation (>1 and <2 cm); Type III, >2 cm of separation. In case of reflux symptoms, patients also underwent pH-(impedance) testing off-therapy [abnormal if acid exposure time higher than 4.2% or number of reflux episodes greater than 54 or positive symptom-reflux association using symptom association probability (SAP+ if ≥95%) and symptom index (SI+ if ≥50%)].

Results: We enrolled 52 [23M/29F; mean age 52 (17–82); mean BMI 24 (17–35)] consecutive outpatients. Based on CC, we identified 32 (62%) patients with EGJ Type I, 8 (15%) with EGJ Type II and 4 (8%) with EGJ Type III, in whom no EGJ changes occurred during standard manometric protocol or after esophageal stimulation or body change position. In contrast, we identified 8 (15%) patients in whom EGJ morphology varied after WS (n=3), MWS (n=3), body change position (n=1) or MWS (n=3). In particular, in 2 patients there was more than one change. All patients with EGJ variation who underwent pH-(impedance) monitoring had an abnormal test (5/5, 100%), whereas this phenomenon occurred only in 13 out of 25 (52%) patients with stable EGJ (p=0.0657). Endoscopy did not vary between the two groups [abnormal in 2/8 (25%) with changed EGJ vs. 8/44 (18%) with stable EGJ, p=0.6415].

Conclusions: Esophago-gastric junction morphology varies only in a minority of patients, suggesting that the single assessment at the beginning of the test has a high per patient reproducibility. On the other hand, EGJ changes occurring during HRM testing are associated with more objective evidence of GERD, thus confirming the major role of EGJ as anti-reflux barrier.

OC.05.9

LONG VS SHORT POEM FOR THE TREATMENT OF ACHALASIA. INTERIM ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL

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Background and aim: The use of Per-Oral Endoscopic Myotomy (POEM) for the treatment of achalasia has been increasing in the last years. However, some technical issues remain to be defined. In the published series a long myotomy (12cm) was usually performed. Surgical myotomy is typically shorter, being protracted for about 8cm.

We report on the interim analysis of a randomized controlled trial that evaluates the outcomes of POEM according to the length of the myotomy.

Material and methods: Patients with type I and type II achalasia were randomly assigned to one of the two study groups, long-myotomy (LM) and short-myotomy (SM).

Patients in the LM-group received a 13cm-long POEM (including 3cm on the stomach); in the SM-group patients received POEM extended for 8 cm (including 3cm on the stomach). During follow-up, HRM, pH-study and EGD were regularly performed and symptoms assessed with the use of the Eckardt score (ECK).

Study outcomes were clinical success (ECK <4), variation of LES pressure, procedure time, prevalence of complications and GERD. The main hypothesis was that the results of a SM are not inferior to the results of a LM (non-inferiority trial). Calculated sample size was 200 patients. Study was approved by the IRB of the Gemelli University Hospital.

Results: Until today, 73 patients were enrolled, 38 in the LM- and 35 in the SM-group. Mean age of patients, gender, achalasia type, mean LES pressure, preoperative ECK, symptoms duration and previous treatments were similar in both groups. POEM was technically successful in all the cases. Procedure time was significantly longer in the LM-group compared to the SM-group (59.2±16.7 minutes vs 47.7±13.2 min, p=0.0018).

A total of 49 patients completed a minimum 6-month follow-up (23 in LM- and 26 in SM-group, mean follow-up 8 months). Clinical success was 100% in both groups. Postoperative ECK (0.5±0.8 vs 0.5±0.8, p=ns) and prevalence of GERD (42.9% vs 65%, p=ns) were similar in the LM- and SM-groups, respectively. LES pressure (17±9.7 mmHg vs 11.4±6.5 mmHg, p=0.02) and 4sIRP (8.6±4.9 mmHg vs 5.9±5.0 mmHg, p=0.06) were lower in the SM-group. No complications occurred, and a similar prevalence of mild procedural adverse events was reported.

Conclusions: This interim analysis demonstrates the feasibility of the study, and the safety and the efficacy of the investigational technique (SM). With the limits of an interim analysis, with a very short follow up, the main hypothesis is confirmed.

OC.06 Miscellanea 1

OC.06.1

ANALYSIS OF THE EFFICACY OF OCA IN PRIMARY BILIARY CIRRHOSIS BY VARYING PATIENT DISEASE SEVERITY ACROSS THREE RANDOMIZED DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIALS

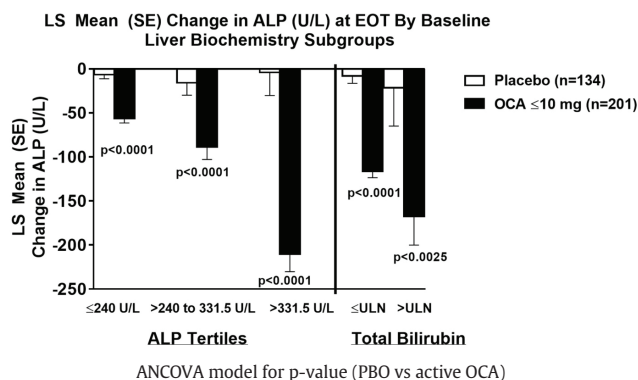
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Background and aim: Obeticholic acid (OCA), a selective and potent farnesoid X receptor (FXR) agonist, produced significant liver biochemistry improvements, including alkaline phosphatase (ALP) and total bilirubin (bili) in 3 randomized, double-blind (DB) placebo (PBO)-controlled trials in primary biliary cirrhosis (PBC). This pooled analysis from the 3 trials evaluates efficacy of OCA across a range of disease severity based on baseline (BL) ALP tertile and total bili. (\leq ULN/ $>$ ULN).

Material and methods: Key inclusion criteria: ALP 1.5 to 10x ULN and conjugated bili \leq 2x ULN for the two 3 month trials and ALP \geq 1.67x ULN or total bili $>$ ULN but $<$ 2x ULN for the 12 month trial. Data were pooled based on end of DB treatment (EOT). Treatment arms were PBO (n=134) and \leq OCA 10 mg (n=201). Endpoints were LS mean (SE) change from BL to EOT for ALP and percent of patients achieving a composite endpoint (ALP $<$ 1.67 ULN, total bili \leq ULN and ALP decrease \geq 15%), shown to be correlated with long-term survival in PBC. Safety and tolerability by disease severity were also assessed.



Results: Significant differences for OCA compared with PBO for both efficacy endpoints were achieved irrespective of PBC disease severity. The magnitude of ALP reduction was proportional to ALP tertile suggesting improved response even in more advanced patients (Figure). The percentage of OCA patients achieving the composite endpoint was inversely proportional to BL tertile (68% low, 54% mid, and 19% upper) and total bili (49% \leq ULN, 17% $>$ ULN). Similar results were observed when subgroups were analyzed by OCA monotherapy or OCA plus UDCA. Pruritus was the most common adverse event. The incidence of pruritus for OCA \leq 10 mg was similar for the low and mid tertiles and slightly higher in patients with more severe disease.

Conclusions: These data demonstrate efficacy of OCA across a range of PBC severity and confirm ALP and total bili both as continuous and categorical variables predictive of clinical outcomes.

This integrated analysis demonstrates robust response with OCA irrespective of BL ALP or total bili. Across the ranges of disease severity, OCA was safe and well-tolerated. These data are clinically relevant given that PBC is a chronic and progressive disease, and demonstrate that even in patients with more advanced disease, OCA

improves parameters shown to correlate with improved clinical outcomes and reduced risk.

OC.06.2

PANCREATIC CANCER IN WOMEN: LATE ONSET OF MENOPAUSE, USE OF HORMONE REPLACEMENT THERAPY AND TWO-PARITY ARE PROTECTIVE FACTORS

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Background and aim: The incidence of Pancreatic ductal adenocarcinoma (PDAC) is slightly higher in men than in women, although the difference in smoking and alcohol consumption between the two genders does not explain this disparity completely. Reproductive and hormonal factors might have an influence, but the few published data are inconsistent.

The aim of this study is to investigate the role of reproductive and hormonal factors on PDAC occurrence in women.

Material and methods: We conducted a unicenter case-control study on women; risk factors were screened through questionnaires about gynecologic and medical history. Cases were matched to controls for age with a 1:2 ratio.

Results: 160 PDAC and 320 matched controls (mean age 70 in both groups) were enrolled. Age of onset of menopause was significantly lower in cases (48.9 vs. 50; $p=0.02$). At a logistic regression multivariate analysis adjusted for smoking, older age at menopause (OR:0.9 per year; 95% CI:0.92-1), use of hormonal replacement therapy (HRT) (OR:0.14; 95% CI:0.04-0.49) and having given birth to two children (OR:0.62; 95% CI:0.39-0.98) were significant, independent protective factors. No difference among cases and controls was found on age of onset of menarche, nulliparity or parity different from two, use of birth control pill or number of abortions.

Conclusions: The results of this study provide support for the hypothesis that PDAC is related to reproductive or hormonal factors. In our cohort of patients, late onset of menopause, use of HRT and having given birth to two children are protective factors for the occurrence of PDAC.

Conversely, age at menarche, history of abortions, multiple abortions, use of OC, years of use of HRT or OC were not related to risk.

These data confirm some previous findings on menopause age and number of births while, to our knowledge, this is the first study to show a protective effect of Hormonal Replacement Therapy.

OC.06.3

PROTECTIVE ACTIVITY OF LACTOBACILLUS RHAMNOSUS GG-DERIVED FACTORS ON PATHOGEN LIPOPOLYSACCHARIDE (LPS)-INDUCED DAMAGE OF HUMAN COLONIC SMOOTH MUSCLE CELLS

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Background and aim: Some of the beneficial effects of probiotics result to be determined by secreted probiotic-derived factors, identified as "postbiotic" mediators. The identification of these soluble factors may represent an opportunity not only to understand their fine mechanisms of action but also to develop new therapeutic strategies, that would avoid risks associated with the administration of live bacteria. Aim of this study was to evaluate if supernatants harvested from LGG cultures protect human smooth muscle cells (SMC) from persistent LPS-induced myogenic damage.

Material and methods: *L. rhamnosus* GG (ATCC 53103 strain) was grown in MRS medium at 37°C and samples were collected in exponential, early, middle and late stationary phases. Supernatants were recovered by centrifugation, filtered and stored at -20°C. The SMC culture was exposed for 24h to purified LPS (1µg/ml) of a pathogen strain of *E.coli* (O111:B4) with and without supernatants. Postbiotics effects were evaluated on morphofunctional alterations and IL-6 production. Data are expressed as mean±SE (p<0.05 significant).

Results: LPS induced persistent significant 20.5%±0.7 cell shortening and 34.5%±2.2 decrease in acetylcholine-induced contraction of human SMC. These morphofunctional alterations were paralleled to a 365.65%±203.13 increase in IL-6 production. All these effects were dose-dependently reduced in the presence of LGG-supernatants. Supernatants of the middle exponential phase already partially restored LPS-induced cell shortening by 57.34%±12.7 and IL6 increase by 145.8%±4.3 but had no effect on inhibition of contraction. Maximal protective effects were instead obtained with supernatants of the late stationary phase with LPS-induced cell shortening restored by 84.1%±4.7, inhibition of contraction by 85.5%±6.4 and IL6 basal production by 92.7%±1.2.

Conclusions: Byproducts produced by LGG are able to directly protect human colonic smooth muscle from LPS-induced myogenic damage. Novel insights are provided about the possibility that LGG-derived products could reduce the risk of progression of a bacterial gastroenteritis to post-infective motor disorders.

OC.06.4

THE OCCURRENCE OF POSTPRANDIAL SYMPTOMS IN IRRITABLE BOWEL SYNDROME IS ASSOCIATED WITH A REDUCTION OF POSTPRANDIAL SENSITIVITY THRESHOLDS

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Background and aim: Irritable bowel syndrome (IBS) is a chronic condition with recurrent abdominal discomfort or pain associated with an alteration of bowel habits (Longstreth, Gastroenterology 2006). The pathophysiology is partially known and alterations of intestinal motility, visceral sensitivity and psycho-emotional aspects have been described, causing alterations of the activity of the brain-gut axis. Patients with IBS very frequently report abdominal symptoms after the ingestion of a meal (Bohn, Am J Gastroenterol 2013), unrelated to functional dyspepsia. Therefore, the aim of this study was the evaluation of visceral sensitivity in fasting condition and after the administration of a meal in a subgroup of IBS patients with postprandial exacerbation of symptoms in comparison with healthy volunteers (HV).

Material and methods: Thirty IBS patients (range 22-63), diagnosed according to Rome III criteria and a group of 10 age- and sex-matched HV were enrolled. In 15 IBS patients postprandial exacerbation of symptom was present, while in the other 15 patients this problem was not present. All subjects underwent the recto-sigmoid barostat test (Di Stefano, Gut 2006). A double lumen polyvinyl tube with an adherent, infinitely compliant plastic balloon was positioned at the recto-sigmoid junction. Basal and postprandial recto-sigmoid sensitivity thresholds were determined by sequential ramp distensions with patients reporting their sensation on a 0-6 scale. The modifications in balloon volume were monitored for 30 minutes during fasting and 60 minutes postprandially (200 Kcal, 200 ml liquid meal). The presence and severity of abdominal symptoms were evaluated by VAL both during fasting and in the postprandial period.

Results: In comparison with HV, both mean fasting and postprandial perception thresholds in IBS patients with or without postprandial exacerbation of symptoms did not show any significant difference (ANOVA=NS). As expected, the mean fasting discomfort threshold was significantly lower in IBS patients than in HV (IBS with postprandial symptoms 13.6±4.5 mmHg, IBS without postprandial symptoms 14.6±4.2 mmHg; HV 20.2±2.3 mmHg, ANOVA p<0.001), but between the two subgroups of IBS there were no differences. On the contrary, the postprandial discomfort threshold was significantly lower than fasting values only in the subgroup of IBS with postprandial symptoms (IBS with postprandial symptoms 8.1±5.6 mmHg, IBS without postprandial symptoms 12.9±5.9 mmHg; HV 19.0±2.5 mmHg, ANOVA p<0.001). Finally, in IBS patients with meal-related symptoms there was a significant increase of abdominal discomfort and bloating during the test. None of the patients suffered from dyspeptic symptoms.

Conclusions: In IBS patients, a further reduction of the discomfort threshold in the postprandial period may represent a pathophysiological mechanism explaining the postprandial occurrence of abdominal symptoms.

OC.06.5

ASSESSING THE RATE OF INCORRECT DIAGNOSIS OF CELIAC DISEASE: DATA FROM A TERTIARY REFERRAL CENTER

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Background and aim: It is not uncommon in clinical practice to deal with patients with a diagnosis of celiac disease (CD) who do not actually fulfill the criteria, in spite of the availability of updated international guidelines. The aim of this study was to identify incorrect diagnostic approaches to patients with suspected CD among referrals to our tertiary center.

Material and methods: The clinical records of all consecutive patients referred for the first clinical evaluation to our outpatient clinic between January 1st 2014 and October 31st, 2015 were evaluated. Patients with known or suspected CD were included. Data on symptoms, serology, duodenal histology were collected, as well as HLA class II profile when available. The current recommendations of the Italian Ministry of Health were used as a reference standard for the diagnosis of CD.

Results: During the study period, 340 patients with a recent or suspected diagnosis of CD were referred for a first evaluation to our outpatient service. An incorrect diagnostic approach was identified in 33 patients (9.7%, 28 females/5 males, median age 33 years, range 24-78) of whom 28 already possessed the medical indemnity for CD despite not fulfilling criteria for CD. The most common diagnostic mistake was the lack of HLA genetic testing and exclusion of other causes in presence of seronegative villous atrophy (n=15), followed by the absence of duodenal histology (n=6) and by tests performed already on a gluten-free diet (GFD, n=6). Five patients had been given a diagnosis of CD even in presence of negative serology and normal duodenal histology and one patient was actually allergic to wheat. The correct completion of the diagnostic work-up was programmed with a median delay of 3 years (range 6 months-9 years), with three patients receiving a final diagnosis of CD, two re-classified as potential CD, 15 in whom CD was ruled out and 12 still waiting for a definite diagnosis.

Conclusions: Despite the presence of established diagnostic criteria for CD, the rate of incorrect diagnosis was surprisingly high in our series, mainly as a consequence of preventable mistakes in the diagnostic process. These results may reflect a relevant burden on

our health system, considering the subsequent diagnostic delay and the number of unnecessary medical indemnities for CD prescribed.

OC.06.6

EFFECTS OF MODIFIED WHEAT GLUTEN ADMINISTRATION IN PATIENTS WITH CELIAC DISEASE: RESULTS OF A DOUBLE-BLIND, GLUTEN-CONTROLLED CLINICAL TRIAL

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Background and aim: The treatment of celiac disease (CD) is based on a lifelong gluten-free diet (GFD). Recent studies showed that biochemical modifications of gluten peptides, induced by microbial transglutaminase (mTG) on wheat flour in the presence of lysine ethyl ester (K-C2-H5), inhibit in vitro their ability to induce the CD-specific immune response. Our aim was to perform a double-blind, gluten-controlled clinical trial to evaluate the safety of a protracted ingestion of mTG-modified wheat flour in CD patients.

Material and methods: Twenty-two but 1 CD patients in remission were randomized to receive, in double blind, rusks made with either mTG-modified (Code A, n = 11) or unmodified (Code B, n = 10) wheat flour. Every month for a total of 3 months, patients were asked to complete an anamnestic card to monitor symptoms using a 100-mm visual analogue scale (VAS), with 0 representing the absence of symptoms. Serum anti-tissue transglutaminase (anti-tTG) and endomysium antibodies (EMA), as well as creatinine concentration were also monitored. At the end of the study, patients underwent upper endoscopy with biopsy for duodenal histology and organ culture system.

Results: Five out of 11 patients who received rusks of Code A and 6 out of 10 patients who received rusks of Code B completed the study. At baseline, all patients who completed the study showed serum anti-tTG and EMA negative results. At the end of the study, one out of 5 (20%) patients ingesting rusks of Code A and 4 out of 6 (66.7%) patients taking rusks of Code B presented serum anti-tTG and EMA positive results. In patients who received rusks of Code B, anti-tTG serum levels determined after treatment were significantly higher (p=0.0313) than those measured at baseline. No significant change was found in the creatinine serum levels after treatment of all patients who completed the study. At the end of the study, one out of 5 (20%) patients ingesting rusks of Code A and 4 out of 6 (66.7%) patients taking rusks of Code B presented intestinal villous atrophy. Consistently, anti-tTG duodenal levels determined in patients who received rusks of Code B tended to be higher than those measured in patients who ate rusks of Code A. Swelling, meteorism and nausea tended to be more severe in patients ingesting rusks of Code B than those taking rusks of Code A.

Conclusions: If data are confirmed, the enzymatic treatment of wheat flour induced by mTG in the presence of K-C2-H5 could become one of the most promising strategies for CD treatment alternative to the GFD.

OC.06.7

RISK OF MISDIAGNOSIS AND OVERTREATMENT IN PATIENTS WITH MAIN PANCREATIC DUCT DILATATION AND SUSPECTED COMBINED/MAIN-DUCT IPMNS

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Background and aim: Segmental/diffuse dilatation of main pancreatic duct (MPD) is the typical feature of combined/main-duct intraductal papillary mucinous neoplasms (CMD-IPMNs). MPD dilation in IPMNs may be also expression of mucus hypersecretion/obstructive chronic pancreatitis (OCP). The aim of this study is to evaluate the presence and extension of MPD involvement by tumor/OCP and assess the risk of overtreatment.

Material and methods: Retrospective analysis of suspected CMD-IPMNs resected between January 2009 and October 2014. Preoperative work-up included CT, MRI/MRCP and eventually EUS with FNA. Pathological correlation among MPD dilatation, IPMN and OCP was searched.

Results: 93 patients (60 males, 33 females; median age 67 years, range 31–80) were resected for suspected CMD-IPMNs. All patients underwent cross-sectional high-resolution imaging. MRI/MRCP was performed in 89 patients (96%) and MDCT in 45 (48%) and 20 patients (22%) had an EUS-FNA. At pathology CMD-IPMNs were found in 69 patients (74%). Branch-duct IPMNs (BD-IPMNs) were found in 8 cases (9%), pancreatic ductal adenocarcinoma (PDAC) in absence of IPMN in 9 (10%), cystic neuroendocrine tumor (NET G2) in 1 (1%), serous cystadenoma (SCA) in 2 (2%), and OCP alone/mucinous metaplasia in 4 patients (4%). Overall, 18 patients (19%) underwent an overtreatment because unnecessary (two BD-IPMNs, 2 serous cystadenomas and 4 OCPs only) or too extensive resections (9 CMD-IPMNs and one PDAC with associated OCP). Total pancreatectomy was the most common procedure (67%) performed in these 18 patients. Preoperative work-up did not significantly differ between patients who underwent overtreatment and the remaining ones, although only 2/18 patients (11%) underwent EUS compared with 18/75 (24%) (P=0.194). Median size of MPD in IPMN-involved area was 12 mm compared with 7 mm when only OCP was found (p < 0.05).

Conclusions: There is a considerable risk of overtreatment in patients with preoperative morphological diagnosis of CMD-IPMNs. In order to improve their diagnostic accuracy, advanced endoscopic techniques including EUS with FNA and pancreatoscopy should be used more frequently. Partial pancreatectomy with margin examination should be performed instead of upfront total pancreatectomy. Radiological observation can be considered in asymptomatic patients with "worrisome" MPD dilatation (5–9 mm) and lacking other high-risk stigmata.

OC.06.8

INTEGRATED ANALYSIS OF EFFICACY OF PHASE II AND III DATA OF OBETICHOIC ACID IN PBC SUBPOPULATIONS BASED ON AGE AND SEX

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Background and aim: A nonresponse to ursodeoxycholic acid (UDCA) is significantly more common in primary biliary cirrhosis (PBC) patients who are diagnosed before age 50 or who are male. Patients with a non-response to UDCA are at significantly increased risk of an adverse outcome such as end-stage liver disease or liver transplantation [1,2]. Obeticholic acid (OCA), a potent and selective farnesoid X receptor (FXR) agonist, induced significant liver biochemistry improvements in 3 randomized, placebo (PBO)-controlled trials in PBC patients both as a monotherapy or in combination with UDCA. This integrated analysis evaluates the efficacy and safety of OCA in PBC subpopulations based on age and sex.

Material and methods: Data were pooled across the 3 trials and endpoints were based on end of double-blind (DB) treatment. Treatment arms: PBO (n=134) and OCA ≤10 mg (n=201). Efficacy endpoints were the LS mean change from baseline (BL) in ALP and a composite endpoint (% of patients achieving an ALP <1.67x ULN, total bilirubin ≤ULN and an ALP decrease ≥15% from BL). Increased serum ALP and bilirubin levels have been strongly associated with reduced transplant-free survival. Safety and tolerability were also assessed.

Results: Irrespective of age, age at PBC diagnosis, or sex, OCA ≤10 mg treatment resulted in significant decreases in ALP and a higher percentage of patients achieving the composite endpoint, compared with PBO (Table). Safety and tolerability were similar across age and gender subgroups. Pruritus was the most frequently occurring TEAE regardless of subgroup. Incidence of pruritus was 63 vs 51% for <65/≥65 y, 62 vs 57% for age at PBC diagnosis <50/≥50 y, and 57 vs 61% for male/female subgroups.

	OCA ≤10 mg ± UDCA					
	Age (y)		Age (y) at PBC Diagnosis		Sex	
	<65 (N=160)	≥65 (N=41)	<50 (N=119)	≥50 (N=82)	Male (N=21)	Female (n=180)
BL						
ALP, Mean (SD)	334 (152)	315 (156)	338 (157)	318 (145)	294 (92)	334 (158)
End of DB Treatment						
ALP, Δ LS Mean (SE)	-133 (13)	-109 (14)	-120 (14)	-120 (13)	-111 (26)	-136 (13)
p-value	<0.0001	<0.0001	<0.0001	<0.0001	0.0009	<0.0001
Responders, n (%)	75 (47)	17 (41)	50 (42)	42 (51)	9 (43)	83 (46)
p-value	<0.0001	0.0004	<0.0001	<0.0001	0.0131	<0.0001

A responder = ALP <1.67x ULN, total bilirubin ≤ULN, and ALP decrease of ≥15% from DB BL.
p-value for comparing active treatments to PBO obtained using ANCOVA model for ALP and Cochran–Mantel–Haenszel General Association test for percent responders.

Conclusions: In contrast to PBO, significant improvements in ALP, highly predictive of outcomes, were observed across age and sex subgroups with OCA ≤10 mg. This is clinically relevant as younger patients and males who do not respond to UDCA are at higher risk of adverse outcomes/poor prognosis. OCA was generally safe and well tolerated.

References

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OC.06.9

IRRITABLE BOWEL SYNDROME: RESULTS OF AIGO SURVEY 2014-2015

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Background and aim: to determine the quality of life of patients (pts) who refer to Italian outpatient Gastroenterology clinics with a known or a first diagnosis of irritable bowel syndrome (IBS) according to Rome III criteria. Secondary aim: to determine whether the distribution of diagnostic resources can be appropriate.

Material and methods: Data from 26 AIGO centres on outpatients affected by IBS, according to Rome III criteria, have been prospectively collected from 1st July 2014 to 30st June 2015. Patients were asked to fill in an anonymous format the following questionnaires: Hospital Anxiety and Depression Scale (HADS), the Short Form (SF12) and the Irritable Bowel Syndrome Severity Scoring System (IBS-SSS). Data on medical care during the course of the previous year were also recorded: number of visits by the general practitioner and gastroenterologist, diagnostic tests, working days lost.

Results: 683 records on IBS pts (mean age 43.1 ± 15.2 yrs, 73% F, 27% M) were collected. 51.2% of the patients were a first diagnosis. Using a visual analogue scale (VAS) (0-100 mm), abdominal pain severity had a mean value of 47.1±23.3, abdominal bloating 53.0±24.4, presence of abdominal pain on a 10 days period 5.2 ± 3.0; satisfaction for bowel habit 28.8±22.9; change in their habits of living and working 47.7±25.7. According to the questionnaire HADS Anxiety, 35.8% had a score greater than 11; according to the HADS Depression, 14.5% had a pathological score (>11). Pts with a first diagnosis of IBS were significantly younger in respect to pts with a known diagnosis, 40.2±14.8 vs 46.1±15.1 (p<0.001) respectively, but did not differ for all other variables included in IBS-SSS and HADS. Data on medical care during the course of the previous year were reported in table 1.

Table 1
Procedures in IBS patients

Procedure	N	350 patients with 1th diagnosis of IBS (%)	333 patients with known diagnosis of IBS (%)
MRI	11	6 (1.7)	5 (1.5)
US abdomen	444	202 (57.7)	242 (72.6)
CT abdomen	33	9 (2.5)	24 (7.2)
Sigmoidoscopy	20	9 (2.5)	11 (3.3)
Colonoscopy	363	147 (42.0)	216 (64.8)

MRI = Magnetic Resonance Imaging ; US = Ultrasound

Conclusions: Data from this survey conducted in the AIGO Italian gastroenterology clinics demonstrated the high degree of disability of pts with IBS that is maintained over the time. The lack of difference between old and new diagnosed IBS shows that current treatments are largely unsatisfying. The use in a large number of pts of invasive procedures, such as colonoscopy, indicates a widespread inappropriateness.

OC.07 UPPER GI

OC.07.1

REFRACTORY PATIENTS WITH NON-ACID REFLUX DISEASE AND THOSE WITH EROSIIVE AND NON-EROSIVE REFLUX DISEASE HAVE SIMILAR RESPONSE TO ANTI-REFLUX SURGICAL THERAPY

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Background and aim: Recent studies clearly demonstrated the increased diagnostic yield of impedance-pH monitoring thanks to its ability to correlate gastro-esophageal reflux disease (GERD) symptoms with both acid and/or non-acid reflux episodes. However, data about the clinical usefulness of this additional diagnostic yield are poor. We aimed to assess whether refractory GERD patients classified by means of endoscopy and impedance-pH as affected by non-acid reflux disease (NARD), erosive and non-erosive reflux disease (ERD and NERD) may equally benefit from anti-reflux surgery.

Material and methods: Consecutive patients with persisting heartburn and/or regurgitation despite 8 weeks of PPI therapy, were prospectively enrolled in this open label trial. All patients underwent endoscopy and impedance-pH off-therapy. We measured esophageal acid exposure time (AET), reflux episodes (acid/non-acid) and symptom-reflux association. Then, patients with ERD (endoscopy+), NERD (endoscopy-, AET>4.2% and/or SAP/SI+ for acid reflux) and NARD (endoscopy-, AET<4.2% and SAP/SI+ for non-acid reflux or both kind of reflux) underwent laparoscopic Nissen fundoplication (LNF). Before and at 1, 6 and 12 months after LNF, reflux symptoms and quality of life were assessed using validated questionnaires. Endoscopy and impedance-pH was repeated 1 year after surgery. Surgical treatment failure was considered in case of: persisting typical reflux symptoms and/or objective evidence of GERD (esophagitis at upper endoscopy, abnormal AET and/or number of refluxes, positive symptom association) and/or poor quality of life.

Results: Out of sixty-five refractory patients, forty-eight (24F/24M; mean age 49; 14 ERD, 22 NERD and 12 NARD) were included. At 1 year follow-up, LNF had similar pathophysiological effects in all groups. Indeed, percentage of patients with abnormal AET (ERD 93% vs 7%, NERD 71% vs 0%) and/or increased number of reflux episodes (ERD 93% vs 0%, NERD 86% vs 0%, NARD 83% vs. 0%), mean AET (ERD 12.9% vs 1.8%, NERD 6.1% vs 0.7, NARD 0.7% vs 0.4%) and median number of total (ERD 100 vs 6, NERD 73 vs 9, NARD 72 vs 10), acid and non-acid refluxes significantly decreased (in all cases, $p<0.01$). As to the surgical outcome, the percentage of patients with resolved or markedly improved typical symptoms at 12 months after LNF was similar among groups (ERD 93% vs. NERD 82% vs NARD 83%, $p=ns$). Quality of life similarly improved in all groups ($p=ns$). Finally, the percentage of failure and/or adverse events did not differ among the groups (ERD 21% vs. NERD 23% vs NARD 17%, $p=ns$).

Conclusions: Our data show that LNF was a safe and effective procedure in relieving typical reflux symptoms in PPI-refractory patients identified as affected by ERD, NERD and NARD, by means of endoscopy and impedance-pH monitoring. Therefore, impedance-pH testing allowed a more clear identification of refractory patients whose symptoms are related to reflux, thus improving their management and outcome.

OC.07.2

FUNCTIONAL HEARTBURN OVERLAPS WITH IRRITABLE BOWEL SYNDROME MORE OFTEN THAN GERD. DEVELOPMENT OF PREDICTIVE MODELS WITH NOMOGRAMS

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Background and aim: Gastroesophageal reflux disease (GERD) and irritable bowel syndrome (IBS) are gastrointestinal disorders affecting a large part of the general population, with relevant impact on quality of life and health care costs. We aimed to evaluate the prevalence of irritable bowel syndrome (IBS) in patients with reflux symptoms as distinguished into gastroesophageal reflux disease (GERD) and functional heartburn (FH) on the basis of multichannel intraluminal impedance (MII)-pH monitoring. We also aimed to develop a predictive model for FH.

Material and methods: Patients underwent a structured interview based on questionnaires for GERD, IBS, anxiety and depression. Upper GI endoscopy and 24h MII-pH monitoring were performed in all cases. In patients with IBS, fecal calprotectin was measured and colonoscopy was scheduled for values >100 mg/Kg to exclude organic disease. Multivariate logistic regression analysis was performed to identify independent risk factors for FH and to develop predictive models.

Results: Of the 701 patients with heartburn who entered the study, 458 (65%) had GERD whereas 243 (35%) had FH. IBS was found in 143/458 (31%) GERD but in 187/243 (77%) FH patients ($P<0.001$). At multivariate analysis IBS, anxiety, and smoking resulted independent risk factors for FH whereas hiatal hernia resulted protective. Two predictive models, based on clinical only (ISAC) or clinical and endoscopic characteristics (ISAA-HH) were developed: the area under the ROC curve did not differ between ISAC (0.861, 95% CI 0.833–0.890) and ISAA-HH (0.872, 95%CI 0.844–0.899) ($P=0.110$).

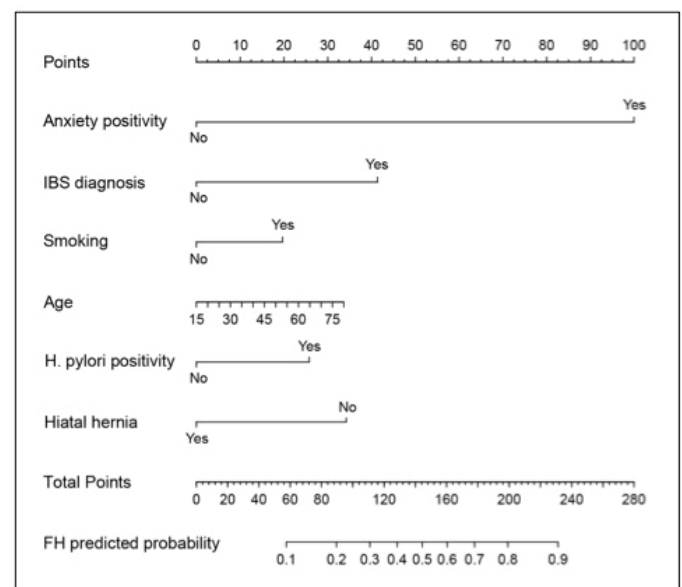


Fig. 1. Nomogram derived from the ISAA-HH (IBS, Smoking, Anxiety, Age, Hiatal hernia, H. pylori positivity) predictive model. Each independent variable corresponds to an axis; in order to obtain the corresponding score, the position on the axis must be reported perpendicularly on the "Points axis" at the top of the figure (e.g., anxiety diagnosis corresponds to 100 points). This passage has to be repeated for all the variables. Then, the total predictive score is obtained by summing all the single scores, and must be reported on the "Total points" axis. The position has to be perpendicularly reported on the "Predicted FH probability" axis to obtain the predicted probability of FH diagnosis.

Conclusions: IBS overlaps more frequently with FH than with GERD, suggesting common pathways and treatment for these two functional GI disorders. The nomograms derived from the ISAC and the ISAA-HH predictive models allow a high level of suspicion for FH and can be useful in clinical practice.

OC.07.3

RECOVERY OF GASTRIC FUNCTION AFTER ACETIUM® ADMINISTRATION: A 2 YEAR PROSPECTIVE STUDY IN PATIENTS WITH CHRONIC, ATROPHIC, BODY GASTRITIS

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Background and aim: The relationship between H.pylori eradication and atrophic changes in the gastric mucosa has not yet been fully elucidated. Although some studies report a partial restoration of pepsinogen I (PGI) levels after eradication, it is not clear whether this finding reflects gastric healing. L-cysteine (Acetium(TM), Biohit Oyj, Finland), an agent capable of reducing acetaldehyde after food intake, has been proposed for prevention of gastric carcinogenesis in patients with body CAG. Present study aims to assess modifications in gastric function after Acetium(TM) administration in body CAG by means of PGI, PGII and G-17 serum levels.

Material and methods: 65 patients (M:F=19:46, mean age 52.2±9.3 years), with histological diagnosis of body CAG (according to the O.L.G.A. staging) and PGI < 25 µg/L, underwent upper GI endoscopy with gastric biopsy samplings and PGI, PGII and G-17 by means of Gastropanel(R) (Biohit Oyj, Helsinki, Finland). Among the patients, 26 had autoimmune gastritis while 39 of them reported previous H.pylorii infection. All the patients were treated with Acetium(TM) (100 mg three times daily) for 24 months. PGI, PGII and G-17 values were measured at baseline and at T+3, T+6, T+12, T+18 and T+24 months and confronted through a General Linear Model adapted for repeated measures.

Results: PGI and PGII values did not significantly differ at the end of follow up (in both cases, GLM p value > 0.05), and covariates such as age, baseline disorders and sex were not associated with a significantly different effect. On the other hand, G-17 values significantly decreased during the follow-up (p = 0.018), in particular after the first year of treatment (46.1±36.9 pmol/L at baseline vs 34.7±28.2 pmol/L at T+12 months, and 28.1±19.8 at T+24). Subjects of male sex (p = 0.022) and post-H.pylorii infection status (p = 0.034) presented the most significant reduction of G-17 values.

Conclusions: After Acetium(TM) administration, patients with body CAG showed improvements of gastric function, reflected by a significant decrease of G-17, with a more evident effect on male subjects and in cases with a previous diagnosis of H. pylori infection. As the reduction of G-17 serological values is more evident after 12 months of treatment, it should not be discontinued even after initial clinically unsatisfying results.

OC.07.4

GASTROESOPHAGEAL REFLUX DISEASE BEFORE AND AFTER LAPAROSCOPIC SLEEVE GASTRECTOMY: LONG TERM RESULTS

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Background and aim: Laparoscopic Sleeve Gastrectomy (LSG) is becoming the most performed bariatric procedure, however, data available on long-term follow-up are scanty. The effects of LSG on GERD remain controversial. Objectives: Evaluate the 5 years efficacy of LSG on weight loss and gastroesophageal reflux disease (GERD) symptoms.

Material and methods: 105 obese patients eligible for bariatric surgery underwent LSG. According to the preoperative Body Mass Index (BMI) obese patients were divided in two Groups: Group 1 (N=61, patients with preoperative BMI ≤ 50 Kg/m²) and Group 2 (N=44, patients with preoperative BMI > 50 Kg/m²). All underwent a preoperative assessment including evaluation of comorbidities, standardized GERD questionnaire, a double-contrast barium swallow (dc-BS), an upper-gastrointestinal endoscopy (UGIE). The postoperative evaluation was performed at 1, 3, 5 year after surgery. At each follow-up visit the following data were collected: weight (expressed as BMI, Delta BMI [BMI at follow-up - preoperative BMI], Total Weight Loss[%TWL]), and GERD symptoms.

Table 1

Linear regression model with the TWL% as dependent variables, and age, gender, post-operative prevalence of GERD, T2DM, hypertension and hyperlipidemia as covariates

Parameter	B	SE	t	Sig	Confidence interval	
					Lower limit	Upper limit
Intercept	51.65	6.07	8.51	0.000	39.57	63.72
Age	-0.43	0.11	-3.89	0.000	-0.65	-0.21
Gender	0.41	2.34	0.18	0.86	-4.23	5.06
Postoperative GERD	-6.26	2.80	-2.24	0.03	-11.83	-0.70
Postoperative T2DM	5.62	7.81	0.72	0.47	-9.93	21.16
Postoperative Hypertension	0.026	3.33	-1.18	0.24	-10.38	2.64
Postoperative Hyperlipidemia	-3.86	3.27	-1.18	0.24	-10.37	2.64

*SE=Standard Error

Results: BMI at surgery was 41±5 Kg/m² in Group1 vs 57±6 Kg/m² in Group2 (p<0.001). Age at surgery was similar in the two Groups (p=0.5). 31% of Group1 vs 25% of Group2 referred preoperative GERD symptoms (p=0.6). In 16% of patients of Group1 and 7% of Group2 the preoperative dc-BS and/or the UGIE revealed the presence of hiatal hernia (HH). Patients with typical GERD symptoms showed a significantly higher prevalence of HH compared to patients without GERD complains (23.1% vs. 6.8%, p=0.02). At 5 years of follow-up, the BMI was 30.1± 4.8 Kg/m² in Group 1 vs 37.8± 8.3 Kg/m² in Group 2 (p<0.001). Delta BMI was significantly higher in Group 2 than in Group 1 at 1-3 and 5 years (p<0.001). Group 2 showed also a significantly higher %TWL (26.6±18.3 vs 33.5±12.9, p=0.006) than Group 1. No significative differences were found in postoperative typical GERD symptoms between Group 1 and Group 2 patients (18.2% vs 20%, p=0.83). Among the patients of Group 1: 65% referred the resolution, 35% the persistence and 15% the new onset of GERD complaints. Among the patients of Group 2, 44% referred the resolution, 56% the persistence and 8% the new onset of GERD complaints. Younger age at surgery and absence of postoperative

GERD were associated with a better %TWL% at 5 years. ($p < 0.001$ and $p = 0.03$) (Table1).

Conclusions: LSG is an effective procedure at long-term, with good weight loss outcomes. Age at surgery and presence of postoperative GERD symptoms could play a role in the long term weight outcomes.

OC.07.5

GASTROINTESTINAL SYMPTOMS AND DYSPEPSIA IN AUTOIMMUNE GASTRITIS: AN OVERLOOKED OCCURRENCE

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Background and aim: Autoimmune gastritis (AG) is characterized by loss of the oxyntic glands with consequent hypochlorhydria, presence of gastric autoantibodies (anti-parietal cell and/or anti-intrinsic factor) and, in a later stage, pernicious anemia. Traditionally, AG is considered a silent disease, however scanty data on the pattern of gastrointestinal symptoms are available. Aim of this study is to assess the occurrence and pattern of symptoms in AG patients.

Material and methods: Gastrointestinal symptoms of 379 AG patients, [70.2% female, median age 55 years (range 17-83)], with (53.6%) or without (46.4%) pernicious anemia, were systematically assessed and retrospectively classified following Rome III Criteria. The anemia pattern, positivity to gastric autoantibodies, *Helicobacter pylori* infection, and concomitant autoimmune disease were evaluated. Univariate analyses were performed by Mann-Whitney and Fisher's exact tests for categorical and continuous variables and odds ratio (OR) and 95% confidence intervals (CIs) were used to describe associations and were obtained by logistic regression analysis. Two-tailed p values < 0.05 were considered statistically significant.

Results: Two hundred fifteen patients (56.7%) complained of gastrointestinal symptoms, 69.8% of them had exclusively upper symptoms, 15.8% only lower and 14.4% concomitant upper and lower symptoms. Among upper GI symptoms, 60.2% reported dyspepsia subtype post-prandial distress syndrome (PDS), 3.8% dyspepsia subtype epigastric pain syndrome (EPS), 7.2% overlap between PDS and EPS, 7.2% gastro-esophageal reflux disease (GERD), 17.7% GERD and dyspepsia, and 3.8% nausea. Logistic regression analysis showed that age < 55 years [OR 1.6 (CI:1-2.5)], absence of smoking habit [OR 2.2 (CI: 1.2-4)] and absence of anemia [OR 3.1 (CI:1.5-6.4)] were independent factors associated to dyspepsia, whereas positivity to gastric autoantibodies, *Helicobacter pylori* infection, and concomitant autoimmune disease were not associated.

Conclusions: This study shows that AG is a condition which in more than half of cases is associated with GI symptoms, mainly dyspepsia, revisiting the concept of a silent disease.

OC.07.6

SERUM BIOMARKERS CAN IDENTIFY PATIENTS WITH AUTOIMMUNE AND H.PYLORI-RELATED ATROPHIC GASTRITIS AND DIFFERENTIATE THOSE WITH ADVANCED GASTRIC CHANGES

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Background and aim: Autoimmune atrophic gastritis (AAG) and multifocal H.pylori-related atrophic gastritis (MAG) are precancerous condition at risk for adenocarcinoma and gastric carcinoid (AAG). The OLGA staging (Operative Link for Gastritis Assessment) has been validated in MAG as well as in AAG. Our aim was to assess whether the determination of simple serum biomarkers allows the prediction of MAG and AAG, the identification of patients with advanced disease and the risk of carcinoid in AAG.

Material and methods: 189 patients with AAG, 157 with MAG and 38 controls (C) underwent endoscopy with at least 5 biopsies (Sydney system) and blood tests (ELISA for Gastrin, PGI and PGII). Statistics included Kolmogorov-Smirnov, Kruskal-Wallis, ROC curves, multivariate and discriminant analysis.

Results: Median values of Pgl, Pgl/PGII and gastrin in AAG, MAG and C were significantly different ($p < 0.0001$ for all comparisons). Same was true for Gastrin/PGI, a new parameter, introduced considering the inverse behaviour of gastrin and Pgl in AAG. Cut-offs, AUCs and accuracy (ACC) for the various parameters are reported in the Table. The cut-offs selected (ROC curves) showed high sensitivity, specificity, PPV, NPV and overall ACC. The distribution of the parameters in AAG according to the OLGA staging was significantly different (stages 0-I vs II-III/IV, $p < 0.0005$ for each). The cut-off for gastrin/Pgl was the same between C and AAG and AAG and MAG. In AAG, Pgl and gastrin/Pgl levels were different in the various stages of ECL hyperplasia (linear, micronodular, nodular, carcinoid, $p < 0.01$ for both). Nodular hyperplasia and carcinoid aggregated in OLGA II-III-IV. A multivariate analysis identified Pgl/PGII and gastrin as independent predictors of the diagnosis. Discriminant Analysis demonstrated a patients correct allocation in 80% of the cases (62.5 of C, 60% of MAG, 85% of AAG).

Table	C vs MAG		C vs AAG		MAG vs AAG		Mean AUC/ACC
	Cut-off	AUC/ACC	Cut-off	AUC/ACC	Cut-off	AUC/ACC	
Pgl ($\mu\text{g/L}$)	70	0.665 0.347	30	0.839 0.767	30	0.861 0.747	0.771 0.620
Pgl/PGII	9	0.682 0.313	3	0.933 0.797	3	0.891 0.741	0.855 0.617
Gastrin (pmol/L)	44	0.711 0.442	83	0.937 0.868	133	0.908 0.812	0.852 0.707
Gastrin/Pgl	3	0.473 0.221	6	0.916 0.786	6	0.904 0.785	0.764 0.597

Conclusions: Pgl/PGII ratio and gastrin differentiate C from patients harboring AAG or MAG, thus confirming the role of their determination in sorting out patients that should undergo endoscopy. Gastrin/Pgl, even though not selected in the multivariate analysis, is a promising biomarker.

OC.07.7

INSULIN-MEDIATED ESOPHAGEAL ADENOCARCINOMA DEVELOPMENT RELATED TO CHRONIC DUODENUM-ESOPHAGEAL REFLUX IN A HYPERINSULINEMIC AND NON-OBESE MURINE MODEL

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Background and aim: Esophageal adenocarcinoma (EAC) is a cancer with a rapidly increasing incidence in the western countries. Barrett's esophagus (BE), its main risk factor and precancerous lesion, related to gastro-duodenum-esophageal reflux disease (GERD), has seen a comparable increase in its incidence as well. Several studies showed that central obesity has a strong correlation with both, EAC and BE onset.

Central obesity is characterized by various hormonal and metabolic changes related to the underlying insulin resistance. Insulin resistance is characterized by compensatory hyperinsulinemia that could have a proliferative and possibly a pro-carcinogenic effect on

epithelial cells. The aim of this study was to evaluate the role of hyperinsulinemia in EAC onset related to GERD, in a murine model of surgically-induced EAC.

Material and methods: We used the transgenic MKR+/+ murine model characterized by marked hyperinsulinemia and a mild dysglycemia, without showing obesity and/or a diabetic phenotype. Twenty-nine wild type and twenty-nine MKR+/+ mice underwent duodenum/jejunum-esophageal anastomosis in order to induce reflux. Thirty weeks after surgery the mice were sacrificed, the esophagus was explanted and the blood was recovered. Serum concentrations of glucose, insulin, C-peptide and leptin were measured by Luminex-XMap-Technology. Histological and insulin signal analysis were performed in the esophageal tissue. Non-operated wild type and MKR+/+ mice were used as controls.

Results: Hyperinsulinemic mice developed very high percentages of EAC (75,9%) compared with normo-insulinemic wild type mice (34,5%). The higher insulin concentration in MKR+/+ mice compared to wild type mice (2474,3 pg/mL and 697,3 pg/mL, respectively; $p=0.038$) corresponded to insulin signal pathway increase in murine esophageal tissue. Insulin signal amplification leads to downstream proteins activation, such as Akt and p70S6K, that are involved on cell survival and proliferation mechanisms. Insulin signal increase in pre-neoplastic lesion suggests an involvement of hyperinsulinemia along disease progression.

Conclusions: Taken together our results suggest a key role of insulin for promoting both, pre-cancerous and cancerous lesions, in chronic duodenum-esophageal reflux condition. Monitoring of serum metabolic parameters in hyperinsulinemic GERD and BE patients and to improve their metabolic status and insulin sensitivity with a correct diet and physical activity could have strong implications for EAC prevention.

OC.07.8

COMBINED USE OF SERUM MARKERS AND MORPHOLOGICAL EVALUATION IN EARLY CHRONIC ATROPHIC GASTRITIS DETECTION: PRELIMINARY RESULTS

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Background and aim: Chronic atrophic gastritis (CAG) is one of the key steps in developing gastric malignancy. Its early diagnosis may be focused by gastric biochemical markers (pepsinogens and gastrin 17); the aetiology may be established by *Helicobacter pylori* (Hp), parietal cell (PCA) and Intrinsic Factor (IF) antibodies.

The aim of the study was to establish the predictive value of serum biomarkers in early detection of chronic atrophic gastritis either infective and/or autoimmune patterns.

Material and methods: From April 2013 to July 2015 in the sera of 1844 subjects (M=641, F=1203, age 44 years, means 6-87), selected on the basis of the presence of dyspeptic (but not alarm) symptoms, microcytic anemia iron therapy resistant or macrocytemia, risk factor for CAG (family, autoimmune thyroid disease, autoimmune multiple syndrome), Pepsinogen I (PGI) and II (PGII), Gastrin 17 (G17) and HP (Biohit, Plc, Finlandia) were detected. PCA (IFA/FEIA methods) and IF (Dot Blot/FEIA methods) were assayed only in patients serologically individuated as CAG which were also submitted to endoscopy (EGDS) and histological evaluation (OLGA System).

Results: 54/1844 patients (2,9%) showed a serum pattern compatible with CAG (8 M, 46 F). 46/54 (85,2%) and 18/54 (33,3%) subjects were PCA and IF positive, respectively; 49/54 (90,7%) CAG were histologically confirmed, while 5 patients who presented slight

low PGI and PGI/II ratio and slight increase of G17 were classified as OLGA 0. HP were found in 40%, 25%, 15,4% and 11,7% of patients from OLGA 0 to OLGA III; PCA positivity was detected in I-IV OLGA patients but not in 0 group, while IF was present only in OLGA II and III but not in the other groups.

Conclusions: Low PGI levels and PGI/II ratio can early indicate a functional CGA. The progression of functional impairment showed by increased G17 levels is well correlated with the atrophy grade. Hp infection seems to be the most relevant aetiological factor in pre-atrophic stages, while autoimmune picture better characterizes the degree of CGA. PCA and IF autoantibodies are suggestive for the presence of atrophy.

OC.07.9

POTENTIAL AUTOIMMUNE ATROPHIC GASTRITIS

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Background and aim: Autoimmune atrophic gastritis (AAG) is an organ specific autoimmune disease characterized by gastric body-fundus atrophy with antrum sparing. AAG diagnosis is based on distinctive features according to the updated Sydney system. Some serological markers, such as parietal cells autoantibodies (PCA), fasting gastrin, vitamin B12, complete blood count and chromogranin A may be useful in the early diagnosis of AAG. The natural history of PCA positive patients is still unknown; in particular in high-risk patients (history of autoimmune diseases, patients with subtle histological alterations). Aim of the present study is to define a risk group of subjects that may develop AAG, therefore defining a potential AAG.

Material and methods: All outpatients referred to our gastro-enterological unit, over a 3-year period, screened for AAG (PCA status and gastric bioptic samples) were enrolled. Among them, patients showing only PCA positivity and those with subtle histological alterations, i.e. gastrin cells hyperplasia, enterochromaffine-like cell (ECL) hyperplasia, low grade atrophy) were evaluated after a year through an upper endoscopy.

Results: Among 2147 patients undergoing upper endoscopy over a 3-yr period, AAG was identified in 202 patients (ratio F:M=2.5:1, mean age 60±18.6 years, range 15-82 years). Fourteen patients (ratio F:M 1:1, mean age 56±16.5) had no or low grade corpus atrophy; all of them had gastrin cell hyperplasia and/or ECL hyperplasia and were PCA positive. All of them underwent upper endoscopy after a year and only one had a total regression of the lesions described, whereas the others developed a frank corpus atrophy

Conclusions: AAG may onset only with scanty histological alterations and PCA positivity may predict the development of the disease. Up to now, natural history of AAG has never been studied. A better characterization of patients may facilitate early detection, identifying a subset of individuals at risk. Finally, patients showing subtle histological alterations should undergo an endoscopic follow-up, as well as those with PCA positivity.

Background and aim: Recently new specifically designed devices for interventional EUS such as Hot-AXIOS™ have significantly changed the technical approach in this setting allowing a simple, safe and

time saving procedure. The aim of this study was to describe a single center experience with the “Hot Axios” stent placement.

Material and methods: The new lumen-apposing metal stent (HOT AXIOS, Xlumen Inc, Mountain View, Calif) is a fully covered, nitinol, braided stent with bilateral anchor flanges. The lumen diameters available are 6, 8, 10 and 15 mm. Clinical applications are various. We retrospectively reviewed all consecutive patients treated with this device in our Unit between March 2014 and October 2015.

Results: Twenty patients were treated by a single operator, with lumen-apposing stent by EUS guided drainage. The population cohort was composed by 9 male and 11 female, with mean age of 66.1 years (ranging from 37-95 y). The indications of EUS drainage were: 12 pancreatic fluid collections (PFC) (2 stents with diameter of 10 mm, 10 with 15 mm of diameter), 1 pancreatic necrosectomy (stent diameter of 15 mm), 6 cholecystitis in patients not fit for surgery (3 with stent diameter of 10 mm, 3 with 15 mm of diameter), 1 cholangitis in patient with papilla of Vater unreachable by ERCP (8 mm of stent diameter). All patients were treated under deep sedation with propofol, with the linear array Olympus GF-UCT-180 series echoendoscopes in combination with the echoprocessor EU-ME2, in a single step fluoroless procedure. The mean duration of EUS procedure was 13.5 minutes (ranging for 10 to 25 m). All stents were successfully positioned without complication and the mean duration of time for stent placement was 1.8 minutes (ranging for 1 to 8). Eighteen stents were placed transgastric, 2 transduodenal. Stent removal was safely performed in 6 patients treated for pancreatic fluid collection, after a median of 3,5 months. No complications occurred during stent placement neither during stent removal.

Conclusions: EUS-guided transmural drainage with the electrocautery-enhanced delivery system is a safe, fast, easy and minimally invasive technique with a high technical and clinical success rate. EUS-guided drainage is now the treatment of choice in case of PFC, allowing their safe puncture under direct view. So far, only ERCP dedicated devices have been adapted for this purposes. In the last years, however, new specifically designed devices for interventional EUS such as Hot-AXIOS™ have significantly changed the technical approach in this setting allowing a simple, safe and time saving procedure.

OC.08.3

DYSPEPTIC PATIENTS WITH NEGATIVE GASTROSCOPY HAVE HIGHER PREVALENCE OF H. PYLORI INFECTION THAN PATIENTS WITH ENDOSCOPIC LESIONS

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Background and aim: In patients with dyspepsia, esophagogastro-duodenoscopy (EGD) is often negative for visible mucosal lesions. Routine biopsies of the normal-appearing gastric body and antrum for the detection of H. pylori infection are not routinely obtained. There are no clinical standards for the performance of such biopsies of normal-appearing mucosa and diagnostic gain is conflicting. The clinical benefit of routine bioptic sampling is still debated and recent Kyoto guidelines suggest to consider H. pylori-related dyspepsia a specific clinical entity, distinguished from functional dyspepsia. The study aim was to assess the prevalence of H. pylori infection and related gastric mucosal changes in patients with dyspepsia without endoscopically visible lesions.

Material and methods: This post-hoc study focuses on endoscopic-histological data from 589 patients (female 67%, median age 57 (40-69) yrs) with dyspepsia obtained during a prospective, nationwide study. Patients with dyspepsia as the sole indication for EGD were included. Exclusion criteria were previous gastric surgery, severe

chronic disease, and prior treatment for H. pylori infection. All patients underwent EGD with standard biopsy sampling to search for H. pylori infection according to the updated Sydney System. Clinical data were collected using a structured clinical questionnaire, including life style items, upper gastrointestinal symptoms, and ongoing treatments (PPIs, H2-antagonists, NSAIDs).

Results: In 349 (59.2%) of patients the gastric mucosa appeared normal. Endoscopic lesions were present in the remaining 40.8%, most frequently gastric or duodenal erosions (18%) or peptic ulcer (3.5%). Overall, 141 (23.9%) of patients were on ongoing anti-secretory treatment.

The prevalence of H. pylori was more frequent in patients without endoscopically visible lesions, exclusively in the corpus (36.4% versus 25.5%, p=0.02, OR 1.67, 95%CI 1.1-2.6), while in the antrum this prevalence was overlapping (OR 0.93; 95%CI 0.6-1.4). Precancerous lesions as corporal atrophy and intestinal metaplasia were similar being present in 6.1% and 6.7% in patients with endoscopically visible lesions compared to 8.4% and 9.3% in patients without visible lesions.

Conclusions: Dyspeptic patients with negative gastroscopy show a nearly 1.7-fold higher probability of having H. pylori infection in the corporal mucosa. These data highlight the need of bioptic mapping in dyspeptic patients when gastroscopy is negative to diagnose H. pylori-related dyspepsia.

OC.08.4

ENDOSCOPIC PAPILLECTOMY: A SINGLE ITALIAN CENTRE EXPERIENCE

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Background and aim: Endoscopic papillectomy (EP) has been recognized as a safe and valuable therapeutic procedure for ampullary adenomas that can obviate the need for potentially major surgical intervention. This study aims to evaluate efficacy, safety and outcome of this technique.

Material and methods: All consecutive patients who underwent endoscopic papillectomy because ampullary tumor at Arcispedale Santa Maria Nuova (Reggio Emilia, Italy) between January 1992 and December 2014 were considered; only patient with diagnosis of ampullary adenoma on the endoscopic resection specimen were included in the analysis.

The primary outcome of the study was the technical success of the papillectomy.

The secondary outcomes were the incidence of adverse events, the incidence of recurrence, and the comparison of these outcomes between patients with sporadic ampullary adenomas (SAA) and patients with FAP-associated ones.

Technical success was achieved when the following criteria were met: a) complete removal, even in multiple sessions, confirmed by the absence of residues at histology at the first follow-up; b) the absence of recurrence in the follow-up.

Technical failure was defined when at least one of the following criteria was met: a) histology > pT1; b) residual adenomatous tissue not suitable of endoscopic resection; c) recurrence: the presence of adenomatous tissue, confirmed by histology, after at least one negative control after papillectomy.

Results: 59 patients were enrolled: 22 FAP and 37 SAA. Technical success was achieved in 24 patients (40.6%): 10 (45.4%) FAP and 14 (37.8%) SAA.

Mortality was 0% and morbidity 9/59 (15.2%) included bleeding in 4 patients, and 5 patients had acute pancreatitis.

During follow-up 23 (39%) patients had recurrence: 11 FAP (50%) and 12 SAA (32.5%). 6 patients (10.2%) were referred to surgery for

technical failure: 1 FAP (4.6%), 5 SAA (13.5%). 6 patients were lost to follow up.

Histology showed: nonspecific changes (8.5%), low grade dysplasia (37.3%), high grade dysplasia (39%) and carcinoma (11.9%). No carcinoma in the FAP group.

Biopsy sampling accuracy was higher for low grade dysplasia (77.3%) compared with high grade dysplasia (17.4%) or carcinoma (14.3%) in both group.

Conclusions: Endoscopic papillectomy of selected ampullary tumors is a safe and effective procedure and, as it can achieve a complete endoscopic resection, it should be established as the first line therapy of ampullary adenomas.

OC.08.5

HAVE INTRAVENOUS PROTON PUMP INHIBITORS BETTER CLINICAL OUTCOME RESPECT TO ORAL PPI IN PATIENTS WITH PEPTIC ULCER BLEEDING: A META-ANALYSIS

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Background and aim: The efficacy of Proton pump inhibitors (PPI) has been proved in peptic ulcer bleeding but the administration route remain controversial. Several studies have shown that oral PPI at high dose is effective as intravenous PPI in reducing recurrent bleeding. However current guideline recommend to use intravenous PPI after endoscopic treatment. To the best of our knowledge a previous metanalysis showed that oral and IV PPI have similar clinical effectiveness but the conclusion was limited by insufficient sample size. To compare the oral and intravenous PPI in patients with peptic ulcer bleeding a metanalysis was performed.

Material and methods: A computerized medical literature search was performed by using MEDLINE, EMBASE, Cochrane Library, from 1980 to March 2015 aimed at identifying available studies that assess efficacy of different route of administration of PPI. We finally analyzed 9 RCTS, involving 1021 patients.

Outcomes were: rebleeding rate, blood transfusion requirement, hospital stay, surgery and mortality.

Results: There was no difference in rebleeding rate (OR 0.94 85%CI 0.62-1.42) and mortality (OR 0.57, 95%CI 0.22-1.49). Of note surgery and need for blood transfusion were higher in iv PPI group (OR 0.32, 95%CI 0.12-0.90; SMD -0.57 95%CI -0.89,-0.25), while hospital stay (SMD -0.73 95%CI -1.70, 0.24) and mortality were equivalent (OR 0.57 95%CI 0.22-1.49).

Conclusions: Intravenous PPI is not superior to oral PPI. Oral PPI seems to have less need for surgery and blood transfusion. More RCTS are warranted to clarify this results.

OC.08.6

EVALUATION OF A NEW THERAPEUTIC LASER SYSTEM FOR ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) IN AN ESTABLISHED ANIMAL MODEL

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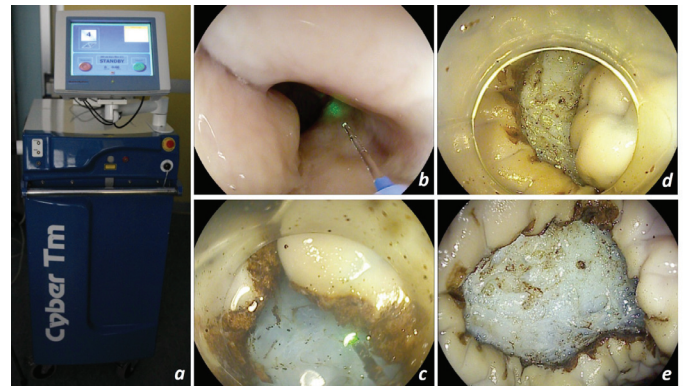
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Background and aim: The Thulium laser system is a novel therapeutic technique for open surgery and endourological treatments [1,2] (fig. a). To date, the experience on the use of the

Thulium laser system in gastrointestinal (GI) endoscopy is very limited [3].

Material and methods: We conducted the first pilot study in an established experimental setting by using the EASIE model to test the feasibility and safety of the newly introduced Thulium laser system (Cyber TM®, Quanta System, Varese, Italy) for endoscopic submucosal dissection (ESD) in GI endoscopy. Therefore, different optical fibers suitable for digestive endoscopy (272 and 365 μ m thick), were evaluated with various power settings (15, 20, 25, 30, and 35 watts), and laser configurations (continued laser shaping or pulse modality). The ESD procedure of artificial lesions of the stomach was performed in standard technique and digitally recorded. An expert GI pathologist performed histopathological analysis.

Results: Neither transmural perforation, nor any muscular layer damage was observed. Both the fiber diameters and the configuration modalities (continued or pulse modality) were safe, effective, and precise. R0 resection was feasible in all cases. A complete ESD of a 35 mm lesion by using the new Thulium Laser system took approximately 70 minutes (fig. b-e). In addition, a fast learning curve was involved.



Conclusions: The new Thulium laser system appears to be an effective technique for ESD in upper GI endoscopy. This novel therapeutic technique for gastrointestinal endoscopy has also shown a high level of precision and safety in an ex vivo animal model. In vivo studies are now highly warranted to confirm these initial results.

References:

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OC.08.7

BILIARY STENT DOES NOT INFLUENCE THE ADEQUACY AND ACCURACY OF EUS-GUIDED TISSUE ACQUISITION WITH FENESTRATED NEEDLES OF PANCREATIC MASSES CAUSING OBSTRUCTIVE JAUNDICE

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Background and aim: Patients with pancreatic masses causing obstructive jaundice candidates to endoscopic ultrasound (EUS) for the diagnosis and staging and to ERCP for stenting, should perform EUS first. However, it is not infrequent to perform EUS when biliary stent is already in situ. While the presence of biliary stent significantly decrease the accuracy of EUS for pancreatic head cancer staging, its impact on the EUS-guided tissue sampling adequacy and accuracy is still debated. Furthermore, data on EUS-fine needle tissue acquisition (EUS-FNTA) with fenestrated needles in patients

with pancreatic mass and biliary stent are lacking. The aim of this study is to evaluate the influence of biliary stent on the adequacy and accuracy of EUS-FNTA performed with fenestrated needles in patients with pancreatic head masses.

Material and methods: All patients who underwent EUS-FNTA with fenestrated needles of solid pancreatic head masses causing obstructive jaundice in a single centre from January 2013 to January 2015, were retrospectively identified. The primary outcome measure was the adequacy, defined as the rate of cases in which a tissue specimen for histological examination was achieved. Secondary outcome measures were the accuracy, defined as the proportion of correct diagnoses made with and without stent and the complication rate. Standard references were the surgical specimen when available or other diagnostic investigations together with long-term follow-up (>6 months).

Results: A total of 109 patients with pancreatic head mass causing biliary obstruction were included in the study: 56 cases of them were sampled without stent and 53 cases with stent in situ (all plastic stents). The adequacy was 96.2% in the stent group and 91.1% in the group without stent ($p=0.582$). Final diagnosis was: 103 (94.5%) cases of adenocarcinoma, 4 focal pancreatitis (3.5%), 1 neuroendocrine carcinoma (1%) and 1 metastasis (1%). No significant differences were observed for sensitivity (88.2% vs. 83.3%), specificity (100% for both groups), and accuracy (88.7% vs. 83.9%) between those with and without stent, respectively. False negative results were encountered in 6/53 (11.3%) cases with stent vs. 9/56 (16%) cases without stent. The accuracy was not influenced by the timing of stenting (<48 hours or ≥ 48 hours before EUS). No EUS-FNTA related complications were recorded.

Conclusions: The presence of plastic biliary stent does not influence the tissue sampling adequacy and the diagnostic accuracy of EUS-FNTA of pancreatic head mass performed with fenestrated needles.

OC.08.8

ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION FOR LARGE STONES EXTRACTION IN PATIENTS WITH PERI-AMPULLARY DIVERTICULA

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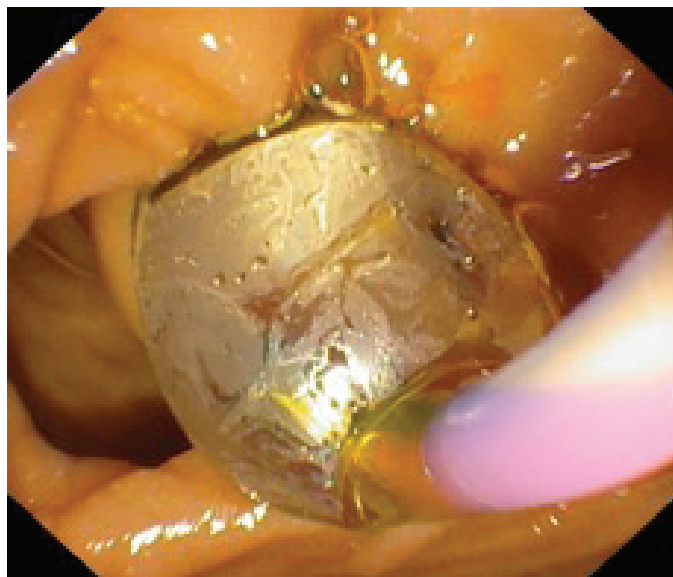
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Background and aim: Dilation Assisted Stone Extraction [DASE] has been proposed as an alternative technique to simple ES for extraction of large common bile duct [CBD] stones extraction (≥ 10 mm). Peri-ampullary diverticula [PAD] can be divided in type 1 (papilla inside the diverticulum), type 2 (papilla on the margin) and type 3 (papilla outside). The presence of PAD is a technical difficulty for stones removal and can cause more complications. We aimed to evaluate the efficacy and safety of DASE for large CBD stone extraction in patients with PAD.

Material and methods: A retrospective analysis of 42 DASE procedures in patients with PAD and large CBD stones was effectuated.

Results: Median age of patients was 75 years, 17 were males and 25 females. About 17% of patients had a type 1 PAD, 33% type 2 and 50% type 3. About 48% of patients had a single large stone. Stones were mainly located in CBD. Mean size of stones was 13.9 ± 4.32 mm. A precut sphincterotomy was effectuated in 4/42 patients. Cannulation rate was 95.2% (40/42). Wirsung was cannulated in 28% of procedures. Stone extraction success was reached 91% (41/45). ML was performed in two cases and use of Dormia was avoided in 38% of cases. Spontaneous stones expulsion occurred in 28% of cases. Pancreatic plastic stent was placed in two patients. Endoscopic evidence of mild self-limiting bleeding, without clinical support,

occurred in 4 patients (9.5%). Only one patient had a clinical evidence of mild bleeding (Hb drop 1.5 g/dL without need for transfusion). One patient had a mild pancreatitis after procedure. No severe or fatal outcomes were observed. No differences in complications rate were observed with respect to Indometacine use. No differences were observed in procedure results regarding papilla location with respect to the diverticula and dilation time (30" or 60").



Conclusions: This is one of the first studies evaluating efficacy and safety of DASE for CBD large stones extraction in patients with PAD. Despite the small number of patients, this technique seems to be safe and effective in patients with PAD, independently of papilla location.

OC.08.9

IMPLEMENTING SPLIT REGIMEN OVER SINGLE DOSE (IMPROVES): A QUALITY IMPROVEMENT (QI) PROJECT TO IMPROVING BOWEL PREPARATION IN CLINICAL PRACTICE. PRELIMINARY RESULTS FROM SIED CAMPANIA NETWORK

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Background and aim: Bowel preparation affects the quality and value of colonoscopy. Split-dosing is considered a key measure for improving bowel preparation. Despite ESGE guideline recommends all patients receiving split-dose, the reporting rates of split regimen are still too low in the real world.

Material and methods: A quality improvement (QI) project was therefore organized in 5 regions of central Italy (Campania, Lazio, Marche, Toscana and Umbria) by using the Plan-Do-Study-Act (PDSA) method with the aim to i) identify ii) measure the problem iii) design a range of interventions designed to overcome the various barriers and suitable to be implemented at local centre and iv) verify whether the interventions worked. Two audit cycles with web data collection were planned with a variable implementation period in between. The regional SIED Coordinators invited centres to provide data of at least 50 routine and screening colonoscopies and monitored the project with an independent timing among regions.

Results: The baseline rate of split-dosing plus same day was 38.3 (1.3% same day) with a large variation among centres. Several gaps and obstacles were identified especially at the organizational and communication level. Some bowel preparations instructions were outdated and in some cases did not include split-dosing information. In general patients did not represent an important barrier to adopting split-dosing. The major obstacle has been the difficulty to inform and motivate patients undergoing routine colonoscopy in an open access regimen who receive written instructions only from “CUP” (Central booking office). Specific protocols and procedures have been developed and adopted for screening cases and for in-patients. Modify the agenda (starting colonoscopy late in the morning) was not considered feasible for most Endoscopy Units. Modified split-dosing PEG 4 L (3 liters + 1 liter) was used for early colonoscopy. Five key areas were identified and targeted for intervention: 1) Organisation and responsibility 2) Education and motivation of health care and administrative personnel 3) protocols and friendly user instructions leaflets 4) Internal and external communication [e.g. primary care physicians; other referring hospital dept.] 5) Specific local problems. The preliminary results from Improves Campania are as follows:

	N°. of centres	Recruiting centres	N°. of centres ≥ 50	N°. of cases	Rates of split
Cycle 1	28	23	15	1206	38.3
Cycle 2	23	22	15	1484	68.4

The variation among centres in the rate of split-dosing between pre- and post-intervention was significantly reduced.

Conclusions: We were able to achieve a 30% increase in the rate of split-dosing over one year in a large sample of Endoscopy units in Campania through a SIED coordinated quality improvement project which involved a system-wide approach to remove barriers to change and move toward high quality colonoscopy.

OC.09 Basic Science

OC.09.1

TRANSLUTAMINASE 2 (TG2) MEDIATES THE CYTOTOXIC EFFECT OF RESVERATROL IN CHOLANGIOCARCINOMA (CC) CELL LINES

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Background and aim: Cholangiocarcinoma (CC) is characterized by a poor prognosis. As curative medical regimen is currently unavailable for patient unsuitable for surgery, new drugs are urgently needed. Resveratrol (RES) has previously been reported to

play a cytotoxic effect on CC cell cultures and the related increase of type 2 transglutaminase (TG2) involved in carcinogenesis and apoptosis. Present study was aimed at evaluating if TG2 inhibition could reduce the cytotoxic effect of RES on CC cell lines.

Material and methods: CC cell lines SK-CHA-1 and MZ-CHA-1, grown on a three dimensional cell culture model, were treated for 72 hours with RES (64 microM, after a dose finding preliminary study) alone or combined with TG2 inhibitors (cystamine and two selective ones, B003 and T101). The following points were investigated: cell viability (clonogenic test), cell morphology (light microscopy -LM, transmission electron microscopy -TEM and immunoistochemistry-IMC), Q-banding (karyotype analysis), and TG2 analysis (colorimetric method and Western Blotting).

Results: RES treatment induced a significant inhibition of cell growth. The co-treatment RES/TG2 inhibitors prevented growth inhibition in both cell lines; the cell growth for SK-CHA-1 with RES 64 microM and the three different inhibitors (respectively cystamine, B003 and T101) increased of the 24%, 42% and 76% vs. percentage of colony growth from cells treated only with RES; for MZ-CHA-1 the cell growth increase was of 75%, 33% and 83% (cystamine, B003 and T101) vs. percentage of colony growth from cells treated only with RES. LM, TEM and IHC results demonstrated a partial protection with T101. The normalization of cell growth was associated to an inhibition of TG2 activity both in MZ-CHA-1 (85% with cystamine, 60% with B003 and 45% with T101 vs. 100% controls) and SK-CHA-1 (95% with cystamine, 30% with B003 and 15% with T101 vs. 100% controls).

Conclusions: Our data demonstrated that the cytotoxic effect of RES in SK-CHA-1 and MZ-CHA-1 is TG2 mediated.

OC.09.2

THE EXTRACELLULAR MATRIX PROTEIN EMILIN2 AS A REGULATOR OF THE MYELOID RESPONSE IN A MODEL OF INFLAMMATION-INDUCED COLON CARCINOGENESIS

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Background and aim: EMILIN2 is an extracellular matrix molecule belonging to the EMI Domain ENdowed (EDEN) protein family that exerts pleiotropic effects in the tumor microenvironment overall functioning as a tumor suppressive molecule. EMILIN2 affects tumor cell viability and proliferation by activating apoptosis and functioning as a negative regulator of the Wnt/ β -catenin axis. Interestingly EMILIN2 expression is down-modulated by methylation in a number of tumors including breast and colorectal cancer. Given its involvement in the regulation of Wnt signaling, a crucial pathway in colon carcinogenesis, and its altered expression in colorectal cancer, we took advantage of the EMILIN2 null mouse model to assess its role in colorectal cancer (CRC) development, subjecting the mice to the inflammation-related AOM/DSS protocol. **Material and methods:** Colorectal tumors were induced subjecting the mice to a AOM/DSS treatment. Tumor development was assessed by colonoscopy. Histopathological and IHC analyses were performed on colon samples from treated mice. β -catenin activation was assessed by Western blot and qPCR. Multiplex serum cytokine analyses from the two mouse models were performed through Luminex Screening and peripheral blood cells were counted. The inflammatory infiltrate was analysed by flow cytometry.

Results: The EMILIN2 KO mice developed a significantly higher number of tumors compared to wt mice. Tumors from EMILIN2 KO mice were more undifferentiated and at an advanced stage compared

to the tumors from control mice. Surprisingly, and contrary to our expectations, tumors from EMILIN2 KO mice did not display any changes in the activation of the Wnt/ β -catenin pathway compared to the controls. Accordingly, the β -catenin target genes cyclin D1 and c-Myc were not altered in the tumors and in the normal mucosa of the two mouse models. Histopathological and IHC analyses indicated that the tumors from EMILIN2 KO mice were characterized by a higher number of macrophages and granulocytes than those from WT mice. Similar alterations in the KO model were found during the acute phase of inflammation: mice subjected to DSS treatment alone developed a more severe colitis than WT mice. Accordingly, the infiltration of myeloid cells within the intestinal mucosa was altered and the serum level of a number of cytokines, including IL-1b, INF- γ , TNF- α and IL-10, was affected.

Conclusions: Our results let us suggest that EMILIN2 may affect colon carcinogenesis impinging on the recruitment and/or the activation of myeloid cells. By altering the inflammatory microenvironment, EMILIN2 may significantly influence colon cancer development.

OC.09.3

PALMITOYLETHANOLAMIDE (PEA) REDUCES COLITIS-INDUCED ANGIOGENESIS THROUGH AKT/MTOR PATHWAY INHIBITION

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Background and aim: In a recent study, we have demonstrated that PEA improves intestinal inflammation in a mouse model of ulcerative colitis. Neovascularization, via the activation of the Akt/mTOR pathway, appears to be crucial in the maintenance of the inflammatory response and might be targeted when developing new treatment strategies in IBD. Given its anti-angiogenic properties, we aimed to evaluate whether PEA affects angiogenesis in mice with DSS-induced colitis.

Material and methods: Six-weeks-old wild-type mice were randomly divided into non-colitic group; colitic group; colitic group receiving PEA (10 mg/kg); colitic group receiving PEA and selective PPAR- α or PPAR- γ antagonists. Colitis was induced by administering 4% DSS in drinking water for 6 consecutive days; PEA alone, or combined with PPAR antagonists, was intraperitoneally administered from day 2 to 6. All animals were sacrificed at day 7. Hemoglobin content measurement and immunohistochemistry for CD31 were performed to evaluate neovascularization. VEGF release was estimated by ELISA, while the expression of VEGF receptor and the activation of the Akt/mTOR pathway were evaluated by western blot analysis.

Results: The hemoglobin content and the expression of CD31 were significantly increased in mice with DSS-induced colitis compared to controls (+390 and +371%; all $p < 0.001$), while a reduction was observed in PEA treated-mice (-60 and -47%; all $p < 0.05$). A significant increase of VEGF release and VEGFR expression was detected in colitis mice (+600 and +247%; all $p < 0.001$). Interestingly, PEA administration significantly reduced both VEGF release and VEGFR expression (-72 and -66%; all $p < 0.01$) in colitis model. We detected a significant higher expression of phospho-Akt-, mTOR and -p70S6 in mice with DSS-colitis (+850, +1600 and +1400%; all $p < 0.001$); whilst PEA reduced the phosphorylation of all these factors (-76.5, -68 and -71%; all $p < 0.01$). PPAR- α antagonist, but not PPAR- γ antagonist, reverted all effects of PEA.

Conclusions: We demonstrated that PEA is able to reduce angiogenesis in a mouse model of colitis. Moreover, we showed that antiangiogenic effect of PEA depends on the specific inhibition of the AKT/mTOR axis, through the activation of PPAR- α pathway. Due to its anti-inflammatory and anti-angiogenic characteristics, PEA represents an interesting candidate for future clinical studies in IBD.

OC.09.4

EXPRESSION OF THE ACTIVATED FORM OF AMPK IS REDUCED IN IBD BUT SELECTIVE ACTIVATION OF THIS KINASE IS NOT SUFFICIENT TO REVERT INTESTINAL INFLAMMATION

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Background and aim: AMP-activated protein kinase (AMPK) is an energy cellular sensor involved in many biological functions, including autophagy, apoptosis and immune cell functions. In mice with dextran sulfate sodium (DSS)-colitis, expression of the active form of AMPK is reduced and treatment with metformin, a known activator of AMPK, promotes resolution of the ongoing colitis.

Aim: To evaluate whether the expression of active AMPK is deregulated in inflammatory bowel disease (IBD) and activation of AMPK is sufficient to revert colitis in mice.

Material and methods: Expression of phosphorylated (active) form of AMPK was evaluated in inflamed biopsy samples of patients with ulcerative colitis (UC), patients with Crohn's disease (CD) and normal controls (CTR) by western blotting and immunohistochemistry. IBD lamina propria mononuclear cells (LPMC) were activated with toll-like receptor ligands in the presence or absence of metformin or A-769662, a specific and selective activator of AMPK. After 24 hours, inflammatory cytokines were evaluated by real-time PCR. To assess the in vivo effect of AMPK activation on the ongoing colitis, DSS-treated mice were given intra-peritoneally metformin or A-769662 after induction of colitis.

Results: Expression of phosphorylated AMPK was reduced in UC samples as compared to CD and controls, and such a decrease was evident in both epithelial and lamina propria compartments. Treatment of IBD LPMC with CpG or poli I:C increased TNF RNA transcripts and this effect was reversed by both metformin and A-769662. Induction of DSS-colitis in mice was accompanied by diminished phosphorylation of AMPK. Mice treated with A-769662 exhibited increased expression of active AMPK in the colons but no resolution of colitis. In contrast, metformin-treated mice showed enhanced phosphorylation of AMPK concomitant with attenuation of colitis.

Conclusions: Expression of active AMPK is decreased in patients with UC and in mice with experimental colitis. Selective activation of AMPK is not sufficient to dampen the ongoing colitis. Data suggest that metformin-mediated resolution of colitis relies on the activation of additional pathways other than AMPK.

OC.09.5

GENERATION AND FUNCTIONAL CHARACTERIZATION OF HUMAN INKT CELL LINES AND CLONES FROM HEALTHY AND INFLAMED INTESTINE

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Background and aim: Invariant natural killer T (iNKT) cells constitute a population of lipid-specific T lymphocytes with multiple functions

in the regulation of gut immune homeostasis. Still, unrestrained iNKT cell activity has been implicated in the pathogenesis of ulcerative colitis (UC), one of the two major forms of Inflammatory Bowel Diseases (IBD) in humans. Up to now, functional analyses of human intestinal iNKT cells under steady state and in IBD have been hampered by a low extraction rate from intestinal specimens, due to the relative rarity of these cells in the gut mucosa with respect to other immune cells.

Material and methods: To evaluate the function of intestinal iNKT cells in IBD patients, we developed two novel methods to generate iNKT cell lines and clones from human intestinal surgical specimens. iNKT cells were isolated from lamina propria mononuclear cells (LPMC) with a 9-color multiparametric FACS-sorting. For the generation of iNKT cell lines, sorted cells were restimulated ex-vivo with phyto-hemoagglutinin (PHA) and allogeneic irradiated peripheral blood mononuclear cells (PBMC), which were used as feeder cells in the presence of human interleukin (IL)-2. After 3 to 4 weeks iNKT cells could be used for phenotypical and functional analyses. For the generation of human iNKT cell clones, we adapted the protocol of cloning by limiting dilution used to clone conventional T cells from peripheral blood (G.De Libero, T cell protocols, Springer ed.). iNKT cells were sorted from LPMC with a 9-color multiparametric FACS-sorting before cloning. After 15 days clones were harvested and checked for growth and specificity.

Results: With these two approaches we succeeded to generate 5 iNKT cell lines, 1 from healthy intestine, 1 from a CD patient, 2 from UC patients and 1 from peripheral blood as internal control. iNKT lineage was confirmed by the expression of specific iNKT surface markers. Intestinal iNKT cells were able to produce both regulatory and inflammatory cytokines, including IL13, IFN γ , IL10 and IL17. A series of in vitro antigen presentation assays with exogenous and endogenous lipid antigens was performed. By the limiting dilution protocol, 250 iNKT cell clones were generated from one UC patient. 50 clones out of 250 were further characterized phenotypically and functionally. 20 out of 50 were used for in vitro antigen presentation assays with exogenous and endogenous lipid antigens.

Conclusions: To our knowledge, this is the first report of the generation of iNKT cell lines and clones from human surgical intestinal specimens. iNKT cells lines and clones display a different phenotypic and functional profile according to the tissue (PB vs gut) and to the inflammatory status of the specimen (healthy vs IBD). They secrete a different array of cytokines and are activated in vitro by both endogenous and exogenous lipid antigens. These results will help to shed light regarding the role of iNKT cells in intestinal inflammation.

OC.09.6

PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA AGONIST REDUCES THE DEVELOPMENT OF NECROTIZING ENTEROCOLITIS IN A NEONATAL RAT MODEL

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Background and aim: Necrotizing enterocolitis (NEC) is the most common neonatal gastrointestinal emergency in preterm infants. Intestinal mucosa and innate immunity play the major role in the pathogenesis of NEC. Factors affecting innate immunity and acting as inflammatory regulators, such as the nuclear peroxisome proliferator-activated receptors (PPARs), could be crucial. We hypothesized that the PPAR γ agonist Pioglitazone (PIO) might be effective in preventing the development of NEC.

Material and methods: We studied a rat model in which NEC was induced using the following protocol: newborn rats were formula fed and stressed twice daily with hypoxia by breathing 100% nitrogen gas in a closed chamber for 60 s, followed by 10 min exposure to 4°C temperature.

Rat pups were divided into two groups: the treatment group (TG; n=30) received enteral PIO (daily dose 10 mg/kg/die divided on six aliquotes) and the control group (n=30) which was not. Animals were sacrificed 96h after birth. NEC was diagnosed evaluating histological ileum changes, and its severity was scored with a standard method. Moreover, we measured levels of RNA of 6 cytokines: IL-4, IL-12, IL-6, IL-10, INF- γ and TNF- α using the qPCR technology. Deposition of extracellular matrix in kidney was tested by Sirius Red staining.

Results: Body rats weights gradually decreased in both groups but the decrease was higher in the CG starting from 48 h (p<0.01) to 96 h (p<0.01).

The occurrence of NEC was significantly higher (p<0.001) in the CG (18/30; 60%) than in the TG (5/30; 16.7%) and was paralleled by a higher NEC score (p<0.001) in the CG than in the TG. Pioglitazone treatment significantly reduced the local intestinal inflammation: pro-inflammatory IL-12 and INF- γ mRNA levels were significantly lower in the TG than in the CG (p=0.02 and 0.04, respectively); conversely, anti-inflammatory IL-4 mRNA level was significantly higher in the TG than in the CG (p=0.02). Finally, extracellular matrix deposition in the kidney was reduced in TG rats compared to CG rats, confirming the overall health improvement in treated rats and the protecting effects of PIO.

Conclusions: Our results demonstrate for the first time that administration of PIO reduces the incidence and severity of NEC in a neonatal rat animal model of the disease.

OC.09.7

INHIBITION OF THE MITOCHONDRIAL ATP SYNTHASE PROMOTES T CELL APOPTOSIS AND SUPPRESSES INTESTINAL INFLAMMATION

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Background and aim: Defective T cell apoptosis occurs in Crohn's disease (CD) thus contributing to sustain the pathogenic inflammatory response. Indeed, drugs that enhance T cell apoptosis (i.e. anti-TNF antibodies and azathioprine) attenuate the CD-associated tissue damaging immune response. We have recently developed an inhibitor of the mitochondrial ATP synthase (ATPase), which increases superoxide formation and consequently induces caspase-dependent and independent T cell apoptosis. This study was aimed at evaluating the ability of such a compound to induce apoptosis in CD lamina propria (LP) T cells and to inhibit T cell-mediated colitis in mice.

Material and methods: Apoptosis and markers of T cell differentiation were analyzed in CD LP T cells either left untreated or treated with the ATPase inhibitor by flow cytometry. The therapeutic effect of the ATPase inhibitor was evaluated in mice with acute or chronic 2,4,6-trinitrobenzene-sulfonic acid (TNBS)-induced colitis or chronic adoptive T cell-transfer colitis.

Results: The ATPase inhibitor promoted CD LP T cell apoptosis even in cells isolated from CD patients resistant to Infliximab. The ATPase-driven apoptosis was associated with reduction of the percentages of T cells expressing Th1/Th17-related markers and no change in Foxp3-expressing regulatory T cells. Mice given orally the ATPase inhibitor showed a marked increase of LP T cell death, down-

regulation of IFN-gamma, TNF-Alpha and IL-17A and were largely protected against TNBS- and transfer-colitis.

Conclusions: Inhibition of ATPase with a specific and selective compound induces intestinal T cell death thereby ameliorating colitis.

OC.09.8

INTERLEUKIN-34 INDUCES CC-CHEMOKINE LIGAND 20 IN GUT EPITHELIAL CELLS

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Background and aim: Production of chemokines by intestinal epithelial cells is a key step in the amplification of the destructive immune-inflammatory response in patients with inflammatory bowel diseases (IBD). In this study, we examined whether intestinal epithelial cells express macrophage colony-stimulating factor receptor 1 (M-CSFR-1), the functional receptor of interleukin-34 (IL-34), a cytokine that is over-produced in IBD and supposed to sustain inflammatory pathways.

Material and methods: M-CSFR-1 expression was evaluated in intestinal samples of IBD patients, controls and in colon epithelial cell lines by real-time PCR, immunohistochemistry and Western blotting. DLD-1 cells were stimulated with IL-34 in the presence or absence of MAP kinase inhibitors, and chemokine induction was assessed by real-time PCR and enzyme-linked immunosorbent assay (ELISA) and MAP kinase activation was monitored by Western blotting. The effect of a neutralizing IL-34 antibody on CCL20 synthesis was tested in ex vivo organ cultures of IBD mucosal explants.

Results: Enhanced expression of M-CSFR-1 RNA transcripts was seen in inflamed mucosa of IBD patients as compared to controls. Immunohistochemical analysis confirmed up-regulation of M-CSFR-1 in IBD and showed that both epithelial and lamina propria mononuclear cells expressed this receptor. Stimulation of DLD-1 with IL-34 increased CCL20 production through an ERK1/2-dependent mechanism. Consistently, treatment of IBD explants with anti-IL-34 reduced CCL20 production.

Conclusions: These data show that intestinal epithelial cells are a target of IL-34 and suggest that this cytokine contributes to mediate the cross talk between epithelial cells and immune cells in IBD.

OC.09.9

PROTECTIVE EFFECT OF INULIN ON LPS-INDUCED INTESTINAL SMOOTH MUSCLE IMPAIRMENT: A PROTEOMIC APPROACH

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Background and aim: Fructans, such as inulin, are dietary fibers which stimulate gastro-intestinal function acting as prebiotics. We recently demonstrated the protective effect of inulin on LPS-induced damage of colonic smooth muscle in an ex vivo experimental model, which seems to be related to presence of oxidative stress. In the present study, the protective role of inulin against LPS-induced

oxidative stress was evaluated on colonic mucosa using a proteomic approach.

Material and methods: Human colonic mucosa and submucosa, obtained from disease-free margins of resected segments for cancer, were sealed between two chambers containing Krebs solution, with the luminal side of the mucosa overlaid with 5 ml of Krebs, or 100 µg/mL LPS solution, or 100 µg/mL LPS +100 mg/mL inulin Fructafit IQ (LPS+INU). The biological system was kept oxygenated for 30 min at 37°C. iTRAQ based analysis was used to separate and compare the total soluble proteomes from human colonic mucosa and submucosa treated. Each sample was labelled by one of four reagents of the iTRAQ 4-plex and then combined into one aliquote. Triplicate labelling were performed, which showed a high level of reproducibility.

Results: Inulin exposure was able to restore, in human colonic mucosa, the LPS-dependent alteration of some proteins involved in the host response and in the intestinal smooth muscle contraction (ZG16, CALM1/MLCK/MYL signaling pathway) and to reduce the upregulation of two proteins involved in the radical-mediated oxidative stress induced by LPS (APEX1, CCT7). Moreover the administration of inulin entails a higher level of some detoxification enzymes (MT2A, GSTK1, and UGT2B4) with respect to LPS treatment. Consistently inulin exposure to colonic mucosa and submucosa was also able to restore the LPS-induced alteration of intestinal smooth muscle contraction as well as it was able to prevent the oxidative damages of LPS-exposed tissues.

Conclusions: Our preliminary data suggest that the exposure of colonic mucosa to inulin is able to prevent LPS-dependent altered expression of some key proteins which promote intestinal motility and the host response, reducing the radical-mediated oxidative stress.

OC.10 Endoscopy 3

OC.10.1

DILATION-ASSISTED STONE EXTRACTION AS ALTERNATIVE, EFFECTIVE AND SAFE METHOD FOR REMOVAL OF COMMON BILE DUCT LARGE STONES: DATA FROM A REFERRAL CENTER

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Background and aim: Large stones of common bile duct (CBD) are a hard challenge after endoscopic sphincterotomy (EST) especially in those that are unable to be managed with standard techniques including mechanical lithotripsy. Dilation-assisted stone extraction (DASE) after EST can be more efficient than EST alone for removal of large CBD stones.

The aim of this study is to report the experience of a referral centre on the efficacy and complications of DASE for CBD large stones treatment.

Material and methods: From January 2013 to September 2015 data of all consecutive patients who underwent DASE due to large stones, evidenced by CT-scan or MRI, were collected and recorded in an electronic database for the final analysis. After selective cannulation of the CBD, an initial cholangiogram was taken before balloon placement. The size of the balloon was matched to the diameters of the bile duct and stones. The balloon was gradually filled with diluted contrast medium under endoscopic and fluoroscopic guidance to observe the gradual disappearance of the waist in the balloon, which was taken to indicate progressive dilation of the

orifice. Once the waist disappeared, the balloon remained inflated for 60 s.

Results: A total of 29 patients with CBD large stones were evaluated: 11 male (38%) / 18 female (62%) with a mean age of 71.9±14.7. Technical success (complete dilation) was reached in all patients (100%) with a median final dilation of 15 mm in diameter: 10 mm in 4 patients (14%), 15 mm in 12 patients (41%), 18 mm in 11 patients (38%), 20 mm in 2 patients (7%). In 6 patients (21%) EST was done before the current procedure and DASE was performed due to stones recurrence. In all patients but two (93%) large stones were successful removed from the CBD (19 with retrieval balloon and 8 with aid of mechanical lithotripsy). In those with DASE failure: 1 was treated with intra-coledocical laser lithotripsy and 1 with surgical approach. Only 2 early complications were recorded (7%): both mild bleeding resolved after endoclips placement. In one patient CBD stones recurred after 2 months.

Conclusions: DASE after EST is an alternative, effective and safe method for removal of CBD large stones.

OC.10.2

QUALITY EVALUATION AND PROFESSIONAL ACCREDITATION IN DIGESTIVE ENDOSCOPY. PRELIMINARY DATA ACQUIRED THROUGH PEER-REVIEWED SITE VISITS

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Background and aim: Although guidelines on quality parameters in digestive endoscopy have been implemented and widely shared, in our country scanty data exist on their evaluation by an external party and the efficacy of corrective interventions after a first report. **Material and methods:** With the support of Kiwa Cermet Italia Certification Company, SIED has recently endorsed a nationwide program of professional accreditation of endoscopy services. Based on a handbook including a checklist to score quality items prepared by Sied Quality Team, an array of site visits has been set up. The first part of the project implies a first visit to spotlight inappropriate or critical issues followed by a second visit to verify the outcome of suggested corrective measures.

Adhesion to the protocol has been on a voluntary basis by the involved department.

The team included: a leader (CM) dedicated to the evaluation of general organization, two gastroenterologists (one for upper GI evaluation, the other one for lower GI evaluation) and a nurse dedicated to the observation of nursing and reprocessing procedures.

Results: So far, 4 centres have been visited; in three a follow-up visit has already been carried out, with a time lag of about 9 months.

During the first visit, the most represented critical issues were:

-Upper GI: Forrest, Los Angeles and Prague classifications; gastric biopsies protocols.

-Lower GI: post-polypectomy surveillance; colo-rectal biopsy protocols in inflammatory bowel diseases and chronic diarrhoea.

-Nursing management/reprocessing: pre and post procedure registration of vital signs; Gloucester scale of post-procedure discomfort; traceability and periodic reports on disinfection procedures; management of histopathological reports.

Items quoted as critical/inadequate at the first visit have been efficaciously managed in two centres, which gained professional accreditation.

The third centre has efficaciously corrected remarks regarding reprocessing, thanks to relevant technological improvements, but

has failed to correct most of other remarks; for these reasons, it has not achieved accreditation.

Conclusions: These data give a preliminary outlook concerning most frequent critical issues in Endoscopy services. Follow-up visits obtained satisfactory results and led to professional accreditation in two out of three centres. These results are in part secondary to a promising cooperation between professionals and health managers. We look forward having more detailed data once a higher number of site visits will be carried out.

OC.10.3

MID TERM RESULTS OF SECOND POEM FOR RECURRENT ACHALASIA: DATA FROM A LARGE COHORT OF PATIENTS

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Background and aim: Peroral Endoscopic Myotomy (POEM) is an emerging non-incisional treatment for achalasia and for other esophageal peristalsis disorders. Despite its efficacy is widely reported as high (% of patients with Eckardt score ≤ 3 after POEM ranges between 91.7-100), recurrent symptoms are reported. Because of the relative novelty of this technique and its high efficacy, long-term follow up results with an adequate number of patients underwent a second POEM are still missing.

Material and methods: We retrospectively reviewed our database of all patients underwent a second POEM. Patient and achalasia characteristics, peri- and post-operative data (including high-resolution manometry, barium swallow and clinical assessment before 1st POEM, 2nd POEM and during follow up) were therefore collected and analyzed. Outcome measures were incidence of intra- and post-operative adverse events for safety issues and % of patients with Eckardt score < 3 after second POEM for efficacy.

Results: Between August 2010 and October 2015, 27 patients underwent a second POEM for recurrent symptoms. Patient and achalasia

Table 1

Baseline characteristics of patients who underwent second POEM

Demographics	
N. of patients	27
Age, median (range), y	45,8 (21-77)
Male, n. (%)	15 (55.6)
BMI, mean (range)	21,2 (14,7-37,2)
Achalasia characteristics	
Duration of symptoms, mean (range), y	9,5 (0,5-32)
Type of Achalasia [†] , n (%)	
I	6 (22,2)
II	6 (22,2)
III	0
Not available	15 (55,6)
Manometry IRP, mean (range), mmHg	23,4 (8-48)
Availability of IRP %	48%
Previous treatments, n (%)	
Pneumatic balloon dilation	14 (51,9)
None	12 (44,4)
Heller Myotomy	1 (3,7)
Esophageal dilation	
None	0
Mild	7 (25,9)
Moderate	19 (70,4)
Severe	1 (3,7)
Eckardt Score, mean (range)	6,6 (2-10)

[†] According to Chicago Classification v. 3.0

characteristics are resumed in table 1. Reason for a second POEM were Eckardt score ≥ 3 after at least one balloon dilation in 17/27 (62.9%) and persistent manometric or barium swallow abnormal findings at follow up in 10/27 (37%). Mean time interval between 1st and 2nd POEM was 13.7 months (range 0.3–32 months). The second POEM procedure was performed by high experienced operators. To reduce the risk of fibrosis, a different route rather than previous POEM access was selected. During 2nd POEM, no serious adverse intra-procedural events were reported. In the first post-operative day, a barium swallow and an esophagogastrroduodenoscopy confirmed the absence of mucosal injuries or procedure-related complications. The clinical course was regular. Second POEM efficacy as Eckardt score <3 was confirmed in 26/27 (96.3%). A woman with persistent Eckardt score of 5 after the 2nd POEM refused to undergo another myotomy and she were managed with repeated pneumatic balloon dilation and clinical surveillance. Four patient complained incomplete remission of symptoms despite Eckardt <3 , reporting chest pain as more frequent discomfort.

Conclusions: In conclusion, second POEM is a safe and effective rescue option for recurrent achalasia in expert hands. A multi-center study, involving a big number of patients and operators with different levels of experience could be helpful to improve the diffusion of second POEM.

OC.10.4

PROSPECTIVE COMMUNITY PRACTICE-BASED STUDY OF ERCP QUALITY

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Background and aim: Background: There are many studies and large series about ERCP that define both the therapeutic success and complications of this procedure, mainly performed in academic centers. Prospective studies with data collected in a community setting are extremely rare. This is particularly critical because the conditions in which endoscopists act in 'real life' are often different from those usually considered in controlled studies.

Aim: The aim of this study is to assess indications, success and complication rate of routinely-performed ERCP in a single region of Italy.

Material and methods: A prospective observational study on consecutive patients undergoing ERCP in 19 hospitals of Lombardia during a period of 6 months was performed. A centralised online ERCP registry was built and used for data storage. The relationship among variables related to patients, procedures and operators were analyzed with descriptive and, when appropriate, inferential statistics. A multivariate analysis was performed to investigate the possible association between these variables and complications.

Results: 39 endoscopists performed a total of 2400 ERCPs of which 2308 (96.0%) with technical success. 69 (2.9%) were purely

diagnostic procedures. Biliary-tract stone disease accounted for the majority of the indications for the procedure (58.4%). 2183 ERCPs (90.9%) were completed reaching the intended goal. The success rate of the procedures was significantly related to the experience of the operator ($p=0.001$). The rate of high-risk conditions and high grade of difficulty of the procedures and the presence of an anesthesiologist was significantly higher in centers with higher ERCP volume ($p=0.02$, $p < 0.001$). The overall complication rate was 10%. Post-ERCP pancreatitis (PEP) occurred in 4.3% of procedures, bleeding in 2.9%, cholangitis in 1.4%, perforation in 0.25%. The mortality rate was 0.4%. The incidence of PEP was not influenced by the volume of the centers or the expertise of the endoscopists. Pancreatic duct injection ($p<0.001$) and precut ($p=0.03$) were identified as risk factors for PEP by multivariate analysis. The prophylaxis of PEP was performed in 19% of the cases using NSAIDs and in 2.8% by pancreatic stenting.

Conclusions: A procedural registry was an important tool to assess and verify the quality of routinely-performed ERCP in the community. It gives incentives to improve the quality of this procedure and the methods by which it is carried out.

OC.10.5

FULLY COVERED SELF-EXPANDABLE METAL STENTS TO DILATE PANCREATIC DUCT STRICTURES DUE TO CHRONIC PANCREATITIS: A PILOT STUDY

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Background and aim: The endoscopic treatment for symptomatic main pancreatic duct (MPD) strictures secondary to chronic pancreatitis (CP) is the insertion of plastic stents obtaining stricture resolution in near 60% of the cases. We evaluate the use of removable fully covered, self expandable metal stents (FC-SEMS) to dilate MPD strictures secondary to CP.

Material and methods: Patients with CP and symptomatic MPD stricture located in the head of the pancreas that persisted 3 months or more after placement of a single plastic stent, were enrolled into a prospective single arm trial. The protocol was approved from the Ethic Committee of our University.

A Nitinol FC-SEMS (Bumpy stent, Taewoong, Korea) was inserted and removed after 6 months. The diameter (6 or 8 mm) and length (3, 4 and 5 cm) of the FC-SEMS were chosen according to MPD diameter and the anatomy of the stricture. Stricture resolution was defined as a satisfactory pancreatico-duodenal contrast medium outflow and absence of pain during continuous flushing with saline (1000 ml/day) for 24 h through a 6 fr nasopancreatic drain positioned after stent removal.

The primary objective was the FC-SEMS removability while the secondary was the MPD stricture resolution rate and the complications.

Follow-up was planned every 6 months during a 2 year period. Pancreatic pain episodes and recurrence of pancreatitis were recorded.

Results: Between December 2012 and October 2014, 15 patients (10 M, mean age 60 years) were enrolled. Pancreatic calcifications were present in 6 (40%) and ESWL was performed in 4 (27%). Four patients had a history of alcohol abuse. In 10 cases the FC-SEMS was inserted through the major papilla, while 5 patients (3 pancreas divisum, 2 dominant dorsal duct) with a prior minor papilla sphincterotomy received the FC-SEMS through the minor papilla. One patient developed cholangitis after 24 h due to occlusion of the biliary sphincterotomy from the FC-SEMS; cholangitis resolved after insertion of a plastic biliary stent.

Before the stent removal, 13 patients were asymptomatic while 2 had recurrent pancreatitis after 4 and 5 months; these 2 patients

had complete distal migration of the FC-SEMS and were treated by insertion of a plastic stent.

FC-SEMS completely migrated in 7 (47%) patients and could be removed endoscopically in the remaining 8 (53%) cases. Four patients developed a tight stricture induced by FC-SEMS at the level of its proximal end; in one case the stricture was overcome only after EUS-guided pancreatic rendez-vous. Follow-up is ongoing. Results are summarized in the table.

Table

	n	%	Follow-up, mean months (range)
Patients	15	–	–
FC-SEMS removability	8/8	100	–
Complete FC-SEMS distal migration	7/15	47	–
FC-SEMS proximal migration	1/8	12	–
MPD stricture resolution	10/15	67	–
SEMS “induced” MPD stricture	4/15	27	–
Asymptomatic	7/13*	54	15.9 (12–24)

* Two patients discontinued the follow-up (pancreatic cancer diagnosed 6 months after stent removal, lost to follow-up).

Conclusions: FC-SEMS removability from the MPD in chronic pancreatitis was feasible in all cases. After a mean follow-up of 15.9 months, 54% of the patients were asymptomatic; this figure is similar to those obtained with a single plastic stent. Occurrence of FC-SEMS induced pancreatic strictures is a major issue and deserves further assessment. According to our experience the use of FC-SEMS in the MPD needs careful evaluation in the setting of clinical trials.

OC.10.6

POST-SPHINCTEROTOMY TRANSPAPILLARY BALLOON DILATION FOR REMOVAL OF LARGE BILE DUCT STONE IS MORE EFFECTIVE AND SAFE COMPARED TO ENDOSCOPIC SPHINCTEROTOMY? A META-ANALYSIS

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Background and aim: Endoscopic sphincterotomy (ES) is a useful method for the removal of common bile duct (CBD) stones. However, in 10-15% of patients, stone removal by ES is unsuccessful. Post-sphincterotomy transpapillary balloon dilation (PSBD), could improve the overall success of stone extraction with low complication rate. A meta-analysis was conducted to establish the efficacy and safety of PSBD compared to ES for removal difficult CBD stones

Material and methods: MEDLINE, EMBASE, Cochrane Library were searched for all articles published from 1990 until June 2015. We finally analyzed 6 RCTs. We included all RCTs comparison of PSBD and ES targeting patients with CBD stones. Outcome were treatment success or morbidity and use of mechanical lithotripsy

Results: PSBD was effective as ES for initial stone removal (OR 1.05 95%CI 0.64–1.70) and overall success rate (OR 1.87 95%CI 0.53–6.55). The use of mechanical lithotripsy was higher in the ES group (OR 0.46, 95%CI 0.23–0.92). Complication rates were higher in ES groups (OR 0.45 95%CI 0.29–0.70). Bleeding, rate were similar in PSBD and ES group (OR 1.50 95%CI 0.43–5.27). Pancreatitis rate was equal in both groups (OR 0.81 95%CI 0.44–1.50). Perforation and infection rates were similar in both groups (0.20 95%CI 0.04–1.71; OR 95%CI 0.21–1.77)

Conclusions: PSBD appears to be a safe and effective method for removal CBD stone reducing the need for mechanical lithotripsy and overall complication while the incidence rate of pancreatitis, bleeding, infection and perforation were equal in both groups

OC.10.7

IMPACT OF BOWEL LAVAGE ON GUT MICROBIOTA

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Background and aim: Colonoscopy is an endoscopic examination frequently performed worldwide as screening tool. The adequate bowel preparation is essential for a successful colonoscopy and to date, few clear information about the impact of the bowel cleansing on the gut microbiota exist.

Material and methods: Design through 16S rDNA Ion Torrent profiling of fecal samples of 10 subjects, we evaluated changes that occurred in the gut microbiota composition immediately after the bowel lavage and one month after the colonoscopy. We studied the gut microbiota at phylum, class and family level.

Results: A significant decrease in Firmicutes abundance and an increase in Proteobacteria abundance after the colon cleansing was observed. γ -proteobacteria was significantly increased after the colonoscopy, but one month after the endoscopic examination this bacterial class was decreased 2.5 fold if compared with baseline samples, as well as α -proteobacteria. Moreover, one month after the bowel lavage a significant reduction in Rikenellaceae, Eubacteriaceae and Lactobacillaceae abundance was observed, while Streptococcaceae were increased 3.0 fold if compared with baseline. Interestingly, immediately after the colonoscopy, Enterobacteriaceae were significantly higher than baseline samples, but one month after the colonoscopy, the abundance of this bacterial family was significantly lower than baseline.

Conclusions: We provide clear evidence about the impact of bowel lavage on the gut microbiota composition. In particular, we highlighted significant changes in the composition of several bacterial families, up to 1 month after the colon cleansing.

OC.10.8

PREDICTION OF TECHNICAL DIFFICULTY OF COLORECTAL ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD): PROSPECTIVE STUDY TO FAVOR ITS PRACTICE IN THE WEST

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Background and aim: Endoscopic submucosal dissection (ESD) is indicated for the en bloc resection of gastrointestinal neoplasms with a risk of submucosal invasion or difficult to be removed by EMR. However, ESD is highly technical demanding, more risky than EMR, and a stepwise model to forecast its success has not yet been identified.

Aim: to identify pre-, intra, and post-operative patient's and lesion's features useful to predict the difficulty of ESD.

Material and methods: Prospective study conducted in a non-academic center by a western endoscopist with a baseline level of competency (1). Inclusion criteria: colorectal neoplasms ≥ 15 or ≥ 20 mm with and without a scar due to previous resection/biopsies, respectively; no features of SM-deep invasion (Kudo pit pattern type V and/or Sano microcapillary pattern type 3B). ESD was performed by the standard technique. The procedure was defined not difficult if the ESD was completed en bloc and the operative speed was 13min/

cm2 (equivalent to: 90 min / lesion with a diameter of 30 mm). The following variables were evaluated: age; sex; location; morphology; size (cm2); nodularity; scar; experience; SM fibrosis; histology.

Results: From 1.2012 to 7.2015, ESD was attempted for 140 lesions (median size 9 cm2, range 1.2–33; colonic 110 (79%); rectal 30 (21%)) in 140 patients (median age 66, range 44–87; females 57, 41%). ESD was en bloc in 129 (92%) cases and with a 13 min/cm2 speed in 82 (59%). Curative resection (R0 with low-LN risk features) was achieved in 132 (94%). Perforations occurred in 7 (5%) cases in the colon and have been treated conservatively in 6. Prognostic variables of a difficult colonic ESD at the multivariate analysis are reported in the Table; no independent variable was identified for rectal ESD.

Table 1

	Rectum (n = 30)	Colon (n = 110)
Easy ESDs, n (%)	15 (50%)	67 (61%)
	Unadj OR (95%CI)	Adj OR (95% CI)
Size >7 cm2	3.14 (0.68– 14.50)	3.93 (1.79–8.64)
Scar positive	0.08 (0.01–0.79)	0.09 (0.01–0.81)
Experience >60 procedures	1.38 (0.29–6.60)	4.14 (1.51–11.36)
SM fibrosis positive	0.18 (0.05–0.61)	0.48 (0.27–0.85)
Histology: T1 cancer	2.15 (0.17–26.67)	0.24 (0.06–0.99)

Conclusions: A difficult ESD has to be expected if the lesion is in the colon, has a scar of previous biopsies/resection, the operator has an overall experience <60 procedures. Lesions <7cm2 in size are resected with a significantly prolonged operative time. Other features of difficulty not evaluable preoperatively are: SM fibrosis, and SM-invasive cancer. Western endoscopists should delay ESD for difficult colonic lesions until an expert level has been achieved.

OC.10.9

DETECTION OF COLONIC ADENOMAS USING DIFFERENT COLONOSCOPY INSERTION TECHNIQUES

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Background and aim: Adenoma detection rate (ADR) is a colonoscopy quality indicator and low ADR predicts the development of interval cancers, especially in the right colon (cecum and ascending). Poor bowel preparation is a notable factor associated with low ADR. We assessed the impact of different insertion techniques on adenoma detection in the right colon and entire colon. We test the hypothesis that the insertion technique that yielded the best bowel preparation score is associated with the highest right colon and entire colon ADR. **Material and methods:** We pooled and compared data on right colon and entire colon ADR stratified according to Boston bowel preparation scale (BBPS) scores. Data were recorded prospectively in 3 similarly designed multicenter randomized controlled trials that compared insertion pain of water exchange (WE, airless insertion and constant suction of opaque water), water immersion (WI, adjunct to insufflation, water infused to facilitate insertion) and insufflation with air or CO2 (AICD).

Results: In 1200 (704 males) subjects randomly allocated to WE (n=395), WI (n=404) or AICD (n=401), demographic and procedural data were comparable. WE showed significantly higher right colon and overall BBPS scores (p values range: 0.003 to <0.0005). In the

right colon WE achieved significantly higher ADR <10 mm than WI and AICD: 11.9% vs 6.9% (p=0.016) and vs 7.2% (p=0.025), respectively; at BBPS 3 significantly higher ADR than WI and AICD for lesions of any size (17.6% vs 7.9%, p=0.008; vs 9.0%, p=0.018, respectively) and for lesions <10 mm (13.3% vs 2.0%, p<0.0005; vs 5.8%, p=0.016, respectively). Proportions of advanced adenomas of any size at BBPS 3 were: WE 3.3%, WI 1.3%, AICD none (vs WE p=0.045). In the entire colon, stratifying ADR by excellent bowel cleanliness (BBPS 9–8), WE revealed significantly higher proportions than the other two groups: 23.8% vs WI 13.1%, p <0.0005; vs AICD 16.2%, p=0.007. At BBPS 9–8 WE achieved also the highest overall advanced adenoma rate (9.6%), vs WI 4.0% p=0.001; vs AICD 5.5% p=0.027. Multivariate analysis confirmed WE as significant predictor of right colon higher adenoma detection at BBPS 3, and higher entire colon adenoma detection at BBPS 9–8. In the remaining colonic segments (hepatic flexure to rectum) overall ADR was comparable among the three techniques, also when stratified by excellent colon cleanliness. Limitations: Secondary outcome analysis, unblinded colonoscopists.

Table 1

Effect of colonoscopy with WE, WI and AICD, and BBPS score on adenoma detection

				P value		
	WE N=395	WI N=404	AICD N=401	WE vs WI	WE vs AICD	WI vs AICD
Right colon ADR, n (%)						
Any size	59 (14.9)	49 (12.1)	48 (12.0)	0.245†	0.219†	1†
<10 mm	47 (11.9)	28 (6.9)	29 (7.2)	0.016†	0.025†	0.862†
BBPS 3	n = 210	n = 152	n = 156			
Any size	37 (17.6)	12 (7.9)	14 (9.0)	0.008†	0.018†	0.729†
<10 mm	28 (13.3)	3 (2.0)	9 (5.8)	<0.0005†	0.016†	0.085†
Right colon advanced adenoma ^{††} rate, n (%)						
Any size	7 (3.3)	2 (1.3)	0	0.313	0.045	0.243
Entire colon ADR, n (%)						
	N=395	N=404	N=401			
	131 (33.2)	117 (29.0)	129 (32.2)	0.199†	0.764†	0.322†
BBPS 9-8	94 (23.8)	53 (13.1)	65 (16.2)	<0.0005†	0.007†	0.215†
Entire colon advanced adenoma ^{††} rate, n (%)						
BBPS 9-8	38 (9.6)	16 (4.0)	22 (5.5)	0.001†	0.027†	0.308†

WE, water exchange; WI, water immersion; AICD, air or CO2 insufflation; ADR, adenoma detection rate; BBPS, Boston Bowel Preparation Scale (cleanliness scores, segmental: 3 excellent, 2 good, >1 poor. Cleanliness scores, total: 9–8 excellent, 7–6 good, >6 poor/insufficient); † Chi-square; /n, sub-group denominator.

^{††}Advanced adenomas: diameter ≥10 mm, or high grade dysplasia, or ≥20% villous component.

Conclusions: WE is a superior insertion technique for detection of adenomas, particularly in the right colon and associated with excellent bowel cleanliness. WE increases also detection of advanced adenomas at excellent cleanliness, in the right colon (vs AICD) and in the entire colon (vs WI and AICD).

OC.11 IBD 2

OC.11.1

INFLAMMATORY BOWEL DISEASE PHENOTYPE AS RISK FACTOR FOR CANCER IN A PROSPECTIVE MULTICENTER NESTED CASE-CONTROL IG-IBD STUDY

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Background and aim: The risk of cancer using immunomodulators for Inflammatory Bowel Disease (IBD) is debated. In a 3-year prospective, multicenter, nested case-control study, we aimed to characterize incident cases of cancer in IBD. The role of clinical characteristics of IBD vs immunomodulators use in determining the cancer risk was also investigated.

Material and methods: From January 2012 to December 2014, all incident cancers in IBD patients referring to 16 IBD Units were recorded. Each patient with cancer (IBD-K) was matched with 2 IBD patients without cancer (IBD-C) for: IBD type, gender, age (± 5 years). Data were expressed as median (range), Wilcoxon test, multivariate logistic regression analysis (OR [95%CI]), Chi-Square test.

Results: Overall, 44,619 IBD patients were considered: 21,953 CD, 22,666 UC. Cancer occurred in 174 IBD patients: 99 CD (CD-K), 75 UC (UC-K). Cancer incidence in IBD was 3.9/1000, being higher in CD (4.5/1000 [99/ 21,953]) than in UC (3.3/1000 [75/22,666]; $p=0.042$). Cancers involved: digestive system (36.8%: CRC 67.2%; ileum 12.5%; others 20.3%), skin (13.2%), urinary tract (12.1%), lung (8.6%), breast (8%), genital (6.9%), thyroid (4.6%), lymphoma (6CD; 3.5%), others (6.3%). The percentage of patients with penetrating CD was higher in CD-K vs CD-C (26%; 26/99 vs 15%; 30/198; $p=0.02$) and with extensive UC in UC-K vs UC-C (55%; 41/75 vs 34%; 51/159; $p=0.003$). In CD, penetrating behavior and combined thiopurines (IS) and TNF α antagonists were risk factors for cancer overall (OR 2.33 [1.01-5.47]; 1.97 [1.1-3.5]), for extracolonic cancers (OR 3.9 [1.56-10.1]; 2.15 [1.17-4.1]), but not for CRC. Risk factors in UC included pancolitis and surgery for cancer overall (OR 2.52 [1.26-5.1]; 5.09 [1.73-17.1]); surgery for CRC (OR 3.6 [1.0-12]); extensive vs distal, subtotal vs distal UC for extracolonic cancers (OR 2.55 [1.15-5.9]; 2.6 [1.04-6.6]).

Conclusions: In a multicenter study, CD phenotype, penetrating CD, extensive UC represented risk factors for cancer overall.

OC.11.2

CROHN'S DISEASE-ASSOCIATED SMALL BOWEL CARCINOMAS SHOW DISTINCTIVE HISTOLOGY AND PHENOTYPE IN COMPARISON TO SPORADIC CASES: AN ITALIAN MULTICENTRE STUDY

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Background and aim: Although the small intestine accounts for 75% of the length of the gastrointestinal tract, non-ampullary small bowel carcinoma (SBC) is a remarkably rare tumor in the general population. Crohn's disease (CD) is associated with an increased risk of development of SBC. Histomorphology and phenotype of CD-associated SBC (CD-SBC) have, however, not been thoroughly examined.

Material and methods: We evaluated histologically 25 cases of CD-SBCs (median age 59 years, range 33-84) in comparison to 24 sporadic SBCs (median age 65 years, range 27-88). Immunoreactions for intestinal markers (CDX2, CD10, CK20), gastric markers (MUC5AC, MUC6), pancreatobiliary marker cytokeratin (CK)7, mismatch repair (MMR) proteins (MLH1, PMS2, MSH2, MSH6), p53 and HER2 were performed. HER2 gene amplification was also investigated by FISH testing in cases with HER2 membranous reactivity.

Results: CD-SBCs were frequently characterized by high grade and/or diffuse histology (poorly cohesive cells with or without overt signet ring cells). CK7 was expressed with significantly ($p<0.005$) higher frequency in CD-SBCs (64%) in comparison to sporadic SBCs (17%). Additionally, MUC5AC was also detected with higher frequency, even not significantly, in CD-SBCs (48%) in comparison to sporadic SBCs (21%). On the contrary, CDX2 and CK20 expression was significantly ($p<0.05$) less frequent in CD-SBCs (both 36%) in comparison to sporadic SBCs (71% and 79%). Moreover, CD10 was also detected with lower frequency, even not significantly, in CD-SBCs (16%) in comparison to sporadic SBCs (42%). There was no difference between sporadic and CD-SBCs regarding MUC6 and p53. Three CD-SBC and 4 sporadic SBC lacked both MLH1 and PMS2. HER2 amplification was observed in two out of 25 CD-SBCs. No significant difference was observed in terms of survival between CD-SBCs and sporadic SBCs.

Conclusions: Compared with sporadic SBCs, SBCs arising in CD had several distinguishing histological and immunophenotypical features, in particular the gastric and, possibly, pancreatobiliary differentiation. HER2 amplification made the two patients with CD-SBCs eligible for treatment with trastuzumab.

OC.11.3

DISEASE COURSE AND COLECTOMY RATE IN ULCERATIVE COLITIS: A FOLLOW-UP COHORT STUDY OF A REFERRAL CENTER IN TUSCANY

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Background and aim: The disease course and colectomy rate of ulcerative colitis (UC) varies largely in population-based and referral center cohorts. In addition the impact of changing treatment paradigms with the increasing use of immunomodulators (IM) and biological agents on the natural history is poorly understood. We retrospectively evaluated our cohort in order to determine the disease course and to identify risk factors, including timing of therapy, that could predict the need for surgery.

Material and methods: A cohort of 1,772 UC patients (1,011 males, mean age 34.8 ± 15.3 yrs) was identified and followed for a mean of 11 ± 9 yrs (range 1 - 49 yrs). The cohort was subdivided according to years of diagnosis: a) before 1980; b) 1981-1990; c) 1999-2000; d) 2001-2013.

Results: Disease extension was E1, E2, and E3 at diagnosis in 20%, 54% and 26% of patients, respectively. At final follow-up, disease extension increased in 20% of cases. Extra-intestinal manifestations (EIMs) were reported by 11% of patients, while use of systemic corticosteroids (CS), IM or anti-TNF α agents were reported in 68.4%, 20%, and 6.4%, respectively. More specifically, in the cohorts 1991-2000 and after 2001, the use of IM was 5-fold increased. In addition, in the cohort diagnosed after 2011, anti-TNF α agents were used in 10.1% of patients. The crude colectomy rate was 5.9% (104 pts), with a Kaplan-Meier estimation of 1.4% at one year (95% CI = 0.9-1.9) increasing up to 13% at 30 years of follow-up (95% CI = 5.1-20.9). The 1-yr colectomy rate did not changed over time (range 0.6-1.9%), while the 5-yrs and 10-yrs colectomy rates were halved in the last two decades compared to the previous ones (P=0.001). At the stepwise logistic regression, disease duration, disease extension, use of systemic steroids and biologics, were independently associated with increased risk of colectomy. The colectomy free survival in patients exposed to IM/anti-TNF α agents within 1, 3 and 5 years from diagnosis compared to those with later or no exposure did not differ significantly.

Conclusions: Colectomy rates in our cohort is rather low and was further reduced in the last two decades. Despite the availability of anti-TNF α agents and earlier use of IM, the 5 and 10 yrs colectomy rates did not differ significantly in the last two decades.

OC.11.4

FOOD PRESERVATIVES AND ADDITIVES EXACERBATE INTESTINAL INFLAMMATION

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Background and aim: In the last decades, there has been an increased incidence of IBD, particularly in previously low incidence areas, and this increase most likely relates to environmental and lifestyle factors. Food preservatives and additives commonly added as emulsifiers, stabilizers coating materials or bulking agents are frequently used in Western diet, and preliminary evidence indicates that daily consumption of some of these compounds could alter

the intestinal microbiota in mice thereby promoting dysbiosis and metabolic syndrome.

In this study, we evaluated whether a diet rich in Propylene Glycol (PG), a diol used as humectant, solvent and preservative, and Maltodextrin (MDX), a polysaccharide used as food additive and energy supplement, can increase the susceptibility of mice to develop intestinal inflammation.

Material and methods: Balb/c wild type mice were exposed to drinking water containing PG or MDX for 5 weeks, while control mice received only water. Colitis was then induced by the addition of dextran-sulfate sodium (DSS) dissolved in drinking water. Mice were sacrificed after 10 days and the colons were harvested for RNA and protein analysis and histopathology.

Results: Mice receiving a diet rich in PG or MDX did not exhibit macroscopic and microscopic signs of intestinal inflammation but had hyperplasia of mucus-producing cells concomitant with an increased expression of Muc2 RNA transcripts. PG or MDX-treated mice expressed high levels of Dual oxidase 2 (DUOX2), an epithelial-specific NADPH oxidase that is increased in early IBD and regulates interactions between the intestinal microbiota and the mucosa. Following DSS administration, mice receiving a diet rich in PG or MDX exhibited a significant weight loss, destruction of intestinal epithelium, and higher infiltration of inflammatory cells in the colon as compared to controls. Moreover, PG and MDX increased colonic expression of TNF- α and IL-6.

Conclusions: A diet rich in PG or MDX can promote morphological changes that alter the interaction between luminal flora and mucosal cells and exacerbate tissue-damaging pathogenic responses. Altogether, these data suggest that daily consumption of PG or MDX may contribute to enhance host's susceptibility to IBD.

OC.11.5

VITAMIN D DEFICIENCY IN EXPERIMENTAL CD-LIKE ILEITIS: A PRELIMINARY STUDY

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Background and aim: Low serum vitamin D (VD) has been associated with inflammatory bowel diseases (IBD). However, whether it is an epiphenomenon or it contributes to disease pathogenesis remains under question. The latter hypothesis is supported by the multiple functions of the VD axis on immune system modulation and mucosal barrier integrity. Dysregulation in the immune system and epithelial barrier dysfunction have been documented in a mouse model of spontaneous, progressive CD-like ileitis, i.e., SAMP1/YitFc (SAMP) mice. The aim of this study was to test VD levels in SAMP mice at different stages of disease progression compared to age-matched healthy controls (AKR/J and C57/BL6 mice). In addition, we determined the correlation between VD levels and progression of ileitis.

Material and methods: 10- and 30-wk old SAMP, and age-matched parental AKR/J and C57/BL6 controls (n=40), raised under the same environmental conditions and fed the same standard diet, were sacrificed. Terminal ilea were collected for histological and stereomicroscopical assessment of ileitis. Serum was obtained to perform 25(OH)D ELISA.

Results: Serum VD levels in SAMP mice were significantly lower compared to AKR/J (p=0.003) and B6 (p<0.0001) mice, independently of age. Analysis within strains revealed statistical difference in VD

levels according to age only in SAMP mice. Pearson's parametric analysis showed a moderate negative correlation between histologic scores and VD levels ($r^2=0.493$, $p=0.096$), and a strong, significant negative correlation between stereomicroscopy scores and VD levels ($r^2=0.742$, $p=0.037$).

Conclusions: In our preliminary study, low VD levels were detected in the early phases, as well as the chronic stage of ileitis in SAMP mice. VD levels were significantly lower in SAMP than in control mice independent of environmental factors or diet type. A negative correlation was found between VD levels and disease severity, and this was particularly true for stereomicroscopic assessment of ileitis. Low VD levels may be a contributing factor to the development of ileitis in this model. These findings provide a rationale for mechanistic studies investigating the effects of dietary VD supplementation and depletion in SAMP mice with CD-like ileitis.

OC.11.6

LOCALIZATION OF EBV IN COLONIC MUCOSAL CELLS OF IBD PATIENTS AND CORRELATION WITH DISEASE ACTIVITY INDEXES

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Background and aim: Epstein-Barr virus (EBV) can establish latency in target cells and reactivate in case of reduced host immunity, as in inflammatory bowel disease (IBD) patients under immunosuppressive therapy, giving rise to systemic and end-organ disease. We previously demonstrated the presence of high EBV DNA load in the intestinal mucosa of refractory IBD patients.

To evaluate the presence of EBV infection in epithelial and immune cells of colonic mucosa of IBD patients, both responders (IBD-R) and non-responders (IBD-NR) to standard therapies, in order to establish its localization, DNA load and correlation with disease activity indexes.

Material and methods: We enrolled 30 IBD-R (19 M, median age 38.5y), 20 IBD-NR (20 M, 49.5y) and 25 healthy controls (HC; 13 M, 49y). Clinical (CDAI: Crohn disease activity index; SCCAI: simple colitis clinical activity index) and endoscopic (CDEIS: Crohn disease endoscopic index of severity; UCEIS: ulcerative colitis endoscopic index of severity) scores were calculated. All subjects underwent lower endoscopy with biopsies for cellular separation by enzymatic digestion. The viral load in enterocytes, intraepithelial lymphocytes (IELs) and lamina propria mononuclear cells (LPMCs) was assessed by quantitative RT-PCR, and expressed as copies/10⁵ cells. The appropriate statistical tests were applied.

Results: EBV DNA was detected in LPMCs of all IBD-NR, 20 IBD-R and 7 HC ($p=0.03$), in IELs of 18 IBD-NR, 16 IBD-R and 9 HC ($p=0.01$), and in enterocytes of 17 IBD-NR, 7 IBD-R and 0 HC ($p=0.02$). A higher viral load was found in all the cell populations of IBD-NR (median 5.605 in LPMCs, 3.876 in IELs, 2.974 in enterocytes) as compared to IBD-R (27.0,0 respectively; $p<0.001$), and to HC (0 in all cell populations, $p<0.001$). No difference was found between IBD-R and HC. Higher

levels of viral DNA were found in all cell populations from inflamed versus non-inflamed mucosa in both the IBD groups ($p<0.001$) and in the inflamed mucosa of IBD-NR versus IBD-R ($p<0.001$). A positive correlation was found between viral load of inflamed mucosa of IBD-NR and SCCAI, CDAI and CDEIS.

Conclusions: Our novel result is the presence of EBV DNA in the epithelial cells of IBD patients, other than in all the immune cells with higher levels in those harvested from inflamed versus non-inflamed mucosa and a positive correlation with both clinical and endoscopic indexes of activity. These data suggest a direct role of EBV in the development of mucosal lesions through an active viral replication in the epithelial cells.

OC.11.7

MOTIVATIONAL INTERVIEWING IN OUTPATIENTS COUNSELLING: DATA FROM A LARGE CASE-CONTROL STUDY IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Background and aim: Motivational interviewing (MI) is a patient-centered counselling also proven useful in inflammatory bowel disease patients. Some skills are at the base of a successful MI: 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 patients. We report data from a case-control study (1:1 ratio) on MI applied to IBD patients.

Material and methods: Between June 2014 and March 2015 we collected data from 2 IBD referral centers both with knowledge on MI skills but only one of these (case group) currently applied this technique during the visits. At the end of visit all patients filled out an anonymous questionnaire.

Results: 200 patients (108 males [54%]) with a mean age of 40.3±15.5 years were evaluated. Ninety-two patients were affected by Crohn's disease (46%), 96 by ulcerative colitis (48%), and 12 by indeterminate colitis (6%). In table 1 are summarized all patients' characteristics. At final analysis 162 patients (81%) were previously evaluated by a gastroenterologist with an acceptable satisfaction rate (68%) which significantly decreased in those at the first outpatient visit (54%, $p<0.001$).

	N=100	N=100
Male, N (%)	51 (51)	57 (57)
Mean age±sd, years	35.5.1±15.1	44±15.1
Median of disease duration (range), months	18 (1-120)	96 (2-612)
Median of symptoms duration before the diagnosis (range), months	8 (1-41)	11.5 (1-276)
Disease, N (%):		
Crohn's disease	48 (48)	44 (44)
Ulcerative colitis	46 (46)	50 (50)
Indeterminate colitis	6 (6)	6 (6)
Family history of inflammatory bowel disease, N (%)	19 (19)	25 (25)
Patients previously evaluated by a gastroenterologist, N (%)	65 (65)	97 (97)
Patients previously evaluated by a general practitioner, N (%)	60 (60)	77 (77)

Satisfaction rate on general practitioner was low both in all patients and in those at the first visit (48% and 28%). The lowest satisfaction rate was reported in patients at the first visit ($p < 0.001$), in patients affected by indeterminate colitis ($p = 0.003$), in patients with long disease duration ($p = 0.004$); 78% of patients would have liked the use of explanatory pictures during the visits. Patients already followed-up in the referral centers reported a good overall satisfaction rate (87%) which reached 100% in those at the first visit. Nevertheless in the latter group, on a scale from 1 to 5, “5” (100% satisfied) was reported by 97% of patients on MI-group (case group) compared to 54% of controls: $p < 0.001$. No differences in terms “physician’s communication skills”, “perceived empathy” and duration of visits (41.9 ± 8.6 vs. 40.2 ± 9.4 minutes) were observed.

Conclusions: Our study showed as IBD patients followed-up in referral centers are satisfied of their physician rather than gastroenterologists without experience on IBD. MI is a communication tool very well appreciated by IBD patients and can help “IBD experts” to reach the best communication skills especially in pts at the first visit. Explanatory pictures should be used to help patients to better understand their clinical condition.

OC.11.8

EFFICACY OF A “CALL CENTER-BASED COMMUNICATION” IN OPTIMIZING THE CARE OF INFLAMMATORY BOWEL DISEASES

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Background and aim: Telephone helplines have been shown to be useful in the management of chronic diseases but data in inflammatory bowel disease (IBD) are still scarce. *Aim:* to analyze our two-years experience with the first IBD-dedicated telephone helpline in Italy, also evaluating the potential benefits for patients and physicians.

Material and methods: Between December 2012 and June 2015 we prospectively collected and analyzed all data deriving from a dedicated contact center (CC) used at our IBD Unit. The helpline was managed by operators specialized in health services. After 2 years, an anonymous questionnaire was administered by telephone operators to assess the effectiveness of the service and the level of satisfaction for patients. Also, we compared the number of outpatient visits in 2014 (active CC) with the number of visits in 2012 (without CC) to directly assess physicians’ benefits. We divided the number of calls in 5 categories (0-5, 6-10, 11-20, 21-30, and > 30), in order to assess the relationship between the number of calls and the risk of hospitalization. Statistical analysis was made by using χ^2 , ANOVA and odd ratio (O.R.); differences were considered significant when $p < 0.05$.

Results: During the first 2 years of activity, CC received a total of 11.080 calls with a number of handled requests of 11.972 (mean 20 calls/day). No difference was evident in terms of gender (M/F 45% vs 55%, $p = \text{N.S.}$); young patients called more frequently than elderly (22% vs 8%; $p < 0.01$). On average, 63% of patients phoned monthly to request medical consultation, while 37% called for non-medical reasons. The monthly peak of calls was on January (18%) and September (15%), while the daily peak was on Monday (30%) ($p < 0.01$). Furthermore, 97% of callers reported full satisfaction about our CC and the number of outpatient visit grow up from 1.658 in 2012 to 1.962 in 2014 ($p < 0.01$). The risk of hospitalization exponentially increased with the number of phone calls: 3% for 0 – 5 calls, 7% for 6 – 10 calls ($p < 0.01$; OR 2.4), 15% for 11 – 20 calls ($p < 0.01$; OR 5.5), 23% for 21 – 30 calls ($p < 0.01$; OR 9.7), up to 41% if patients called > 30 times in 2 years ($p < 0.01$; OR 21.6).

Conclusions: A dedicated telephone helpline for IBD patients could provide clinical guidance, care, support and, when necessary,

allow specific additional interventions to supplement the routine outpatient service.

OC.11.9

IBD-NURSE IN PATIENTS’ HEALTH STATUS ASSESSMENT: DATA FROM A PILOT STUDY COMPARING ABILITY OF IBD-NURSE AND GASTROENTEROLOGIST IN USING IBD-CLINICAL SCORES

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Background and aim: Inflammatory Bowel Diseases (IBD) are life-long chronic diseases which require a multidisciplinary team to optimise patients’ care. In this scenario IBD-nurses can play a strategic role both in the assessment and management of IBD-patients especially in those affected by severe disease that requires biologic treatment. The purpose of this pilot study is to evaluate the role of IBD-nurse in patients’ health status assessment (of those treated with biologics) by filling-out IBD clinical scores.

Material and methods: From July to September 2015 all consecutive IBD-patients treated with biologics were enrolled. For each patient both gastroenterologists and nurses filled-out separately an IBD clinical score depending on the type of disease: the Harvey-Bradshaw Index (HBI) for Crohn’s disease (CD) patients and the partial MAYO score for ulcerative colitis (UC) patients. All data were recorded in an electronic database for the final analysis.

Results: At the end of the study 40 patients were enrolled: 18 male (45%) and 22 female (55%). Twenty-six patients were affected by Crohn’s disease (65%) and 14 by ulcerative colitis (35%). The median value of HBI was 4 (range 1-13) in those evaluated by the gastroenterologist and 6 (0-14) in those evaluated by the IBD-nurse ($p = \text{ns}$). No differences were recorded through the different items of the HBI score (median values were reported): 1) patients well-being (1 vs. 0, $p = \text{ns}$); 2) abdominal pain (0 vs. 0, $p = \text{ns}$); 3) number of liquid or soft stools in the previous day (3 vs. 3, $p = \text{ns}$); 4) abdominal mass (0 vs. 0, $p = \text{ns}$); 5) complications (0 vs. 0, $p = \text{ns}$). Considering UC patients the median value of partial MAYO score was 1.5 (0-5) in those evaluated by the gastroenterologist and 1.5 (0-7) in those evaluated by the IBD-nurse ($p = \text{ns}$). No differences were recorded through the different items of the partial MAYO score (median values): 1) stool frequency per day (1.5 vs. 1, $p = \text{ns}$); 2) rectal bleeding (0 vs. 0, $p = \text{ns}$); 3) global assessment (0 vs. 0, $p = \text{ns}$).

Conclusions: Our study shows as IBD-nurses are able to determine correctly the current health status of IBD-patients through IBD clinical scores use. This can be a solid basis for evaluating the response to treatment and/or for planning the appropriate therapeutic interventions, helping gastroenterologist in improving patients’ care.

OC.12 Miscellanea 2

OC.12.1

ARE BASELINE IMPEDANCE LEVELS ASSESSED DURING ESOPHAGEAL IMPEDANCE MANOMETRY HELPFUL IN DISCRIMINATING PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE FROM THOSE WITHOUT? A PILOT STUDY

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Background and aim: Previous studies by means of 24h impedance-pH monitoring (MII-pH) highlighted the correlation between baseline impedance levels (BI) and integrity of the esophageal mucosa and the possibility to use this parameter to discriminate between subtypes of GERD. No previous studies investigated the possibility to achieve similar results by using impedance-manometry, a test requiring shorter time and providing further data about esophageal motility. We aimed to measure BI during manometric assessment and to correlate them with those obtained at MII-pH monitoring.

Material and methods: Consecutive patients with typical reflux symptoms underwent upper endoscopy and multiple biopsies were taken at Z-line and 2 cm above it to assess presence and severity of microscopic esophagitis. Within 3 days from endoscopy, patients underwent esophageal imp-manometry and imp-pH testing off-therapy. We evaluated BI values for at least 30 seconds during impedance manometry, expressed as mean value over 3 intervals of 10 secs each. BI at 3 and 5cm above the LES, was assessed on MII-pH recording during the overnight rest, for at least 30 minutes. Twenty healthy volunteers (HVs) who underwent the same procedures were also used as controls.

Results: We included 38 patients (M/F 17/11; BMI 27; age 46) classified according to endoscopy and MII-pH as: 8 grade A erosive esophagitis (EE), 10 non-erosive reflux disease (NERD), 10 hypersensitive esophagus (HE) and 10 with functional heartburn (FH). Twenty HVs [11F/9M; BMI 24; mean age 44] were included. BI values during impedance-manometry were lower in patients with GERD (2290; 95%CI: 1518-3476) than in those without (FH/HVs; 3677, 95%CI: 2648-5074; $p<0.05$). AUC 0.797; Sens 71.4 Spec 92.3; cut off $\leq 3159\Omega$. BI levels were lower in patients with ME than those without (2178 vs 3328; $p<0.05$). AUC 0.724; Sens 65.4 Spec 78.6; cut off $\leq 3353\Omega$. Although BI levels progressively decreased with the increasing severity of mucosal damage (EE<NERD<HE), a statistical significance was not reached. Finally, BI values assessed during manometry showed a positive correlation with BI levels assessed during MII-pH monitoring ($r=0.37$).

Conclusions: Baseline impedance levels measured during esophageal impedance-manometry have been associated to the diagnosis of GERD in patients with typical reflux symptoms. In patients with limited compliance this may represent an alternative method in order to investigate GERD. Due to the complexity of this disorder, miscellaneous manifestations and inconstant benefit of treatment, MII-pH study remains crucial in the management of patients referred to tertiary centers.

OC.12.2

HLA TESTING IN ADULT-ONSET CELIAC DISEASE: RELATIONSHIP WITH CLINICAL PRESENTATION AND MUCOSAL DAMAGE

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Background and aim: Genetic predisposition plays a key role in celiac disease (CD). Indeed, CD is strongly associated with specific HLA class II genes known as HLA-DQ2 and HLA-DQ8 located on chromosome 6p21.

Our aim was to assess the relationship between HLA phenotypes and clinical, serological and histological characteristics in a homogeneous cohort of patients with adult-onset CD, diagnosed in two referral centers from Sicily.

Material and methods: Age at diagnosis, clinical presentation (classical, atypical, silent), serological markers – anti - tissue transglutaminase antibodies (tTGA) and antiendomysium antibodies (EMA), degree of mucosal damage according to Marsh-Oberhuber classification, were registered on a shared database. HLA-DR and DQ alleles were performed on genomic DNA extracted from peripheral blood lymphocytes by PCR. According to HLA phenotype, patients were divided into three groups: HLA-DQ2 (homozygous or heterozygous for DQ2), HLA-DQ2-DQ8 and HLA-DQ8 (DQ8 homozygous or heterozygous). Data were analyzed by SPSS 13.0.

Results: 309 patients with CD were consecutively diagnosed between January 2004 and August 2014. 132 patients were tested for HLA-DQ2/DQ8. Most patients expressed HLA-DQ2 (56.9%), followed by HLA-DQ8 (31.8%) and HLA-DQ2 / DQ8 (11.3%). 82,6% were females. Mean age was $39,21\pm 14,7$ (range 12-80). 59,85% presented as classic CD (C-CD), 26,51% showed an atypical presentation (A-CD), 13,6% had silent disease (S-CD). 16,6% of patients had a previous diagnosis of autoimmune disease. There was no relationship between phenotype and sex. HLA-DQ2 was related to an earlier age of onset ($38,3\pm 14,6$) compared with HLA-DQ8 ($p<0.05$). There was no relationship between clinical presentation and genotype, but in HLA-DQ2 / DQ8 patients, levels of hemoglobin and ferritin were lower ($p<0,05$). Genotype did not influence the presence of autoimmune disorders. Serological markers (EMA and TGA) were significantly associated with DQ2 ($p=0,05$). No significant difference was observed in the three HLA- groups concerning the degree of mucosal damage.

Conclusions: The most frequent HLA haplotype in this sicilian population with CD is HLA-DQ2. However, the prevalence of HLA-DQ8 was greater than expected, according with rates reported in other Mediterranean series. Patients with HLA-DQ2 alone or in combination with DQ8 have a more aggressive clinical presentation with lower levels of hemoglobin and ferritin and higher levels of TTGA and EMA. HLA genotype is not related to severity of histological damage. Our results suggest that HLA testing has not only a diagnostic role, but could predict disease course.

OC.12.3

SUSTAINED IMPROVEMENT OF A CASE WITH REFRACTORY CELIAC DISEASE (RCD) BY SERIAL INFUSIONS OF AUTOLOGOUS BONE MARROW-DERIVED MESENCHYMAL STEM CELLS

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Background and aim: Mesenchymal stem cells (MSC) are an attractive therapeutic tool thanks to their multilineage differentiation, powerful action on all immune cells, homing to inflamed sites, and immune-privileged status which allows their transplantation across HLA barriers. RCD represents a clinical challenge since no standardized therapy is available and the prognosis is dismal. This is due to a progressive accumulation of aberrant intra-epithelial lymphocytes (IELs) triggered and sustained by overexpression of interleukin (IL)-15.

We investigated the feasibility, safety and efficacy of serial infusions of autologous bone marrow-derived MSC in a 51-year-old woman suffering from severe malabsorption syndrome due to type II RCD, as diagnosed following widely accepted criteria.

Material and methods: After systemic steroid therapy was undertaken with no improvement of her clinical condition and continuous need of parenteral nutrition and electrolyte correction, serial intravenous infusions of MSC scheduled every 4 months were proposed as rescue therapy. Monitoring of malabsorption indexes, mucosal architecture, rate of aberrant IELs and circulating FoxP3+ T-cells during the 12 months treatment period and the following 6 months was performed. The levels of IL-15 and its receptor on mucosal samples were also evaluated by means of Western blotting.

Results: A total of 3.9×10^8 MSC were obtained and the patient underwent 4 intravenous infusions of 2×10^6 MSC/kg. At baseline she had severe malnutrition (BMI 14.9 kg/m², albumin 1.9 g/dL, potassium 1.99 mEq/L, xylose 2.2 mg/dL), Marsh 3 lesions at histology with monoclonal rearrangement of TCR γ -chain, 94% of aberrant IELs, and 0% of FoxP3+ T-cells. During the treatment, there was a gradual improvement with normalization of all parameters after 12 months (BMI 19 kg/m², albumin 3.9 g/dL, potassium 3.5 mEq/L, xylose 58.6 mg/dL). Moreover, a complete recovery of both mucosal architecture and FoxP3+ T-cell percentage (45%) was observed, although the persistence of monoclonal rearrangement and aberrant IELs. The high levels of both IL-15 and IL-15R α found at baseline almost completely disappeared at the end of treatment.

Conclusions: MSC serial infusions in RCD appears feasible, safe and effective in terms of clinical and mucosal recovery. The inhibitory effects on IL-15 pathway and the recovery of normal values of regulatory FoxP3+ T cells may play a role in silencing the specific pathogenic mechanism leading to tissue injury.

OC.12.4

TEMPOROMANDIBULAR DISORDERS (TMD) IN PATIENTS WITH IRRITABLE BOWEL SYNDROME (IBS)

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Background and aim: Patients with IBS often have at least one co-morbid somatic complaint and many IBS patients meet diagnostic criteria for other functional disorders. Studies on the association between IBS and Temporomandibular disorders (TMD), that encompass a group of musculoskeletal and neuromuscular conditions that involve the temporomandibular joints (TMJs), the masticatory muscles, and all associated tissues, are scanty. Moreover, it is not known whether the association of IBS and TMD depends on the level of severity or the predominant symptom of the intestinal disorder. The aim of this study was to evaluate the prevalence of

TMD in patients with IBS and the association of TMD with patterns and severity of the intestinal disorder.

Material and methods: Seventy-seven consecutive patients diagnosed as having IBS, according to Rome III Diagnostic Criteria and 48 healthy controls, negative for IBS, were included in the study. IBS patients were classified into three different patterns according to the predominant bowel symptom and into three levels of severity using the irritable bowel severity scoring system (IBS-SSS) by Francis et al. In all participants, evaluation of TMD was carried out according to Axis I and Axis II of the Research Diagnostic Criteria for TMD (RDC/TMD).

Results: The prevalence of facial pain in the last month and jaw click were significantly increased in patients with IBS compared with controls (39% vs 20.8%, $p = 0.03$ and 42.9% vs. 20.8%, $p = 0.01$, respectively). The prevalence of depressive symptoms and non-specific physical symptoms (included and excluded the painful symptoms) were significantly higher in patients with IBS than controls (71.4% vs 52.1% $p = 0.028$, 85.7% vs 60.4% $p = 0.001$ and 83.1% and 47.9% $p = 0.000$, respectively). The severity of chronic facial pain was significantly correlated to the severity of IBS ($p = 0.029$), while no significant correlation was found between the severity of chronic facial pain and the patterns of IBS. Moreover, a significant correlation was found between the facial pain score (0-10 VAS) and the abdominal pain on a 100-point VAS ($p = 0.009$).

Conclusions: TMD occur frequently with irritable bowel syndrome. The severity of TMD and IBS are positively correlated. Further studies on somatic and visceral sensitivity in patients affected by different degrees of severity of IBS and TMD are clearly needed for a better pathophysiological understatement and management of these syndromes.

OC.12.5

ESOPHAGEAL SHORTENING IS ASSOCIATED TO SWALLOW-INDUCED LES RELAXATION AND INCOMPLETE TLES RELAXATIONS IN NERD PATIENTS AND HEALTHY CONTROLS

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Background and aim: Background: Transient lower esophageal sphincter relaxations (TLESRs) contribute to episodes of reflux. It has been demonstrated that longitudinal muscle contraction occurs during swallows and may play a role in eliciting TLESRs. LES lift, evaluated by means of high-resolution manometry (HRM), is a possible marker of the longitudinal muscle contraction of the esophagus.

Aim: To assess the length of esophago-gastric junction (EGJ) lift during liquid swallows and incomplete TLESRs in non-erosive reflux disease patients and healthy volunteers (HVs).

Material and methods: 15 NERD patients with typical symptoms, without hiatal hernia, and 15 HVs, underwent HRM combined with impedance (HRM-MI), before and 60 min. after a standardized solid/liquid meal, in a sitting position. Before meal, a total of 10 liquid (5ml) swallows, at 30-sec intervals, were performed. A catheter with 36 solid-state pressure sensors and 9 impedance segments was used. Color HRM plots were analyzed to determine the lower edge of the LES lift during swallow-induced LES relaxation as well as during incomplete TLESRs. Incomplete TLESRs were recognized when the end-expiratory LES pressure during relaxation was more than 5 mmHg. Average intra-esophageal pressures were measured before and during incomplete TLESRs.

Results: In the post-prandial period, a total of 68 and 59 incomplete TLESRs were recorded in NERD and HVs, respectively. The frequency of complete TLESRs did not differ between NERD patients and HVs. TLESRs in patients were more often associated with reflux episodes than in HV [129 (79% of TLESRs) vs 94 (66% of TLESRs), $p < 0.05$]. Mean

shortening length during incomplete TLESRs and wet swallows was 1.5 ± 0.31 cm and 0.8 ± 0.14 cm in patients, and 0.9 ± 0.14 cm ($p < 0.05$) and 0.6 ± 0.15 cm. (p : ns) in HVs. Increases of esophageal pressure during incomplete TLESRs were of 4.2 ± 0.4 mmHg in patients and 3.8 ± 0.2 mmHg in HVs (p : ns). A linear direct correlation between intra-esophageal pressure increases and length of LES lifts was found (R 0.76, $p < 0.05$).

Conclusions: Shortening can be clearly appreciated during incomplete TLESRs and wet swallows. In contrast to swallow-induced LES relaxation, the degree of esophageal shortening during an incomplete TLESR is more pronounced. EGJ might be an initial event contributing to LES opening and a key factor involved in GERD pathogenesis.

OC.12.6

THE ROLE OF S100B IN THE DEVELOPING ENTERIC NERVOUS SYSTEM

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Background and aim: S100B is a Ca²⁺ binding protein, which is predominantly produced by glial cells. Previous studies have shown that S100B is first expressed at embryonic day (E)14.5 by post-mitotic enteric glial cells. However, currently little is known about its possible function and whether the specific onset of expression is important for the developing the enteric nervous system (ENS).

Material and methods: We cultured intact E13.5 gut in the presence of arundic acid (300 μ M), an inhibitor of S100B protein synthesis, for 2 days in vitro. We then analysed changes in the numbers of enteric neurons, glia and ENS progenitors by performing immunohistochemistry against HuC/D, S100B and Sox10.

Results: In control cultures, S100B expression was identified in the rostral small intestine. This expression was successfully inhibited by arundic acid. Exposure to arundic acid did not affect the number of HuC/D+ neurons but significantly reduced the number of Sox10+ cells. The remaining Sox10+ cells also showed weaker immunoreactivity. Surprisingly, a subpopulation of HuC/D+ cells also exhibited Sox10-immunoreactivity in their nucleus. This was observed only in arundic acid cultures, but not in control conditions.

Conclusions: Our data suggest that the timely appearance of S100B is important for the development of the ENS. Inhibition of the onset of S100B expression could redirect fate specification of neurons and glia. We are currently investigating the identity of the HuC/D and Sox10 co-expressing cells that appear as a result of inhibition of S100B expression.

OC.12.7

BILE DUCT INVOLVEMENT IN AUTOIMMUNE PANCREATITIS: CLINICAL FEATURES AND PROGNOSTIC ASPECTS IN 92 PATIENTS

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Background and aim: Autoimmune pancreatitis (AIP) is a peculiar form of pancreatitis classified in type 1, type 2 and type NOS by International Consensus Diagnostic Criteria (ICDC). Disease relapse can be observed in up to 50% of patients, more frequently in type 1 and NOS AIP. Risk factors for recurrences are IgG4 serum levels and extra-pancreatic involvement, particularly intra-hepatic.

Aim of the study was to evaluate the bile duct involvement as prognostic factor for recurrences and the relationship between

intra-hepatic bile duct involvement, IgG4 serum levels and extra-pancreatic involvement.

Material and methods: We enrolled AIP patients observed in our center in the period 2009-2014. AIP was diagnosed according to ICDC. We evaluated MRI/MRCP to evaluate the biliary involvement, classified in normal (N), intra-hepatic±extrahepatic (IE), and only extra-hepatic (EE). Exclusion criteria were patients who underwent surgery (pancreatic or biliary) or patients without imaging at clinical onset.

Results: A total of 92 patients (70 males, 22 females, median age 48.7 ± 17.9 years) were included, 51 (55%) in N group, 21 (23%) in IE, and 20 (22%) in EE. IE patients are older ($p = 0.017$), suffering more frequently from type 1 AIP ($p = 0.003$), with kidney involvement ($p = 0.004$). IgG4 serum levels are higher in IE (688.6 ± 678.4 mg/dl) than in EE and N (290.3 ± 319.3 mg/dl) ($p = 0.005$). Patients with intrahepatic bile duct involvements relapse more frequently in comparison with others groups but the difference did not reach the statistical significance ($p = ns$).

Conclusions: AIP with intra-hepatic involvement is a more aggressive disease and, probably, a manifestation of IgG4-related systemic disease.

OC.12.8

LONG-TERM SAFETY OF OBETICHOIC ACID IN PATIENTS WITH PRIMARY BILIARY CIRRHOSIS

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Background and aim: Obeticholic Acid (OCA) is a potent and selective farnesoid X receptor (FXR) agonist developed for treatment of primary biliary cirrhosis (PBC). 216 patients with PBC were treated in a randomized, double blind (DB), placebo (PBO) controlled Phase 3 clinical study to evaluate the efficacy and safety of OCA. 198 patients completed the DB phase of the study and 193 enrolled in a long term safety extension (LTSE) phase. Exposure to OCA during the DB phase resulted in statistically significant liver biochemistry improvements and was generally well tolerated.

Material and methods: All patients enrolled in the LTSE first met the inclusion criteria for the DB study, which included PBC diagnosis, ALP $\geq 1.67 \times$ ULN and/or total bilirubin $>ULN$ to $<2 \times$ ULN, stable UDCA or unable to tolerate UDCA. During the DB phase, patients were randomized to placebo, OCA 5 mg titrating to 10 mg after 6 months based on tolerability/clinical response, or OCA 10 mg. In the LTSE, all patients started at OCA 5 mg with the option to increase by 5 mg every 3 months. An interim safety analysis was conducted after the initial 12 month LTSE period.

Results: Long-term OCA treatment demonstrated durability of therapeutic response and safety out to 2 years; no new safety signals emerged during the LTSE. The overall incidence of new adverse events (AEs) during the LTSE was lower for patients who received OCA during the DB phase, suggesting improved tolerability. Pruritus was the most common AE. As with the overall AE rate, the incidence of new pruritus was lower during the LTSE phase (DB: 56% OCA titration, 68% OCA 10 mg; LTSE: 15% OCA 5 mg, 21% OCA 10 mg). The use of an OCA titration strategy improved study retention; 0% PBO, 1% OCA titration, and 10% OCA 10 mg discontinued due to pruritus in the DB phase and $<1\%$ patients withdrew due to pruritus in the LTSE. After 2 years of OCA treatment, LDL remained comparable to baseline while the decrease observed in HDL during the DB remained unchanged in the LTSE. During the LTSE, the overall SAE incidence was low (9% OCA 5 mg, 7% OCA 10 mg), none were related to OCA and there continued to be no trend in the types of SAEs that were observed.

Conclusions: Continued treatment with OCA for up to 2 years was safe and generally well tolerated, with trends for improved tolerability.

OC.12.9

FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT C. DIFFICILE INFECTION: A 2-YEAR EXPERIENCE FROM A EUROPEAN REFERRAL CENTRE

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Background and aim: Fecal microbiota transplantation (FMT) from healthy donors is considered an effective treatment against recurrent *Clostridium difficile* infection (rCDI). To date, however, FMT is available only in few Centers worldwide. FMT was implemented in our Centre since June 2013. Our aim is to report outcomes of a large series of patients treated with FMT for rCDI in a European academic tertiary care Centre after 2 years of experience.

Material and methods: All patients treated with FMT for rCDI in our Centre were prospectively identified. Follow-up data, including diarrhea, *C. difficile* toxin status and adverse events were collected and analyzed.

Results: 45 subjects M/F: 23/22; mean age 70, range 29-91) received FMT from healthy donors because of rCDI (mean n° of recurrences: 3, range 2-6). Mean Charlson Comorbidity Index score was 3. Inpatient/outpatient ratio was 2.5. Twelve patients received multiple infusions, for a total of 66 procedures. All procedures were performed by colonoscopy. In 13 patients, endoscopic appearance of pseudomembranous colitis (PMC) was observed. The mean follow-up was 12 months (range 1-27 months). Resolution of rCDI occurred in 43 of the 45 treated patients (96%). No patients experienced further recurrences after FMT. Fecal material was provided by unrelated donors in 38 procedures. Both fresh and frozen feces were used. *K. Pneumoniae*-related sepsis occurred in one patient (3%) 24 h after the transplant, and resolved after antibiotic treatment. In 2 patients (6%), all suffering from concomitant urinary infections, a transient, self-limiting bacteremia was observed 1 to 6 days after FMT. Two subjects died because of overwhelming CDI from 1 to 10 days after FMT failure. Eight patients died 6 to 12 months after FMT, because of their own comorbidities (mainly cardiovascular disease) not relatable to the procedure.

Conclusions: FMT by colonoscopy achieved a 96% resolution rate of rCDI in our series. Our results confirm the efficacy of FMT in the treatment of rCDI in a large series of European patients, with a mean follow-up of 9 months. Dissemination of FMT is warranted to provide a better management of patients with rCDI.

Video

V.01 Video 1

V.01.1

GASTROSCOPIC REMOVAL OF A MIGRATED ADJUSTABLE GASTRIC BAND: A CASE REPORT

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Background and aim: Laparoscopic gastric banding is a popular method for treating morbid obesity. Intra-gastric band migration in an unusual but major complication of gastric banding. When migration occurs, band removal is mandatory to prevent intra-abdominal infection, gastrointestinal obstruction or life threatening hemorrhage and the treatment is usually reoperation.

Material and methods: A 43 years old female patient, with suspected band migration caused by vomit, underwent an upper endoscopy showing a partial transgastric migration of the laparoscopic adjustable silicone gastric band (LASGB). With the patient under general anesthesia, through a cutaneous exploration at the port-site, the silicone connecting tube was resected and the injection port extracted. The band was then retrieved endoscopically.

Results: After insertion of the gastroscope and insufflation of the stomach with CO₂ the migrated band was identified. A standard ERCP guidewire was introduced into the working port of the endoscope and passed between the partially migrated LASGB and the stomach wall and picked up at the other side of the LASGB, creating a noose around the band. Both end of the guidewire were externalized through the mouth. The metal spiral sheath of a mechanical ERCP lithotripter was passed over both ends of the wire. The metal tube (containing the guidewire looped around the intra-gastric band) was passed through the esophagus to the stomach. By twisting the handle of the gastric lithotripter the band was cut under direct vision. The band was then retrieved endoscopically by using a polypectomy snare. Finally the gastroscope was again introduced to check visually the full integrity of the gastric wall. No other complementary postoperative examination was performed and the patient was discharged the day after. The patient was reexamined gastroscopically one month after the removal of the LASGB to confirm adequate closure of the migration defect.

Conclusions: In this case report we show that a band penetrating the gastric wall can be treated endoscopically using standard equipment. It seems that this technique is simpler than reoperation and is beneficial even when the intraluminal migration is partial. The use of standard endoscopic equipment makes the procedure feasible in almost all the endoscopic units.

V.01.2

PER-ORAL ENDOSCOPIC MYOTOMY (POEM) WITH A NEW THERAPEUTIC LASER SYSTEM: FIRST STUDY IN AN EX VIVO ANIMAL MODEL (WITH VIDEO)

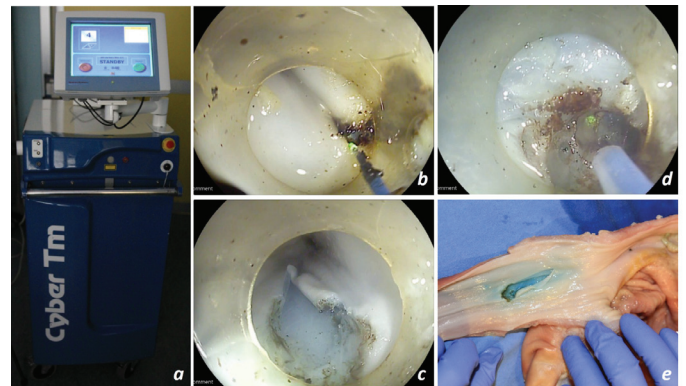
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Background and aim: Several therapeutic laser systems are established for surgical and endourlogical interventions [1-2]. Most recently, a new therapeutic laser system with a wavelength of 2µm has been developed to provide constant speed of cutting and vaporization (i.e. "vaporesction") with a precise control on depth and lateral tissue penetration to avoid inadvertent injury (fig. a). To date, no study has assessed the efficacy of the new device for gastrointestinal endoscopy. We conducted the first pilot study to test the feasibility of the newly introduced Thulium laser system (Cyber TM®, Quanta System, Varese, Italy) for POEM by using an established experimental setting (EASIE model).

Material and methods: The POEM procedure was performed following a standard technique. All steps were performed just by using the new Laser system and video-recorded. Subsequent to the endoscopic procedure, specimens were evaluated by an expert pathologist.

Results: A complete POEM by using the Thulium laser took approximately 20 minutes. No perforation to the luminal side (i.e. mucosal) occurred (fig. b-e). For laser power settings the most effective choice was 25-35 watts for mucosal excision and 15-25 watts for submucosal and muscular excision. Histopathology confirmed a clean and safe cutting of the different layers.



Conclusions: This is the first study of the newly introduced Thulium laser system showing the safety and efficacy of the new device for performing POEM procedures. These promising results should now be confirmed in additional in vivo studies.

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1. Rieken M & Bachmann. Nat Rev Urol 2014.
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V.01.3

ENDOSCOPIC BANDING FOR ABLATION OF DUODENAL FLAT LESIONS IN HIGH RISK PATIENTS

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Background and aim: Non-ampullary duodenal flat lesions are usually managed with endoscopic mucosal resection (EMR) but a high rate of perforation and bleeding has been reported.

Aim was to evaluate the safety and effectiveness of endoscopic banding (EB) as an alternative technique to EMR for ablation of duodenal flat polyps in patients at high risk for complications.

Material and methods: From May 2013 to May 2015, we treated five patients (3 M, age 34-70) with high (#2) or low (#3) grade dysplastic adenomatous flat polyps (8-15 mm) of the duodenum. In four cases

lateral-viewing duodenoscopy and colonoscopy excluded polyposis syndromes; Lynch syndrome was present in one patient. EB ablation was considered because of complicated advanced liver disease (#3), previous mucosal resection complicated with bleeding (#1) and suboptimal lifting (#1). Lesions were located at post-pyloric area (#1), anterior wall of the bulb (#1) and descending duodenum (#3), respectively. During upper endoscopy under conscious sedation, a multiband ligator was used to lift flat lesions. Snare resection was avoided in all cases. Chromoendoscopy and sampling were used to better assess marginal area of the polyps before ablation and to exclude residual or recurrent adenoma. Endoscopic controls were planned at 2 and 6 months until eradication and yearly thereafter.

Results: Complete ablation was achieved in all patients in one session. One (#3) or three (#2) bands were needed. No periprocedural complications occurred. At a median of 12 months (5–29) follow-up, no recurrent adenoma was detected.

Conclusions: EB ablation represents a safe and effective option to treat small duodenal flat lesions in patients at high risk for complications.

V.01.4

EUS-GUIDED DRAINAGE OF AN INFECTED PANCREATIC PSEUDOCYST AND SUCCESSIVE TREATMENT WITH HEMOSTATIC POWDER FOR A LATE INTRACYSTIC BLEEDING

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Background and aim: EUS-guided drainage is an effective treatment for infected pancreatic pseudocysts but complications such as bleeding, perforation, pancreatitis or stent migration can occur.

Material and methods: A 68-year-old patient developed the infection of a 10 cm pseudocyst in the body of the pancreas two months after an acute pancreatitis. A transgastric EUS-guided placement of a covered double flanged self-expandable metal stent (Taewoong Nagi stent, 16 mm wide, 2 cm long) was done. After its release, the stent was dilated with a 12mm TTS balloon for allowing a fast and complete outlet of the purulent material. Symptoms rapidly improved but seven days later the patient developed hematemesis; EGDS showed blood in the stomach without visible bleeding lesions. Thus the pseudocystic cavity was explored with a standard gastroscope: some fresh blood and a few small adherent clots were present in the pseudocyst. The fearsome rupture of a large vessel such as the splenic artery seemed improbable and an urgent radiologic or surgical intervention was not ruled out. The erosion of some small vessels within the pseudocystic wall appeared the most likely cause of hemorrhage and we treated the pseudocystic cavity with hemostatic powder (Endo Clot).

Results: This is a case report of an EUS-guided drainage of an infected pancreatic pseudocyst; the use of a large self expandable metal stent allowed us to get a rapid and complete emptying of the purulent collection, with a prompt clinical (fever, pain and leukocytosis improved after two days) and technical (a CT scan effected five days after the procedure showed a complete resolution of the collection) success. This treatment was complicated by a late intracystic bleeding one week after the stent placement: the presence of a wide stent allowed us to enter the cavity and to perform a topic treatment with an hemostatic powder. Neither recurrence of fluid development nor relapse of intracystic bleeding occurred in the following weeks.

Conclusions: EUS-guided placement of a large self expandable metal stent is still the best choice for treating infected pancreatic pseudocysts. The occurrence of mild intracystic bleeding can be endoscopically managed and the treatment with hemostatic powder is a promising option.

V.01.5

A SIMPLE AND SAFE METHOD FOR REMOVAL OF AN ESOPHAGEAL FISTULIZING FULLY-COVERED SELF-EXPANDING METAL STENT

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Background and aim: Malignant dysphagia can be due to esophageal cancer or neoplastic extrinsic compression. Treatment of patients with unresectable malignant stenosis is palliative. Self-expandable metal stents (SEMS) are nowadays recommended as preferred method for palliation of malignant dysphagia. Potential stent-related complications include obstruction, perforation, migration, esophageal-respiratory fistulas. Stent-associated esophageal-respiratory fistulas developed in 4% of patients with esophageal stenting. We describe a simple and safe method to remove a fistulising esophageal SEMS.

Material and methods: A 62 years old man with unresectable mediastinal mass stenosing the esophagus was treated with fully covered SEMS placement (FCSEMS) and following chemotherapy. After about five months recurrent dysphagia and pneumonia occurred. A contrast-swallow showed extra luminal spreading of contrast from the proximal end of FCSEMS into the trachea. Bronchoscopy demonstrated the presence of tracheoesophageal fistula (TEF) with half of the proximal edge of the FCSEMS prolapsing into the tracheal lumen. A computed tomography confirmed the leak of the proximal esophageal wall with the FCSEMS penetrating through the posterior tracheal wall. The patient was unfit for any surgical intervention, so we decided to remove FCSEMS with a previous overtube placement, to reduce traumatic risks and treat TEF with a new esophageal and a tracheal FCSEMSs.

Results: Initially the distal end of the stent was grasped using a rat-tooth forceps and pushed distally. An overtube was used to protect the esophageal mucosa during removal. The scope was withdrawn and the overtube was pre-loaded onto the scope. The scope was reinserted and overtube advanced into place. The proximal retrieval lasso was grasped and the stent was successfully retracted into the overtube. Then both scope and overtube with the FCSEMS inside were removed. No other damage to the esophageal wall was noted. Finally a new esophageal FCSEMS and a tracheal FCSEMS were placed. No complications occurred. Patient had symptomatic improvement.

Conclusions: Stent-associated tracheoesophageal fistula is uncommon complication and can often present as a potentially life threatening emergency. Additional insertion of FCSEMS is an effective treatment in this case, but initial FCSEMS removal could be traumatic and could lead to further tissue damage. We describe a simple and safe method to remove a fistulising esophageal FCSEMS before a new stent insertion and fistula treatment.

V.01.6

STONE IMPACTION IN THE PAPILLA: IS AN URGENT ERCP INDICATED?

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Background and aim: Indications to urgent endoscopic retrograde cholangiopancreatography (ErCP) include acute cholangitis, early biliary pancreatitis and acute pancreatitis associated with biliary obstruction.

Stone impaction in the papilla may be responsible of intractable pain and biliary obstruction.

Indication to ErCP in these cases is universally recognized but recommendations regarding its timing are not clear.

Material and methods: We report our experience with urgent Ercp (defined as a procedure performed within 12 hours after clinical presentation) at our institution in the period January 2013 – September 2015.

The indication to urgent Ercp was severe pain associated with biliary obstruction, with imaging (computerized tomography scan, magnetic resonance, endosonography) evidence of stone impaction in the papilla.

The series consisted of 7 patients, 4 males; mean age 46 years, range 19–92.

Results: In 4 cases an urgent Ercp has been performed, with fast and satisfactory resolution of the clinical picture and no complication observed; in three this has not been possible and the procedure has been executed 2–3 days later: in two cases pain has been very difficult to control and in one patient an acute pancreatitis has developed.

Conclusions: Our experience suggests to make all efforts to perform an early Ercp in patients with stone impaction in the papilla, due to possible development of intractable pain and unpreventable complications.

V.01.7

ENDOSCOPIC ULTRASOUND-GUIDED SINGLE-INCISION WITH NEEDLE KNIFE AND DEEP TISSUE BIOPSY FOR THE DIAGNOSIS OF A GASTRIC SUBEPITHELIAL TUMOR

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Background and aim: Gastrointestinal subepithelial tumors (SETs) includes a variety of neoplastic and non-neoplastic lesions that can be difficult to diagnose. Endoscopic ultrasound (EUS) is currently recommended as a first choice for examining SETs, even if its diagnostic yield seems to be suboptimal. Therefore, several other techniques for sampling SETs have been utilized.

Material and methods: An 80-year-old man was referred to our unit for the evaluation of a gastric SET. An EUS revealed a 25 mm homogenous hypoechoic well-circumscribed tumor, originating from muscular layer. An EUS-fine needle biopsy of the lesion resulted inconclusive. Therefore a EUS-guided single-incision with needle knife (EUS-SINK) biopsy was performed using a linear echoendoscope guiding a 10-mm linear incision over the lesion through a needle-knife sphincterotome connected to an electrosurgical unit. Then a conventional biopsy forceps were introduced to obtain deep tissue samples. Subsequently, the incision was closed with an endoclip. Procedure was uneventful.

Results: Histology showed a group of spindled-shaped cells resulted positive for CD117 and DOG-1 while negative for desmin, smooth muscle actin and S-100 expression on immunohistochemistry, in keeping with a gastrointestinal stromal tumor. The patient underwent surgical resection.

Conclusions: In this article we report on a more accurate diagnostic possibility offered by EUS-SINK with deep tissue biopsy for pathologic diagnosis of a gastric SET.

V.01.8

HAEMOSTATIC TREATMENT WITH A NEW THERAPEUTIC LASER SYSTEM – FIRST IN VIVO EXPERIENCE (WITH VIDEO)

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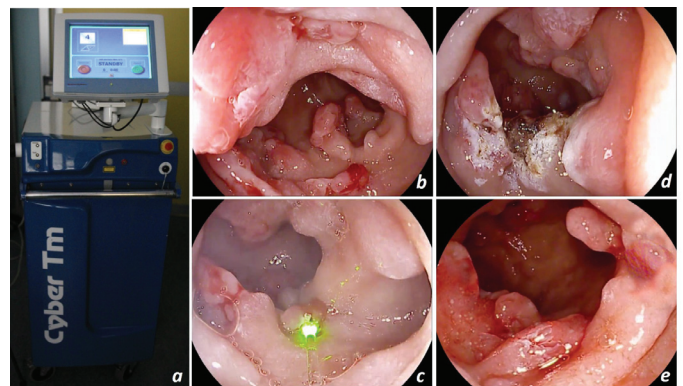
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Background and aim: The Thulium laser system (fig. a) is an established therapeutic technology for surgical resection [1]. By adjusting the power, its wavelength of 2µm provides a precise control on penetration depth (0.2–0.4mm) for ablation and vaporesction purposes in luminal endoscopy [2]. Here, we report on the first in vivo haemostatic treatment in humans, with this newly introduced tool during ongoing gastrointestinal bleeding, which had not been controlled by means of conventional haemostatic methods.

Material and methods: The new therapeutic laser system was used in a 67-year old man with recurrent oozing duodenal bleeding from a large post-inflammatory elevated lesion placed along the proximal duodenum. One year before, the patient had undergone a rescue treatment with selective arterial embolization for persistent active bleeding despite several endoscopic attempts in a huge and deep peptic ulcer located at the same part of the duodenum. The patient developed a large post-inflammatory duodenal lesion with recurrent oozing bleedings, which were unsatisfactorily controlled by standard thermal, cytochemical, and mechanical devices [3]. The endoscopic examination was performed using a high-definition videogastroscope and digitally video-recorded.

Results: Under conscious sedation, the endoscope was advanced into the duodenum, thereby showing two areas of oozing bleeding within the post-inflammatory lesion (fig. b). Then, a 550 µm optical fiber was introduced into the working channel, placing the tip at a distance of approximately 1 cm from the endoscope and from each targets. Using an integrated green laser as a pilot light for tissue targeting (fig. c), the Thulium laser system was used as a paintbrush to carefully vaporise the mucosal surface under a 5 watts continued modality. When active bleeding from an exposed vessel occurred, the focal administration of 10 watts power resulted in an immediate and persistent haemostatic ablation (fig. d). Patient was discharged home 4 hours after the procedure and no adverse event was recorded. Four weeks later, the endoscopic control revealed an initial mucosal healing upon the targeted area (fig. e).



Conclusions: The Thulium laser system appears to be safe and effective for in vivo haemostatic therapy of active bleeding lesions in the upper GI-tract, which are not amendable with conventionally haemostatic therapies. Multicenter studies should now confirm these initial results in a prospective setting.

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V.01.9

ENDOSCOPIC CLOSURE OF IATROGENIC DUODENAL PERFORATION SUCCESSFULLY TREATED WITH A NEW OVER-THE-SCOPE CLIPAnderloni A.¹, Bianchetti M.^{*2}, Di Leo M.¹, Repici A.¹¹Istituto clinico Humanitas, Milano, Italy, ²Istituto clinico Humanitas - Mater Domini, Castellanza, Italy

Background and aim: Although rare (0,09%), duodenal perforation is one of the most critical complication of endoscopic ultrasound (EUS), with significant morbidity and mortality. With the introduction of “over the scope” systems, clips and stents, endoscopic management has become the treatment of choice of the gastrointestinal perforation in the place of traditional surgical procedures.

Material and methods: We present a case of a 62-years old man with jaundice, referred to our unit to undergo EUS-FNA of solid lesion of pancreatic head followed by ERCP for biliary drainage. The patient underwent EUS performed with a linear echoendoscope (GF-UCT140, Olympus Optical Co., Ltd., Tokyo, Japan) under CO2 insufflation and deep sedation with propofol. During the scope withdrawal in the duodenum, we noticed a full thickness break of about 13 mm diameter at the upper duodenal knee. Then the echoendoscope was immediately retrieved.

Results: With a diagnostic gastroscope loaded with the new OTSC Padlock Clip (C910001, Aponos Medical Co., Kingston, USA) we reached the perforation site in the duodenum. The Padlock clip is a new OTSC device ergonomically designed to be placed on the tip of the scope without occupying the operative working channel. Since the diameter of the hole was too wide to be aspirated into the cap, we used a twin grasper to approach the edges of the perforation before releasing the OTSC (Video). X-ray with Gastrografin (Bayer AG, Germany, Leverkusen, Germany) showed the complete closure of the perforation with no contrast medium leakage. Broad-spectrum antibiotics were administered intravenously and a CT-scan performed three hours later confirmed the efficacy of the maneuver. The patient remained afebrile, asymptomatic with stabile vital signs. Semiliquid diet was allowed 24 hours later. Three days later, the patient underwent percutaneous transhepatic cholangiography and biliary drainage with positioning of a metallic stent. On day 7 postoperatively, the patient was discharged asymptomatic and with reduction of bilirubin level.

Conclusions: OTSC is a potentially surgery-sparing device and can be a useful tool for the immediate closure of duodenal defects. OTSC should be ready accessible and endoscopist should be trained in their appropriate use. The Padlock Clip is a new OTSC device readily deployed, ergonomically designed, that does not occupy a working channel making the interventional procedure more quick and easy to perform, with a high technical and clinical success rate.

V.01.10

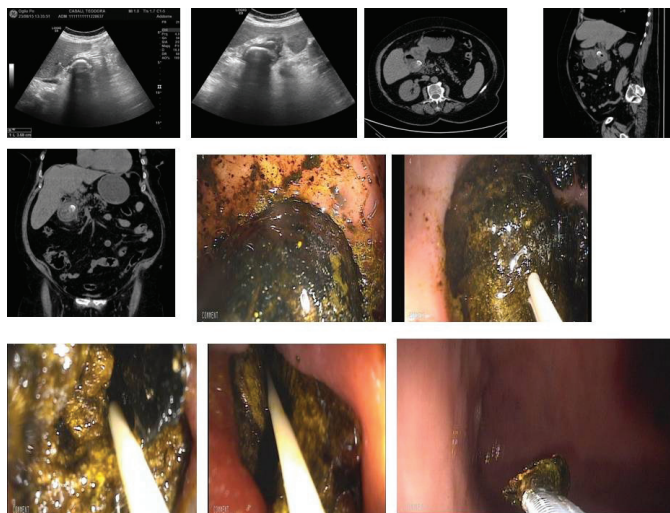
“DISSECTING THE STONE”: SUCCESSFUL ENDOSCOPIC “LITHO HYDRO-JET TRIPSY, LHJT” OF A BOUVERET SYNDROMEStaiano T.^{*2}, Repici A.³, Mutignani M.⁴, Martinotti M.¹, Rispo A.⁵, Buffoli F.⁶

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Background and aim: Bouveret's syndrome, is an uncommon cause for small bowel obstruction. Less than 3% of cases are due

to a gallstone impacted in the duodenum or pylorus resulting in a gastric outlet obstruction following the passage of a gallstone from the gallbladder to the duodenum via a cholecystoduodenal or choledochoduodenal fistula. Most of the successful therapeutic maneuvers described involve open surgical removal of the stone through either a gastrotomy or duodenotomy, and reported morbidity is not insignificant. We report a case of successful endoscopic removal of a large stone impacted in the duodenal bulb by means of a modified intracorporeal lithotripsy using hydro-jet probe connected to an electrosurgical unit.

Material and methods: An 86 yo woman was admitted to our hospital for severe epigastric pain, vomiting and nausea. Abdominal US (Fig 1A) suggested the diagnosis of a biliary fistula and CT scan detected pneumobilia, a thickened pyloric wall in continuity with the the gallbladder and stone impacted in the duodenal bulb (Fig. 1 B). EGDs revealed a large (50 x 60 mm) gallstone impacted in the duodenal bulb (Fig. 1 C), prohibiting passage of the endoscope downstream. Because of the size and location of the stone, fragmentation with mechanical lithotripsy was not feasible. Therefore, we performed intracorporeal endoscopic modified electrohydraulic lithotripsy using an ERBE JET® flexible probe (Ø1,3 mm; L 2,2 m) for ERBEHydro-Jet connected to electrosurgical unit at a setting of 50 watts. The probe was advanced through the operative channel and the cut distal end was applied to the stone for lithotripsy (Hydro-Jet Lithotripsy, HJL). HJL was repeatedly applied to the stone with subsequent applications to break the stone into multiple fragments (Fig. 1 D, VIDEO).



Results: Loose stone bigger fragments were dragged into the stomach with a snare, in order to prevent escape into the small bowel with consequent obstruction of the terminal ileum due to gallstone ileus. The patient improved clinically. The patient was fully recovered and was discharged after 6 days of hospitalisation.

Conclusions: Here, we described the first case of lithotripsy using an ERBE JET® hydro-jet flexible probe for a successful endotherapy of Bouveret syndrome. The limitation of this method is the risk involved with inadvertent focusing of the “hydro-jet waves” onto the surrounding tissue with consequent bleeding and perforation. Key factors for a successful endotherapy are: excellent stone visualization, adequate water immersion of the stone, correct technique (adequate devices handling and electrosurgical setting) and a skilled endoscopist. In conclusion, endoscopic management of Bouveret's syndrome offers an exceptional minimally invasive option compared to surgery.

V.01.11**IN VIVO ASSESSMENT OF TUMOR ANGIOGENESIS IN COLORECTAL CANCER: ROLE OF CONFOCAL LASER ENDOMICROSCOPY**

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Background and aim: Tumor neoangiogenesis is a key factor for tumor progression and metastatic spread. The possibility to assess tumor angiogenesis might provide prognostic information. Aim of the study was to establish the role of probe-based Confocal Laser Endomicroscopy (p-CLE) in the identification of vascular architecture and specific morphological patterns in normal colorectal mucosa and malignant lesions, during routine endoscopy.

Material and methods: Fourteen consecutive patients with colorectal cancer were included. The following features were identified and then compared between normal and neoplastic mucosa on p-CLE images: vessel shape (straight vs irregular); vessel diameter; the "branching patterns"; vessel permeability (fluorescein leakage) and blood flow (normal vs defective flux). Immunohistochemistry was used to confirm the presence and to study the morphology of vascular structures (CD-34 staining) and "neo-vessels" (WT-1 staining) on tumor and normal mucosa sections.

Results: Tumor vessels appeared as irregular, ectatic and with a highly variable caliber and branching patterns on p-CLE images. Mean diameter of tumor vessels was significantly larger when compared with normal mucosa (WMD, 3.38, 95% CI 2.65, 4.11, $p=0.01$). Similarly, "vessel branching" (OR, 2.74, 95% CI 1.23, 6.14, $p=0.01$), fluorescent dye "extravasation" (OR, 3.46, 95% CI 1.39, 8.57, $p=0.01$) were significantly more frequent in colorectal cancer than in normal colorectal mucosa. Immunohistochemistry corroborated p-CLE findings, showing higher vascularity in tumor sections due to neo-formed vessels, presenting irregular patterns as shown at p-CLE images.

Conclusions: P-CLE provides a non-invasive characterization of the microvascular architecture of colonic mucosa. Different morphological patterns have been described, discriminating from normal and malignant microvascular networks in colorectal mucosa.

V.01.12**OVER-THE-SCOPE CLIP-ASSISTED ENDOSCOPIC FULL THICKNESS RESECTION AFTER INCOMPLETE RESECTION OF RECTAL ADENOCARCINOMA: CASE AND VIDEO REPORT**

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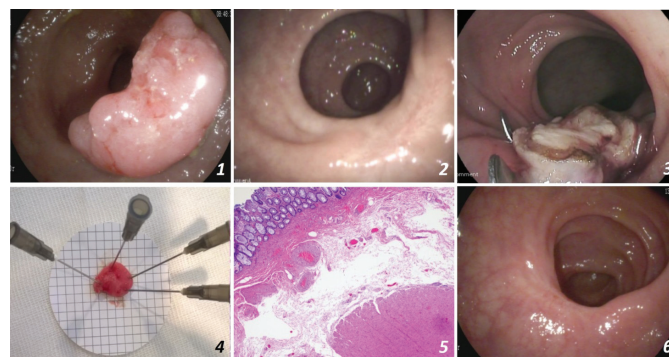
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Background and aim: The endoscopic resection is a valuable therapeutic option for early colorectal cancer (CRC), especially in high-risk surgical patients [1]. A novel endoscopic full-thickness resection device (FTRD; Ovesco Endoscopy, Tübingen, Germany) has been recently introduced to achieve complete resection of early CRC during ongoing endoscopy [2].

Material and methods: Here, we report the case of a 78-year-old man with a history of coronary disorders and recent pulmonary embolism who underwent colonoscopy for hematochezia. A 3 cm, non-pedunculated colorectal polyp with adenomatous pit pattern (Kudo IV) was observed 5 cm above the dentate line (fig.1). An en bloc endoscopic mucosal resection was performed. Histology revealed adenocarcinoma pT1 G2 Sm3, while total body CT scan and rectal endoscopic ultrasound reveal no lymphatic or metastatic disease.

Based on patient's comorbidities, we used FTRD to achieve the R0 resection (Video) after antibiotic prophylaxis with intravenous cefalosporine.

Results: First, lateral margins of the scarred resection site were marked with argon plasma coagulation (fig.2). The device was mounted on the tip of a standard gastroscope and, through a tissue anchor, the whole scarred lesion was pulled in to the cap and the OTSC was deployed. The pseudopolyp tissue created by the OTSC was resected using the pre-loaded snare and standard electrosurgical setting (VIO® ERBE Elektromedizin GmbH, Tübingen, Germany). The procedure took about 8 minutes and no bleeding nor perforation occurred (fig. 3). Patient reintroduced anticoagulant agents and was discharged in perfect condition the following day. On the full-thickness 15 mm-large specimen (fig.4), histological analysis revealed no remnant dysplasia (fig.5), as well as in the biopsy samples taken from the clear rectal scar 3 months later (Fig 6). Following endoscopic ultrasound and CT scan confirmed the absence of lymphatic or metastatic disease and abscess.



Conclusions: This case is interesting for several reasons. First, we have performed for the first time a full-thickness endoscopic resection for early CRC in the distal rectum, where standard surgery imply considerable risks and aggressive strategies. Secondly, we evaluated the potential of the novel FTRD in a high-risk patient with ongoing anticoagulants therapy. In addition, we have shown in detail the long-term clinical and endoscopic outcomes of this advanced endoscopic treatment.

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V.01.13**ENDOSCOPIC LIGATION AND RESECTION OF A LARGE SYMPTOMATIC SUBEPITHELIAL TUMOR OF THE DUODENUM**

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Background and aim: Subepithelial tumors (SETs) are frequent findings during endoscopy. Definitive diagnosis based on endoscopic biopsies is often not feasible, while endoscopic ultrasonography (EUS) is good to differentiate the nature of SET and can help guide decisions about treatment. Surgical resection is the gold standard for treatment of symptomatic gastrointestinal SETs, however novel endoscopic procedures represent an alternative to surgery in selective cases.

Material and methods: We here report a case of a 55 years-old woman presented for severe anemia and melena with an history of nonsteroidal anti-inflammatory drugs use. Upper endoscopy revealed a pedunculated SET of about 30 mm, ulcerated with a central bleeding stigmata, located in the second part of the duodenum. Biopsy of the lesion were inconclusive. EUS revealed

an heterogeneously hypoechoic mass with cystic anechoic spaces, arising from the third layer. We planned to perform an endoscopic resection. The excision of the SET was performed by standard oval electrosurgical snare after placement of a detachable nylon endoloop to the base of the stalk. Non procedure-related complication occurred. An endoclip was applied to secure the stalk. The resected lesion was then placed in a net polyp retriever and extracted back through the mouth. It was a well-circumscribed mass of 30×20 mm, with an ulcerated surface and yellowish tissue on resection margin. Histopathologic examination established a diagnosis of lipoma without atypical cells. After 3 months follow-up, patient was persistently asymptomatic and an upper endoscopy was performed without any evidence of lesions.

Results: Endoscopic resection of large lipomas may be associated with complications, as the low water content of fat makes it poor conductor of electrosurgical current. The use of a detachable snare may reduce the risk of bleeding. EUS in this case has proven to be essential for determining the original layer of SET and subsequent treatment.

Conclusions: Endoloop-assisted endoscopic resection can be one of the reliable therapeutic options for patients with peduncolated symptomatic SETs, given its low risk profile and provision for effective en bloc removal.

V.02 Video 2

V.02.1

4 CASES OF ENDOSCOPIC FULL-THICKNESS RESECTION OF COLONIC LESIONS USING OVESCO FTRD® SYSTEM: OUR EXPERIENCE

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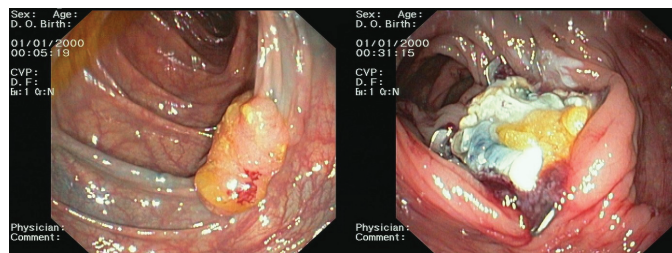
Background and aim: OVESCO AG recently proposed a novel therapeutic tool (FTRD® system) for the resection of adenomas of the colon and the rectum. It permits an endoscopic full-thickness resection (eFTR) of lesions, enabling the endoscopist to resect all layers of suitable lesions including the serosa. We discuss here the first 4 cases of eFTR performed in our Endoscopic Unit.

Material and methods: From March 2015 we performed 4 FTRD to 4 patients, 2 men and 2 women, mean age 65 years (range 54-81). Lesion localization was 1 hepatic flexure, 1 transverse colon, 1 sigma and 1 rectum. Lesions had different morphological characteristics as to Paris-Kyoto classification: 0 – IIc, 0 – IIc + IIa, 0 – IIa + IIc and 0 – Is. Lifting sign was negative in all lesions. 2 lesions were recurrent polyps after prior polypectomy. Histopathology showed an early carcinoma and 3 adenomas with high-grade dysplasia. One patient was not eligible to surgery due to atrial fibrillation, severe ischemic cardiomyopathy and chronic renal failure.

FTRD® system consists on a 21 mm cap with a clip and a snare, applied on the tip of a standard endoscope, which is covered with a sleeve. It slightly reduces visibility and handling of the scope during the exam. The procedure has 4 steps: marking, grasping inside the cap, releasing the clip then electrical snare cut of the lesion.

Results: eFTR was successful in 3 of 4 procedures. In one patient eFTR failed due the inability to retrieve the complete lesion inside

the cap, therefore she was referred to surgery. Elective surgery revealed a neoplasm invading the perirectal fat. The other 3 patients had a complete lesion removal confirmed by histology. All patients were dismissed after a 3 hours observation period after the procedure without any symptom. No adverse events were observed in a minimum 4 months follow-up. Patients with successful eFTR underwent a control colonoscopy after 2-3 months revealing a good healing of the resection.



Conclusions: eFTR with OVESCO FTRD® system is easy to perform and permits a radical resection of advanced adenomas not resectable with standard endoscopic techniques. Due to its safety profile, it can be indicated in patients with high surgical risk or not eligible to surgery.

V.02.2

ENDOSCOPIC ULTRASOUND GUIDED RADIOFREQUENCY ABLATION OF A PANCREATIC NEUROENDOCRINE TUMOUR (WITH VIDEO)

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Background and aim: The standard of care of pancreatic neuroendocrine tumours recommends surgical resection of functioning nodules or of large or high grade non-functioning ones (>2cm, G2-G3), with relevant costs and post-operative complications. Local endoscopic ultrasound guided ablative therapy is described, yet.

Radiofrequency ablation (RFA) is a method to obtain tumour necrosis by cell protein denaturation induced by tissue heating above 45°C, applied to treat several malignancies.

Energy is provided by an RFA current generator connected to an active electrode needle placed into the tumour under imaging guidance. Induced lesions have variable diameter, depending on current intensity, active tip length and time.

Recently a novel RFA needle has been developed to be used under endoscopic ultrasound (EUS) guidance. It is an 18G water cooled needle, with a 5 to 30 mm long active tip, connected to a radiofrequency generator (EUSRATM RF Electrode-Viva RF generator, STARmed, Koyang, Korea).

Material and methods: A 76-year-old man was referred for a pancreatic nodule. Labs were within normal ranges. An abdominal computed tomography (CT) showed an hypervascular 20mm nodule in the pancreatic tail. EUS-guided fine needle aspiration revealed a pancreatic neuroendocrine tumour with a Ki67 proliferative index >5% to yield a G2 grade.

Results: The patient refused surgical resection and we decided to treat the lesion by EUS-guided RFA. Under general sedation the nodule was ablated in a single session, with two passes by a 10mm long exposed tip needle. The patient remained asymptomatic, with normal serum pancreatic enzymes and was discharged on the third day. CT and contrast-enhanced EUS confirmed a complete radiological ablation on follow-up. No complication was observed and the patient is disease free to now.

Conclusions: In the reported case EUS-guided RFA appeared feasible and effective, remarkably with no complication and a short time hospital stay.

V.02.3

WALLED-OFF PANCREATIC NECROSIS: THE NEW ERA OF ENDOSCOPIC TREATMENT

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Background and aim: Nowadays, the interventional strategy for walled-off pancreatic necrosis (WOPN) is the minimally invasive step-up approach, including endoscopic drainage. Recently new specifically electrocautery-enhanced delivery system for interventional EUS such as Hot-AXIOS™ has significantly changed the technical approach in this setting allowing a simple, safe and time saving procedure.

Material and methods: We described a case of WOPN treated by endoscopic technique. A 68-year-old woman with a history of previous (two months) acute necrotic biliary pancreatitis was admitted to our hospital for management of symptomatic WOPN. The patient underwent a CT scan that showed a capsulated necrotic collection, with diameter of 18 cm, compressing the gastric wall. EUS examination confirmed CT scan finding. In the same session a 15 mm diameter, double-flange, lumen apposing, metal stent was deployed under EUS guidance across the gastric antrum in a fluoroles manner.

Results: EUS-guided transmural drainage with the Hot AXIOS system had none complication and was successful. Few days later the patient was treated by three endoscopic necrosectomy sessions combined with nasocystic drainage. During necrosectomy endoscopic debridement and irrigation with betadine and oxygenated water was performed. A significant reduction in collection diameter was seen on the CT scan repeated after the procedures, so nasocystic drainage was removed and the patient started enteral feeding regimen. The patient was discharged after 7 days asymptomatic and in good clinical conditions. The stent was endoscopically easily removed after three months.

Conclusions: Hot AXIOS system allows a safe, fast and easy EUS-guided fluoroles transmural drainage of pancreatic collection and in the same time provides easy entry to the cavity in order to perform possible necrosectomy. So far, only ERCP dedicated devices have been adapted for this purposes. In the last years, however, new specifically designed devices for interventional EUS such as Hot-AXIOS™ have significantly changed the technical approach to WOPN allowing a simple, safe and time saving procedure.

V.02.4

NOVEL SINGLE OPERATOR DIGITAL COLANGIOSCOPE FOR A DIAGNOSIS OF CYSTIC DUCT CARCINOMA: A CASE REPORT

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Background and aim: Cystic duct carcinoma (CDC) is a rare tumor with only few cases have been reported in the literature. Usually, this cancer is detected only when it is in an advanced stage and became clinically relevant with obstructive jaundice by compressing the hepatic hilum or the common hepatic duct. Several classifications of CDC were reported and the definitions were essentially the same: a part of gallbladder cancer in which the center is located in the cystic duct.

Material and methods: We present a case of an 83-year-old man, admitted to our Institution, for jaundice and abdominal pain. His

past medical history revealed coronary artery bypass, type II diabetes and chronic kidney disease.

MRI demonstrated dilatation of proximal common bile duct (CBD) and of the intrahepatic biliary ducts, with an obstacle at the insertion of the cystic duct. The subsequent EUS revealed an hypoechoic lesion (7 mm diameter) with irregular margins in the cystic duct (Fig 2). The lesion was punctured with a 25-gauge needle but the cytological examination was inconclusive.

Results: A colangioscopy was performed, using a novel single operator colangioscope (SpyGlass Direct Visualization System, Boston Scientific, Natick, Mass, USA) that revealed an adenomatous ulcerating mass in the cystic duct proximal to the confluence with the common bile duct.

Endoscopic biopsies (SpyBite biopsy forcep, Boston Scientific) performed under direct visualization revealed an adenocarcinoma of the cystic duct (Video).

Eventually the patient died two weeks after the endoscopic procedure due to a heart attack.

Conclusions: The single-operator peroral cholangioscopy technique is an advanced technique for intraluminal visual inspection, and for therapeutic intervention of the biliary and pancreatic ducts. The novel digital colangioscope (Spy Glass DS) seems easy to use and offer an accurate visualization of the biliary duct. It allows to reach specific area of the biliary tree and to perform biopsies under direct visualization. This new endoscopic instrument seems very useful to define the cause of indeterminate biliary obstruction.

V.02.5

EUS GUIDED RE-ESTABLISHMENT OF BOWEL CONTINUITY AFTER COMPLETE CLOSURE OF COLORECTAL ANASTOMOSIS (WITH VIDEO)

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Background and aim: Stenosis of a surgical anastomosis is a common complication of rectal surgery. While endoscopic treatment is relatively simple when a residual lumen is identifiable, it may be challenging when the obstruction is complete. We report a case of eus guided endoscopic re-establishment of bowel continuity. A complete video documentation is offered.

Material and methods: A 73 year-old man underwent a low anterior resection with a loop colostomy for treatment of a colorectal neoplasm. The procedure was complicated by deiscence of the anastomosis, requiring a second surgical look. During preoperative study for colonostomy reversal, a complete obstruction of the anastomosis was found.

Results: Using a double endoscopic access (standard endoscopy trough the colostomy and endoscopic ultrasound trough the rectum). The pre-anastomotic loop was filled with water and ultrasonographically identified. Under EUS guidance a 19G Access needle was inserted into the preanastomotic loop then a 0.035 inch guidewire was passed trough and caught up by a forcep. A 10 mm pneumatic dilation was performed.

Later on a 30x12 mm biflanged fully covered self expandable metal stent (Nagi, Taewong, Corea) was deployed across the anastomosis under endoscopic view.

Postoperative course was uneventful.

Conclusions: This is a further demonstration of the great capability of endoscopic ultrasound to lead complex interventional endoscopic procedure.

EUS guided re-establishment of bowel continuity is feasible and may be an alternative to challenging surgical procedures.

V.02.6

ENDOSCOPIC SUBMUCOSAL DISSECTION OF A LARGE PSEUDO-DEPRESSED SUPERFICIAL NEOPLASM OF THE TERMINAL ILEUMIacopini F.^{*1}, Grossi C.¹, Saito Y.², Rigato P.⁴, Gotoda T.³¹Endoscopy Unit, Ospedale S. Giuseppe, Albano L., Rome, Italy,²Endoscopy Division, National Cancer Center Hospital, Tokyo, Japan,³GI & Endoscopy Unit, Tokyo University, Tokyo, Japan, ⁴pathology Unit, Ospedale S. Giuseppe, Marino, Rome, Italy

Background and aim: It is recognized that superficial tumors of the duodenum, jejunum and terminal ileum pose a higher degree of complexity for endoscopic resection and surgical treatment is sometimes required in cases of incomplete resection. ESD achieves significantly higher en bloc and complete (R0) resection than conventional snare resection but is associated with a higher risk of adverse events, i.e. perforation.

Material and methods: We report one very rare case of a large superficial neoplasm of the terminal ileum treated by endoscopic submucosal dissection (ESD).

Results: A 73-year-old woman underwent colonoscopy for abdominal pain after a previous examination performed 3 years before.

At routine ileoscopy, a large 30x25 mm laterally spreading tumor non granular with a central pseudodepression (LST-NG PD type) was incidentally diagnosed. At chromoscopy with indigo carmine and narrow band imaging, endoscopy showed a Kudo pit pattern type IIIa and a Sano microcapillary pattern type 3A.

The tumor was resected en bloc by ESD with a combination of a small-caliber-tip transparent hood, insulated and noninsulated knives, no complication occurred.

Technical difficulties were: identification of neoplasm borders; the incision of the mucosal layer due to the presence of villi; the access into the submucosal layer. A whitish minute (2 mm) submucosal nodule resulted to be a Peyer's patch was observed.

Histology of the resected specimen showed an adenoma with low grade dysplasia with negative lateral and vertical margins.

Conclusions: ESD in the terminal ileum requires proper anatomical knowledge but may achieve successful curative resection with standard devices without complications.

V.02.7

ENDOSCOPIC RESECTION OF A LARGE PYLORIC GLAND ADENOMA OF THE CARDIATogliani T.^{*}, Mantovani N., Vitetta E., Savioli A., Troiano L., Pilati S.

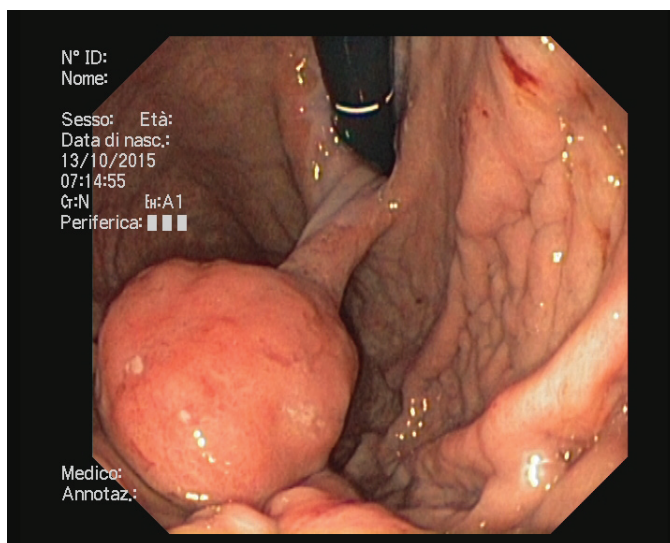
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Background and aim: Pyloric gland adenomas represent less than 3% of gastric polyps, with a strong predominance in elderly females. In the stomach the gastric body is the most common location, although extragastric sites such as duodenum, gallbladder, Wirsung duct and uterus have been described. They are characterized by closely packed pyloric gland-type tubules that express MUC6, and an association with intestinal metaplasia, autoimmune gastritis or dysplasia is not rare. Anemia, which is the most common clinical onset, can be due either to blood loss or to vitamin B12 deficiency in the setting of atrophic gastritis. Given the risk of coexisting cancer, an endoscopic or surgical resection is advisable.

Material and methods: A 69-year-old man presented with iron-deficiency anemia. Colonoscopy was unrevealing. Upper GI endoscopy showed a 4 cm round peduncolated lesion hanging in the gastric fundus from the cardia, with some small erosions on the overlying mucosa. At EUS the head of the polyp consisted of a slightly hyperechoic inhomogeneous submucosal mass with internal anechoic cystic spaces; the superficial mucosal layer was

normal; no Doppler-positive structures were visible in the stalk; no regional lymph nodes were visible. Afterwards, using a large working channel gastroscope, we put an endo-loop at the base of the stalk, we resected the lesion with a snare and we retrieved the polyp for histology.

Results: No early complications occurred and the patient was discharged two hours after the procedure. Histology revealed a 4.5 cm pyloric gland adenoma with no dysplastic alterations; the superficial epithelium showed a lymphocytic *Helicobacter pylori*-positive chronic gastritis. At the time of writing this paper neither an upper GI endoscopy nor a blood cell count have been repeated yet.



Conclusions: This is a case report of a rare large pyloric gland adenoma; its anatomical location and the male sex of the patient make the case much more uncommon. A preliminary EUS allowed to exclude major inner vascular structures before polypectomy; the endoscopic resection was complete and without complications. Given the need for an en-bloc removal, for providing the pathologist an intact polyp, the extraction of a big lesion through the cardia and the upper esophageal sphincter can represent the main technical difficulty of the procedure.

V.02.8

EFFECTIVE ENDOSCOPIC HOLMIUM LASER LITHOTRIPSY IN THE TREATMENT OF A LARGE IMPACTED GALLSTONE IN THE DUODENUMMirante V.G.^{*}, Bertani H., Grande G., Manno M., Caruso A., Mangiafico S., Conigliaro R.

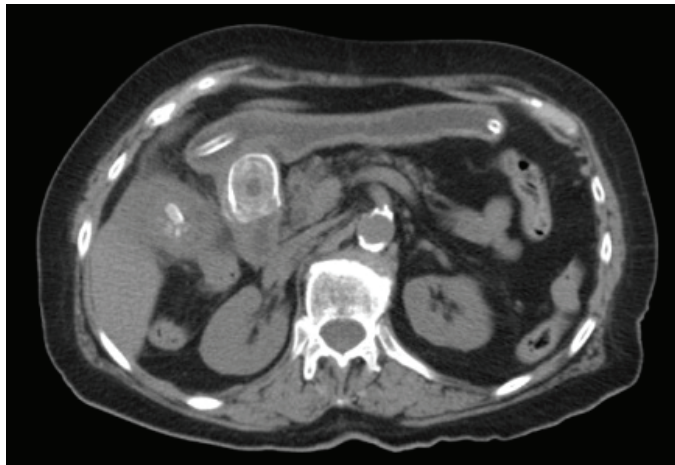
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Background and aim: Gallstone ileus is caused by the passage of one or more large gallstones (at least 2.5 cm in size) in the gastrointestinal tract through a bilio-enteric fistula. It accounts for 1-4% of all cases of mechanical small bowel obstruction. The obstructing gallstone usually impacts the terminal ileum, rarely the duodenum. CT scan usually reveals mechanical bowel obstruction, pneumobilia and ectopic stone in the intestinal lumen (Ringer's triad). Although surgery is considered the gold-standard treatment, a less invasive endoscopic approach is advisable in high risk patients.

Material and methods: A 87 years old woman was admitted to the emergency department complaining of abdominal pain and vomiting for three days. CT scan showed a large, calcified ring in the duodenum and aerobilia. An upper endoscopy revealed the

presence of a large obstructive stone in the duodenal bulb, unable to be removed endoscopically even after pyloric dilation. To improve the obstructive symptoms, the patient underwent gastro-jejunal anastomosis with partial relief of the obstruction. In order to fragment the stone, we performed another endoscopic procedure. A laser Holmium YAG 30 W (HLS30W, Olympus GmbH) treatment was applied for a total of about 200 minutes which resulted in stone's fragmentation into small parts removed by extraction basket and retrieval device.

Results: The patient was discharged 15 days after with a complete resolution of the occlusive symptoms. The cholecystectomy was cancelled.



Conclusions: Holmium laser lithotripsy is safe and effective in the treatment of a large impacted gallstone in the duodenum.

V.02.9

AN INDETERMINATE BILIARY STRICTURES ASSESSED USING THE NEXT GENERATION SPYGLASS DS SYSTEM: A VIDEO CASE

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Background and aim: Cholangiocarcinoma typically presents as biliary strictures; an accurate diagnosis is fundamental to address the best management. Although intraductal brushing during ERCP is the designated method for tissue sampling of biliary strictures, its sensitivity is low varying between of 27% to 56%. Spyglass system also known as Peroral cholangioscopy (POC) permits direct visualization and biopsies of the biliary tree for diagnostic procedures. The aim of this video case was to show the usefulness of the next generation of Spyglass system for the characterization of an indeterminate biliary stricture.

Material and methods: A 70 years old male with a suspected lesion located in the head of the pancreas, identified at CT scan and associated with a biliary stricture underwent EUS and ERCP. At that time brush cytology and fine needle aspiration (FNA) were performed and a plastic biliary stent was successfully placed. Despite the improvement of the patient symptoms, a certain diagnosis was not made due to inconclusive results of brush cytology and FNA. After a few months, following the worsening of the patient conditions, a next generation of Spyglass system was performed during the ERCP in order to characterise the indeterminate biliary stricture.

Results: During the ERCP a clogged plastic biliary stent (Olympus double layer, 6cm 10 Fr) was identified in placed and removed using a polypectomy snare. Once the cholangiography was performed, a stricture located in the distal common bile duct was identified and dilated using a 12mm balloon dilatation. A SpyGlass assessment of the biliary tract was then successfully performed and an endophytizing

irregular and ulcerated lesion was located in the distal common bile duct. Multiple targeted biopsies were then taken through the spyglass biopsies channel using a dedicated biopsies forceps. A 6 cm uncovered metallic stent was then placed. The histopathological analysis confirmed a pancreatic neoplasia involving the biliary duct.

Conclusions: The next generation SpyGlass system appeared to be an useful and safe technique that allows the characterization of an indeterminate biliary stricture and it can be easily performed by one operator. In addition, the improvement of the images quality, compare to the previous generation of SpyGlass system, allows an accurate inspection of the biliary tract.

V.02.10

AN INNOVATIVE EVALUATION OF PANCREATIC CYSTS BY CONFOCAL LASER ENDOMICROSCOPY AND FIBER OPTIC LIGHTING DIRECT VISUALIZATION SYSTEM

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Background and aim: Pancreatic cysts are a frequent diagnostic challenge. Endoscopic ultrasound (EUS) with Fine Needle Aspiration is often used for differential diagnosis, but both cytology and cystic fluid analysis are often inconclusive.

Material and methods: We report a video showing the exploration of two different pancreatic cysts with both confocal laser endomicroscopy (CLE) probe by Cellvizio (AQ flex probe; Mauna Kea Technologies) and direct visualization by SpyGlass System (Boston Scientific).

Case A: a 75-year-old woman presented with an incidentally discovered, 4 cm cyst of the pancreatic body identified on CT scan.

Case B: a 45-year-old woman presented with a slightly growing 6 cm cyst of the pancreatic tail and two previous episodes of acute pancreatitis. On EUS exploration contrast enhanced thin peripheral septa were detected.

The cysts were punctured with a 19 gauge Expect Flexible Needle (Boston Scientific) in which the CLE probe and SpyGlass optic fiber were introduced.

Results: Macroscopic and microscopic images of the pancreatic wall are provided in the VIDEO and the utility of CLE and Spyglass is discussed comparing the diagnostic yield of these innovative procedures with cyst cytology and CEA/amylase levels in the cystic fluid.

Conclusions: New promising devices are available to obtain a definite diagnosis of pancreatic cysts by direct endoscopic and microscopic exploration.

V.02.11

EUS GUIDED CISTO-GASTRIC DRAINAGE AFTER EUS-GUIDED GASTRO-GASTRIC ANASTOMOSIS TO TREAT A SYMPTOMATIC PANCREATIC PSEUDOCYST IN PATIENT WITH ROUX-EN-Y GASTRIC BY-PASS: THE DREAM BECAME REALITY!

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Background and aim: From 10% to 15% of acute pancreatitis is complicated by pancreatic pseudocysts, which show spontaneous resolution in 50% of the cases. Treatment is indicated in symptomatic or complicated persistent pseudocysts. Drainage of pancreatic pseudocysts using endoscopic techniques is the current preferred method.

We report a case of endoscopic drainage of a pancreatic pseudocyst through a gastro-gastro-cyst anastomosis in a patient who underwent a laparoscopic Roux-en-Y gastric bypass for obesity.

Material and methods: A 33-year-old female with Roux-en-Y gastric bypass was admitted to our hospital because of a CT evidence of symptomatic 7 cm pancreatic cystic lesion. Laboratory indicated iron deficiency anaemia. An endoscopic ultrasound (EUS) evaluation was performed. From gastric stump a cystic lesion of 7 cm in size was observed, but the excluded gastric pouch was interposed. A fine needle aspiration with a 19G needle (ECHO-19, Cook Medical) was performed. The cytological analysis showed granulocytes, histiocytes and was negative for malignant cells. Amylase and CEA levels were respectively 6785 U/ml and <5 ng/ml. Then we proposed an endoscopic approach. Initially an EUS-guided puncture from the gastric stump with a 19 G needle was performed and an access to excluded gastric lumen was obtained; after injection of contrast medium, a 0.035-guidewire was then placed into the excluded gastric pouch, and a gastrogastrocystic fistula was created by pushing a 10Fr cystoenterostome (XS 1341, Endoflex) on the guidewire. Finally, a 10Fr-20mm, SEMS (Nagi stent; Taewoong Medical) was left in place. After 2 weeks, failing to go through the gastrogastrocystic anastomosis with a therapeutic echoendoscope (Pentax), SEMS was substituted by a 20Fr-60mm enteral fully covered SEMS (Taewoong Medical). One month later it was possible to reach the excluded gastric pouch with a therapeutic echoendoscope (Pentax) passing through the enteral stent. Then an EUS guided puncture from the gastric pouch with a 19-gauge needle was achieved and a 0.035-guidewire was placed into the cyst; a gastrocystic fistula was created by pushing a 10Fr cystoenterostome on the guidewire. Finally a 16 Fr -20mm, SEMS (Nagi stent; Taewoong Medical) was left in place. Passage of air in the peritoneal cavity occurred. It was evacuated by placement of a XX needle under CT guidance. The patient was discharged 72 h later healthy. Two months later CT showed complete drainage of the cyst.



Results: Two months later cross sectional imaging showed complete drainage of the cyst.

Conclusions: In selected cases and in experienced hands, EUS guided drainage of pancreatic pseudocysts is a viable therapeutic alternative also in patients with previous digestive surgery.

V.02.12

PERORAL CHOLANGIOSCOPY VIA SPYGLASS SYSTEM FOR INDETERMINATE BILIARY STRICTURES: AN EFFECTIVE AND SAFE TOOL TO DISTINGUISH MALIGNANT FROM BENIGN LESIONS WHEN CONVENTIONAL METHODS HAVE FAILED

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Background and aim: Diagnosing malignant etiologies of biliary strictures is a difficult challenge. ERCP cytologic or tissue diagnosis with brushing, biopsies, or both is limited by their poor sensitivity. Peroral Cholangioscopy (POC) via the SpyGlass cholangioscopy system (Spyglass®) is a safe and effective adjunctive tool with ERCP for evaluation of bile duct strictures when conventional methods have failed. We report a video-case of an indeterminate hilar biliary stricture in whom SpyGlass was used for diagnostic purpose.

Material and methods: A 71-year-old man with a recent history of jaundice and weight loss (about 6 kg) and CT scan evidence of a "mass forming" hilar biliary strictures, already underwent in another hospital to PTBD, exploratory laparotomy and cholecystectomy with inconclusive biopsy on the hilar mass, was admitted to our hospital because of recurrent cholangitis.

A new CT scan showed increase in the size of the mass.

An EUS with FNA was performed but cytological sample was not representative.

CPRE showed the presence of proximal third bile duct stricture. Cyto-histological sampling was performed by brushing and biopsies, and were placed two plastic stents.

Since, cyto-histological examination was negative for malignant cells, it was decided to refer the patient to Peroral Cholangioscopy (POC) via the SpyGlass cholangioscopy system (Spyglass®) (VIDEO).

Results: Direct visualization of the stenosis showed irregular nodulations with erosions but no clear signs of malignancy (Intraductal nodular/villosus masses; oozing and irregular vascular patterns with an irregular surface). Histological examination showing chronic inflammation without malignant cells, allowed us to exclude the presence of malignancy.

Conclusions: Peroral Cholangioscopy (POC) via the SpyGlass cholangioscopy system (Spyglass®) provides direct visualization of strictures and allows for targeted biopsies, which may help to diagnose or rule out malignancy in indeterminate strictures. Future trials should develop algorithmic approaches incorporating cholangioscopy targeted biopsies and validate them in diagnosing patients with indeterminate biliary strictures.

V.02.13

METASTATIC MELANOMA OF THE GALLBLADDER DIAGNOSED BY ENDOSCOPIC ULTRASOUND-GUIDED FINE NEEDLE BIOPSY

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Background and aim: A 73 year-old woman with a history of malignant cutaneous melanoma (BRAF wild type) of the groin excised four years before, was referred for further characterization of an asymptomatic gallbladder mass discovered during follow-up on abdominal US then also detected on CT scan. Blood tests showed mild elevation of gamma glutamyltransferase, erythrocyte sedimentation rate and carcinoembryonic antigen. Endoscopic ultrasound (EUS) confirmed a 30 mm irregular mass rising from the gallbladder wall and extending into the lumen.

Material and methods: A EUS-guided fine-needle biopsy (EUS-FNB) of the lesion was performed using a 25 fenestrated needle in a single pass changing the position of the echoendoscope to safely target the solid tissue only without going through the gallbladder lumen. Antibiotic prophylaxis was used. Procedure was uneventful. Adequate tissue specimen was obtained for histopathological assessment and proved to be metastatic melanoma with BRAF mutation. Thus, the patient started on BRAF inhibitor Vemurafenib with rapid response.

Results: Metastases of melanoma to the gallbladder are rare and generally associated with widespread multi-visceral disease where prognosis is poor. In this case EUS-FNB consented to diagnose a limited metastatic disease involving an unusual location and provided tissue for repeated genetic test that was crucial to address the following treatment.

Conclusions: To our knowledge, this is the first case reported in literature of metastatic melanoma of the gallbladder diagnosed by EUS-FNB.

V.02.14

THE DIAGNOSIS OF AMOEBIC COLITIS IN NORTHERN ITALY: NOT AN EASY TASK!

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Background and aim: Amoebic colitis can mimic closely inflammatory bowel disease from clinical and endoscopic point of views and create severe management problems given a totally different therapeutic approach.

Furthermore, the paucity of observed cases make its recognition troublesome.

Material and methods: We describe the case of a 42 years old Albanian woman working as a caregiver of an old lady who had a previous history of world-wide journeys.

She has been admitted in another hospital with a 9 months history of chronic bloody diarrhea, with previous evidence of non-specific proctitis.

The clinical picture had dramatically evolved in the week before admission, with development of bloody diarrhoea, abdominal pain and fever, mild anaemia, leukocytosis and elevation of C-reactive protein. A standard search for stools parasites gave negative results. She has been treated with a combination of iv. steroids and iv. metronidazole.

Once transferred to our ward a colonoscopy revealed flask-shaped multiple ulcerations in the left colon, with histology suggesting acute ulcerative colitis; the examination of fresh stool specimens revealed trophozoites of *Entamoeba histolytica*.

Results: Withdrawal of prednisone and continuation of metronidazole allowed complete clinical recovery.

Conclusions: The clinical case we report stresses :

- the importance of taking an accurate history, since the old lady has probably been the source of the infection of the caregiver due to her state of healthy carrier passing *Entamoeba* cysts in the stools.
- the possibility of an insidious course in patients with amoebic colitis
- the necessity to examine fresh stools specimens to diagnose an infestation by *Entamoeba histolytica*.
- the possibility to misinterpret colorectal flask-shaped ulcers, in spite of their specificity.
- histology is not helpful.

Posters

P.01 Liver 1

P.01.1

A SINGLE INFUSION OF FERRIC CARBOXYMALTOSE EFFECTIVELY IMPROVES IRON-DEFICIENCY ANEMIA IN PATIENTS WITH GASTROINTESTINAL AND LIVER DISEASE: A HOSPITAL-BASED SURVEY

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Background and aim: Disease of the gastrointestinal (GI) tract and the liver are common causes of Iron deficiency anemia (IDA). Traditional therapy with oral iron is often ineffective or is linked to gastrointestinal side effects. Conventional intravenous (IV) iron is effective but requires repeated infusions. Ferric carboxymaltose (FCM) is a novel intravenous iron preparation that can be administered in single doses. In this retrospective study we aimed to evaluate efficacy and safety of FCM in a cohort of patients with IDA related to gastro-intestinal disease.

Material and methods: We report data of 63 consecutive patients admitted to our day-care unit because of IDA from January 2014 to September 2015. Anemia (defined as Hb < 13 g/dl in men, Hb < 12 g/dl in non-pregnant women) was classified as IDA if ferritin value was < 30 ng/ml. There were 27 (43%) patients with Inflammatory Bowel Disease, 17 (27%) with liver cirrhosis, 4 (6%) with celiac disease, 15 (24%) with other G-I disease. Clinical-demographic characteristics were registered on a dedicated database. We evaluated Hb, serum iron and ferritin values at baseline, after 2 and 8 weeks. FCM was administered by intravenous infusion of 500 mg in 15 minutes. We also evaluated the need for a second infusion of FCM and number of blood transfusions at baseline and after iron therapy. Safety was also assessed.

Results: By a single infusion of FCM, we obtained a mean increase of 1,3 g/dl in Hb values (Hb levels at baseline 9.5 ± 1.2 g/dl, 10.8 ± 1.5 g/dl at week 2) ($p < 0.001$). Significant increases in mean levels of serum iron (31 ± 23 at baseline, 60 ± 33 µg/dL at 2 weeks, $\Delta 27$ µg/dL; $p < 0.001$) and ferritin (21.6 ± 47 at baseline, 126 ± 85 ng/mL at 2 weeks, $\Delta 105$ ng/mL; $p < 0.001$) were also observed. A second infusion of FCM was necessary in 30% of patients. 11 patients (17%) had required at least one transfusion before FCM treatment while only 5 patients (8%) needed transfusions after FCM. Only one adverse event was observed (skin rash). FCM was well tolerated also in 4 patients with a previous history of anaphylactoid reaction to iv iron.

Conclusions: A single infusion of FCM significantly improves Hb and iron status in patients with IDA due to GI disease. Safety profile was excellent even in patients with liver disease and those with a previous history of allergic reaction to iron sucrose preparations. The use of FCM benefits reduces the impact of treatment on everyday life and work productivity and allowing a more efficient utilization of hospital resources.

P.01.2

HBV INFECTION PREVALENCE AND VACCINATION IN AN IMMIGRANT POPULATION IN ROME

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Background and aim: HBV chronically infects about 400 million people, in some geographical areas reaching and exceeding an 8% prevalence. Italy is placed in a HBV low prevalence range (about 1%) among native population. Still lack of information is observed about the diffusion of HBV infection in immigrant populations. Aim of the study is to improve immigrant's access to screening, diagnosis and treatment.

Material and methods: Between March 2013 and June 2014 a screening for HBV infection was proposed to 516 immigrants coming from different high and intermediate endemic areas. 449 of them accepted the blood test.

Vaccination against Hepatitis B was offered to the 209 patients negative for all markers of HBV infection.

Results: HBsAg positivity prevalence in patients accessing the Outpatient Clinic of NIHMP was 7.7%, (41% of them coming from East Europe, 39% from Africa, 20% from Asia). 67,3% of patients were males, mean age was 39.5 ± 11 .

Among the 449 patients submitted to serological screening, 35 were positive for HBV infection (HBsAg positive), while 414 patients were negative for HBV infection (163 patients with immune response generated by previous infection, 42 with immune response generated by vaccination and 209 negative for all markers). The prevalence of HBV infection in the cohort studied is 7.7% (35/449).

Among the 209 patients who received the vaccination against HBV infection, 68 (32.5%) refused the vaccination, while 141 (67.4%) began the vaccination cycle.

In addition, the screening showed the low percentage (9.3%) of patients that had been vaccinated against HBV (42/449), due to a lack of health education and of vaccination campaigns in their countries of origin.

Conclusions: In the cohort of patients studied, HBV infection prevalence resulted higher than in the general Italian population (7,7% versus 1%). The reason for this difference can be explained by considering immigrant's places of origin, which are often countries with high endemic HBV infection. We emphasize that, besides offering the screening test, also the vaccination option was offered to the immigrants resulting HBV sero-negative; in particular it is crucial to extend vaccination to cohabiting people and sexual partners of HBsAg positive subjects.

P.01.3

EFFICACY OF MEDITERRANEAN DIET AND ANTIOXIDANTS IN OVERWEIGHT PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Background and aim: Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide. The only currently recommended treatment for NAFLD is lifestyle modification. However, literature reports many studies on the use of antioxidant supplementation. The aim of this report is to describe the effects of Mediterranean diet associated with the administration of antioxidants (Bilirel – BIL; Pharnaluce, Republic of San Marino) in overweight patients with NAFLD.

Material and methods: Forty overweight patients with NAFLD were consecutively enrolled in this prospective study. The patients were randomized into two groups (n:20 and n:20). The first group was treated by Mediterranean diet (1300 kcal/day), and the second

group by Mediterranean diet and BIL (active components: silymarin 75 mg, chlorogenic acid 3.75 mg, protopine 0.02 mg, L-methionine 75 mg, and L-glutathione 75 mg), orally twice daily. All patients underwent clinical and biochemical evaluations, and ultrasound staging of liver steatosis according to the Hamaguchi score, in pre- and post-intervention period, after six months follow up.

Results: Before the treatment there was no significant difference between the two groups with respect to average age, BMI and gender, lipid profile, transaminase levels, serum insulin level, Homeostasis Model Assessment (HOMA) index for insulin-resistance and ultrasound degree of steatosis. After six months treatment, a statistically significant reduction was observed in BMI ($p<0.001$), lipid profile ($p<0.007$), transaminase levels ($p<0.01$), and liver steatosis degree ($p<0.01$) in both groups. However, a statistically significant reduction in serum insulin ($p<0.01$) and glucose levels ($p<0.05$), and HOMA index ($p<0.03$) was observed in Mediterranean diet plus BIL group.

Conclusions: Our data suggest the efficacy of Mediterranean diet plus BIL, on transaminase levels, BMI and hepatic fat accumulation in overweight patients with NAFLD. Also we report the improvement of glucose and lipid metabolisms.

P.01.4

ENDOCAN AS SERUM MARKER OF ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE AND/OR TYPE 2 DIABETES

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Background and aim: Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in Western countries, and is emerging as an independent cardiovascular risk factor.

Recently, Endocan, a 50 kDa circulating proteoglycan, produced specifically by non sinusoidal endothelial cells has been studied as an early marker of endothelial dysfunction. Aim of the study was to evaluate the serum levels of Endocan in patients with diagnosis of NAFLD and/or type 2 diabetes.

Material and methods: We enrolled 56 patients: 19 with NAFLD and 37 with type 2 diabetes, compared to 25 healthy controls. Endocan was measured by using ELISA EndoMark H1 assay (Lunginnov SAS, Lille, France).

Results: Endocan has been found to increase in NAFLD patients, independently from the presence of type 2 diabetes (1.23 ± 1.51 vs 0.68 ± 0.4 ng/mL; $p=0.016$), and in diabetes patients itself, compared to healthy subject (1.54 ± 1.76 vs 0.68 ± 0.4 ng/mL; $p=0.01$).

Specifically, we showed a statistically significant increase ($p=0.047$) in diabetes subject without liver disease, compared to NAFLD patients without diabetes (1.61 ± 1.61 vs 0.72 ± 0.58 ng/mL); moreover, we observed that Endocan was more elevated in NAFLD patients with diabetes compared to non diabetic ones (1.56 ± 0.81 vs 0.72 ± 0.58 ng/mL), even without statistic significance ($p=0.05$). Non diabetic patients didn't reach a relevant result compared to controls, even though they showed higher serum levels of our marker (0.72 ± 0.58 vs 0.68 ± 0.4 ng/mL; $p=n.s.$). Finally, we observed an increase of circulating Endocan in patients with metabolic syndrome vs controls ($p=n.s.$), especially with the adding of NASH (2.86 ± 3.15 vs 0.68 ± 0.4 ng/mL; $p=0.047$), based on the impact that this syndrome has on vascular system.

Conclusions: Our study demonstrate the increase of Endocan serum levels in NAFLD patients. In patients with type 2 diabetes and/or metabolic syndrome, Endocan serum levels are even higher, because

of a more important scientific evident endothelial dysfunction in these pathologies.

P.01.5

NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) AS POTENTIAL RISK FACTOR OF CARDIOVASCULAR DISEASE AND ONCOLOGICAL DISEASE IN DIABETIC TYPE 2 PATIENTS

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Background and aim: NAFLD is an increasingly cause of liver damage in western countries associated with obesity, hypercaloric diet and the sedentary lifestyle. The increasingly high prevalence of Nafld and its possible damage on several organs due to its inflammatory effects (cardiovascular risk and oncological risk) will lead to a priority health care problem in the next future. Validated prognostic scores for NAFLD and for cardiovascular risk in diabetics patients were respectively Fatty liver index (FLI) and UK Prospective Diabetes Study (UKPDS risk engine). The aims of our study are to assess the real correlation between FLI and UKPDS risk with cardiovascular (CE) and oncological events (OE) in a cohort of diabetic type 2 patients, in order to identify with accuracy the best predictor.

Material and methods: 2004 patients referred to our Diabetics Center Ambulatory and in a regular follow-up were retrospectively tested. UKPDS risk and FLI were calculated for each patient. Data such as CE, OE, anthropometric, biochemical and metabolic features were also collected. T test for unpaired data and Pearson Chi-squared test were performed.

Results: 304/2004 pt (15%), 211 M and 93 F, were FLI >60; in this group we observed 14 (5%) OE (7 M and 7 F) and 81 (27%) CE (64 M and 17 F). 743/2004 pt (37%), 638 M and 17 F, were FLI < 20; in this other group we observed 9 (1%) OE (6 M and 3 F) and 74 (10%) CE (47 M and 27 F). The statistical analysis showed that patients with FLI>60 have a higher risk of OE ($p=0.0006$) or CE ($p=0.0001$) compared to patients FLI<20. We identified also two peculiar profiles of cardiovascular risk, in fact male gender patients with FLI>60 presented a significant higher risk of developing CE than female ($p<0.05$); instead female gender patients with FLI<20 presented a significant higher risk of developing CE than male ($p<0.001$). No statistical significance was found between FLI > 60 +UKPDS >20 and CE ($p=0.754$). FLI>60 and FLI<20 patients also significantly differed respectively for mean age 62,2 vs 68,4 y ($p=0.02$), duration of diabetes 4,9 y vs 13,24 y ($p=0.002$) and mean glycated hemoglobin 8.7y vs 7,9 ($p=0.009$).

Conclusions: An early and aggressive program of follow-up and treatment could be established in diabetic type 2 patients with FLI>60 and so with reasonable suspicion of NAFLD because this population have higher risk to develop CE and OE in comparison to FLI<20 (or FLI negative and not suspicion of NAFLD). The simultaneous UKPDS and FLI positivity doesn't improve accuracy in predicting CE.

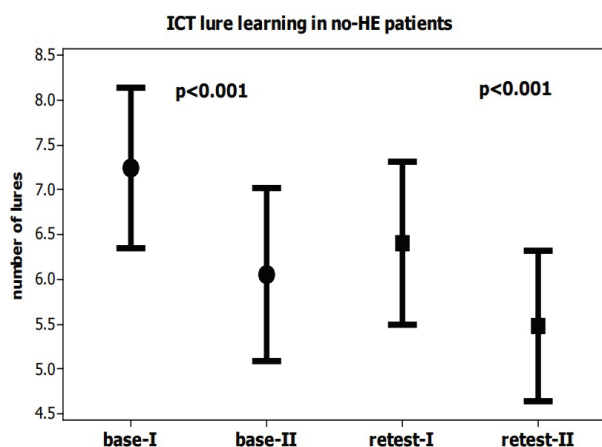
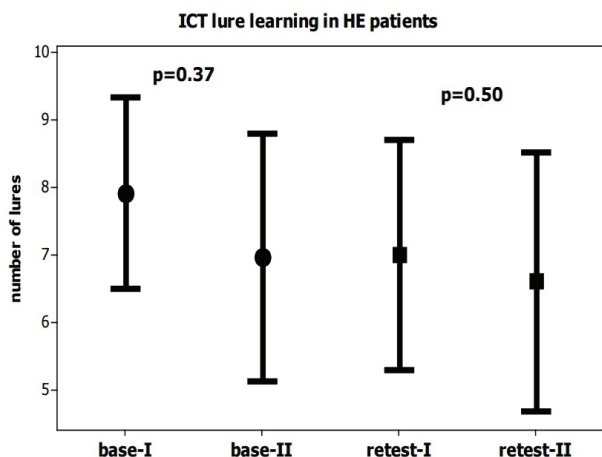
P.01.6

HEPATIC ENCEPHALOPATHY IS ASSOCIATED WITH PERSISTENT COGNITIVE DEFICITS DESPITE ADEQUATE MEDICAL TREATMENT: A MULTI-CENTER, INTERNATIONAL STUDY

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Background and aim: Hepatic encephalopathy (HE) is considered reversible regarding mental status (alertness, orientation) but may not be from a cognitive standpoint (performance on specialized tests that reflect daily function). Poor cognitive function despite treatment for HE has been shown in single-center studies. The aim of this study was to evaluate persistence of cognitive impairment in patients treated for HE compared to those who never experienced HE (no-HE) patients in a multi-center study.



Material and methods: 174 outpatient cirrhotics from 3 centers (94 subjects from Virginia, 30 from Ohio and 50 from Rome, Italy) underwent cognitive test using Psychometric hepatic encephalopathy score (PHES) and Inhibitory control test (ICT); patients were tested at baseline and re-tested at least 7 days apart without intervening change in liver disease severity. ICT learning (change in 2nd half lures compared to 1st half) was compared between HE and no-HE patients at baseline and at the re-testing visits.

The changes in the PHES individual sub-tests between baseline and re-testing visits were compared between HE and no-HE patients.

Results: Thirty six patients had prior HE; all were controlled on lactulose and 9 were on additional rifaximin. All HE patients were completely alert and oriented at the time of the testing (minimal score >25). HE patients had a higher MELD score compared to no-HE patients (16 vs. 10, $p<0.0001$). HE patients had worse performance on all tests compared to no-HE patients at baseline; a significant improvement (learning) (1st half 7.1 vs. 6.2, 2nd half, $p<0.0001$) was observed in no-HE patients and not in HE patients (1st half 7.9 vs. 7.8, $p=0.1$). All patients were retested a median of

20 days later without change in cirrhosis severity, medications or complications. No HE patients had significant learning or reduction in lures (1st half 6.0 vs. 2nd half 5.4, $p<0.0001$), while in HE patients again did not show ICT learning (1st half 7.8 vs. 2nd half 6.9, $p=0.37$). As regards Psychometric Hepatic Encephalopathy Score (PHES), no-HE patients shown an improvement in 4 PHES sub-tests instead of HE patients had an improvement only in 2 PHES sub-tests.

Conclusions: In this multi-center study, patients with prior HE showed persistent significant learning impairment compared to those without prior HE, despite adequate medical therapy. This persistent change should increase efforts to reduce the first HE episode.

P.01.7

MICROWAVE ABLATION OF LARGE HCCS BY SIMULTANEOUS MULTIPLE ANTENNAE INSERTION: LONG TERM FOLLOW-UP

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Background and aim: To report long term results of microwave (MW) ablation with simultaneous insertion of multiple antennae for large hepatocellular carcinoma (HCC).

Material and methods: Between October 2008 and September 2013, 36 cirrhotics with a single HCC nodule >3 cm (range :3.2-7.0cm; mean: 4.4 cm) underwent MW ablation in a single session by simultaneous insertion of multiple 13-gauge-MW-antennae (Viva-Wave, Covidien, USA). All patients underwent intraoperative evaluation of efficacy with contrast enhanced ultrasound (CEUS). Residual viable tumor at CEUS was treated in the same session by reinsertion of 2-3 MW antennae in the tumor. Efficacy of ablation was definitely assessed with three-phase computed tomography (CT) after one month. After treatment, scheduled follow-up entailed US every 3 months and CT every 12 months.

Results: 10 and 18 patients were treated with a single insertion of 2 and 3 synchronous antennae, respectively. 8 patients were treated with 2 insertions of 3 antennae in the same session. Intraoperative CEUS showed residual tumor in 12 patients. 9 out of these patients underwent an additional insertion of two antennae and 3 patients of three antennae. Intraoperative CEUS at the end of the procedure showed complete necrosis in all patients. 1month-CT showed complete necrosis in 33/36 patients. A severe hemoperitoneum, treated with blood transfusion, occurred in one patient after treatment. No major complication occurred in the other patients. Follow-up ranged from 18 to 78 months (mean: 42 months). During follow-up, local recurrence occurred in 7 patients within 3 to 12 months (mean: 6 months). Recurrences in other liver segments occurred in 35/36 patients within 6 to 24 months (mean: 15 months). Extrahepatic metastasis from HCC were observed in 1 patient 24 months after treatment. 16 patients died within 18-60 months (mean: 36 months), for tumor progression in 11 cases, decompensation of cirrhosis in 4 cases, hemorrhagic stroke in 1 case, respectively. 20 patients were alive at 18-78 months follow-up (mean: 42 months).

Conclusions: Ablation of large HCC by simultaneous insertion of multiple MW antennae is a safe and effective treatment and can result in long survival of patients.

P.01.8

PERCUTANEOUS ELECTROCHEMOTHERAPY OF MALIGNANT MAIN PORTAL VEINS THROMBOSIS: A PROSPECTIVE CASE SERIES

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Background and aim: Cirrhotic patients with malignant main portal vein thrombosis (MMPVT) from hepatocellular carcinoma (HCC) are excluded from any known curative treatment. A single previous report advocated a possible role of Radiofrequency Thermal Ablation (RF). Electrochemotherapy (ECT) is a non-thermal local tumor ablation modality using electroporation, a physical method that enhances cell membrane permeability, and enables chemotherapeutic agents to enter tumor cells. This technique is virtually able to damage tumor cells without affecting stromal structures and normal cells proximal to the tumor. In order to evaluate the effectiveness and safety of the technique, we treated with ECT, in a prospective study, a series of patients with liver cirrhosis and MMPVT from HCC.

Material and methods: Six patients were enrolled. All of them underwent pre-treatment three-phase abdominal computed tomography (CT), contrast enhanced ultrasound (CEUS), and ultrasound (US) guided percutaneous biopsy of the thrombus. We performed ECT in general anesthesia, with intubation. Under US guidance, four to six electrode-needles were inserted percutaneously along the external margin of the thrombosed portal vessel. The electrodes were connected to independently controlled generator outputs of the Cliniporator Vitae (IGEA, Carpi, Italy). 8 minutes after intravenous injection of a Bleomycin bolus (15,000 IU/m²), electric pulses were delivered. All patients underwent percutaneous US guided biopsy of the treated tumor. Short term control of efficacy of the ECT was performed with intraoperatively CEUS, at the end of the procedure, and an additional CEUS after 24 hours. All patients were followed up with monthly color-doppler US (CDUS) and CEUS for six months. Three-phase CT was repeated as soon as CDUS showed recanalization of treated portal vein.

Results: The follow-up ranged from 2 to 9 months. Monthly post-treatment CEUS demonstrated complete absence of enhancement of the thrombosis in all cases. Pre-treatment biopsy was adequate and showed viable HCC in 4/5 cases. Post treatment biopsy showed severe involutive changes of tumor cells with cellular apoptosis and areas of necrosis. In 2 cases, the specimen included the portal vein wall that showed normal endothelium and normal stromal aspects of the wall. The first patient (9 months follow-up) showed a completely patent portal vein at CDUS, CT and CEUS within 2 months from the ECT. 2 patients (6 and 5 months follow-up) showed partial recanalization of the treated portal vessel. The other 3 patients (2, 5, and 3 months follow-up, respectively) showed avascular thrombus at monthly CEUS and CDUS, and at 2-month CT.

Conclusions: ECT seems an effective and safe procedure for curative treatment of MMPVT. This technique does not affect hilar biliary structures and vessels. Results on larger series of patients are needed to confirm these preliminary results.

P.01.9

THE GUT MICROBIOTA OF CIRRHOTIC PATIENTS WITH POOR NUTRITIONAL STATUS: PRELIMINARY EVIDENCES

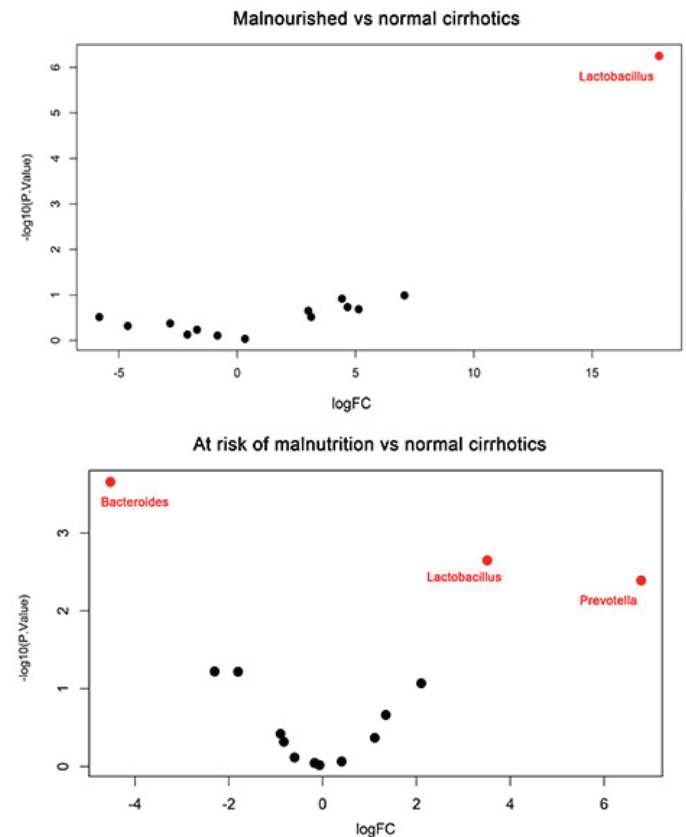
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Background and aim: Gut microbiota (GM) modifications have been reported in malnourished populations. Liver cirrhosis is often associated with malnutrition and sarcopenia but GM changes in this setting have not been investigated yet.

The aim of the present study was to investigate changes in GM composition according to nutritional status in patients affected by liver cirrhosis.

Material and methods: Fecal samples of cirrhotic patients without exposure to antibiotics, pre-/pro-biotics and bowel colonoscopy preparation for at least one month were collected. Nutritional status was assessed by a multi-dimensional questionnaire including clinical and anthropometric parameters (Mini Nutritional Assessment, MNA). GM composition was assessed by a metagenomic gene-targeted approach (16S rRNA) using the Roche 454 GS Junior and Qiime pipeline. Biostatistic analysis was performed using R-statistics packages.



Results: Twenty cirrhotic patients were included in the study; median age was 60 years, Child-Pugh A/B/C 10/4/6, 13 (65%) were well-nourished, 5 (25%) at risk of malnutrition and 2 (10%) severely malnourished according to MNA. Nonmetric multidimensional scaling (NMDS) ordination on Bray Curtis distance revealed a significant clustering according to nutritional status rather than to Child-Pugh score ($p=0.014$ vs $p=0.06$ PERMANOVA). Malnutrition was associated with increased abundance of Lactobacillus and Prevotella and a reduction in Bacteroides (adj. p -value <0.05 ; Figure 1). This

finding was different from that observed after stratifying patients according to Child-Pugh score; indeed, advanced liver disease was associated with decrease in *Bacteroides*, *Parabacteroides*, *Faecalibacterium*, *Veillonella*, *Clostridium*, *Oscillospira* and *Blautia* (adj. p-value <0.05).

Conclusions: GM composition is influenced by nutritional status in patients with liver cirrhosis. Although the increase in beneficial bacteria such as *Lactobacilli* may suggest a possible compensatory mechanism, metabolomic analyses should be performed to reveal the significance of these alterations and to evaluate potential therapeutic approaches.

P.01.10

CLINICAL OUTCOME OF IMMUNOSUPPRESSION IN PATIENTS WITH AUTOIMMUNE HEPATITIS: A SICILIAN COHORT STUDY

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Background and aim: Autoimmune Hepatitis (AIH) is a disease with unknown aetiology. It predominantly affects female patients, and is characterized by elevated transaminase and immunoglobulin G levels, circulating autoantibodies and interface hepatitis at liver biopsy. AIH is responsive to immunosuppressive treatment, which should be started to promote remission and long-term survival. The aim of this work was to assess the clinical, biochemical and serological features associated with clinical outcome of AIH Sicilian patients.

Material and methods: Clinical, biochemical immunological features and treatment response of 99 sicilian patients with AIH have been evaluated.

Results: We included 99 cases (mean age of 50.4 years, 86 women). Type 1 has been found in 92 cases. Liver fibrosis and cirrhosis have been found in 61.9% and 24.1% respectively. Combination of steroids and azathioprine or steroid alone was used in 76 patients. Complete remission has been documented in 69% of patients, whereas partial/null response has noticed in remaining patients. At multivariate time-dependent analysis complete responders showed a lower risk of disease progression, or the onset of complications such as portal hypertension ($p < 0.0001$), thrombocytopenia ($p < 0.0001$), esophageal varices, increase of liver stiffness, hepatic cirrhosis, liver failure, hepatocellular carcinoma (HCC) and death.

Conclusions: AIH appears to have similar features in male and female patients. The combination of azathioprine and steroids has proven to be an appropriate therapy in the setting of AIH, reducing the risk of the aforementioned disease progression.

P.02 Pancreas

P.02.1

VITAMIN D DEFICIENCY AS A RISK FACTOR IN PANCREATIC NEUROENDOCRINE NEOPLASMS: REPORT FROM A SERIES AT A SINGLE INSTITUTE

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Background and aim: Vitamin D deficiency (VitDdef) is hypothesized to represent a risk factor in several neoplasms (i.e. colorectal cancer, pancreatic cancer, hepatocellular carcinoma). To our knowledge, vitamin D levels have not been previously evaluated

in patients newly diagnosed with pancreatic neuroendocrine neoplasms (pNENs).

Aim: to determine whether VitDdef may represent a risk factor for pNENs and whether may be associated with overall survival (OS) and progression-free survival (PFS).

Material and methods: From September 2009 to September 2014, pNEN was newly diagnosed in 47 patients (M/F= 17/30, median age 61 yrs, range 26-86 yrs). Grading was G1, G2 and G3 in 32 (68.1%), 14 (29.8%) and one (2.1%) patient, respectively. Again, TNM stage was I, II, III and IV in 16, 17, 2 and 12 cases, respectively. Serum 25-hydroxyvitamin D (25OHvitD) levels were measured at baseline in all the patients and its deficiency was defined when facing with values <20 ng/mL. Again, the possible associations of 25OHvitD levels with PFS and OS was evaluated by the Cox proportional hazards regression. The possible correlation between 25OHvitD and disease grading and staging was also considered.

Results: Median 25OHvitD levels were 12.5 ng/ml (range 4-29.5); in detail, they were < 20 ng/ml in 38 patients (80%) with 20 cases (42.5%) showing levels even < 10 ng/ml. No correlation was observed between serum 25OHvitD and disease grading and staging. At Cox proportional hazards regression, serum 25OHvitD levels did not result associated with OS or PFS ($p = n.s.$).

Conclusions: Among patients with pNENs, VitDdef was highly prevalent. The role of VitDdef in both the disease pathogenesis and progression remains to be clarified. The growing awareness of the role of vitamin D of pNENs could lead to improved therapeutic strategies. Further studies are needed to confirm this observation.

P.02.2

SYSTEMATIC REVIEW AND META-ANALYSIS: PREVALENCE OF INCIDENTALLY DETECTED PANCREATIC CYSTIC LESIONS IN ASYMPTOMATIC INDIVIDUALS

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Background and aim: Pancreatic cystic lesions (PCLs) are frequently occasionally detected in patients undergoing cross-sectional imaging investigations for other medical indications. As most PCLs would require follow-up, it is important to know their expected prevalence in asymptomatic individuals. However, published studies are heterogeneous, and a wide range of PCLs' prevalence has been reported. We therefore aimed at performing a systematic review and meta-analysis to determine the rate of PCLs in asymptomatic individuals.

Material and methods: a systematic search was conducted and studies investigating the prevalence of occasionally detected PCLs asymptomatic subjects were included. The prevalence of positive studies for PCLs was pooled across studies. A random effect model was used with assessment of heterogeneity by the I² statistic.

Results: 10 studies including 13,147 patients were included in the meta-analysis. All studies were unicentre, and all but one retrospective. Four studies were conducted in the US, 4 in Europe, 1 in Japan and 1 in Brasil. The pooled prevalence of positive tests for PCLs was 11% (95% CI 6%–20%) with important heterogeneity ($I^2 = 99\%$). Four studies employed MRCP and showed a higher pooled prevalence of 26% (95% CI 13%–45%) with still important heterogeneity ($I^2 = 98\%$), while studies not employing MRCP had a lower prevalence rate of PCLs (5.9%; 95% CI 3%–11%). The 6 studies investigating subjects with a mean age >55 years showed a higher rate of PCLs (16%; 95% CI 7%–32%; $I^2 = 98\%$). Only 3 studies reported the pooled prevalence of PCLs defined as IPMN, with a pooled rate of 16% (95% CI 5%–44%) with important heterogeneity ($I^2 = 98\%$). Country of origin, year of publication and number of patients did not explain heterogeneity.

Conclusions: This is the first meta-analysis evaluating the rate of occasionally detected PCLs in asymptomatic individuals. The rate is as high as 11%, and is higher in older subjects, and in studies employing MRCP. IPMNs seem the most common occasionally detected PCL. These findings underline the importance of better defined follow-up policies for asymptomatic IPMNs.

P.02.3

ASPIRIN, STATINS AND PANCREATIC CANCER: IS THERE ROOM FOR CHEMOPREVENTION?

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Background and aim: Pancreatic ductal adenocarcinoma (PDAC) has increasing incidence and poor prognosis, mostly due to delayed diagnosis. Prevention can be a cornerstone in the fight against this deadly cancer. In this context, chemopreventive action of aspirin and statins might prove interesting. However, published data are conflicting, with effect sometimes limited to subgroups; the possible combined effect of the two drugs has never been explored.

The aim of the study is to investigate the possible protective role of aspirin and statin use and their combination on PDAC.

Material and methods: This is a case-control study, with risk factors screened through questionnaires about environmental factors, family and medical history. PDAC cases were matched to controls for age and gender with a 1:2 ratio.

We performed a power calculation analysis, considering an exposure of 22% and 23% respectively for aspirin and statins recorded in the first 200 controls; to have a 80% power of identifying a <0.61 OR for aspirin and <0.62 OR for statins 345 cases and 690 controls were needed. With a 10% rate for the combined use of aspirin and statins among controls, the same number of subjects allows to detect an OR of 0.47 with 80% of power.

Results: 346 patients with PDAC and 692 matched controls (54% males, mean age 69 in both groups) were enrolled. Aspirin (19.1% vs 23.8%) use was similar in both case and control group. Neither >5-year use of aspirin (7.2% vs 10.8%) nor its combination with statin (10.1% vs 11.3%) showed different prevalence among cases and controls. Statin use was significantly higher in the control group (19.1% vs 24.9%); a protective effect was also demonstrated in multivariate logistic regression (OR 0.66, 95%CI: 0.46-0.96).

In multivariate logistic regression analysis smoking (OR:1.61, CI95%: 1.56-2.26), heavy drinking (OR:2.08, CI95%:1.31-3.29), history of previous diabetes (OR:1.6, CI95%: 1.01-2.54), chronic pancreatitis (OR:16.96, CI95%:2.01-143.03) and family history of PDAC (OR:3.92, CI95%: 1.9-8.07) were all significant risk factors.

Conclusions: This study suggested a chemopreventive effect for statins, but not for aspirin (OR similar to that recently reported in another large C-C study in the US). The possible combined chemopreventive effect of aspirin and statins was hereby analyzed for the first time with null results. All known factors associated with increased risk for PDAC were confirmed, supporting the genuineness of our population.

P.02.4

REASSESSMENT OF HISTOLOGICAL FEATURES AT DISEASE PROGRESSION DURING THE FOLLOW-UP OF NEUROENDOCRINE TUMOURS

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Background and aim: Neuroendocrine Neoplasms (NENs) are relatively rare diseases with an heterogeneous clinical behaviour. The proliferative index ki-67 is the most important prognostic factor. However, whether repeating histological assessment at time of disease progression (DP) is still debated, since there are few data regarding potential Ki-67 modification during the course of disease. Our aim is to investigate modification of ki-67 index at time of DP in NENs.

Material and methods: Retrospective analysis of sporadic NENs patients in which histological sampling (bioptic or surgical) was repeated at time of DP. Histological evaluation was assessed according with WHO 2010 classification by a pathologist blinded about the disease clinical course.

Results: 29 pts, median age 59 (range 37-74 yr), repeated histological evaluation at time of DP, and were included. Of these, 17 (58.6%) showed increase in lesions number/size, whereas 12 (41.4%) had recurrent disease after previous radical surgery. Primary tumour sites were: distal jejunum/ileum (14, 48.2%), pancreas (9, 31%), bronchial (3, 10.3%), unknown (2, 6.8%), colonic (1, 3.4%). At time of initial evaluation, a total of 15 pts (51.7%) had G1 tumor, whereas 14 (48.3%) had G2 tumor. Median ki-67 was 2% (range 1%-20%).

The median interval between initial assessment and repeated histology was 51 months. At DP, 22 pts (75.8%) experienced ki-67% changes (9 pancreatic NENs, 8 intestinal NENs, 5 other primary NENs). Of these, 10 (34.4%) underwent G modifications. In detail, 3 patients changed grading from G2 to G3 (3 pancreatic NENs), 5 from G1 to G2, and the remaining 2 pts from G2 to G1. Overall, median ki67 at time of DP was 5% (range 1%-70%; p=0.006 vs Ki67 at time of initial assessment). No difference was observed neither in ki-67 nor in grading changes between patients who underwent increase in lesions number/size and those who had recurrent disease after previous radical surgery.

Conclusions: Significant increase in Ki-67 index occur in a relevant group of NEN patients at time of DP, thus suggest the usefulness of repeating histology before planning medical treatments in these patients.

P.02.5

PREVALENCE OF CHRONIC PANCREATITIS IN THE PRIMARY CARE SETTING

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Background and aim: Data on the prevalence of chronic pancreatitis are scanty, as a formal diagnosis is often difficult to be made. Moreover, most epidemiological studies are hospital-based and therefore might not represent the general population.

We aimed at investigating the prevalence of chronic pancreatitis in the general population.

Material and methods: About 160 primary care physicians (PCPs) were invited to take part in clinical meetings on chronic pancreatitis (CP) and pancreatic exocrine insufficiency (PEI). Afterwards, a survey was conducted among the participants. Each PCP was asked to report his total number of assisted individuals, and the number affected by definite or suspected CP, filling in a form with details about environmental factors and disease characteristics of each CP patient. The forms were reviewed and patients with "uncertain" diagnosis of CP were invited to our pancreatic disease unit for a specialist appointment.

Results: 23 PCPs accepted to take part to our study. Their pooled assisted population was of 34.000 individuals. According with

PCPs' judgment, 38 patients had CP diagnosis. After reviewing each patient data and disease characteristics, 11 resulted having a definite diagnosis of CP according with M-ANNHEIM classification, while 3 had a probable diagnosis, 15 a borderline diagnosis and 9 were uncertain, suggesting a prevalence of definite/probable CP of 41/100.000. Of the 14 patients with definite/probable diagnosis 21% had a M-ANNHEIM stage 0, 15% had stage I, 50% stage II, 7% stage III, 7% stage IV. Mean age at diagnosis was 50.2, 30% being males; etiology was toxic-metabolic in 28%, idiopathic in 29%, post-recurrent or severe acute pancreatitis in 36%, obstructive in 7%. All the patients underwent radiologic imaging: 47.6% ultrasound only, 23.8% CT scan, 23.8% MRI. Mean BMI was 26.4 kg/m², 35.7% of the patients were reported having PEI, although fecal elastase was never dosed, and 64% received PERT (mean dosage being 4.4 tablets per day of 10.000 pancrelipase units). 28% of the patients had endocrine insufficiency, 43% patients reported abdominal pain and 28% had osteoporosis.

Conclusions: This is the first study on the prevalence of chronic pancreatitis in the general population. Our preliminary data suggest that the prevalence of chronic pancreatitis is around 41/100.000, a figure that is in line or higher to those of previous studies conducted in specialist centres. Most cases are secondary to severe or recurrent acute pancreatitis or toxic causes. This study is also highlighting the lack in the investigation of PEI and frequent incorrect prescription of PERT (either suboptimal doses or wrong indication).

P.02.6

ACUTE PANCREATITIS IN CAMPANIA: PROPOSALS FOR A RESOURCES SAVING REGIONAL ORGANIZATION

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Background and aim: Acute Pancreatitis (AP) has an incidence ranging from 13 to 45/100,000 persons and the moderate and severe forms, representing the 15%, are characterized by larger mortality and greater use of resources. AIGO Campania in collaboration with experts from local health government, report data regarding AP inferred from DRGs of the year 2013 in Campania to propose a more efficient and cost saving regional organization in this field.

Material and methods: DAFs (Discharge Abstract Forms) of the year 2013 in Regione Campania were retrospectively analyzed and the All-Patient-Refined-DRG system was applied to the DRG 204 (disease of the pancreas except malignancies). APR-DRG is a validated program based on two sets of subclasses, severity of illness and risk of mortality, able to correlate clinical severity to the absorption of resources in the care process.

Results: In Regione Campania G.I. diseases is the most frequent cause of hospital discharge (12.7%) pooling both ordinary and day hospital modality. AP has an incidence of 36.3 per 100.000 persons and a mortality of 1.4%, figures comparable with data in western world. APs were mainly hospitalized in Internal Medicine, Surgery, or Gastroenterology Units (41%, 39% and 10.8% respectively). Seven classes ranging from 1 (mild) to 7 (extremely severe) were identified on the basis of APR-DRG. The moderate and severe forms (classes from 4 to 7), represented the 12% and presented a double days in hospital stay compared to less severe forms (17.3 vs 8.9 days). Milder forms (classes from 1 to 3) were discharged in decreasing order from the Units of Surgery, Internal Medicine, Gastroenterology (40.6%, 39.2%, 11.0% respectively).

Conclusions: On the light of the APR-DRGs system only 12% of APs could be considered moderate-severe needing a multidisciplinary approach in specialist center equipped with sophisticated

endoscopic and radiologic technologies while milder forms require minor supportive and cheaper measures. Actually more than 40% of the latest were discharged by Surgery Units so that these admissions could look improper. We suggest that Regione Campania, in order to save resources, needs a territorial hub-spoke organization with only few advanced Gastroenterology Units able to handle moderate and severe APs connected in a network with a sufficient number of territorial Gastroenterology or Medicine Units for a more efficient management of milder AP forms.

P.02.7

FREQUENCY AND CLINICAL-INSTRUMENTAL CHARACTERIZATION OF ACUTE PANCREATITIS FROM HYPERTRIGLYCERIDEMIA IN A CONSECUTIVE SERIES OF 105 PATIENTS

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Background and aim: Hypertriglyceridemia (HyperTG) severe, defined as levels of triglyceride (TG) in serum >1000 mg/dl, it is a cause of acute pancreatitis (AP) in 1-10% of cases, but its aetiopathogenetic role is unknown. Moreover HyperTG mild to moderate (TG 150-999 mg/dl) seems to correlate with increased severity of the AP, independent of the cause of disease. The causes of HyperTG are divided into primary (genetic, eg. Deficit of lipoproteinlipase - LPL) and secondary ones. It was recently approved by European Medicine Agency a gene therapy for LPL deficiency. The aims of this study are an epidemiological and clinical-instrumental characterization of AP hypertriglyceridemia-correlated and the description of the relationship between mild to moderate HyperTG and the severity of AP.

Material and methods: We reviewed the patients observed in the period 2010-2015 with a diagnosis of first episode of PA, with a dosage of TG within 72 hours and abdominal CT performed at least 48-72 hours. We were collected clinical-instrumental data of patients.

Results: The average age of patients with AP HyperTG-correlated was lower than in controls (40.3 ± 7.3 vs 55.1 ± 19.2 years, p = 0.002). Patients with HyperTG have higher frequency of family history of dyslipidemia (67% vs 21%; p = 0.009) and smoking status (73% vs 34%, p = 0.019), with the highest number of cigarettes /day in smokers (27.1 ± 12.2 vs 15.9 ± 10.7, p = 0.027). The AP for HyperTG was more severe than the AP from other causes, with greater occurrence of organ failure (50% vs 17%, p = 0.025) and need for hospitalization in Intensive Care Unit (ICU) (50% vs. 11%, p = 0.006). Patients, regardless of the cause of disease, are increasing severity in the three groups of serum triglycerides (<150, 150-999, ≥1000 mg / dl) with increase in average length of stay (18.6 ± 16.3, 22.6 ± 15, 30.7 ± 34 days, p = 0.0001), organ failure (14%, 29%, 50%, p = 0.015), ICU (8%, 23%, 50%, p = 0.0001).

Conclusions: The AP HyperTG-correlated is not uncommon and TG levels correlate with the severity of the disease regardless of the cause.

P.02.8

CAN SERUM AMYLASE AND LIPASE LEVELS BE USED AS DIAGNOSTIC MARKERS TO DISTINGUISH BETWEEN PATIENTS WITH MUCINOUS CYSTIC LESIONS OF THE PANCREAS, CHRONIC PANCREATITIS AND PANCREATIC DUCTAL ADENOCARCINOMA?

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Background and aim: To assess the presence of pancreatic hyperenzymemia in patients with pancreatic cystic lesions as compared to other chronic diseases of the pancreas.

Material and methods: Ninety-one patients were studied. Thirty-two patients had mucinous cystic lesions, 35 had chronic pancreatitis and 24 pancreatic ductal adenocarcinoma. Surgery was carried out in 10 of the 32 mucinous cystic lesion patients (7 of them had severe dysplasia), in 5 patients with chronic pancreatitis and in 9 pancreatic ductal adenocarcinoma patients.

Results: Abnormally high serum pancreatic isoamylase activity was present in 11 patients (34.4%) with mucinous cystic lesions, in 14 chronic pancreatitis patients (40.0%) and none of pancreatic ductal adenocarcinoma patients ($P=0.002$) whereas serum lipase activity was abnormally high in 8 mucinous cystic lesion patients (25.0%), in 17 (48.6%) chronic pancreatitis patients and in 3 (12.5%) pancreatic ductal adenocarcinoma patients ($P=0.009$). In seven patients with mucinous cystic lesions who had histologically confirmed severe dysplasia, abnormally high levels of both serum pancreatic isoamylase and lipase were present in 3 patients (42.9%).

Conclusions: High serum concentrations of amylase and lipase were found in no more than half of the patients with mucinous cystic lesions, but high levels of these enzymes were not associated with greater risk of malignancy.

P.02.9

ELASTPQ-POINT SHARE WAVE ELASTOGRAPHY (ELASTPQ®-PSWE) IN CHRONIC PANCREATITIS. A PROMISING TOOL FOR STAGING DISEASE SEVERITY

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Background and aim: ElastPQ®-pSWE, an emerging non-invasive US technique developed to estimate tissue stiffness, has recently been evaluated to stage liver fibrosis in patients with chronic liver diseases whereas few data, mainly using strain imaging, are currently available for the pancreas.

Present study was aimed at assessing both the feasibility and reproducibility of pancreatic stiffness in a cohort of patients with chronic pancreatitis of different etiology and at evaluating the possible relation between this parameter and major clinical and laboratory data in reflecting disease severity. Another aim was to correlate ElastPQ®-pSWE to Fibroscan results for the assessment of liver stiffness.

Material and methods: 45 consecutive patients (33 M, 12 F) mean age \pm SD 62 \pm 25 years with chronic pancreatitis (CP) underwent hepatic and pancreatic US scan and ElastPQ-pSWE (iU22, Philips) (10 valid measurements). Liver stiffness was also measured by transient elastography (Echosens, Paris) (10 valid measurements, SR >60%, IQR <30%). 27 healthy subjects (10 M, 17 F) mean age \pm SD 39 \pm 21 years served as controls (CRL). Interobserver agreement for pancreatic ElastPQ®-pSWE was analyzed in 20 cases using the intraclass correlation coefficient (ICC). The effect of some clinical, laboratory and US data on pancreatic stiffness measurements will be evaluated by fitting linear regression models.

Results: ElastPQ-pSWE was feasible in all but one patient in the CP. Pancreatic stiffness was significantly higher in CP than CRL (4.2 vs 2.9 kPa, $p<0.05$). Moreover in CP group, those with longer disease duration (>10 years) had significantly higher ElastPQ-pSWE value than those with shorter one (7.0 vs 3.8 kPa; $p<0.01$), as those on chronic analgesic drugs as compared to those not (5.9 vs 3.7 kPa, $p<0.05$). Finally in both groups (CP and CTL) pancreatic stiffness was

significantly related to age and decrease in BMI. No correlation with laboratory data was found. The ICC for pancreatic stiffness was 0.80. As concerns hepatic stiffness a high correlation was found between ElastPQ and Fibroscan (4,89 \pm 1,96 kPa and 5,9 \pm 3,37 kPa) ($p<0.0001$, $r=0.74$).

Conclusions: ElastPQ has been proven to be promising and reproducible in assessing pancreatic stiffness. Values at ElastPQ reflected disease severity and length. Accordingly, this performance could be of value in stratifying CP patients by identifying those with more serious disease.

P.02.10

CLINICAL AND RADIOLOGICAL FEATURES OF 40 PATIENTS WITH SEROUS CYSTADENOMA OF THE PANCREAS

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Background and aim: Serous cystadenomas (SCA) are benign cystic tumours of the pancreas and represents 10–16% of cystic pancreatic lesions. Most of the patients are asymptomatic and surgical treatment is indicated only for symptomatic patients or in case of uncertain diagnosis. The aim of the study was to evaluate clinical, radiological and laboratory findings in patients with SCA. We also assessed the factors associated with a higher growth-pattern.

Material and methods: Patients with SCA diagnosed on the basis of magnetic resonance imaging (MRI) observed between 2010-2015 in our gastroenterological Unit were retrospectively enrolled and classified in microcystic/mixed or macrocystic.

Results: 40 patients (33 females, 7 males, mean age 61.5 \pm 15.6 years at diagnosis) were included. Symptoms reported by patients are non-specific abdominal pain (22.5%), pancreatitis (2.5%), diabetes (10%), none (65%). MR pattern was microcystic in 25 patients (62.5%) and macrocystic in 15 (37.5%) Average follow-up was 2.7 \pm 1.4 years. An increase in diameter was observed in 4 patients (10%) (growth rate: 28 mm/year), 3 of whom with a macrocystic pattern.

Conclusions: After 3 years follow-up, the majority of the patients were asymptomatic, and only in a small percentage of these patients size slowly increased. Macrocystic pattern seems associated with a higher growth rate and these patients need a more accurate follow-up.

P.02.11

EXOCRINE PANCREATIC INSUFFICIENCY IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASM (IPMN) WITH WIDESPREAD GLANDULAR INVOLVEMENT

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Background and aim: Pathological and radiological findings of Intraductal Papillary Mucinous Neoplasm (IPMN) are characterized by acinar and duct alterations, probably responsible for a significant impairment of exocrine function. Similar alterations are present in chronic pancreatitis and in the pathological process of aging in which a certain degree of pancreatic exocrine insufficiency (PEI) has been demonstrated. These changes may be responsible for malabsorption and specific nutritional deficiency and thus prompt enzyme replacement therapy. Until now these aspects of IPMN have scarcely been taken into account.

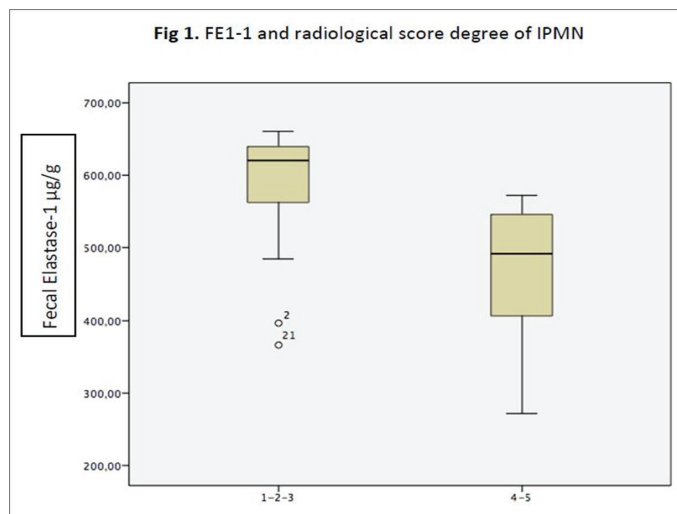
The aim of this study was the evaluation of pancreatic exocrine insufficiency (PEI) in patients with stable IPMN (Main Duct, Branch Duct and combined) with evidence of a widespread involvement of the pancreatic gland.

Material and methods: Eighty-nine patients with magnetic resonance cholangiopancreatography (MRCP) findings of cystic lesions compatible with IPMN were evaluated. Patients with other possible causes of PEI (pancreatic or gastric resection, diabetes mellitus, inflammatory bowel disease and celiac disease, etc.) were excluded. Twenty six patients with 3 or more cystic lesions were enrolled and followed up for at least 1 year. Exocrine pancreatic function was evaluated by determination of fecal elastase-1 (FE-1). A five degree radiological score system, based on MRCP, was specifically created to judge glandular involvement (Table 1).

Table 1
Degree of glandular involvement of IPMN

Degree 1	Millimeter ductal ectasia
Degree 2	Few moderately diffuse ductal ectasia
Degree 3	Diffuse ductal ectasia
Degree 4	Ductal ectasia with glandular hypotrophy
Degree 5	Main duct ectasia and/or severe glandular subverting

Results: The Pearson test was used to correlate FE-1 values with age. The Spearman test was used to correlate FE-1 with the radiological score. The ANOVA test was used to evaluate mean FE-1 values for each involvement degree. Statistical significance was set at $p < 0.05$. Mean FE-1 values were $539.4 \pm 111.5 \mu\text{g/g}$. FE-1 was inversely related to age ($r = -0.465$; $p = 0.017$) and to radiological score system ($r_s = -0.478$; $p = 0.013$). Mean FE-1 values, adjusted for age, were significantly lower in patients with more severe glandular involvement, such as pancreatic atrophy and main duct or combined type (degree 4-5), than in patients with a mild to moderate degree (different degrees of impairment by BD-IPMN; degree 1,2 and 3) ($p = 0.003$) (Fig. 1).



Conclusions: Patients with more severe glandular involvement, such as pancreatic atrophy and main duct ectasia, have lower values of FE-1. Further studies on a larger number of patients with a high degree of IPMN glandular involvement could identify different conditions of IPE.

P.02.12

THE USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE IS FREQUENT IN PATIENTS WITH PANCREATIC DISORDERS

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Background and aim: Herbal remedies and other not conventional medicines (CAM) are widely used for the treatment of various chronic diseases including gastrointestinal and liver disorders. Some 30% of patients with liver disease and inflammatory bowel diseases have been reported to use CAM. CAM users are mainly women, with high education level. The most common reason for use is dissatisfaction with conventional care. However, there are no data regarding CAM use in patients with pancreatic disorder, including their potential pancreatotoxic effects.

Aim: To assess the prevalence of CAM use in patients with pancreatic diseases and screen pancreatotoxicity.

Material and methods: Cross-sectional survey of consecutive patients seen at a pancreatic disorders outpatient clinic. Data were collected using a questionnaire regarding demographics, CAM usage, reasons for CAM use, and respondent experiences of effects from CAM.

Descriptive statistics were used to analyse the prevalence and the patterns of CAM use. Fisher test or t-test were used to determine any association between CAM use, demographics and lifestyle factors.

Results: 108 consecutive patients were enrolled (52% male; mean age 65 ± 12.74). The 44% of patients used CAM (44,6% male; mean age 64 ± 13) and the 30% for more than 1 year. 47% of patients with previous acute pancreatitis, 35% with chronic pancreatitis and 41% with IPMN used CAM. 62% of patients reported advantages with treatment. CAM users were more often female (55% vs 43 in no CAM), with higher school degree (42% vs 36% in no-CAM), performed physical activity more than once a week (51% vs 41% in no-CAM) and reported anxiety (43% vs 31% in no-CAM) more frequently. However, none of these differences were statistically significant.

Of the 47 patients using CAM, three reported use of serenoa repens that has been previously associated with pancreatotoxicity.

Conclusions: The 44% rate of CAM use in patients with pancreatic disease is similar or higher to those reported in other GI diseases. CAM usage is higher in patients with previous AP. 60% of patients report benefit with CAM. The use seems more frequent in female with higher education level and "healthier lifestyle". Patients might not be aware of potential pancreatotoxicity of CAM, which should be carefully considered by physicians.

P.02.13

INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMNS): RESULTS OF A THREE-YEAR FOLLOW-UP STUDY

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Background and aim: Intraductal papillary mucinous neoplasms (IPMNs) of the pancreas are neoplasms characterized by ductal dilation, intraductal papillary growth, and thick mucus secretion. The prevalence is high almost 20%, whereby the majority of these neoplasms are discovered incidentally. Imaging investigations, such as CT scan, MRI, and endoscopic ultrasound (EUS), allow to distinguish three subtypes of IPMN according to location, namely the main duct IPMN [MD-IPMN], branch duct IPMN [BD-IPMN], and mixed type IPMN. Natural history of IPMN, especially BD-IPMN, is not well-established and the proper management and follow-up strategy of BD-IPMN still remain to be fully defined. Aim of the study was to assess the clinical characteristic and outcome of IPMN.

Material and methods: From January 2011 to October 2014, all consecutive patients with IPMN referred to our pancreatic disease day service were enrolled and followed up with clinical visits, EUS and/or MRI according to available guidelines.

Results: A total of 41 patients, 16 males and 25 females (median age: 68 years, range 35–87 years), with diagnosis of IPMN without worrisome features were followed up for a median period of 38 months. At baseline clinical observation, all patients reported the presence of abdominal pain and/or showed increased serum levels of amylase and lipase. A family history of pancreatic cancer was present in 3 patients whereas a personal history of malignancy was present in 10 patients. Diagnosis of IPMN was reached by CT scan in 14 patients, MRI in 20 patients, and EUS in 7 patients: 26 patients had a BD-IPMN, 6 patients a MD-IMPEN, and 9 patients a mixed type IPMN. During follow-up, 3/41 patients (7%) underwent surgical resection due to a nodule (one mural intraductal and one parenchymal) in two patients and an enlargement (>5 cm) of the cystic lesion in another patient. IPMN features remained unmodified in the remaining 38/41 patients (93%). All three patients operated had not family or personal history of malignancy.

Conclusions: IPMN may progress toward pancreatic cancer. Patients with IPMN should undergo careful surveillance, including EUS or MRI, in order to promptly adopt a surgical strategy. Whether the development and course of IPMN may be influenced by a family history of pancreatic cancer and personal history of malignancy remains to be clarified.

P.02.14

ACUTE PANCREATITIS IN ELDERLY PATIENTS: A RETROSPECTIVE EVALUATION AT HOSPITAL ADMISSION

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Background and aim: Acute pancreatitis (AP) in elderly may have an aggressive course due to co-morbidity high rate and severe presentation. We retrospectively evaluated AP severity and its underlying factors in a group of elderly patients compared with an adult population sample.

Material and methods: Forty-two elderly patients (65–102 years) and 48 controls (19–64 years) admitted at our Unit for biliary or alcoholic AP were retrospectively enrolled. AP severity was evaluated by Atlanta classification and Ransom score. Laboratory investigations and demographic data were collected. Comparison between the two groups was performed by t-test, ANOVA or Fisher's exact test. A multinomial logistic regression was used to determine factors affecting AP severity.

Results: Elderly patients showed more severe Atlanta score (1.81 ± 0.75 vs 1.29 ± 0.46 ; $p=0.007$), as well as higher Ransom score (2.52 ± 1.57 vs 0.75 ± 0.73 ; $p<0.0001$), even if no death was observed. Elderly patients assumed more drugs than controls, and had a higher rate of cardiovascular, pulmonary and renal co-morbidity. They showed higher creatinine (1.09 ± 0.41 vs 0.81 ± 0.18 ; $p=0.004$) and lower calcium levels (8.43 ± 0.48 vs 8.88 ± 0.44 ; $p=0.002$) than controls. AP severity was influenced by white blood cell (WBC) count (OR=1.94; 95% CI 1.14–2.86; $p=0.048$), aspartate-transaminase (AST) levels (OR=1.97; 95% CI 1.91–2.18; $p=0.02$), serum lactate-dehydrogenase (LDH) (OR=1.07; 95% CI 1.008–1.168; $p=0.047$) and Ransom score (OR=70.4; 95% CI 45.7–134.8; $p=0.036$). The etiology (biliary or alcoholic) did not influence the severity.

Conclusions: Elderly patients usually undergo a severe AP course, but without increase of mortality. High WBC, LDH, AST and Ransom score at the onset may predict AP severity.

P.03 Endo/EUS 1

P.03.1

DIAGNOSTIC ACCURACY AND THERAPEUTIC IMPACT OF EUS IN PATIENTS WITH INTERMEDIATE SUSPICION OF CHOLEDOCHOLITHIASIS AND NEGATIVE MRCP

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Background and aim: Endoscopic ultrasonography (EUS) and magnetic resonance cholangiography (MRCP) are accurate procedures in diagnosing common bile duct stones, thus suggesting the possibility to avoid invasive endoscopic retrograde cholangiopancreatography. MRCP is non-invasive diagnostic procedure but its accuracy decreases in presence of microlithiasis.

Aim: To study the diagnostic accuracy and the therapeutic impact of EUS in patients with intermediate likelihood of choledocholithiasis and negative MRCP.

Material and methods: Between January 2013 and August 2015, all consecutive patients with clinical intermediate suspicion of choledocholithiasis according to the ASGE guidelines and undergone a negative MRCP for lithiasis, were retrospectively reviewed. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of EUS, carried out within 7 days of the initial clinical presentation, were determined. Also, the clinical impact of EUS in the management of these patients was assessed.

Results: A total of 53 patients were included in the study. EUS detected choledocholithiasis in 17 out of 53 patients with negative MRCP. The subsequent ERCP confirmed lithiasis in 16 out of 17 patients (94%). Thus, EUS showed a diagnostic accuracy of 98% for detection of CBD stones. Sensitivity, specificity, positive predictive value, negative predictive value were: 100% (95% C.I. 74–100%), 97.3% (95% C.I. 85–99%), 94% (95% C.I. 71–99%) and 100% (95% C.I. 90–100%), respectively. The diagnostic gain of EUS compared to MRCP was 32% with an EUS/MRCP agreement of about 70% ($k=0.68$, $p<0.01$).

Conclusions: EUS is a highly accurate diagnostic tool for the common bile duct stones detection. EUS findings change the management of patients with intermediate suspicion of choledocholithiasis and a negative MRCP allowing the diagnosis of lithiasis in 1/3 of them.

P.03.2

IS THERE A LINK BETWEEN PERIAMPULLARY DIVERTICULA AND BILIOPANCREATIC DISEASES? AN EUS APPROACH TO ANSWER THE QUESTION

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Background and aim: The prevalence of periampullary diverticula (PAD) varies in literature from 0.16 to 27%. Many studies, all in an ERCP setting, have been conducted to establish if a link exists between PAD and biliopancreatic diseases but contradictory results were obtained and the issue is still debated.

Material and methods: We retrospectively reviewed our EUS database from January 2001 to December 2014 enrolling patients scheduled for EUS with an indication that entailed the exploration of the second duodenum. Oblique viewing (50–55 degrees) echoendoscopes from Olympus were employed. For each patient

with PAD, 6 controls were randomly selected for statistical analysis. The presence of a PAD was diagnosed either endoscopically or by its characteristic EUS appearance after instilling 100-200 ml of water to fill and extend the duodenal lumen.

Results: 2475 patients met the inclusion criteria. Among them 185 subjects with PAD were found (prevalence 7.5%), 1110 subjects served as controls. Patients with PAD were older than controls (mean age 69.8 ± 11.3 vs 61.4 ± 13.86 years; $p < 0.0001$), had a higher prevalence of common bile duct (CBD) dilation (44.3 vs 28.2% ; OR 2.03 $p < 0.0001$), a higher prevalence of CBD stones (34 vs 19.6% ; OR 2.11, $p < 0.0001$) and a higher prevalence of cholangitis in their clinical history (8.1 vs 2.2% ; OR 3.99, $p < 0.0001$). No differences between PAD patients and controls were found as far as gender, history of jaundice, of acute/recurrent pancreatitis or EUS signs of chronic pancreatitis are concerned.

Conclusions: To our knowledge, this is the first study that has assessed PAD prevalence using EUS. We demonstrated that PAD can be seen either endoscopically (at least using an oblique viewing echoendoscope) or endosonographically and found a prevalence that is in keeping with the existent literature. As other Authors in an ERCP setting, we demonstrated a link between PAD and biliary disease. Despite some anecdotal reports, we could not confirm a link between PAD and pancreatic disease.

P.03.3

USEFULNESS OF ENDOSCOPIC ULTRASONOGRAPHY TO GUIDE THE RATIONAL USE OF ERCP: STRATIFY THE LIKELIHOOD OF CHOLEDOCHOLITHIASIS IN THE CLINICAL SUSPICION OF PERSISTENT BILE DUCT STONE

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Background and aim: Bile duct stones are a common clinical problem and endoscopic retrograde cholangiopancreatography (ERCP) is highly effective in relieving biliary obstruction despite can carries adverse events related to the procedure or the sedation. Endoscopic ultrasonography (EUS) is a very sensitive and specific technique for diagnosing biliary diseases and represents lower-risk alternative to confirm or exclude choledocholithiasis.

The aim of the study is to evaluate the role of EUS in predicting choledocholithiasis, stratifying patients with clinical suspicion of persistent bile duct stone who would benefit from ERCP.

Material and methods: We collected data on all consecutive patients from November 2014 to January 2015 suspected for choledocholithiasis according to ASGE criteria for choledocholithiasis on initial presentation: intermediate risk (a serum bilirubin of 1,8 to 4 mg/dl or dilated common bile duct on ultrasound and/or abnormal liver biochemical test other than bilirubin, age older than 55 years, clinical gallstone pancreatitis) and high-probability (image of stone inside the common duct, acute cholangitis and serum bilirubin greater than 4 mg/dl and/or a serum bilirubin of 1,8 to 4 mg/dl or dilated common bile duct on ultrasound). Then we re-classified subjects' risk of choledocholithiasis according to new biochemistry in order to perform (or not) EUS.

Results: We enrolled 51 patients (male [53%], mean age of 63 ± 15 year): 14 (27%) and 37 (73%) patients were respectively at intermediate and high risk. All patients were re-classified after a median of 7 days (4-8). Patients at intermediate risk underwent: EUS (5/14 [36%]), cholangio-RM or CT-scan (7/14, [50%]) and ERCP due to increased risk (2/14, [14%]); for those evaluated with EUS in 2/5 (40%) ERCP was not performed due to absence of stones. Patients at high risk: 8/37 (22%) underwent ERCP (due to persistence of high risk), 7/37 (19%) underwent CT-scan and 22/37 (59%) underwent EUS. In those evaluated with CT-scan 4 underwent EUS also as third

test due to mild reduction of bilirubin levels in absence of stones at imaging (EUS was "positive" in all 4 patients who underwent ERCP with stones removal). In the 22 patients evaluated with EUS as second instrumental test (due to decrease of bilirubin levels), 9/22 (41%) did not underwent ERCP because of not evidence of stones (these patients were discharged after 4-7 days asymptomatic and with normal values of bilirubin); 13/22 (59%) resulted "positive" for stones at EUS and underwent ERCP. Finally considering patients reclassified with EUS (second or third test) we "saved" 9 (41%) of ERCP in those classified as "high risk" at admittance.

Conclusions: Our experience shows as EUS, according to assessment of laboratory values, can help to improve the risk stratification of those with suspicion of persistent bile duct stone eliminating unnecessary diagnostic ERCP especially in patients classified as "high risk" at admittance.

P.03.4

ENDOSCOPIC ULTRASOUND-GUIDED BILIARY DRAINAGE FOR MALIGNANT BILIARY OBSTRUCTION AFTER FAILED ERCP: A SINGLE ITALIAN CENTER EXPERIENCE

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Background and aim: Endoscopic ultrasonography-guided biliary drainage (EGBD) has been proposed as an alternative drainage technique for percutaneous transhepatic biliary drainage (PTBD) in patients with obstructive jaundice where endoscopic retrograde cholangiopancreatography (ERCP) has failed.

Material and methods: All patients afferent to Santa Maria Nuova Hospital in Reggio Emilia, between January 2011 and December 2014, with malignant obstructive jaundice, in whom ERCP had failed, were enrolled. Inclusion criteria are: patients over 18 years old, malignant bile duct obstruction with unsuccessful ERCP drainage. Patients with benign stricture were excluded.

The end points were to evaluate technical and clinical success rate, adverse events rate and follow-up of direct transluminal EGBD.

Technical success was defined as success of stent placement in the desired location. Early clinical success was defined as a drop in the bilirubin level by 50% at 2 weeks and late clinical success as a drop to below 3 (level that allows patients to undergo chemotherapy) at 4 weeks.

Results: During the study period, 23 patients (8 men; median age 69; interquartile range, 61 to 76) underwent EGBD. Reason for EGBD was obscured ampulla by invasive cancer in 39.1% (9/23), postsurgical anatomy in 30.4% (7/23), failed deep biliary cannulation in 21.7% (5/23), hepaticojunostomy stricture in 4.4% (1/23) gastric outlet obstruction 4.4% (1/23).

EUS-guided cholangiography was successful and confirmed a distal common bile duct stricture in 20 patients (87.0%). Technical success in EGBD was achieved in 95.0% (19/20) of patient with a successful cholangiography. Early clinical success was reached in 75.0% (15/20) and late clinical success in 45.0% (9/20).

One (5%) procedure-related severe adverse event occurred in 1 patient. It was a severe cholangitis in a patient with several comorbidities that died after 9 days after the procedure for multiorgan failure.

Conclusions: EGBD is a safe and effective procedure to provide biliary access and drainage after failed ERCP. EGBD provides a viable alternative to PTBD, and limited available data suggest equivalent efficacy and safety.

P.03.5**REPETITION OR SIMULTANEOUS SAMPLING OF PRIMARY AND METASTATIC LESIONS IMPROVE DIAGNOSTIC ACCURACY OF EUS-FNA IN THE ASSESSMENT OF SUSPECTED NEOPLASTIC PANCREATIC MASS**

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Background and aim: Endoscopic ultrasound-fine needle aspiration (EUS-FNA) is a relatively low invasive technique for diagnosing a suspected neoplastic pancreatic mass. Several factors may influence the adequacy of tissue collection leading to not conclusive findings. Aim of the study was to evaluate if repetition or simultaneous sampling of primary and metastatic lesions improve diagnostic accuracy of EUS-FNA in patients with suspected pancreatic malignancy.

Material and methods: All patients with suspected malignancy of the pancreas were submitted to EUS-FNA. In case of suspected metastasis in the liver or lymph nodes, EUS-FNA of primary and secondary lesions was performed in a same session. Final diagnosis was defined according to surgical histopathology or clinical follow-up.

Results: A total of 126 patients (73 males, median age: 68 years, range: 41–86) with a pancreatic mass underwent 142 EUS-FNAs: 102/126 patients (81%) with no evidence of metastasis underwent EUS-FNA of pancreatic mass while in 24/126 patients (19%) simultaneous EUS-FNA of primary lesion and metastases in the liver (8 patients) or lymph nodes (16 patients) was performed. EUS-FNA was repeated in 16/102 patients (15%) with no metastasis due to non conclusive findings of first procedure. Both repetition of sampling or simultaneous EUS-FNA of primary and metastatic lesions resulted to improve sensitivity and diagnostic accuracy of the procedure (see Table).

	Primary Lesion Single EUS-FNA	Primary Lesion Repeating EUS-FNA	Primary Lesion & Metastasis EUS-FNA
Sensitivity	68	81	89
Specificity	100	100	100
Diagnostic accuracy	73	85	92

Conclusions: Simultaneous sampling of primary lesion and metastasis may increase EUS-FNA diagnostic accuracy and reduce the need to repeat sampling due to non diagnostic findings in patients with suspected neoplastic pancreatic mass.

P.03.6**COMPARING EUS-FNA AND ERCP-BRUSHING IN THE DIAGNOSTIC WORKOUT OF SUSPECTED CHOLANGIOCARCINOMA: A RETROSPECTIVE SINGLE-CENTER ANALYSIS**

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Background and aim: Cholangiocarcinoma is an aggressive tumor and diagnosis still remains cumbersome.

Although novel intraductal techniques are emerging in the diagnostic workout, cytology is still the gold standard. Diagnostic yield can also depend on tumor location and characteristics as well as endoscopist skill. EUS-FNA and ERCP brushing/biopsies are the most common methods to obtain samples, although with conflicting data.

Data comparing these two techniques, for earlier diagnosis and patient management are still lacking.

Aim of the study was to compare the diagnostic yield of EUS-FNA vs ERCP brushing cytology in the diagnosis of cholangiocarcinoma biliary strictures.

Material and methods: A retrospective analysis was conducted on the Endoscopy Database, from January 2013 and October 2015, querying for patients undergone to EUS and/or ERCP for suspected primary malignant biliary strictures. Patients demographics and biliary ducts characteristics were recorded. Procedures were performed under deep sedation, with anesthesiology assistance by endoscopists expert in bilio-pancreatic procedures. Samples were evaluated "on site" by expert cytotechnologist, after quick hematoxylin eosin standardized staining for qualitative adequacy and reviewed by an expert cyto-pathologist, for final diagnosis. Final diagnosis was based on surgical pathology findings, where available, and cythology. Lesions were divided into groups according to EUS features and site. Data were analyzed with Student's t-test and chi squared test, assuming a significant p-value of 0.05.

Results: 62 patients (33M, mean age 70±9.8 years) underwent EUS and/or ERCP during the study period. Out of these, in 51/62 pts (82%) we reached a histo/cytological final diagnosis. In 45/51 pts (88%) cholangiocarcinoma, in 2/51 pts (4%) pancreatic adenocarcinoma and in 4/51 pts (8%) other etiology were reported.

EUS-FNA diagnosed cholangiocarcinoma in 19/22 pts (sensitivity 86%), whereas ERCP-brushing 23/36 pts (sensitivity 64%) (p=0.06).

EUS-FNA was more sensitive and accurate than ERCP-brushing in mass-forming lesions (100% vs 80%), intra-ductal vegetations (100% vs 33%; p < 0.05), and duct wall thickness associated to solid nodules (78% vs 59%), whereas ERCP-brushing was superior in case of duct wall thickness (50% vs 0%).

Furthermore, in case of mass-forming cholangiocarcinoma, in which both techniques were applied (5/22 pts; 23%), final diagnosis was achieved only with EUS-FNA.

Conclusions: In the diagnosis of cholangiocarcinoma EUS-FNA is superior to ERCP-brushing in case of mass-forming lesions and intra-ductal vegetations, although not statistically significant.

Depending on lesions characteristics, EUS-FNA should be considered as first choice in the cholangiocarcinoma diagnostic armamentarium. In case of ductal thickness ERCP-brushing is still superior. Further prospective studies, also using novel endoductal techniques are needed.

P.03.7**EUS-GUIDED FINE NEEDLE ASPIRATION OF SOLID PANCREATIC TUMORS IN YOUNG PATIENTS: EXPERIENCE IN A TERTIARY REFERRAL CENTER**

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Background and aim: Pancreatic solid lesions in young patients are relatively rare and, to our knowledge, the clinical value of pancreatic masses fine needle aspiration (FNA) in patients < 40 years of age remains limited.

Aim of this study was to evaluate the clinical value of EUS-FNA for diagnostic evaluation of young patients with a pancreatic solid lesion.

Material and methods: A computerized search of our database was performed for a period of 7 years. All pancreatic EUS-FNA cases performed on patients less than 40 years of age were identified. Age, gender, and the cytologic diagnosis were recorded for each patient with pancreatic solid lesion. All available corresponding surgical pathology reports or at least 6 months of follow-up were reviewed.

Results: From October 2008 to October 2015, 3371 patients underwent pancreatic EUS with FNA for solid or cystic pancreatic tumor. Among these, 125 (3.7%) were aged between 11 and 40 age.

Median age was 32.44 and 72 were women. 80 patients (2.4%) had a solid lesion. The final diagnosis was pancreatic neuroendocrine tumor (pNET) in 38 patients, adenocarcinoma in 23 patients, pseudopapillary solid tumor in 11 patients, autoimmune pancreatitis in 3 patients, focal pancreatitis in 3 patients, intrapancreatic accessory spleen in 1 patient. Cytology was not diagnostic in 1 patient, the diagnosis was granulocytic sarcoma at surgical histology. All cases of adenocarcinoma were observed between 31 and 40 years, pNETs were observed between 19 and 39 years. Among pNETs, Ki67 index was evaluated on cytological samples in 63% of cases.

Review of medical records for the 6 patients with negative FNA diagnoses who did not have surgical follow-up was performed for at least 6 months following the FNA, and none of these patients were demonstrated to having neoplasms during follow-up period. The sensitivity and specificity of EUS-guided FNA to identify malignancy were 98% and 100% respectively.

Conclusions: In our series, solid pancreatic tumors occurring in young adults younger than 40 years were rare (<3% of our population). Of the 73 malignant diagnoses, pNET was the most common and accounted for 52% of cases. Our experience demonstrates that EUS-FNA has fundamental clinical value for diagnostic evaluation of younger patients who present solid masses of the pancreas.

P.03.8

ACCESSING TO THE LEFT PARATRACHEAL (#4L) AND THE AORTOPULMONARY WINDOW (#5) MEDIASTINAL LYMPH NODES BY ENDOSCOPIC ULTRASOUND WITH FINE NEEDLE ASPIRATION (EUS-FNA)

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Background and aim: Accurate lymph node staging is mandatory in case of enlarged mediastinal lymph nodes (MLN) in patients with suspected lung cancer or extrathoracic neoplasia. Efficacy of less invasive technique for lymph node biopsies is well established. Many authors believe that surgery is the preferred approach to biopsy the 4 and 5 lymph nodes because poor efficacy of EUS-FNA in these mediastinal nodal stations. We evaluated accessing the left paratracheal (#4L) and aortopulmonary window (#5) stations by EUS FNA.

Material and methods: In our series of 211 EUS FNA, performed in 200 consecutive patients (127 men) with median age of 65 years from January 2011 to January 2015, we examined by EUS the lower mediastinal nodes (stations #8 and #9), the nodes of the aorto-pulmonary window (station #5), the left paratracheal nodes (stations #2L and #4L), the retrotracheal nodes (station #3P), the subcarinal nodes (station #7) and paraesophageal lung masses. In 154 of these patients (77%) we performed EUS-FNA only on enlarged MLN.

EUS-FNA was performed on the following mediastinal sites according to the regional lymph-node map definitions: on station #7 (subcarinal area dorsally to the origin of the left pulmonary artery and cranial to the left atrium) in 123 cases; on station #4L (to the left of the left lateral border of the trachea, medial to the ligamentum arteriosum; between upper margin of the aortic arch and upper rim of the left main pulmonary artery) in 15 cases; on station #5 (laterally to station #4L with ligamentum arteriosum as anatomic border) in 16 cases.

Results: The overall sensitivity of EUS FNA in this series was 81.1% with a corresponding negative predictive value (NPV) of 52.1% and accuracy of 85%. In lymph node station #7 the sensitivity of EUS-FNA to detect malignancy was 82.1%, VPN was 55% and accuracy 87.5%; in station #4L sensitivity was 70%, VPN was 57% and accuracy 78.5%; in station #5 sensitivity was 80%, VPN was 25% and accuracy 81.2%.

In our series sensitivity of EUS FNA for station #4L and #5 was higher than reported in other study.

Conclusions: These results suggest that routine use of EUS-FNA as an initial investigation after a staging CT scan or/and PET for enlarged MLN results in a better approach than surgery in mediastinal stations. Furthermore we think that also #4L and #5 stations are reachable by trained operator by transesophageal EUS FNA with a good performance, safe and accuracy.

P.03.9

IS ENDOSCOPIC ULTRASONOGRAPHY USEFUL IN SUBJECTS HAVING ASYMPTOMATIC CHRONIC PANCREATIC HYPERENZYMEMIA?

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Background and aim: We have previously shown that at least 50% of patients having asymptomatic chronic pancreatic hyperenzymemia (ACPH) may develop morphological pancreatic alterations. In addition, it has been shown that endoscopic ultrasonography (EUS) may detect small lesions and its sensitivity appears to be higher than other imaging techniques. The aim of this study was to evaluate if EUS may modify the management of patients having ACPH.

Material and methods: In two referral centers for pancreatic disease, a retrospective analysis of prospectively enrolled patients with ACPH was conducted.

Results: 73 patients with ACPH were enrolled for the purpose of this study (35 males, 38 females, mean age 58.9 years, range 22-91 years). The mean±SD duration of pancreatic hyperenzymemia was 8.7 years±4.6 years. Mean amylase concentration was 304 IU/L (range 101-2082, upper reference limit 110) and mean lipase concentration was 248 IU/L (range 25-2941, upper reference limit 60). Seven subjects had a familial ACPH and their amylase and lipase concentration were not statistically different as compared to those of 66 patients having sporadic ACPH (P=0.790). 61 patients (83.5%) underwent abdominal ultrasonography, magnetic resonance imaging (MRI) associated with MRI cholangiopancreatography was carried out in 41 (56.1%), contrast-enhanced computed tomography in 32 (43.8%), and ERCP was performed in one patient (1.3%). All these imaging studies did not revealed pancreaticobiliary disease. In 45 patients (61.6%) an EUS was also performed. Using this technique in 7 subjects abnormalities were found: 3 branch-duct IPMNs (having a size more than 10 mm), 1 duodenal diverticulum, 1 annular pancreas, 1 findings suggestive of chronic pancreatitis, and 1 undefined cyst (<5 mm).

Conclusions: EUS is able to detect alteration not found by other imaging technique in 15.5% (7/45) of patients with ACPH and may be useful to select those patients who requires a more strict follow-up.

P.04 Upper GI Disorders

P.04.1

CORRELATION BETWEEN SEASONAL EXACERBATIONS OF UPPER GI SYMPTOMS AND NUMBER OF 13C-UREA BREATH TESTS PERFORMED IN A LARGE UNIVERSITY HOSPITAL

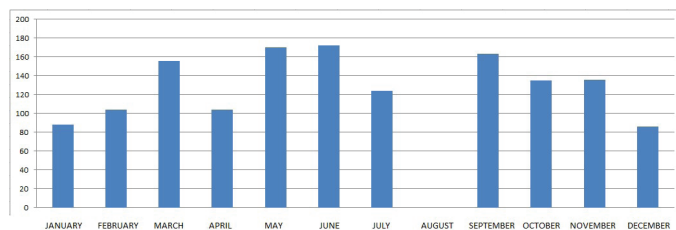
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Background and aim: *H. pylori* infection is the main cause of gastritis and as a consequence of upper GI symptoms. On the other hand, several studies reported a seasonal variation of the occurrence of upper GI symptoms. Usually, the occurrence or exacerbation of upper GI symptoms is the main reason why patients perform 13C-Urea Breath Test (UBT). The aim of our study was to assess whether there is a seasonal variability of the number of UBT performed in our outpatient facility.

Material and methods: We enrolled 1438 consecutive patients (920F and 515M, mean age 49 ± 17), from May 2014 to April 2015, except for August when the facility was closed, who performed UBT for the first time for upper GI symptoms. We collected data and analyzed them comparing the number of the tests performed each month.

Results: We observed a monthly fluctuation of the number of UBT performed; lower values were obtained in December and January, while the highest values in May and June ($p < 0.0001$). By stratifying the data for each season, spring was the one with the highest number of UBT performed compared to winter ($p < 0.001$).



Conclusions: There are solid evidences to conclude that there is a strong correlation between seasonal exacerbation of gastritis, upper GI symptoms and number of UBT performed. The lowest number of UBT has been performed in December and January. Compared to previous studies there has been a shift from April to May/June and from October to November.

P.04.2

MORPHO-FUNCTIONAL MODIFICATIONS OF THE GASTRIC REMNANT AFTER ROUX-EN-Y GASTRIC BYPASS (RYGB): THE (NOT SO) SLEEPING REMNANT?

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Background and aim: The endoscopic inaccessibility of the excluded stomach after Roux-en-Y gastric bypass (RYGB) still represents an unsolved issue for this kind of procedure. The aim of this study is to evaluate the morpho-functional modifications of the gastric remnant by using an immunoenzymatic test already validated for non-bariatric patients: the Gastropanel®.

Material and methods: A cohort of 20 patients submitted to RYGB was prospectively enrolled and evaluated preoperatively, at 3 months and 3 years postoperatively. In addition to Gastropanel® data (Pepsinogen I, Pepsinogen II, Gastrin 17, and anti-*H. pylori* IgG class antibodies), biometrical and clinical data were registered. Continuous variables were confronted through Kruskal-Wallis for independent samples. A multivariate analysis was then performed by calculating a general linear model: Pepsinogen I, Pepsinogen II, Gastrin 17 and *H. pylori* IgG were taken in account as dependent variables, whereas BMI and age were evaluated as covariates and sex was considered as a fixed factor. All calculations were performed with SPSS 22.0.

Results: In general, all Gastropanel® elements showed a reduction during follow up in respect of T0 samples. In Pepsigen I ($p < 0.001$) and Gastrin 17 ($p = 0.044$), the model appeared of statistical significance, whereas for Pepsinogen II ($p = 0.349$) and *H. pylori* IgG class antibodies (0.817) the observed reduction in serological values appears not statistically significant. When the general linear model was applied, statistical difference among stages was confirmed both for G17 and Pepsinogen 1 ($p < .0001$ in both cases), whereas correction for BMI and age of patients at the start of follow up suggested a significant trend for *H. pylori* ($p = 0.084$). Interestingly enough, multivariate model showed as Pepsinogen I and not G17 main determinant was BMI at the time of sample, suggesting the results as a direct effect of reduced weight rather than a physiological consequence of the stomach exclusion.

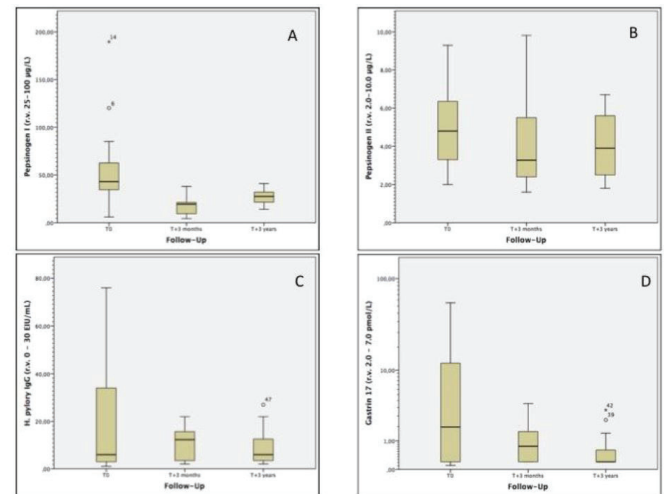


Figure 1. Pictures A to D shows the time trend during the follow up of the Gastropanel® components. In general, all components (Pepsinogen I and II, Gastrin 17, *H. pylori* IgG class antibodies) showed a significant reduction in confront with T0. Please pay attention to the logarithmic scale of Gastrin 17 picture.

Conclusions: RYGB, compared to LAGB, produces, along with a higher weight loss and comorbidity resolution, a higher QoL, more evident starting from 6 month postoperative and more significant at 12 month. The change of QoL, is dependent on type of intervention (RYGB), independent from BMI preoperative and from changes of comorbidities during the follow up. Satisfaction intervention, appears greater in patients undergoing RYGB, directly proportional to reduction of BMI, negatively to SF-36 and independent from resolution of comorbidities. An additional parameter for assessing the effectiveness of the intervention of RYGB, is the best food dissatisfaction compared to LAGB.

P.04.3

SERUM PEPSINOGEN II LEVELS AND IGG ANTI HELICOBACTER PYLORI ANTIBODIES MAY REPRESENT A NON-INVASIVE METHOD FOR THE DIAGNOSIS AND MONITORING OF H PYLORI-RELATED GASTRITIS

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Background and aim: Serum concentration of Pepsinogen II (PGII) increases in patients affected by chronic gastritis due to *Hp* infection; this enhancement is correlated to the degree of gastric

inflammation. The positive effect of the eradicator Hp treatment may also produce a reduction in serum levels of PGII.

The aim of the study was to assess the combined role of PGII and anti IgG Hp antibodies (Hp abs) serum levels in the diagnosis of Hp-related gastritis and in the follow-up after eradication.

Material and methods: A total of 657 dyspeptic patients (M=219, F=438, mean age=44.4±14.0 ys, range=18-86 ys) were evaluated. PGII concentrations and Hp abs were determined via an ELISA test (GastroPanel, Biohit Oyi, Helsinki, Finland) in fasting serum samples. Patients affected by chronic atrophic gastritis were excluded from the study. Patients in proton pump inhibitors (PPI) were included.

Results: 170 patients of 657 (25.9%) were Hp positive and 487 Hp negative (74.1%). The table shows the result of age, PGII and Hp abs in the four groups of patients.

Table 1

H pylori status	No PPI treatment			With PPI treatment		
	Age	PGII	IgG Hp	Age	PGII	IgG Hp
Negative	38.4±10.8	5.8±2.5	6.5±10.4	42.4±13.4	8.4±4.2	7.1±8.7
Positive	39.1±10.8	12.9±6.7	90.3±24.5	43.7±14.0	17.3±12.1	83.5±30.8
Eradicated (Hp-ve)	45.6±13.3	5.8±1.6	30.7±31.3	55.1±13.1	8.1±4.1	24.0±23.2
Non eradicated (Hp+ve)	54.2±13.2	12.4±3.8	86.5±30.7	52.9±13.5	19.9±14.4	81.8±36.5

Conclusions: The combined use of serum PGII (>10 ug/L) and Hp abs (>=30 EIU) levels most accurately defines a picture of Hp-related gastritis; the reduction of PGII concentrations under 10 ug/L as well as Hp abs <30 EIU could be may be an aid in evaluating the efficacy of eradication therapy.

P.04.4

THE SHOWER IS NOT WARM ENOUGH!

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Background and aim: A 30 years old Caucasian female, presented with a 7 years history of nausea and non bloody hyperemesis 5 times daily. She had multiple hospitalizations and emergency accesses during the past years for intermittent abdominal pain, nausea and vomiting and referred important weight loss (of about 15 Kg in the last 3 years).

Material and methods: An extensive medical workup had demonstrated negative, including upper and lower endoscopy, magnetic resonance enterography (jejunal thickening), PET scan, push endoscopy. Moreover in the last three years she reported a progressive increase of the systolic pressure, mean values over 160 mmHg, an ultrasound study of the renal arteries showed no arterial obstruction.

Results: At the admission to our Clinic the physical examination showed increased levels of blood pressure (160/90 mmHg), routinary laboratory tests were unremarkable. She reported smoking one cigarette daily and occasional alcohol use in social settings. No family history of hypertension or gastrointestinal disorders was declared.

During the first days of hospitalization she actually presented an intractable vomit of whitish watery secretions associated to abdominal pain and continuous nausea, antiemetics, including metoclopramide and onansetron, were not effective in relieving the symptoms, she reported that the only strategy that could help relieve her nausea was hot water, complaining that the hospital showers were not warm enough. Her workups included: upper GI with barium, gastric emptying studies (14C-octanoic acid gastric emptying breath test), US abdomen, abdominal computerized

tomography; none of these investigations revealed pathology. After a few days, the symptoms underwent to spontaneous relapse, in those days she returned to normal bath habits.

Conclusions: In order to exclude toxic ingestion other tests were performed and showed the presence of cannabis in urine and blood stools. She admitted smoking cannabis from at least 8 years.

The diagnosis of "cannabinoid hyperemesis syndrome" was made, we recommend to quit smoking. On follow-up 6 months later, she had remained free of cannabis use and she had no symptoms of nausea, vomiting or compulsive bathing, moreover the blood pressure levels returned normal.

P.04.5

PROGNOSIS OF GASTRIC GISTS BASED ON TUMOR SIZE

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Background and aim: Gastric GISTs range from small benign lesions to large metastatic tumors; EUS provides diagnostic and prognostic information that help deciding between follow up or surgery. The aim of this study was to establish the prognostic value of the size of gastric GISTs.

Material and methods: We retrospectively studied patients with an EUS diagnosis of gastric GIST without metastases; we divided them according to the initial size of the tumor: Group A (≤2 cm), Group B (>2 cm). The clinical onset and the EUS characteristics were recorded. For the prognostic evaluation one among these follow up data was required: an EUS control after ≥6 months, the histologic diagnosis in operated patients, or the documentation of a GIST-related death.

Results: Fifty-two patients were included. Group A was composed of 24 patients. The onset was dyspepsia in 21 cases, anemia in 2, a CT suspect of GIST in 1. EUS worrisome criteria (inhomogeneity, irregular borders, enlarged lymph nodes, ulceration) were present in 5 cases. After a mean of 45 months EUS controls showed no changes in 19 patients and a little worsening (a mild enlargement or the appearance of a second <1 cm GIST) in 4; 1 patient died after GIST bleeding. No patients were operated. Group B was composed of 28 patients. The onset was dyspepsia in 11 cases, anemia in 1, upper GI bleeding in 6, a CT suspect of GIST in 10. EUS worrisome criteria other than size were present in 25 patients. In the 22 operated patients histology revealed 4 GISTs with high mitotic rate, 13 GISTs with low mitotic rate, 5 other benign tumors. Because of their poor general condition, 6 patients were not operated: 3 showed no EUS worsening during follow up, 3 died for GIST progression.

Conclusions: In Group A and Group B an alarming onset was present in 13% and 61%, other initial EUS worrisome criteria were visible in 21% and 89%, signs of a bad evolution (an EUS worsening during follow up, a high risk histology after resection or a tumor-related death) were seen in 21% and 32%, respectively. GISTs belonging to Group A and B probably represent the same disease diagnosed in different moments: ≤2 cm GISTs were accidentally found in younger patients (mean age 59 years) while >2 cm GISTs were seen in older subjects (mean age 69 years) in whom tumors had more time to grow, becoming symptomatic. Thus, as a minority of small GISTs showed a slow and late progression, these patients can initially avoid surgery but a long EUS follow up is mandatory (e.g. every 1-2 years for at least 10 years).

P.04.6**PREVALENCE OF H. PYLORI INFECTION IN SEXUAL PARTNERS OF H. PYLORI INFECTED SUBJECTS: ROLE OF GASTROESOPHAGEAL REFLUX**

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Background and aim: Transmission of *H. pylori* infection is through fecal-oral or oral-oral routes. Whether *H. pylori* infection is more prevalent in sexual partners of *H. pylori*-infected subjects is not completely clear. Our aim was to evaluate the prevalence of *H. pylori* infection in sexual partners of *H. pylori*-infected subjects. Also we evaluated the prevalence of gastroesophageal reflux (GER) symptoms in *H. pylori*-infected subjects and their sexual partners.

Material and methods: We studied 100 *H. pylori*-infected subjects (M, F, age range, median age) and their sexual partners (M, F, age range, median age). Control group consisted of 100 dyspeptic subjects matched for sex and age; 2) *H. pylori* infection was assessed by 13C Urea Breath Test (UBT); 3) prevalence of upper GI symptoms, including GER symptoms, was assessed through the Leeds scale; 4) significance of differences was assessed by chi-square test and a *p* value of < 0.05 was considered statistically significant.

Results: 1) Prevalence of *H. pylori* infection in sexual partners of *H. pylori*-infected subjects was 75/100 (75%) whereas prevalence of *H. pylori* infection in the control group was 33/100 (33%), *p*<0.05; 2) in the 75 couples with both members infected with *H. pylori*, prevalence of GER symptoms in at least one member of the couple was 50/75 (67%) whereas in the 25 couples with no transmission of *H. pylori* infection, prevalence of GER in *H. pylori*-infected subjects was 10/25 (40%), *p*<0.05.

Conclusions: 1) Prevalence of *H. pylori* infection is significantly higher in sexual partners of *H. pylori*-infected subjects than in a control group of dyspeptic patients; 2) Prevalence of GER symptoms is significantly higher in *H. pylori*-infected subjects whose sexual partner is *H. pylori*-infected than in those whose sexual partner is not; 3) We hypothesize that sexual partners of *H. pylori*-infected subjects are at risk of being infected and that therefore should be tested for *H. pylori* infection; 4) We postulate that transmission of *H. pylori* infection might be, at least in part, contributed to by GER, probably through an oral-oral route.

P.04.7**PREVALENCE OF H. PYLORI INFECTION AMONG PATIENTS COMING FROM DIFFERENT COUNTRIES AND LIVING IN ROME AREA**

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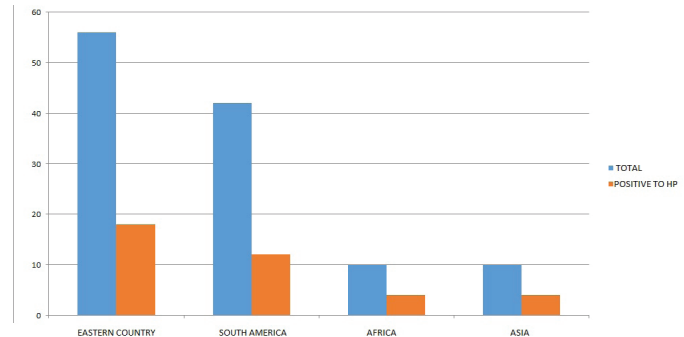
Background and aim: Rome is a multi-ethnic metropolis and many patients, Italians or non-Italians are referred to our outpatients Gastroenterology unit to perform 13C-urea breath test (UBT) because of the occurrence of upper GI symptoms. The aim of this study was to assess the prevalence of *Helicobacter pylori* (HP) infection and DOB values in Italian and non-italian patients.

Material and methods: 258 patients (198F; 60M, mean age 47±15 years) performed UBT between November 2014 and April 2015 in our Gastroenterology Unit according to international guidelines. We considered positive to HP infection with a DOB>3.5%. Among patients, 138 (104F 34M, mean age 48±17 years) were Italians, meanwhile 120 (94F 26M, mean age 46±13 years) were from

different countries, as assessed by the place of birth (56 Eastern Countries, especially from Romania, 42 South America, Ecuador above all, 10 Africa and 10 Asia).

Results: Among 138 Italian patients, 23% resulted infected by HP, compared to 37% of non-Italians subjects (*p*<0.04).

The positivity of HP infection among patients from Eastern Countries, South America, Africa and Asia were 32%, 28%, 40%, 40% respectively. Interestingly, we found significant lower DOB values in Italians compared to non-Italian patients (mean DOB 36±27 vs 69±32; *p*<0.0001).



Conclusions: Our data shows that around 50% of pts referred to our outpatients unit come from foreign Countries and most of them are from Eastern Europe. Prevalence of HP is lower in Italians compared with non-Italian patients, with a significantly lower level of DOB value, which deserves further investigations.

P.04.8**PREVALENCE OF H. PYLORI INFECTION IN A POPULATION OF ITALIANS AND IMMIGRANTS IN ROME AND RATE OF RESPONSE TO THERAPY**

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Background and aim: It is estimated that *Helicobacter Pylori* (HP) infection affects approximately half of the world's population, causing diseases such as gastritis, peptic ulcer and gastric neoplasms. Although its impact in developed countries has been reduced over the last decades, the prevalence of the disease remains high, equal to 10-20% in individuals under the age of 50 and to 40-50% in individuals over the age of 50.

However in developing countries, the prevalence of the infection is higher compared to developed countries (reaching up to 90% in some African and Asian countries).

Aims of the study are: 1) to assess the prevalence of HP infection in a population of Italians and immigrants with chronic dyspepsia 2) to evaluate the rate of responders to first line therapy.

Material and methods: Between January 2014 and February 2015, 366 patients with dyspeptic symptoms attending the outpatient clinic of NIHMP were visited. Among these, 311 were submitted to urea breath test (UBT) for the diagnosis of HP infection.

The distribution by gender demonstrates a slight prevalence of males (51.4%) with a mean age of 43.1 years. The distribution of patients, related to the geographical areas of origin, was the following: Europe 50.2% (of which Italy was 23.5%), Africa 29.3%, Asia 10%, South America 10.6%.

HP positive patients after UBT were submitted to first line therapy. First line therapy was differentiated on the basis of the country of origin: individuals from countries with a high percentage (>20%) of antibiotic resistance to clarithromycin (Europe, Asia) were treated

with sequential therapy, whereas individuals from countries with a low percentage (<20%) of antibiotic resistance to clarithromycin (Africa, America) were treated with standard triple therapy with clarithromycin.

Results: Among the 311 patients submitted to UBT, 188 (67.6%) were HP positive, and among these 163 began a treatment cycle.

Among the 101 patients that were examined post-therapy, the overall response rate was 75.2%, of which 80.6% concerned sequential therapy and 78.3% standard triple therapy.

Conclusions: The prevalence of HP infection in the cohort studied is high (67.6%); this confirms that HP infection represents one of the main causes of chronic dyspepsia.

P.04.9

DIAGNOSIS OF CHRONIC ATROPHIC GASTRITIS IN PRIMARY CARE SETTING BY MEANS OF GASTROANEL®: A POPULATION STUDY ON 10,000 CONSECUTIVE PATIENTS

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Background and aim: Chronic atrophic gastritis (CAG) is a stomach precancerous condition, often related to *Helicobacter pylori* (H.p.) infection. This condition is characterized by hypo- or achloridria due to loss of appropriate gastric glands. Gastropanel® is a non-invasive test able to detect both CAG and H.p. infection. This test, which provides information on

both morphological and functional status of the gastric mucosa, is often referred to as “serological biopsy”. The aim of the present study is to investigate, by means of Gastropanel®, the prevalence of CAG in a large primary care population.

Material and methods: Ten thousand dyspeptic patients, from two different areas of North-East of Italy, were enrolled. The first one (Group A) included 7,400 patients (M:F=1.2:2.0 mean age 53 years) from 2003 to 2014 while the second one (Group B) involved 2,600 patients (M:F=1.5:2.3, mean age 56 years) from 2011 to 2013. Upper GI endoscopy with biopsies sampling, evaluated histologically according to the Sydney classification and the O.L.G.A. staging system, as well as Gastropanel® (Biohit Oyj, Helsinki, Finland) were performed in every patient.

Serological diagnosis of CAG was made when PGI serum levels were < 25 microg/L and G-17 concentrations > 14 pmol/L. Histological diagnosis of CAG followed the criteria of both Sydney system and O.L.G.A. staging.

Results: Overall, CAG was diagnosed by serology in 716 out of 10,000 patients. In Group A population, 608 patients (mean age 57 years old) has a CAG, 2,492 (mean age 54) a non-atrophic gastritis related with H.p. infection was performed while 879 patients (mean age 44 years) presented with a normal gastric morpho-functional assessment. In Group B population, CAG was found in 108 patients (mean age 58 years) and H.p.-related gastritis in 643 (mean age 59) while a normal pattern was detected in 721 patients (mean age 47).

Conclusions: Overall, in a primary care setting, a picture of CAG was found in 7.2% of patients. The prevalence was higher in Group A than in Group B (8.2% and 4.2%, respectively) for unknown reasons. The

mean age of subjects with CAG was higher than that of patients with NAG H.pylori-related and normal population in both areas.

P.04.10

GASTRIC CANCER AND SIMULTANEOUS CARE: PRELIMINARY REPORT ABOUT THE TAKE CHARGE APPROACH

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Background and aim: In multimodal therapy era, surgery is considered the main treatment for gastric cancer (GC). Yet, the main topic of National Health Service is GC treatments' costs. In Italy, the cost due to GC's care, results in loss of productivity (LP), and is 134% higher than average cancer costs. Among its proposed actions, “National Cancer Plan” intends to reduce migration of the health care and better utilize the available resources so to reduce LP's. We present our preliminary results of the first Italian simultaneous care model with the intent to increase relationship between oncology and territory, and reduce treatment costs.

Material and methods: Como has 600,000 people. Incidence of GC, standardized for age, is the highest in North Italy: 18.7 vs 17.1. An average of 110 patients/year undergo a GC surgery, with a migration value of 30%-35%. Erone onlus (oncological volunteer association) has organized a plan of simultaneous care model. In February 2014, in collaboration with Valduce (religious hospital), organized a two-days conference on “Oncology and territory”. The first day dedicated for everybody while the second day for general practitioners (GP). After a year, we examined and compared the results with the historic database of Como Local Health Authority

Results: Como has a “Dipartimento Interaziendale Provinciale Oncologico”, that treats all oncological patients, nonetheless in 2013 the migration index was of 30.5%. Following our event in 2014, that had an attendance of over 600 people, the migration index decreased to 24.5%. A cutback of migration of health care means a better use of the available resources. Compared to 2013, gastroscopy increased of 4% (up 27% in surgery endoscopy); a sign that GPs paid more importance to upper gastrointestinal symptoms of their patients. Moreover in 2015, first time in Italy, Valduce described an integrated multidisciplinary clinical protocol, on treatment of GC.

Conclusions: As the fifth most commonly diagnosed cancer and the fourth leading cause of cancer-related death, GC is a major clinical and financial burden with significant differences in territorial distribution. Multimodal progress is extremely costly and the results often end in marginal survival benefit, therefore, excellence in surgery should be achieved. A new program for a simultaneous care model is one of several changes required to improve the intended actions of GC surgical treatment. Our preliminary results on this model, demonstrate an advantage in territory, reducing the migration index

P.05 Clinical Cases

P.05.1

ENDOSCOPIC REMOVAL OF A LARGE SYMPTOMATIC IMPACTED BONE IN THE COLON

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Background and aim: Most foreign bodies pass through the gastrointestinal tract without any consequence. A very small

percentage perforate the bowel, leading to acute abdomen and requiring surgical intervention. Foreign bodies such as dentures, fish bones, chicken bones, toothpicks and cocktail sticks have been known to cause bowel perforation

Impaction, perforation, or obstruction often occurs at GI angulations or narrowing. Hence, patients with previous GI tract surgery or congenital gut malformations are at increased risk

Material and methods: We report the case of a 75 years-old male patient without previous surgery presented with intermittent abdominal cramps and diarrhea of 2 months' duration. Two months earlier, he had also experienced hematochezia on three occasions. On physical examination, bowel sounds were normal and there was no abdominal organ enlargement, tenderness, or rebounding pain. Digital rectal examination was unremarkable. Physical examination showed a diffuse tenderness of abdomen without defense. Clinical and biochemical data were negative. An x-ray of the abdomen showed in hypogastrium a calcific body compatible with bone fragment that was projected at the level of the sigmoid colon. Excluded perforation we proceeded to recto-sigmoidoscopy previous preparation with macrogol.

Results: At 25 cm from the anal verge, the mucosa was edematous and hyperemic and an impacted foreign body was present. We proceeded to remove it using biopsy forceps, a silk tie was looped around the impacted bone and then gently pulled caudally as it exited the anus. No evidence of perforation or other complications except presence of one pressure ulcer on the mucosal wall. After removal of the bone, the patient became asymptomatic without any residual symptom.

Conclusions: It is therefore described a case in which poorly suggestive symptoms and a non-specific examination has allowed early detection and to target a targeted endoscopy with a rapid resolution of symptoms. Our patient was not aware of the ingestion of the foreign body.

Osseous esophageal foreign bodies are potentially dangerous as the risk perforation always exist. Safe extraction or dislodgment of an osseous foreign body can almost always be performed with the endoscope stating an adequate preliminary evaluation and the selection of proper equipment. After recognition of the impacted foreign body, the patient was managed endoscopically with resolution of symptoms.

P.05.2

FIRST CASE OF SMALL BOWEL ADENOCARCINOMA DETECTED WITH THE NEW 360° PANORAMIC-VIEWING CAPSULE ENDOSCOPY SYSTEM

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Background and aim: Small bowel tumors (SBT) are rare, accounting for only 1-3% of all gastrointestinal neoplasms [1]. Nonetheless, among patients undergoing small bowel capsule endoscopy (SBCE), neoplastic lesions can be detected in 2-9% of cases [2,3].

Material and methods: Here, we report the case of a 52 years old outpatient presented for iron deficiency anaemia (Hb 7.4 g/dl, ferritin 7 ng/ml), asthenia and dark discharge stools occurred after oral intake of non-steroidal anti-inflammatory drugs without any gastroprotection.

An immediate esophagogastroduodenoscopy showed antral erosive gastritis with no evidence of *Helicobacter pylori* infection and subsequent ileo-colonoscopy was negative. Overt bleeding stopped spontaneously and patient received medical treatments based on proton pump inhibitors (esomeprazole 40 mg/24h) and

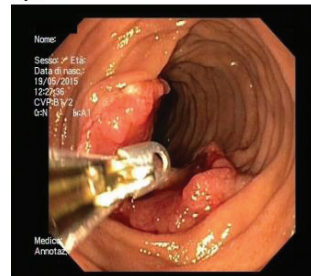
iron supplement. One month later, blood tests revealed persistent iron deficiency anaemia (Hb 9 g/dl, MCV 72 fL, ferritin 10 ng/ml) and positive fecal occult bleeding tests (3/3 samples). Therefore, SBCE was performed using the newly introduced CapsoCam® SV1 (CapsoVision Inc, Saratoga, USA).

Results: The SBCE explored the entire small bowel and the video image quality always scored as optimal. The lateral view allowed a clear visualization of an ulcerated nonbleeding lesion with central depression in the proximal jejunum (fig A). The following enteroscopic inspection confirmed the lesion site and the macroscopic appearance (fig B). Histological analysis lead to the diagnosis of adenocarcinoma and to surgical resection.

Fig A



Fig B



Conclusions: The newly introduced CapsoCam® SV1 is a wire-free device for SBCE with long lasting battery life, and 12-20 frames per second captured by four lateral cameras to enable a 360° panoramic view of the entire small bowel [4,5]. CapsoCam® SV1 has a detection rate and a safety profile comparable to other SBCE with frontal view in patients suffering from obscure gastro-intestinal bleeding or with suspected Crohn disease [4-6]. This represents the first case of jejunal adenocarcinoma discovered with Capsocam® SV1. Further study should now evaluate the role of CapsoCam® SV1 as a new standard in patients suspected for to have SBT.

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P.05.3

A RARE CASE OF GASTROINTESTINAL BLEEDING

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Background and aim: A 48 old male was admitted to our clinic for investigate a recurrent low gastrointestinal pain. In 2013 he presented an episode of important lower gastrointestinal bleeding causing severe anaemia which subsided spontaneously. In that occasion a colonoscopy showed dilated tortuous sub-mucosal veins through the entire explored tract (until the trasverse colon). A contrast abdominal TC excluded vascular stenosis. Two sessile polyps found in the sigma were excised in a second time, the histology revealed a tubular adenoma with severe dysplasia. A

new endoscopy performed 6 months later confirmed the varices. An upper gastrointestinal endoscopy showed no evidence of esophageal, gastric varices.

Material and methods: In 11/2014 he was admitted for further evaluation. He reported recurrent abdominal pain, denied other episodes of hematochezia. He declared to smoke 10 cigarettes qd, no alcohol abuse or illicit drug use was noted. Both his father and his grandfather died for a colon malignancy. The physical examination was unremarkable. Laboratory investigations were within normal limits except a small thrombocytopenia (PLT 120 000/ul) and hyperhomocysteinemia (heterozygous MTHFR variant).

Results: Doppler ultrasound revealed normal liver size and echo texture, normal flows and no evidence of collaterals. A TC showed varicose ectasia in the submucosa on the anterior side of the sigma until the distal descending colon, the rectum-anal passage and even in the jejunal-ileal tract in absence of stenosis. A selective angiography of mesenteric artery exhibited a normal enhancement in arterial phase while the venous phase confirmed stasis of the contrast medium from the upper rectum into the terminal ileum, no evidence of portal venous obstruction. Although no hepatic involvement was suspected after clinical examination, other laboratory tests for identifying liver diseases were ordered, an elastography/liver biopsy resulted normal; a portogram revealed normal flow and superior mesenteric artery.

Conclusions: We discussed if submit the patient to a preventive colonic resection, both considering the elevated hemorrhagic risk and the neoplastic familiar attitude or to a conservative strategy with oral therapy. After collegial discussion, we decided for the second option, propranolol was started at 20 mg bid and titrated to 40 mg bid over three weeks. After 6 months a new endoscopy was performed and for the first time of the patient history it was complete until the ileo-cecal valve which appeared recovered by adenomatous mucosa (histology: tubular adenoma with dysplasia) and a polyp was found in the ascendant tract.

One year later from the diagnosis of idiopathic ileo colonic varices, the patient conditions are stable, at the moment, no gastrointestinal bleeding has occurred.

P.05.4

A RARE CASE OF MIXED ADENO-NEUROENDOCRINE GASTRIC CARCINOMA (MANEC) ASSOCIATED TO AUTOIMMUNE METAPLASTIC ATROPHIC GASTRITIS (AMAG)

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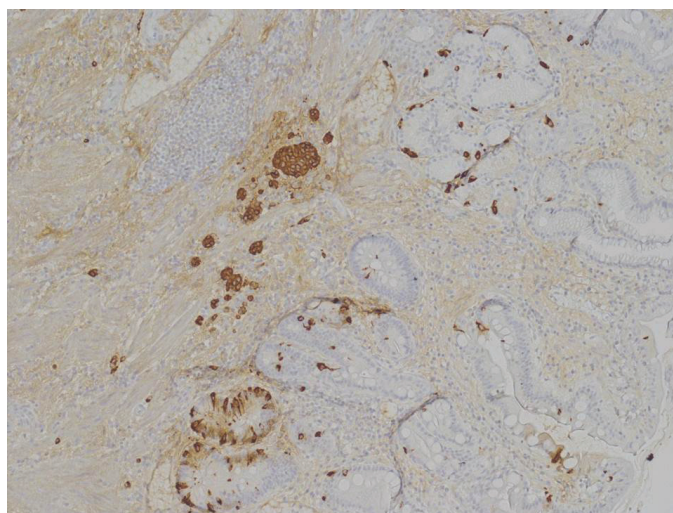
Background and aim: AMAG is characterised by body and fundus atrophy, antral preservation and positive antiparietal cell antibody as result of parietal cells destruction and acid/intrinsic factor reduction. Gastrin stimulates parietal cells and enterochromaffine-like cells to proliferate and secrete more acid and histamine, leading to hypo/achlorhydria, and pernicious anemia. Patients with AMAG have up to 3–6 fold increased risk of developing gastro-intestinal squamous tumors and adenocarcinomas (ADK), in addition to neuroendocrine tumors (NET). Mixed adenoneuroendocrine carcinoma (MANEC) is a rare condition in which ADK and NET cells coexist for at least 30% each.

Material and methods: A 76 years old man with AMAG showed a 3 cm sessile lesion of the gastric body. The biopsy showed tubulovillous adenoma with high grade dysplasia associated with superficial. *Helicobacter pylori* was negative. AFP, CEA, CA 19-9, cytokeratin-19 fragment, and 5-hydroxy indoleacetic were normal. EUS showed suspect of slight submucosal infiltration, CT scan

and PET-CT were negative for metastasis, Endoscopic submucosal dissection was scheduled.

Results: Histological examination revealed poorly differentiated ADK deeply invading the submucosa with high grade budding, no vascular invasion and small cell neuroendocrine carcinoma (SC-NEC). The latter was positive for pankeratin, chromogranin A, synaptophysin, CDX2, and negative for TTF1. Ki67 labeling index was 60%. As the NEC component was more than 30%, diagnosis of MANEC was posed.

Subsequently total gastrectomy was performed showing complete tumor removal and one metastatic glandular lymph node positive over 29. Tumor was pT1bN1M0, stage IB according to the 7th TNM classification. Any chemotherapy was prescribed for age and comorbidity. The patient is alive without signs of recurrence after 8 months.



Conclusions: AMAG has an increased risk of cancer development. The pathway is still unclear. The 2 most validated hypotheses suggest: ADK cells dedifferentiate to NET cells during tumor progression or monoclonal pluripotent epithelial stem cells differentiate into 2 components. In case of AMAG, mixed lesion must be suspected. Boost endoscopic surveillance in patients with AMAG possibly with the help of HD endoscopy must be taken in account in order to improve their management.

P.05.5

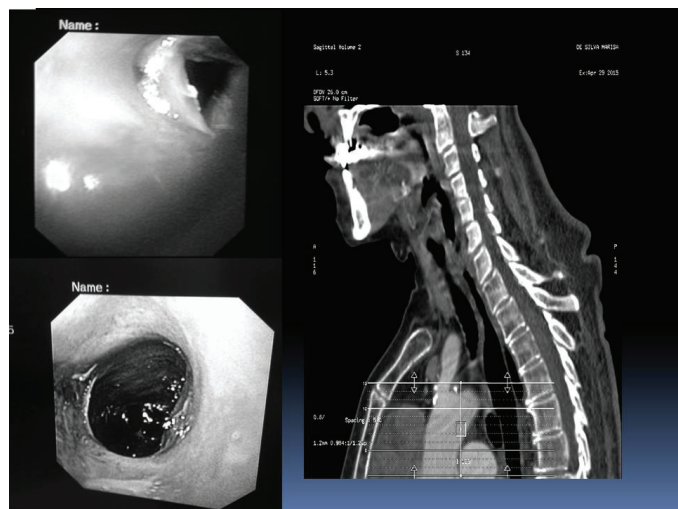
AN UNUSUAL CASE OF DYSPHAGIA

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Background and aim: Dysphagia is a common symptom especially in elderly. Esophageal dysphagia is caused by both malignant and benign diseases. A carefully conducted patient history can be of help to make a proper diagnosis.

Material and methods: We here describe the case of a 77 year old woman who was admitted to the hospital because of solid food dysphagia. She suffered from hypertension and diabetes. The upper gastrointestinal examination revealed the presence of a severe stricture of the upper third of the esophagus (Fig. 1) on which multiple biopsies were taken. A MR scan of the neck revealed a 2-cm thickened esophagus along the C6-C7 vertebra with stenosis of the lumen. There were no lesions of the peri-esophageal fat (Fig 2). A second endoscopic examination with the ultra-slim endoscope was performed to complete the study of the upper gastrointestinal tract and was negative for other diseases. Biopsies were negative for malignancy and for epithelial dysplasia. However, the pathologist

reported the hydropic degeneration of basal layer, subepithelial T cell infiltrate, epithelial hyperplasia, hyperkeratosis, acanthosis, necrotic keratinocytes. The picture was compatible with the diagnosis of lichen planus. A second anamnesis revealed the presence of a long lasting oral lichen planus nearby a mobile dental bridge. Patient was treated with endoscopic dilatations by the use of bougies over a Savary guidewire by increasing the diameters until 9 French (fig 3).



Results: Patient reported an immediate symptoms relief. Dilatation in lichen planus stenosis is not the first choice due to the risk of Koebner phenomenon but this patient the comorbidity did not allowed systemic steroid therapy.

Conclusions: Lichen planus is an idiopathic disorder with clinical manifestation in the skin, mucous membranes, genitalia, hair and nails. Esophageal involvement by lichen planus is rare, more commonly found in middle-aged woman, mostly associated with oral lesions. It can be missed because a long time (years) is necessary from the disease onset and the development of dysphagia. Even if esophageal localization of lichen is rare, it must be considered in the differential diagnosis of dysphagia and esophageal stricture especially in elderly women, along with peptic disease and esophageal adenocarcinoma.

Our case demonstrated that clinical, endoscopic and histologic data may narrow a broad list of differential diagnoses for the esophageal stricture and in this case allowed the diagnosis of the rare esophageal lichen planus.

P.05.6

A RARE CASE OF CELIAC DISEASE IN A PATIENT WITH COMMON VARIABLE IMMUNODEFICIENCY: WHEN VILLOUS ATROPHY IS NOT ENOUGH

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Background and aim: We present a case of a woman with a diagnosis of celiac disease (CD) histological documented by villous atrophy; other test demonstrated the presence of common variable immunodeficiency (CVID) complicated by *Giardia Lamblia* infection, an other cause of villous atrophy. In this case, HLA and histological

response to a glutenfree diet (GFD) confirmed CD and GFD resolved clinical manifestation and villous atrophy.

Material and methods: A 40 years old woman presented with chronic diarrhea, weight loss of about 8 kg in 2 months, and iron deficiency anemia (Hb:8 g/dl); in 2013 patient receive diagnosis of CD based on histological characteristics (marked chronic inflammation with intraepithelial lymphocytosis, severe flattening of the villi “March 3 C”). She started gluten free diet. For persistence of clinical symptoms despite GFD, an other planned disease reevaluation was performed in 2014. Research of abnormal hemoglobin chains showed no tassemia and other hemoglobinopathies; laboratory test showed negative celiac markers (transglutaminase IgA and IgG antibodies) but very low levels of all classes of immunoglobulin (Ig) (IgA <6.67 mg / dl, IgG <119 mg / dl, IgM <4.17 mg / dl. Abdomen ultrasound showed only mild splenomegaly (Dt 13 cm). The esofagogastroduodenoscopy (EGDS) showed on duodenum mucosa, nodules of various sizes, up to 5 mm. At Hystological exam: severe villous atrophy, nodular lymphoid infiltration of the lamina propria, no evidence of plasma cells, presence of many spheroidal morphology forms compatible with *Giardia lamblia* (GI). (Fig 1A,B,C); CD5 glycoprotein expression positive (as a marker of intraepithelial T lymphocytes); CD20 negative (B-lymphocytes absent) (Fig. 2A,B,C); switch on D-Immunoglobulin (IgD) for absence of other classes of Immunoglobulin in CVID (Fig 3). There was also follicular lymphoid hyperplasia. CVID complicated by GI infection was diagnosed; patient started antibiotic therapy with metronidazole; CD was excluded so it was placed indication to practice free diet. Patient had an increase of weight but diarrhea and anemia not resolved. A new research of GI in the stool was negative.

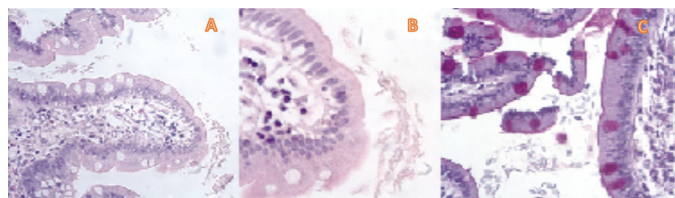


Fig. 1. (A,B) Histological view of duodenitis by *Giardia Lamblia*: many spheroidal morphology forms CPAS positive staining (x40 magnification). (C) the trophozoites of *Giardia Lamblia*. This parasitic infection is typical of patients with CVID and is associated with villous atrophy.

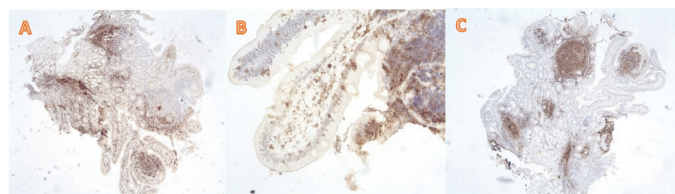


Fig. 2. (A,B,C) CD5 glycoprotein expression positive (as a marker of intraepithelial T lymphocytes); CD20 glycoprotein are negative (B-lymphocytes absent).

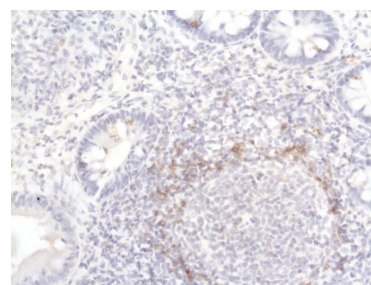


Fig. 3 The switch on D-Immunoglobulin (IgD) for absence of other classes of Immunoglobulin in CVID.

Results: The patient was referred to our Gastroenterology Unit. We decided to perform genetic test with evidence of HLA-DQ2

typing. We asked the patient to restart gluten-free diet. EGDS was performed in 2015 (after 18 month) and showed a normal duodenum mucosa. Histological exam showed no villous atrophy, not inflammatory infiltrate. CD diagnosis was confirmed and patient resolved gastrointestinal manifestation and anemia.

Conclusions: Villous atrophy can be seen in patients with CVID. Infectious agents may be responsible, whereas in others, CD may be the cause. Our case report demonstrates that celiac antibodies gave conflicting results and were of no help in CVID diagnosis. HLA-DQ typing is important for exclusion of CD. Histologic response to a GFD allowed a diagnosis of CD and remains the only diagnostic criteria for CD.

P.05.7

SYSTEMATIC REVIEW AND META-ANALYSIS OF STUDIES COMPARING METAL OR PLASTIC STENTS FOR PREOPERATIVE BILIARY DRAINAGE IN RESECTABLE PANCREATIC CANCER

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Background and aim: In resectable pancreatic cancer, preoperative biliary drainage (PBD) increases complications compared with early surgery without PBD. However PBD may be necessary in patients with marked hyperbilirubinemia or in patients undergoing neoadjuvant therapy. Metal stents seem to be more effective than plastic stents in these settings.

Material and methods: Systematic review and meta-analysis of studies comparing metal versus plastic stents in patients undergoing endoscopic PBD for resectable pancreatic cancer. Primary outcome was the rate of endoscopic reintervention (ER), meaning stent failure of preoperative biliary drainage before surgery. Secondary outcomes were rate of overall complications related to preoperative biliary drainage, before and after surgery such as anastomotic leakage, intra-abdominal abscesses, delayed gastric emptying, wound infection, portal vein thrombosis, pancreatic fistulas, biliary anastomotic leak and mortality.

Results: One Cohort prospective Trial and four retrospective cohort trials were identified including 704 patients comparing metal vs plastic stents. Of these, 202 patients (29.5%) were treated with metal stents and 502 patients (70.5%) with plastic stents. The majority of patients had a pancreatic adenocarcinoma 610 (86.4%). The methodological quality assessment for each of the included studies was considered as "fair". The rate of ER was significantly lower in the metal stent group than in the plastic group (3.4% vs 14.8%, $p = 0.0009$). In addition, rate of postoperative pancreatic fistulas resulted significantly lower in the metal stent group 5.1% vs 11.8% ($p=0.04$). No significant difference was found in the other secondary outcomes.

Conclusions: Even though early surgery remains the standard preference in most patients suffering from jaundice with a resectable pancreatic tumour, metal stents should be preferred for PBD when surgery must be delayed.

P.05.8

RECURRENT LIFE-THREATENING GASTROINTESTINAL BLEEDING DUE TO MECKEL'S DIVERTICULUM

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Background and aim: This is a case of a 34 year old man presented with a further episode of gastrointestinal bleeding (GB) motivating admission in the department of Medicine.

Material and methods: His previous history began two years before, with three episodes of GB, presenting as melena, with haemorrhagic shock in one occasion, and plenty transfusions during the episodes. Five upper endoscopic and 6 coloscopic exams, both urgent and elective, had been performed, only finding an angiodysplasia of the cecum, that was treated with argon plasma coagulation. Moreover, no other sources were found at two small bowel capsule studies and at two enteroscopic exams. After discharge lanreotide was started. Eleven months later, a new episode on GB occurred. After admission, melena persisted despite optimal medical treatment. Further urgent both upper and lower endoscopy, angioCT and angiographic exams, did not find bleeding sources. Due to the development of haemorrhagic shock, a surgical emergency procedure was performed during which Meckel's diverticulum (MD) with bleeding ulcers was found and surgically removed at about 60 cm from ileo-cecal valve (Fig 1).



Results: Histological examination confirmed MD with ulcerated ectopic gastric mucosa. The patient was dismissed after few days and no further episodes of GB occurred during follow up.

Conclusions: MD is the vestigial remnant of the omphalomesenteric duct and represents the most common congenital anomaly of the gastrointestinal tract. MD known complications are intestinal obstruction, intussusceptions, ulceration, hemorrhage, vesico-diverticular fistulae and tumors. However, whether GB represents the most common complications of MD in children, it is a rare complication in adults. Both endoscopic, radiological exams and scintigraphy are useful but not always address the diagnosis. Our report suggests that a diagnosis of MD should be considered in young adults with recurrent gastrointestinal bleeding of otherwise unknown cause.

P.05.9

GASTROINTESTINAL NEUROENDOCRINE TUMORS OF UNKNOWN PRIMARY SITE: REPORT FROM A SERIES AT A SINGLE INSTITUTE

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Background and aim: Neuroendocrine neoplasms (NENs) are a heterogeneous group of neoplasms, which differ in biologic behavior, histologic features and response to treatment.

The behavior and therapeutic options of NENs depend on the location of the primary tumors.

NENs with unknown primary site (NENs-UP) account for 10 to 13 percent of all NENs.

Aim: To describe clinical and histological findings and the diagnostic work-up of patients with histologically proven metastatic NENs of unknown primary.

Material and methods: Study period: Between January 2005 to January 2015, 93 patients with metastatic gastrointestinal NENs were referred to our Institution.

Patients: Among 93 patients, 17 (18%) presented with immunohistochemically proven neuroendocrine metastases, without evidence of primary site.

Of these, 11 were male and six female. The median age at the diagnosis was 64 years (range 33–74). In all the cases, an exhaustive work-up based on computed tomography (CT), magnetic resonance (MRI) and somatostatin receptor scintigraphy (SRS) / Gallium-68 PET was performed.

Results: 14 of the 17 patients with NENs-UP (82%), showed hepatic metastases, whereas in three patients an abdominal nodal involvement was detected.

In 14 of the 17 cases (82%), liver or nodal metastases were firstly diagnosed by abdominal ultrasound, performed during surveillance of chronic diseases in six patients and for gastrointestinal symptoms in eight.

16 of the 17 tumors (88%) were well differentiated (G1 in five cases and G2 in 11), with a poorly differentiated carcinoma in one patient. Hormonal syndrome was diagnosed in 11 cases (65%). In particular carcinoid syndrome was present in 8 patients, Zollinger-Ellison syndrome in two and Verner-Morrison syndrome in one.

In the course of a strict work-up, the primary tumor was diagnosed in 12 cases (71%), after a median of 8.5 months (range 3–120), of these eight (67%) had a functioning form.

The primary site was identified as pancreas by a repeated abdominal CT (#3); terminal ileum (#2) and colon (#1) by colonoscopy; central ileum by double balloon enteroscopy (#1) and pancreas by endoscopic ultrasound (EUS) (#1).

Again, laparoscopy identified a jejunal, ileal, Meckel's diverticulum and pancreatic primary tumor in further four patients.

In our series, five cases are still classified as NENs-UP.

Conclusions: Despite the continuous advances in diagnostic techniques, including radiologic, endoscopic and immunohistochemical methods, metastatic NENs still represent a clinical challenge, involving multidisciplinary expertise.

In the present series, NENs remain of unknown primary origin in a relevant proportion of cases (5/93, 5.3%), even after an in-depth work-up. Data from our series suggest that NENs-UP may derive more frequently from the gastrointestinal tract. The presence of hormone-related symptoms may help to better localize the primary site.

P.05.10

DUODENAL NEUROENDOCRINE TUMORS – DATA FROM A SINGLE CENTRE

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Background and aim: Duodenal neuroendocrine neoplasms (D-NENs) are heterogeneous tumors, previously classified as foregut

NET, whose prognosis can be good as for gastric neuroendocrine tumors or bad when facing with more aggressive forms. Their optimal management remains to be clarified, even if endoscopic resection is increasingly performed instead of surgery. Present series was aimed at reporting a single-centre experience.

Material and methods: Retrospective analysis of patients with histologically confirmed diagnosis of D-NENs managed at our Institution.

Results: From 2004 to 2014, 12 patients (9 M and 3 F, median age of 67 years, range 26–79) were diagnosed and treated. The D-NEN was single in all but one patient who was diagnosed with MEN1 syndrome and had both a D-NEN and multiple pancreatic NENs. Two patients had a peri-ampullary D-NEN. The median diameter was 20 mm (range 5–37). A non-functioning D-NEN was incidentally diagnosed in seven cases, a gastrinoma in three and a somatostatinoma in two cases, respectively. According to 2010 WHO classification, D-NEN was G2 in three cases and G1 in nine. At enrolment, four patients (33%) had metastases, to lymph nodes (#2), liver (#1) and both (#1). D-NEN was removed in 10 cases (83%), endoscopically (#3) or surgically (#7). An elder patient, with 8 mm non metastatic gastrinoma unsuitable for surgery, was only followed-up. One patient was lost at follow-up. Over a median follow-up of 33 months (range 2–133), two patients died of the disease (metastatic somatostatinoma and gastrinoma, respectively, both progressive after surgery and not responsive to somatostatin analog, chemotherapy and peptide receptor radionuclide therapy treatments).

Conclusions: D-NENs may be metastatic at the diagnosis in up to 33% of the cases, thus nuclear imaging should be performed to exclude distant metastases. Endoscopy and surgery play a primary role in the management of the disease. Prognosis may be highly variable. Further studies are needed to better define standardised dedicated guidelines for D-NENs, including the optimal management and the perfect follow-up intervals.

P.05.11

UNUSUAL ONSET OF COLONIC SARCOIDOSIS: A CASE REPORT

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Background and aim: Sarcoidosis is a multisystem chronic inflammatory condition of unknown etiology that has the potential to involve every tissue in the body. Sarcoidosis in the gastrointestinal system, and particularly the colon, is very rare.

Material and methods: We report a case of a 57-year-old man in apparent good health who presented with newly onset abdominal pain and symptoms related to colonic obstruction. The patient was healthy until three to four weeks prior to presentation, when new-onset constipation developed and he began passing pencil-like stools. A physical examination of the patient revealed mild abdominal distention and tenderness of the right lower abdominal quadrant. Routine hematology and biochemistry analyses were normal; Carcinoembryonic antigen levels were slightly elevated (3.6 ng/mL). A colonoscopy revealed a stenotic obstructive lesion at the cecum-ascending colon transition and we were unable to advance the colonoscope beyond this area. Biopsy specimens obtained from this site showed no evidence of a neoplastic lesion, but rather an acute inflammatory infiltration of the submucosa. An abdominal CT revealed marked symmetric concentric wall thickening in the cecum-ascending colon, which notably reduced the enteral lumen and was associated with a heterogeneous hyperdensity of perivisceral fat tissue and multiple satellite lymphadenopathies along the ileocolic vessels. A malignant colonic lesion was suspected, despite the unclear histology results. The patient underwent an exploratory laparotomy.

Results: Exploratory laparotomy revealed a 4 cm stenotic lesion in the cecum-ascending colon, with numerous peritoneal micro-nodules and adjacent lymphadenopathies. A carcinologic right hemicolectomy was performed. Examination of the resected specimen revealed a stenotic ulcerated lesion in the colonic wall in proximity to the ileocecal valve and microscopic examination showed multiple noncaseous granulomas composed of a central core of epithelioid cells and multinucleated giant cells surrounded by a lymphocyte cuff. In absence of acid-fast bacilli or foreign bodies at Ziehl-Neelsen staining, a diagnosis of sarcoidosis was made.

Conclusions: Only histologic examination of the surgical specimen can yield a diagnosis of gastrointestinal sarcoidosis due to the non-specificity of endoscopic and radiologic findings.

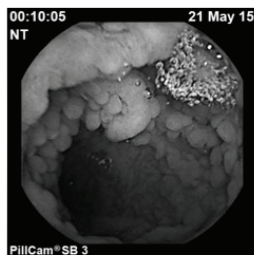
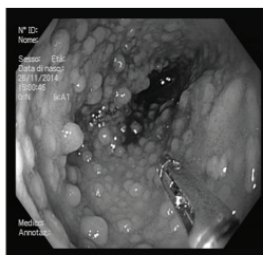
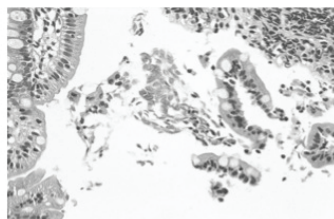
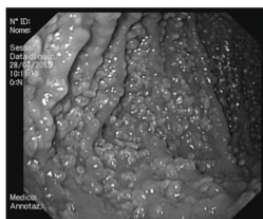
P.05.12

DIFFUSE INTESTINAL NODULAR LYMPHOID HYPERPLASIA (DNHL) IN A PATIENT WITH EPIGASTRIC PAIN: A CASE REPORT

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Background and aim: Diffuse intestinal nodular lymphoid hyperplasia (DNHL) is a rare disease involving either the entire small intestine or the large intestine or both, characterized by the presence of multiple small nodules, normally between 2 and 10 mm in diameter. DNHL has been observed more frequently in children and more rarely in adults in whom it is often associated with common variable immunodeficiency (CVID) [1]. Symptoms include epigastric pain, chronic diarrhea and intestinal obstruction. Pathogenesis is often unclear.



Material and methods: We report the case of a patient with DNHL in whom *Giardia lamblia* and *Helicobacter pylori* eradication relieved symptoms. In October 2014 a 44 - year- old woman was admitted to our clinic for epigastric pain and diarrhea present since June. Gastroscopy (EGDS) revealed inflammation of the gastric antrum mucosa and multiple millimetric polypoid lesions in the duodenum. Histological findings showed *Helicobacter Pylori* gastritis and lymphoid follicular hyperplasia in the duodenum with *Giardia* infection. The patient's biochemical, serologic and stool tests were normal except for serum Ig A reduction [2]. CVID was therefore suspected. Ileo-colonoscopy and video endoscopic capsule also revealed multiple polypoid lesions. HP was eradicated and *Giardia*

was treated with metronidazole. The patient was referred to an immunologist for complete investigation.

Results: Both treatments completely relieved symptoms. The endoscopic picture at 6 and 12 months was unchanged and histology showed post treatment Hp and *Giardia lamblia* eradication.

Conclusions: Despite improvement of symptoms following treatment, endoscopic and histological findings of DNHL persist in time.

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P.05.13

PANCREATIC MUCINOUS CYSTIC ADENOCARCINOMA METASTASIS TO THE RECTUM

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Background and aim: Most patients with pancreatic cancer have a metastatic disease at the moment of diagnosis. Usually pancreatic cancer spreads to the liver, lymph nodes, and lung.

Material and methods: A 38 years old woman presented with a pancreatic mass and a rectal cancer. She was admitted to another hospital because of abdominal pain. A colonoscopy revealed a rectal adenocarcinoma. At CT a mass was observed in the pancreatic tail. The patient was addressed to our Hospital for a multidisciplinary approach. An endoscopic ultrasound (EUS) showed a malignant mucinous cystic neoplasm of the pancreatic tail with infiltration of the surrounding pancreatic parenchyma. An EUS-FNA confirmed mucinous material.

Results: A rectal EUS showed an ulcerative lesion, with convergence of mucosal folds, corresponding to a thickened rectal wall with loss of the layers structure that was strictly adhering to a nodule in the mesorectum. It looked more like something coming from outside the rectal wall, than a primitive rectal cancer, so that other biopsies were obtained. The histological examination reported an adenocarcinoma. The immunohistochemical (IHC) staining was positive for cytokeratin 7, cytokeratin 20, and mildly positive for CDX2. The final diagnosis was a rectal metastasis from pancreatic cancer. A 18F-FDG-PET confirmed the hyperaccumulation in the pancreatic tail and rectum. The patient received systemic chemotherapy. At restaging, the rectal EUS showed a response, with initial reconstruction of the layers. She underwent a distal pancreatic resection. The pathological examination reported a mucinous cystic adenocarcinoma (CK7+, CK20+, CDX2-/+), pT3N1R0.

Conclusions: Pancreatic cancer metastasis to the rectum is very rare. EUS can be helpful to differentiate a primitive rectal cancer from an infiltration from the mesorectum. IHC staining for CK7 and CK20 can help in diagnosing metastasis from pancreatic cancer.

P.05.14

MUCOSAL TEARS OCCURRED DURING COLONOSCOPY IN OUTPATIENT WITH ULCERATIVE COLITIS: A CASE REPORT

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Background and aim: The term of Mucosal Tears (MT) is used by several authors to describe linear mucosal defects and sharp longitudinal ulcers, as a characteristic colonoscopic findings in patients with collagenous colitis. We report a rare case of MT

occurred during colonoscopy in outpatient suffering from ulcerative colitis (UC), which was successfully treated with endoscopic clipping.

Material and methods: In april 2015, we observed an outpatient 42 years old man with UC from 21 years, was sent at our hospital to undergo a routine surveillance colonoscopy in our Unit of Digestive Endoscopy. His past family and medical history, and physical examination were unremarkable. Routine laboratory tests and complete blood analysis were normal. The patient was in clinical remission and actually treated with mesalazine 3,2 gr./daily. A total colonoscopy, with conscious sedation and without the use of CO2 insufflation, at that time not available, was performed after standard bowel preparation with 4 liters of polyethylene glycol lavage solution using a split-dose regimen. Colonoscopic findings revealed a mild erythema with granular mucosa in the rectum, and evidence of multiple scars in left colonic segment explored.

Results: During withdrawal of the endoscope, two longitudinal MT with a length of about 8 and 12 millimeters involving mucosa and submucosa were revealed in sigmoid colon, whereas such MT were not observed during the insertion of the endoscope. Therefore, immediately, ten endoclips Resolution™ (Boston Scientific Corporation, Natick, USA) were used for mucosal clousure of the colon wall, without evidence of active bleeding. The patient was hospitalized in the department of surgery, and to exclude the suspicion of a perforation, an abdominal CT scan was performed, which showed the absence of pneumoperitoneum. The patient's postoperative clinical course was uneventful, with a liquid diet and parenteral antibiotic therapy, and he was discharged three days after admission.

Conclusions: MT are rare and uncommon complication during colonoscopy, have not been reported in the colonic mucosa of patients with UC. Mucosal inflammation alone is not sufficient to explain the cause of MT. One possible mechanism for MT could be attributed to the stiffness of the mucosal and submucosal layers, as well as the presence of multiple scars, possibly in combination with the pressure of the air resulting from endoscopic insufflation, leading to stretching of the colon wall mucosa and subsequent tearing.

P.06 Coeliac Disease 1

P.06.1

USEFULNESS OF LASER DOPPLER PERFUSION IMAGING TO OBJECTIFY THE ORAL MUCOSA PATCH TEST IN THE DIAGNOSIS OF ALLERGIC CONTACT MUCOSITIS IN NICKEL-SENSITIVE PATIENTS

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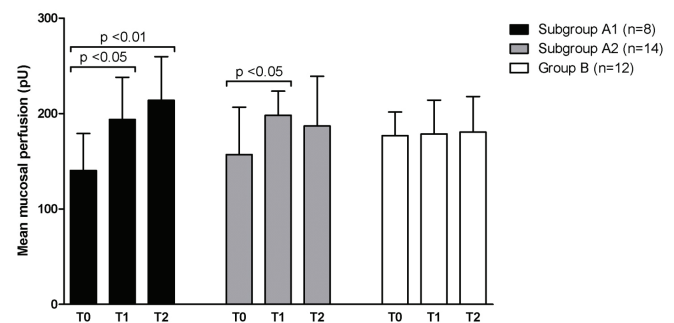
Background and aim: Nickel (Ni) is often the trigger of gastrointestinal and systemic disorders: the exposure of intestinal mucosa to Ni may cause an Allergic Contact Mucositis (ACM), identifiable by means of the Ni oral mucosa Patch Test (omPT). The effectiveness of omPT has already been proven, but up today an objective diagnostic approach to Ni ACM still lacks.

AIM: Laser Doppler Perfusion Imaging (LDPI) was tested to support omPT in Ni ACM diagnosis.

Material and methods: Popultaion: Group A: 22 patients with intestinal and/or systemic symptoms related to the ingestion of Ni-containing foods. Group B: 12 asymptomatic volunteers. Ni-related

gastrointestinal and/or extra-intestinal symptoms and their severity were tested by a specific alimentary-symptom questionnaire. All patients underwent Ni omPT with clinical evaluation at baseline (T0), after 30 minutes (T1), after 2 hours (T2) and after 24-48 hours (T3). LDPI was performed to evaluate the mean mucosal perfusion at T0, T1 and T2. Statistical analysis was performed by ANOVA test and Bonferroni multiple-comparison test.

Results: All 22 Ni-sensitive patients (group A) presented oral mucosa hyperemia and/or edema at T2. Eight out of the same 22 patients presented a local delayed vesicular reaction at T3 (group A1), unlike the remaining 14 out of 22 patients (group A2). All 12 patients belonging to control group B did not show any alteration. Mean mucosal perfusion calculated with LDPI showed an increase in both subgroup A1 and A2. In group B, no significant perfusion variations were observed.



Conclusions: omPT properly supported by LDPI may actually be used for diagnostic purposes in ACM to Ni. This also applies to those symptomatic Ni-sensitive patients who do not have the typical aphthous stomatitis after 24-48 hours from Ni omPT and could risk to miss the diagnosis.

P.06.2

HOW MUCH DO CELIAC PATIENTS KNOW ABOUT GLUTEN FREE DIET?

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Background and aim: The only treatment for Celiac Disease at present is a strict lifelong gluten-free diet (GFD) which decreases disease-related mortality and has a role in preventing some of the long-term complications. Adherence to GFD has been the object of many studies but few have investigated its essential requisite: a thorough knowledge of gluten sources. Our aim was to measure celiac patients' knowledge of GFD and assess its determinants.

Material and methods: Between March and December 2014 a 20-item questionnaire was submitted to our celiac outpatients who were asked to indicate which foods or situations might be at risk of gluten intake. Half of the questions involved foods/situations that really expose patients at risk of consuming gluten while the other half concerned products that are gluten-free. A 20-point rating scale was built giving one point for each correct answer.

Results: 154 patients were enrolled. The mean score of the knowledge test was 14.3 ± 2.9 . Focusing on the incorrect responses, only 20.8% of them would have placed patients at risk of consuming gluten while the other 79.2% concerned foods or situations that were unnecessarily avoided by the patients. A statistically significant lower score was obtained by patients aged over 60 years ($p=0.0002$), without a degree or diploma ($p=0.0016$), non-members of the Italian Celiac Association ($p=0.043$), who never logged to the Association website ($p=0.0002$) and never ate outside ($p=0.0009$). Conversely no significant correlation was observed between gender, kind of

information on GFD received at the time of diagnosis and disease duration.

Conclusions: In our reality celiac patients seem to be well informed about GFD. Frequently they unnecessarily avoid foods that are safe because gluten free. We identified some categories of celiac patients at risk of less knowledge of GFD who deserve special training and attention.

P.06.3

FODMAPS FREE DIET: AN EFFECTIVE SOLUTION FOR SYMPTOMATIC COELIAC PATIENTS ON GLUTEN FREE DIET

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Background and aim: Recent studies have shown high efficacy of a FODMAPs free diet (FFD) in patients suffering from non-coeliac wheat sensitive (NCWS) and irritable bowel syndrome (IBS), but data on this kind of dietary approach in coeliac disease (CD) are still scarce. **Aim:** to establish the efficacy of FFD in symptomatic CD patients despite being on gluten free diet (GFD), also comparing this outcome with that of subjects affected by IBS.

Material and methods: From January 2016 to September 2016 we carried out an observational prospective study including all consecutive adult CD patients (Group A) who were symptomatic (abdominal pain, diarrhoea, bloating, constipation) despite performing a strict GFD. Also, we enrolled all consecutive adult IBS patients (Group B) referred to our general Ambulatory. We administered a personalized FFD and 2 questionnaires (IBS-SSS with a pain score from 0-minimum to 3-maximum, and SF-36 with 8 different domains) at the time of the first visit (T0), 1 month after (T1) and at 3 months (T3) from the beginning of FFD. Statistical analysis included ANOVA test with and without covariates adjustment. All results were considered significant with a $p < 0.05$.

Results: Finally, 66 patients were enrolled (Group A: 23 vs Group B: 43). All CD patients were on GFD from at least 1 year and showed negative EMA and anti-transglutaminases. No differences were noted in terms of age and gender ($P = NS$). When analyzing the IBS-SSS results, the symptomatic score dropped in both Groups after starting FFD (Group A: 2.04 at T0, 1.26 at T1 and 1.09 at T3 ($P < 0.01$); Group B: 2.35 at T0, 1.42 at T1 and 1.07 at T3 ($P < 0.01$)). However, no statistically significant differences were noted between the two Groups ($P = NS$). When analyzing the results from SF-36, no differences were noted between the two Groups, even though both CD and IBS population significantly improved their own status with the regards of the 8 domains of SF-36, both at T1 ($P < 0.01$) and at T3 ($P < 0.01$).

Conclusions: FFD leads to a significant improvement of gastrointestinal symptoms in CD patients who were persistently symptomatic despite GFD. GFD in association with FFD should be considered a first-line therapy CD this population.

P.06.4

ADULT CELIAC PATIENTS ADHERENCE TO A FOLLOW-UP PROGRAM IN THE FIRST YEAR OF GLUTEN-FREE DIET: A SINGLE CENTER STUDY

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Background and aim: Coeliac disease (CD) is an immune-mediated enteropathy. The treatment for CD is a gluten-free diet (GFD), which requires significant patient education, motivation and follow-up.

Usually celiac patients are not included in a standardized follow-up neither for the first year, nor for the subsequent years. Aim of this study was to assess the patients adherence to time-based protocol in the first year of GFD and if clinical characteristics and histological parameters could affect the adherence to follow-up.

Material and methods: 226 consecutive newly diagnosed outpatients with biopsy-proven atrophic CD, diagnosed between 2002 and 2014 (median age 33yrs, 16-72; 79% female), were included. Clinical data were collected using a structured clinical questionnaire, including life style items, gastrointestinal symptoms, biochemical values and histological score. Moreover each patient was instructed, by a specific sheet, to follow a follow-up program that included five items: after 3 months of GFD: 1) outpatient visit; after 1 year of GFD: 2) serologic testing for specific antibody assay and 3) nutritional parameters, 4) endoscopy with biopsy and 5) outpatient visit including a validated questionnaire for GFD adherence. Full adherence to the program was defined when patients underwent to all five controls. Adherence $>50\%$ and $<50\%$ were defined when the patients underwent at least three or four controls of five and at least one or two of five, respectively. Statistical analysis was performed using the Cochran-Armitage for trend in order to compare groups with different adherence to the follow-up program.

Results: 41.9% of patients had full adherence to the program, while 23.6% did not undergo any control. A first degree familiarity for CD positively affected the adherence to follow-up ($p=0.04$), and the presence of symptoms at diagnosis affected it negatively ($p=0.04$). Among patients with full adherence to the follow-up protocol 87.5% had adequate compliance to GFD, while only 40% of patients with $<50\%$ adherence to follow-up showed an adequate compliance to diet ($p=0.0001$).

Conclusions: This study showed that full adhesion to the follow-up program in the first year of GFD in adult patients occurred in only 41.9% of patients influencing positively the adherence to GFD. A scheduled follow-up program should be proposed in the adult celiac patients management.

P.06.5

HIGH SMAD7 IN REFRACTORY CELIAC DISEASE SUSTAINS INFLAMMATORY CYTOKINE RESPONSE

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Background and aim: Background. Refractory celiac disease (RCD) is a severe form of celiac disease (CD) resistant to gluten-free diet and associated with elevated risk of complications. Enhanced production of inflammatory cytokines is supposed to contribute to the RCD-associated lesions, even though it remains unclear if tissue destructive inflammatory response is also sustained by defects in counter-regulatory mechanisms. One such a mechanism could involve transforming growth factor (TGF) $\beta 1$, an immunosuppressive cytokine that negatively regulates inflammatory responses in the gut.

Aim. To determine whether RCD-related inflammation is marked by elevated levels of Smad7, an intracellular inhibitor of TGF- $\beta 1$ activity.

Material and methods: Methods. Smad7 expression was evaluated in duodenal biopsy samples of patients with RCD, patients with active CD (ACD), patients with inactive CD (ICD), and normal controls by western blotting, immunohistochemistry and RT-PCR. In biopsy samples taken from the same groups of patients and controls, TGF $\beta 1$ and phosphorylated Smad2/3 were evaluated by ELISA and immunohistochemistry respectively. Expression of proinflammatory cytokines was assessed in RCD biopsy samples cultured with Smad7 sense or antisense oligonucleotide by RT-PCR.

Results: Results. Smad7 protein, but not RNA, expression was increased in RCD samples compared to normal controls, while there was no difference between ACD or ICD and normal controls. In RCD duodenal mucosa, Smad7-positive cells were abundant in both the epithelial and lamina propria compartments. TGF β 1 protein content did not differ among groups. However, TGF β 1-associated Smad2/3 phosphorylation was less pronounced in RCD as compared to controls. Knockdown of Smad7 in RCD biopsy samples reduced RNA expression of interleukin (IL)-15, IL-6 and TNF α , all cytokines that are over-produced in RCD mucosa.

Conclusions: Conclusions. High Smad7 associates with defective TGF β 1 signalling in RCD, thus suggesting a novel mechanism by which the ongoing mucosal inflammation is sustained and perpetuated in this disorder.

P.06.6

SUBTYPES OF CHRONIC GASTRITIS IN PATIENTS WITH COELIAC DISEASE BEFORE AND AFTER GLUTEN-FREE DIET

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Background and aim: Chronic gastritis appears to be more common in patients with coeliac disease (CD). Aim of this study is to evaluate the frequency of lymphocytic gastritis (LG), chronic active gastritis (CAG) and chronic inactive gastritis (CIG) in a cohort of patients with CD, and their histological changes after treatment with a gluten-free diet.

Material and methods: A five-year prospective study including all consecutive patients with a new diagnosis of CD performed at our GI Unit, in the period between January 2010 and January 2015. All gastric and duodenal biopsy specimens at the time of the diagnosis of CD and at the first endoscopic control after 18-24 months on gluten free diet were analyzed. CD diagnosis was made in the presence of anti-tissue transglutaminases and/or anti-endomysial antibodies associated with specific alterations at histological evaluation of duodenal biopsies, according to the modified Marsh-Oberhuber classification. Gastric lesions were classified according to the Updated Sydney System. Giemsa staining was used for histological diagnosis of *Helicobacter pylori* infection and immunohistochemical staining for the diagnosis of LG, defined as a dense proliferation of intraepithelial lymphocytes (more than 25 lymphocytes per 100 epithelial cells). Anti-gastric parietal cell antibodies were assayed by enzyme-linked immunosorbent assay (ELISA). Demographic, clinical, and laboratory data were collected.

Results: 250 patients with CD were enrolled (191 F, 59 M, mean age 34 years at the diagnosis). At the time of CD diagnosis, histological examination showed normal gastric mucosa in 78 patients (31.2%), LG in 32 (12.8%), CAG in 74 (29.6%), and CIG in 66 (26.4%).

Out of 32 patients with LG, 20 (62.5%) were *H. pylori* negative and all of them showed an improvement of gastritis after gluten free diet.

Out of 74 patients with CAG, 30 (40.5%) were *H. pylori* negative and one third of them showed an improvement of gastritis after gluten free diet.

Out of 66 patients with CIG, 63 (95.4%) patients were *H. pylori* negative.

LG is significantly associated to histological improvement after gluten-free diet compared to other types of gastritis ($p = 0.0039$).

Conclusions: Subtypes of gastritis have different probability to be influenced by the gluten-free diet. LG is present in a significant number (13%) of CD patients and seems to improve as well as duodenal lesions after gluten free diet. Two thirds of LG are not associated with *H. pylori* infection. Both CAG and CIG are also

significantly associated with coeliac disease, despite less influenced by gluten free diet.

P.06.7

GLIADIN EFFECT ON THE OXIDATIVE BALANCE AND DNA DAMAGE IN CACO-2 CELL LINE

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Background and aim: Wheat has been identified as a key environmental factor in different human disorders (celiac disease, food allergies and non-celiac gluten sensitivity). As its components (gliadins) can induce different cellular and biological noxious alterations, present study was aimed at evaluating the gliadin effect on oxidative/reductive balance and assessing the possible oxidative/genotoxic damage.

Material and methods: Caco-2 cells were exposed for 12-24 h to increasing concentrations (from 250 to 1000 μ g/mL) of digested gliadin, then investigating : i) cytotoxicity (MTT test); ii) oxidative balance (DCFDA ROS evaluation); iii) DNA damage by means of comet assay (Alkaline and with ENDO III e Fpg enzymes) to identify single and double strand DNA breaks; iv) transglutaminase type 2 (TG2) activity in different cellular compartments (including nucleus, cytoskeleton, membranes and cytoplasm) with ELISA assay.

Results: Gliadin treatment did not significantly reduce cell viability after 24h at different concentration (250 μ g/mL-1000 μ g/mL). Conversely, gliadin induced a significant increase of ROS production after 12h of exposition at the concentrations of 500 μ g/mL and 1000 μ g/mL. Alkaline comet analysis revealed a DNA damage in all of the analyzed parameters (Tail length, Tail moment and % DNA), the damage being particularly evident at the dose of 1000 μ g/mL. Moreover, comet analysis with enzymes showed an increase in the delta tail moment at 1000 μ g/mL, consist of oxidative origin of the damage. After gliadin treatment, TG2 activity increased from 191% to 310% into the cytoskeleton and from 117% to 153% into the nucleus. The analysis of cellular compartments evidenced a TG2 translocation from the cytoplasm to the nucleus and cytoskeleton suggesting a proapoptotic process.

Conclusions: Present findings demonstrated with a gliadin-induced genotoxic damage associated to both an oxidative imbalance and an apoptotic process.

P.06.8

SERUM 25-HYDROXYCHOLECALCIFEROL LEVELS AT CELIAC DISEASE DIAGNOSIS PREDICT BONE MINERAL DENSITY RECOVERY AFTER GLUTEN EXCLUSION

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Background and aim: Celiac disease (CD) patients at presentation variably show reduced bone mineral density (BMD) and altered bone-related serology, including serum 25-hydroxycholecalciferol (25[OH]VitD). Gluten-free diet (GFD) has been shown to promote repair in children and to a smaller extent in adults. However, complete bone mineral recovery is uncertain and predictive markers are lacking.

Aims of this study were to evaluate the prevalence of reduced BMD (as Z-score) at CD presentation, assess BMD recovery and identify potential predictors under GFD.

Material and methods: Adult anti-tTG positive, biopsy proven CD patients. BMD scores were obtained by Dual Energy X-Ray Absorptiometry.

Results: We evaluated 161 celiac adults (mean age=39.2ys, F/M=5:1) at diagnosis and after adequate GFD (mean duration 7.4±6.8ys). Histology was graded according to the Corazza-Villanacci classification (A 10.6%, B 50.9%, C 38.5%). Mean anti-tTG levels at onset were 73.3±35.4U/dl (mean±SD), while at inclusion 4.4±2.3U/dl. BMD Z-scores were lower at diagnosis (-1.6±1.09 vs -0.9±0.89, p<0.001), showing no correlation with sex but moderately with age (r=-0.221, p=0.04). Prevalence of normal vs low BMD (< -1.0 DS) at onset and inclusion was 18.6% vs 81.4%, and 27% vs 73%, respectively. Prevalence of severely reduced BMD (< -2.5 DS) was 14.8% vs 1.2% after GFD. Mean 25[OH]VitD levels before GFD were 17.07±6.44 vs 26.71±6.74ng/dl after (p<0.001). Prevalence of deficit and insufficiency were 20.8%/66.7% vs 4.9%/62.3% after GFD, respectively. BMD at diagnosis did not correlate to outcome (r=-0.41, p=0.581). 25[OH]VitD levels showed no correlation to BMD at onset. However, they correlated to outcome BMD (r=0.419, p=0.041). In particular, a cut-off=20ng/dl was significantly associated to restored BMD values (-1.12±0.94 vs -0.24±0.85, p=0.033). Overall, GFD duration to achieve significant BMD increase from onset was 48 months (-1.46±1.05 vs -1.04±0.85, p=0.029).

Conclusions: Reduced BMD is common in adult celiacs at diagnosis and generally responds slowly to GFD, taking up to 4ys before significantly improving. Initial severity of BMD loss does not seem to impair recovery. Serum 25[OH]VitD at onset positively correlates to outcome BMD; a cut-off=20ng/dl in our sample predicted a full BMD recovery. Further studies are needed to confirm this potential predictor of outcome under GFD.

P.06.9

VILLOUS ATROPHY WITHOUT COELIAC ANTIBODIES

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Background and aim: Small bowel villous atrophy (VA) is mainly related to coeliac disease (CD), whose diagnosis requires positive endomysial/tissue transglutaminase antibodies while on a gluten-containing diet (GCD) [1]. VA without CD antibodies can be due to IgA deficiency, common variable immune-deficiency (CVID), autoimmune enteropathy, small bowel malignancies, medication-related enteropathies, and seronegative CD [2]. Epidemiology of these different forms of VA without coeliac antibodies are little known. Our aim was, therefore, to study causes and mortality of these rare enteropathies in patients directly diagnosed in our centre in the last 15 years.

Material and methods: We retrospectively collected age at diagnosis, sex, clinical and laboratory data of all the adult patients with duodenal biopsies showing VA while on a GCD.

Results: Between September 1999 and June 2015 we found 274 patients with VA. 260 of them were affected by CD (82 M, mean age at diagnosis 35±12 years, 116 with classical presentation) while 14 had an EMA negative VA (12 M, mean age 49±16, 10 with classical presentation). More precisely, 5 of these 14 patients were affected by CVID, 3 by dermatitis herpetiformis, 2 IgA deficiency, 2 abdominal lymphomas, 1 olmesartan enteropathy, 1 seronegative CD. Four of the 260 coeliac patients developed complications (1 refractory CD, 1 B cell lymphoma, 1 small bowel carcinoma, 1 enteropathy associated T cell lymphoma), 4 died (3 unrelated causes and 1 enteropathy-

associated T cell lymphoma), and 18 were lost to follow-up. In the EMA negative VA group 4/14 patients died (2 lymphomas, 1 B lymphoma in CVID, 1 sepsis), and 1 was lost to follow-up.

Conclusions: Our preliminary results show that patients with VA and negative coeliac serology are very rare. However, these forms of VA recognize a specific etiology that can be diagnosed directly and not with a diagnosis of exclusion. These patients are affected by a very high mortality.

References:

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P.06.10

USE OF VIDEOCAPSULE ENTEROSCOPY IN COMPLICATED CELIAC DISEASE: A META-ANALYSIS

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Background and aim: Video capsule enteroscopy (VCE) is considered the gold standard for detection of small bowel (SB) tumors originating from the mucosal layer. These kind of malignancies (especially T cell lymphoma and adenocarcinoma) are the most fearful complications of celiac disease (CD) with an increased relative risk ranging from 2 to 300, even if data from the literature are controversial.

Aim of this meta-analysis was to obtain a summary value by pooling data of primary studies that investigated the diagnostic yield of VCE for SB malignancy and/or of preneoplastic conditions.

Material and methods: An extensive search of studies estimating the accuracy (diagnostic yield) of VCE in predicting the presence of a SB tumors or ulcerative jejunoileitis (as pre-cancer condition) was performed in the principal databases. Two investigators independently conducted the search and extraction of data. Data from eligible studies were collected and analyzed. The DerSimonian and Laird random effects method was used to pool the log transformed proportions of patients with the events. Three meta-analyses were performed considering the following events: jejunoileitis alone, neoplasia alone and the composite of the two.

Results: Out of the 97 titles originally generated by the literature search, 11 studies, 6 prospective and 5 retrospective, including 461 patients met the inclusion criteria and were eligible for the metanalysis. In all studies VCE was performed to assess the presence of intestinal abnormalities.

Overall, 14 patients showed a SB malignancy and 13 an ulcerative jejunoileitis. The summary diagnostic yields of VCE were 4.4% (95% CI 2.7-7.0), 4.3% (95% CI 2.2. -8.2) and 7.3% (95% CI 4.2 -12.3%) for neoplasia, ulcerative jejunoileitis and neoplasia plus ulcerative jejunoileitis, respectively.

Conclusions: VCE is a powerful and efficient diagnostic tool for SB malignancies' detection in CD.

P.06.11

SEVERE WHEAT ALLERGY AND CELIAC DISEASE IN THE SAME PATIENT: A DANGEROUS COEXISTENCE

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Background and aim: Dietary intake of cereals can cause two distinct immunologically mediated diseases with gastrointestinal manifestations, celiac disease, and immunoglobulin (Ig)E mediated food allergy. The pathogenic mechanisms underlying these diseases are different and the coexistence of both diseases seems to be rare.

Material and methods: The biopsy proven celiac patient undergone gluten-free diet (GFD) for 5 years, with moderate benefits. Two years ago she presented anaphylaxis, after eating a salty wheat pancake, that was granted to be gluten-free. Subsequently, she presented Food Dependent Exercise Induced Anaphylaxis (FDEIA), commonly found in adults, diagnosed by an exercise challenge test following wheat ingestion: the most severe response is attributed to one ω gliadin that is a relative of the protein that causes celiac disease. We performed skin prick tests (mm) that were positive for *Parietaria judaica* (20), grass pollen (5), peach containing uniquely lipid transfer protein (Pru p3, 30 mg/mL; ALK-Abelló, Denmark) (5), kiwi (5), wheat (10), zucchini (5), corn (5), rye (10). Prick-prick tests were positive for wheat flour (5), crude corn (7) [3].

Results: Blood cell count, biochemistry, and Ig determinations were normal. Total serum IgE was 215 kU/L. Values for specific IgE (Phadia-CAP, Uppsala, Sweden) in kUA/L were as follows: wheat gluten (16.4), rye (11.3), barley (11.0), corn (0.46), rPru p3 (0.38), Phl p2 (0.58), wheat (27.5). rTri a 19 ω -5 gliadin was found negative, rTri a 14 (Ltp of wheat) 19.3 was positive.

Despite the daily administration of high-dose of inhaled combined fluticasone/salmeterol (2000/200 Ig) and montelukast tablet (10 mg), the patient suffered constantly from respiratory symptoms. The patient has allergy to pollen and dust mites. Because of celiac disease has not been carried food challenge either at rest or after exercise. She is still following a dietary regime for celiac patients. We gradually reduced the restriction on wheat consumption for gluten-free products.

Conclusions: In both cereal allergy and celiac disease (CD), the reaction to gluten is mediated by T-cell activation in the gastrointestinal mucosa. However, in cereal allergy it is the cross-linking of immunoglobulin (Ig)E by repeat sequences in gluten peptides (for example, serine-glutamine-glutamine -glutamine-(glutamine-) proline-proline-phenylalanine) that triggers the release of chemical mediators, such as histamine, from basophils and mast cells [1]. In contrast, CD is an autoimmune disorder, as demonstrated by specific serologic autoantibodies. anti TG and EMA. The diagnosis of IgE-mediated allergy is based on the clinical history and presence of IgE-antibodies (IgE-Ab) in skin or blood, and the result of an oral food challenge. In our knowledge, the coexistence in the same patient of both these wheat related disease is very rare.

P.07 IBD 1

P.07.1

GUT MICROBIOTA MOLECULAR SPECTRUM IN HEALTHY CONTROLS, DIVERTICULAR DISEASE, IBS AND IBD PATIENTS: TIME FOR MICROBIAL MARKER OF GASTROINTESTINAL DISORDERS?

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Background and aim: Increasing evidences have emerged on the analysis of bacterial species making up the gastrointestinal microbiota. However few data exist on differences in gut microbiota composition in GI diseases, such as IBD, IBS and diverticular disease compared to healthy controls.

Material and methods: Aim of our study was to evaluate the differences in gut microbiota composition between IBD, IBS and

diverticular disease (DD) patients. 10 Crohn's Disease (CD), 5 Ulcerative Colitis (UC), 4 DD, 3 IBS patients, and 8 controls (CD) were enrolled and fecal samples collected from each. Microbiota composition was assessed by a metagenomic gene-targeted approach (16S rRNA) using the Roche 454 GS Junior, following DNA isolation from stool samples stored at -80 °C. Data were analyzed in QIIME. Individual species richness was estimated using Chao1 alpha-diversity index. We also explored the differential relative abundance of several taxa of interest, selected according to literature.

Results: Bacteria amplicons were detected in all samples. Prevalent classes of bacteria were: Bacteroidia (min 13,06% - max 91,55%), Firmicutes (min 7,48% - max 86,10%) and Proteobacteria (min 0,48% - max 46,48%). Fusobacteria were found only in CD and DD patients (min 0,67% - max 50,71%). IBD microbiota composition differed significantly compared to all other. In particular, UC patients showed a reduced concentration in Bacteroidetes and an increased presence of Firmicutes vs. CT, DD and IBS. On the other side, Bacteroidetes and Firmicutes composition varied among CD patients, being increased or reduced when compared to the other groups. Proteobacteria were increased in all diseased group compared to CT, being more represented in CD and IBS-D. Moreover, Actinobacteria were increased in IBD and DD vs. IBS and CT. The most represented species in IBD and DD vs. other groups was *Collinsella aerofaciens*. Rikenellaceae were suppressed in IBD patients, as well as *Fecalibacterium prausnitzii*. *Akkermansia muciniphila* was present only in IBS patients. Enterobacteriaceae were increased only in CD patients vs. other groups. Finally, while Chao1 score was similar between CT, IBS and DD, it was deeply reduced in IBD patients.

Conclusions: These preliminary data show that starting from microbiota, GI disease can be a continuous pathological spectrum where IBD display one extreme in gut microbiota composition while controls display the other. Furthermore, GI diseases share some microbial patterns, sharing perhaps common pathophysiological pathways. New analyses are needed to confirm this hypothesis and evaluate therapeutic implications.

P.07.2

BEYOND MUCOSAL HEALING: TRANSMURAL AND EXTRAMURAL HEALING AFTER ONE-YEAR ANTI-TNFA THERAPY IN CROHN'S DISEASE

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Background and aim: Crohn's disease (CD) is characterized by transmural (full-thickness) inflammation, frequently with extra-mural complications beyond to the mesentery and adjacent organs. The capability of anti-TNF α therapies in achieving and maintaining both clinical remission and mucosal healing (MH) has repeatedly been described, while only one study was designed to assess prospectively their role in transmural healing. Aim of this study was to analyze transmural healing (TH) in consecutive CD patients after a 1-year treatment with anti-TNF α and to correlate TH with endoscopic and clinical activity as well as biological markers.

Material and methods: 13 patients with moderate to severe ileocolic CD were enrolled. All underwent ileocolonoscopy and MRI-enterography before and after 1-year treatment with anti-TNF α ; clinical remission was defined as CDAI<150, response as a 70-point reduction from baseline. CRP and fecal calprotectin (FC) (positivity cut-off respectively >0,50 mg/dl and >150 μ g/gr) were also measured. Endoscopic activity was assessed by SES-CD, range 0-40, with mucosal healing defined as score <3 and response as a 50% decrease

from baseline. MRI activity was measured by MRI-enterography global score (MEGS), range 0-296, a score which takes into account transmural and extramural features, with active disease defined as a score ≥ 1 , and response as above.

Results: We enrolled 6M/7F, mean age 36 ± 12 ys, mean disease duration 7 ± 5 ys. According to the Montreal classification the phenotype was L1 in 31%, L2 in 7% and L3 in 62%; the behaviour was B1 in 8%, B2 in 69% and B3 in 23%. Resectional surgery related to CD was observed in 15%. Signs of mesenteric inflammation were only lymph node enlargement or comb-sign. 3 patients were treated with IFX, 10 with ADA (all naive to anti TNF α). Mean SES-CD, MEGS, CDAI, CRP and FC values significantly decreased at one year (table). 53% had clinical remission, 77% clinical response. Biological remission was achieved in 69% and 53% according to FC and CRP respectively. MH was achieved 38%, endoscopic response in 46%. Normalization of MRI finding was achieved in 15%, 31% had transmural improvement; before therapy 85% showed at least one extramural sign of inflammation, after 1 year at least one sign persisted in 54% ($p=ns$). MEGS score after one year didn't change significantly between patients with endoscopic remission/improvement and those without ($p=0.7$). CRP positivity at one year was correlated with presence of extramural involvement only ($p=0.02$) and mean CRP level were higher (2.3 ± 2.4 vs 0.30 ± 0.50 mg/dl) in the presence of comb-sign ($p=0.03$).

	Baseline	After one year	p value
SES-CD	10 ± 4	6 ± 4	$p=0.002$
MEGS	29 ± 13	17 ± 12	$p=0.001$
Transmural	22 ± 11	12 ± 9	$p=0.001$
Extramural	85% (at least one sign)	54% (at least one sign)	$p=ns$
CDAI	227 ± 88	147 ± 103	$p=0.03$
PCR	3.7 ± 4.1	1.2 ± 1.8	$p=0.03$
FC	388 ± 277	177 ± 148	$p=0.03$

Conclusions: Biological therapy is effective in inducing clinical, biochemical and endoscopic remission of CD while transmural inflammation may persist longer than one year. Transmural, mainly extramural, healing probably needs longer therapy to be achieved, and his activity was unrelated to endoscopic improvement while closely relates to CRP positivity and levels.

P.07.3

MAINTENANCE OF CLINICAL REMISSION IN IBD PATIENTS AFTER DISCONTINUATION OF ANTI-TNF AGENTS, AN ITALIAN EXPERIENCE

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Background and aim: Despite the long experience in the treatment of Inflammatory Bowel Disease (IBD) with antiTNF agents, we still don't know whether and when stopping the biological treatment in patients that are in clinical remission. Aim of our study was to assess the risk of relapse in an Italian cohort of IBD patients who discontinued antiTNF therapy because of clinical benefit and to evaluate if the mucosa healing is associated to a better outcome.

Material and methods: Consecutive patients followed in three Italian referral center for IBD, affected by Crohn Disease (CD) or Ulcerative Colitis (UC), and who received an antiTNF agent, infliximab (IFX) or adalimumab (ADA) for a period ≥ 12 months and discontinued the drug because in clinical remission, were included. All patients had an endoscopy performed before and after the treatment with antiTNF. Demographic, clinical and endoscopic characteristics of

patients were collected. Relapse was defined as need for rescue therapy (corticosteroids or new cycle of antiTNF) or surgery.

Results: 126 patients were included, 99 were affected by CD (78.6%) and 27 by UC (21.4%). Median age was 35 years old (range 15-78yrs). 56% were male. 29.4% of patients underwent surgery in the past. 108 patients received IFX (85.7%) and 18 ADA (14.3%). A concomitant treatment with immunosuppressant therapy (ISS) was seen in 65.9% of patients. Mucosal healing was achieved in 77 patients (61.6%). Kaplan-Meier curves showed a cumulative probability of a disease free course at 1 year of 78%. After 2 years from stopping antiTNF 64% of patients were on remission. Probability of relapse after 5 years was 54%. In the univariate analysis, the following variables resulted related to the probability of maintenance clinical remission: gender (male, 0.001), age (≥ 35 ys, 0.05), and concomitant immunosuppression (0.02). Mucosa healing was not associated to a better outcome.

Conclusions: In our cohort, composed by IBD patients treated with antiTNF at least for 1 year, who discontinued the treatment because in clinical remission, the probability to maintenance clinical benefit at 2 years was 64%. Risk of relapse was more frequent in the first 2 years from withdrawal. healing was not associated to a better outcome in our cohort. Prospective studies are needed to identify patients with a low risk to relapse.

P.07.4

HEMOGLOBIN AND FERRITIN VALUES ARE ASSOCIATED WITH INCREASED RATE OF MUCOSAL HEALING IN PATIENTS WITH CROHN'S DISEASE TREATED WITH ANTI-TNF ALPHA

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Background and aim: In the era of biologics, mucosal healing (MH) has become a relevant treatment goal in inflammatory bowel disease (IBD), since it is associated with a lower rate of relapse, hospitalization and surgery. In this study, we aimed to evaluate rate and predictive factors of MH in a homogeneous cohort of Sicilian patients with Crohn's disease (CD) treated with anti-TNF agents.

Material and methods: We report data of 43 consecutive patients with Crohn's disease (CD), treated with anti-TNF alpha at our IBD clinic from January 2012 to September 2015. Clinical-demographic characteristics (sex, age, smoking habits, familial predisposition, disease location and behavior (Montreal), activity (Harvey-Bradshaw Index [HBI]), indications to biologic therapy, concomitant medications, and serum biomarkers (CRP, haemoglobin [Hb], ferritin) were registered on a dedicated database. Each patient underwent ileocolonoscopy at the beginning of treatment and after 12 months. Simple Endoscopic Score for Crohn's Disease (SES-CD) was used to assess endoscopic activity. Mucosal healing was defined as a SES-CD score between 0 and 3.

Results: Mean duration of CD of the 43 patients (22 males; mean age 43.9 ± 14.2 years) was 126 ± 77 months. Thirty-two patient were treated with adalimumab (74%) and 11 with infliximab (26%). Mucosal healing was observed in 25 patients (58%). Infliximab achieved a higher, though not significant, endoscopic response rate as compared to adalimumab (88% vs 50% $p=0.065$). Clinical remission (HBI < 5) was obtained in all patients with MH and in 13 of 18 patients that didn't get it (100% vs 72%, $p=0.005$). No difference concerning duration, extent, behavior was detected. Mean Hb values at baseline (13.3 ± 1.2 ; $p=0.023$) and after 12 months (13.7 ± 1.2 ; $p=0.05$) were higher in patients who obtained MH. Ferritin values > 30 ng/ml was significantly more frequent in patients with MH, both at baseline ($p=0.030$) and after 12 months ($p=0.017$). No significant difference as far as concerns CRP was found.

Conclusions: As previously reported, biologics induce endoscopic response at 12 months in more than 50% of patients with CD. Disease features did not predict MH. Hemoglobin and ferritin were the only laboratory parameters significantly related to MH, while no significant difference was observed for CRP. Our results could suggest to use these parameters to drive timing of endoscopic reassessment in patients with CD on biological therapy.

P.07.5

ON THE ORIGIN OF CRP IN CROHN'S DISEASE: ROLE OF THE EXTRAMURAL COMPONENT

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Background and aim: Due to the full thickness involvement of the bowel wall or complications, Crohn's disease (CD) evaluation is the result of an integration of endoscopy (the gold standard) with clinical, laboratory and radiological data. The role of MRI, which excels in identifying extramural signs of inflammation, is still unclear in CD follow-up. Moreover it is still debated whether CRP serum levels increase is due to mucosal or mural/extramural inflammation, not only via liver production but also from extrahepatic sources such as of the mesenteric fat hypertrophy (MFH), a CD common feature, which assessed by CT was found to correlate with plasma CRP levels in CD patients. Aim was to correlate enteric and extraenteric inflammatory MRI findings with endoscopic severity and CRP in a group of CD patients.

Material and methods: 52 consecutive patients with endoscopically proven CD underwent MRI enterography for the staging at diagnosis or activity assessment (68/32%). Endoscopic activity was scored through the SES-CD (range 0-40) with active mild, moderate and severe disease defined as 4-10, 11-19 and >20 respectively. MRI activity was scored through the MEGS score (range 0-296), which integrates both mural and extramural items, namely lymph node, fistula, abscess and comb sign, with active disease defined as ≥ 1 score. For all participants CDAI was completed and CRP and fecal calprotectin (FC) were measured (positivity cut-off respectively >0,50mg/dl and >150µg/gr). MFH was qualitatively defined a bowel loop separation ≥ 3 cm.

	SES-CD	CDAI	CRP	FC
SES-CD		r=0,51 p<0.001	r=0,39 p<0.005	r=0.35 p<0.01
MEGS	r=0,42 p<0.001	r=0,59 p<0.001	r=0,43 p<0.005	r=0.27 p<0.01

Results: We enrolled 20M/32F, mean age 38±15 ys, mean CD duration 5±5 ys. SES-CD and MEGS correlated well between them and with clinical and biological activity (table). According to SES-CD 62% of patients had mild, 19% moderate and 5% severe disease. Increasing severity at endoscopy was significantly correlated with traslmural/extramural involvement, only with CRP positivity (p=0.007). MRI did not show ability to distinguish endoscopic severity (p=0.14), but revealed traslmural/extramural signs of inflammation in 60% of patients in remission, 84% mild and 100% with moderate and severe disease, mostly with CRP positivity. Moreover CRP positivity was associated with the presence of extraintestinal (p=0.006; lymph nodes p=0.009, comb sign p=0.001 and abscess p=0.005), not of mural involvement (p=0.4). Mean CRP levels increased according to the number of extramural signs of inflammation (from absence to 4

signs p=0.01). Patients with MFH showed higher levels of CRP than those without (4,2±4 mg/dl vs 1,9±3,2 p=0.005).

Conclusions: Transmural inflammation, which is more frequent in severe disease, may still be present regardless of endoscopic activity. Positive CRP is significantly correlated to extramural activity in CD patients, thus suggesting the need of MRI for the staging of the disease independently from endoscopic severity. Moreover these data suggest that mesenteric fat may contribute to the increased CRP production

P.07.6

ROLE OF DIFFUSION-WEIGHTED IMAGING (DWI) IN MRI-ENTEROGRAPHY FOR THE EVALUATION OF SURGICAL RISK IN PATIENTS WITH CROHN'S DISEASE

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Background and aim: In Crohn's disease (CD) it's useful to discriminate inflammatory from fibrotic lesions. MRI-Diffusion Weighted Imaging (DWI) is able to identify active inflammation in most pathological tissues. **Aim:** To define the role of DWI sequences in the evaluation of the risk of surgery in patients with CD.

Material and methods: From March 2011 to June 2013 we performed an observational prospective study including all consecutive CD patients with active disease undergone a MRI-enterography. MRI study included: measurement of bowel wall thickness (BWT), CD extension, enhancement pattern, pre-stenotic dilation, presence of oedema and/or comb-sign, presence of fistulas/abscesses, (T2 weighted, T1-weighted gadolinium-based contrast material uptake). Furthermore, all patients were studied by DWI sequences defining: visual analysis of iperintensity corresponding to a qualitative value of reduction of diffusion on a scale (0-4), quantitative analysis of Apparent Diffusion Coefficient (ADC) maps (max, min and medium). The medical/surgical treatments during the following 12 months were also recorded. Statistical analysis was performed dividing all patients in 2 groups (operated vs not operated) using T-student test for continue variables and X-square test for dichotomic variables. To identify the variables associated to surgical risk, we performed a logistic multiple regression expressing the risk in terms of Odd Ratio. A p value lower of 0.05 was considered significant. Finally, the diagnostic accuracy was tested by a ROC curve.

Results: 110 patients (61M/49F) were enrolled in our study (median age 37,6 years) and 127 bowel segments resulted pathologic at MRI. 26 patients (23,6%) and 31 segments were resected during the follow-up period. At all pathological segments, the iperintensity in DWI sequences, the reduction of ADC max, ADC medium and the presence of fistulas/abscesses were significantly associated with a subsequent surgical intervention (p<0.05). In particular, the presence of CD complication was the variable with the highest risk of surgery (p=0.08; OR 3.9; 95% CI 1.4-10.7). When excluding the patients with complications, we reported a significant correlation of DWI iper-intensity, ADC max and medium with surgical intervention. Interestingly, the reduction of ADC medium was the variable with the highest risk of surgery (p=0,03; OR 2.0; 95% CI 0,79-0,92). The cut-off value for discriminating patients at risk of surgery was 1,081x10⁻³ mm²/s (sensitivity 55.6%, specificity 70.3%, PPV 33.3%, NPV 85%).

Conclusions: The presence of fistulas/abscesses remains the variable most associated with surgical risk in CD. In not complicated CD, the evaluation of DWI sequences at MRI-Enterography, and in particular the reduction of ADC medium, correlates with the need of surgery. High value of ADC medium shows high NPV for surgery in CD patients.

P.07.7**CROHN'S DISEASE IS A REAL TIME SENSITIVE EVOLUTIVE PATHOLOGY BASED ON LÉMANN INDEX? PRELIMINARY DATA FROM A TERTIARY PEDIATRIC IBD CENTER**

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Background and aim: Crohn's disease (CD) is a chronic and progressive condition that, due to disease complication, leads to surgical resection in the majority of cases. Recently, a panel of expert developed the Lémann Index (LI), a new tool aimed to assess the progressive bowel damage due to disease course. The LI takes into account disease extension and the presence of stenotic and penetrating lesions, providing a quantitative score of disease which seems to increase over time in adult patients. Data on pediatric population in this regard are lacking. The aim of our investigation was to measure the LI in a pediatric cohort at diagnosis and the trend of LI during the time.

Material and methods: We retrospectively selected 48 consecutive pediatric patients who were firstly diagnosed in our hospital by abdominal Magnetic Resonance Imaging, Colonoscopy and upper GI endoscopy and in case of perianal disease, a pelvic MRI. Patients were included in case of age between 6 to 17 years. We evaluated LI and deltaLI from the diagnosis to the last pediatric outpatient visit or to the transition to adult outpatient.

Results: We included in our investigation a total of 48 CD pediatric patients (21 male, median age of 18 years, range 11-34, median age of diagnosis 13 years, range 7-17) who were followed-up for a median of 42 months (range 3-117). Among them, 35 (72.9%) patients had a stable LI during the follow up, whereas 13 (23.1%) increased their LI during the time. There was no statistical significant difference between median LI at beginning and end of follow-up (1.8, range 0.3-10 vs 1.8, range 0.3-7.6. P=0.51). Moreover, analyzing data from patients who utilized anti-TNF therapies, we found out no significant difference among LI at beginning and end of follow-up (3, range 0.3-10 vs 2.3, range 0.8-7.6. P=0.86).

Conclusions: In contrast to adult population, our data suggest that LI in pediatric population is not a useful tool to assess disease progression. Moreover, independently from therapy used, we observed that LI remain stable in the majority of our pediatric CD patients during a long-term follow up.

P.07.8**IL-33/ST2 AXIS MODULATES EPITHELIAL REPAIR AND GUT MUCOSAL WOUND HEALING IN DSS-COLITIC MICE**

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Background and aim: Increasing evidence confirms that IL-33 and ST2 are important factors in the pathogenesis of IBD. The aim was to characterize the precise role of the IL-33/ST2 axis following acute epithelial injury and mucosal repair in DSS-induced colitic mice.

Material and methods: 3% DSS was administered for 5d to C57/BL6 wild-type (WT), IL-33 KO and ST2 KO mice. DSS was then replaced with drinking water for 2 wks (recovery period). Another group of WT mice received DSS for 5d and IL-33 (33ug/kg, i.p.) or vehicle (VEH) every other day during the recovery period. Mice were sacrificed either after DSS challenge or after 1 or 2 wks of recovery. Body weight, occult blood test, and stool consistency were measured

daily to calculate DAI, and endoscopic and histological evaluation of colons were performed. IHC, qPCR and Western blots were done on full-thickness colons for IL-33 and ST2 localization, mRNA expression, and evaluation of protein isoforms, respectively.

Results: DSS administered to WT mice resulted in increased body weight loss and DAI. More severe colitis was observed following DSS+1wk recovery vs. after 5d of DSS, which decreased after DSS+2wks recovery. IL-33 mRNA transcripts were elevated after DSS, and even more so following DSS+recovery vs. CT, but similar to CT after DSS+2wks recovery. ST2 mRNA expression was also increased after DSS+recovery vs. CT, while no difference was found between 5d of DSS challenge and CT and after DSS+2wks recovery. Full-length, bioactive IL33, ST2L and sST2 were expressed in all experimental groups; the cleaved, less active form of IL33 was increased in only DSS exposed mice vs. CT. IHC showed intense IL-33 and ST2 staining within the inflamed and ulcerated mucosa of DSS-treated mice. ST2 staining was more evident during the recovery phase following DSS, notably localized to subepithelial myofibroblasts in close proximity to areas of re-epithelialization. Both IL-33 and ST2 KO mice showed increased colonic inflammation after 2 wks recovery compared to after 5d DSS and vs also WT. IL-33 treatment of WT mice resulted in increased body weight, reduced DAI, and decreased colonic inflammation after 2 wks recovery vs. VEH.

Conclusions: Our results suggest that activation of the IL-33/ST2 axis promotes epithelial repair and mucosal healing following acute epithelial injury during DSS-induced colitis.

P.07.9**EFFECTIVENESS OF PSYCHOLOGICAL SUPPORT ON QUALITY OF LIFE IN IBD PATIENTS**

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Background and aim: Inflammatory bowel diseases (IBD), with their typical chronic relapsing course, often induce both a constant basal stress, and periods of acute stress in the case of an exacerbation, a therapeutic change or surgery.

This study aims to assess whether a psychological treatment can help patients in facing the disease better, reducing anxiety, improving the management of emotions, stress and quality of life.

We proposed to the patients a group of psychological support, designed to promote a better management of the disease and the emotional states associated.

Material and methods: We enrolled 43 consecutive patients with Ulcerative Colitis and Crohn's Disease, with a mild / moderate activity according to the Mayo score or Simple Index respectively. They participated in the psychological support groups: each group was made up of 5-6 persons, and consisted in a meeting a week for a 6 week period. Twenty-six IBD patients with similar disease characteristics, not participating in the groups, were enrolled as control group.

All the 69 patients underwent a psychological assessment at the first visit and after 6 weeks (duration time of the psychological treatment), with self-administered tests (CES-D; STAI-Y, TAS-20; BRIEF COPE; BRIEF-IPQ; IBDQ), validated for Italians samples and customarily used. We made a comparison of the average values of the parameters at week 0 and at week 6 both in the treated group than in the control group.

Statistical analysis was performed by using the Anderson-Darling test, Bartlett test, the Fisher Exact Test for nominal variables, the

Paired Sample T-Test and the analysis of covariance (ANCOVA) when appropriate.

Results: In the treatment group, we observed a significant reduction of situation and basic attitude anxiety (STAI-Y; $t=-2.69$ $p=0.01$ for the status anxiety and $t=-3.87$ $p=0.0004$ for trait anxiety), an improvement in the ability to identify emotions (DIS subscale of the TAS-20; $t=-3.47$ $p=0.001$) and to address the disease by decreasing its denial (denial of stairs BRIEF-COPE $t = -1.8$ $p=0.07$). Moreover, the psychological support provided evidence to improve the management of less negative situation of the disease (positive subscale restructuring BRIEF-COPE $t=3.26$ $p=0.002$) (subscale emotional functioning IBDQ) which is reflected in a significant increase in quality of life (measured with the IBDQ $t=2.14$ $p=0.039$) and a decrease in the perception of negative emotions due to illness (BRIEF-IPQ $t=-1.72$ $p=0.09$).

No significant change was found in control group. As far as quality of life is concerned, IBDQ showed an increase in the treatment group, significantly higher if compared to control group (7.91 vs -3.2) ($t=2.14$ $p=0.039$).

Conclusions: The psychological treatment proved to be successful in reducing anxiety and depression as well as improving quality of life in IBD patients. This kind of psychological support is easy to use, even in the hospital setting, and can also be defined cheap.

P.07.10

FAECAL-ASSOCIATED AND MUCOSAL-ASSOCIATED MICROBIOTA IN INFLAMMATORY BOWEL DISEASE PATIENTS AND HEALTHY SUBJECTS: PRELIMINARY EVIDENCE

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Background and aim: Over the last few years, growing evidence has supported the potential role of intestinal microbiota in the pathophysiology and symptom generation of several gastrointestinal (GI) diseases, such as Inflammatory Bowel Disease (IBD). The existing literature on the intestinal microbiota in IBD does not reveal uniform alterations in microbiota composition among all patients. Several studies have seen abnormal GI microbiotas; however, the relevance of such studies has been hampered by the fact that the analyses were focused only on the faecal microbiota, which differs substantially from that adhering to the gut mucosa. In the present study, we evaluated the microbiota composition in intestinal mucosal biopsies and faecal samples of IBD patients and control subjects (CTRLs) in a case-control study exploited by 16S rRNA targeted metagenomics-based approach (phylotyping, PH).

Material and methods: Faecal specimens were collected from 12 IBD patients and from 11 healthy subjects, undergone to colonoscopy for screening. Colonic mucosal specimens were obtained during colonoscopy from the proximal descending colon. All patients filled out a standardized questionnaire for the GI symptoms and the quality of life. All the patients were enrolled only after signing the informed consent. PH was assessed by pyrosequencing as follows. Genomic DNA was isolated from the entire set of samples using the QIAamp DNA Stool Mini Kit (Qiagen, Germany). The V1-V3 region of 16S rRNA locus was amplified on a 454-Junior Genome Sequencer (Roche 454 Life Sciences, Branford, USA). Reads were analyzed by Quantitative Insights into Microbial Ecology (QIIME, v.1.8.0), grouped into operational taxonomic units (OTUs) at a sequence similarity level of 97% by PyNAST for taxonomic assignment, and aligned by UCLUST for OTUs matching against Greengenes database (v. 13.8).

Results: In adult IBD patients colonic biopsies showed a statistically significant increase of Proteobacteria and decrease of Firmicutes, compared to CTRLs, with main OTUs in IBDs being Enterobacteriaceae and Clostridiales compared to Ruminococcaceae, Prevotella, Bacteroides and Faecalibacterium prausnitzii in CTRLs ($p<0.05$). The analysis of IBD faecal samples reproduced these data except for a significant reduction of Clostridiales in IBD faecal samples, compared to CTRLs.

Conclusions: Our data suggest the potential of microbiota profiling in the description of disease-related microbiota enterogradient.

P.07.11

ASSOCIATION BETWEEN INFLAMMATORY BOWEL DISEASE AND VITAMIN D DEFICIENCY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and aim: Vitamin D plays a role in several immune-mediated diseases, but its association with inflammatory bowel disease (IBD) is unclear. We conducted a systematic review and meta-analysis to assess the association between IBD and vitamin D deficiency.

Material and methods: We searched electronic databases from inception to December 2014 for observational studies reporting the presence of vitamin D deficiency (defined as serum 25-hydroxycholecalciferol [25(OH)D] level of ≤ 20 ng/ml) in IBD patients and having a control group without IBD. Odds ratios (OR) were combined using a random effects model. Meta-regression was performed using latitude as a moderator. Study quality was assessed using the Newcastle-Ottawa scale.

Results: Out of 816 citations, 14 eligible studies were identified, comprising 1891 participants (938 IBD cases and 953 controls). Meta-analysis showed that patients with IBD had 64% higher odds of vitamin D deficiency when compared to controls (OR=1.64; 95% CI: 1.30, 2.08; I² = 7%; $p < 0.0001$). UC patients had more than double the odds of vitamin D deficiency when compared to normal controls (OR=2.28; CI: 1.18, 4.41; I² = 41%; $p=0.01$). Meta-analysis of the 3 studies reporting on children showed that 177 pediatric cases with IBD had a higher, although not significant, odds of vitamin D deficiency compared with 413 non-IBD controls (OR = 1.36; 95% CI: 0.91, 2.04; I²=18%; $p=0.14$). Latitude did not influence the association between IBD and vitamin D deficiency ($p = 0.34$). All studies were of moderate to high quality as assessed by the Newcastle-Ottawa scale. Generalizability of our results might be limited as we summarized unadjusted ORs, due to non-availability of adjusted ORs in individual studies.

Conclusions: IBD is significantly associated with having higher odds of vitamin D deficiency. Well-designed RCTs and longitudinal studies are needed to further clarify the role of vitamin D in IBD pathogenesis and its therapy.

P.07.12

BETA-GLUCAN, INOSITOL AND DIGESTIVE ENZYMES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE ASSOCIATED WITH IRRITABLE BOWEL SYNDROME

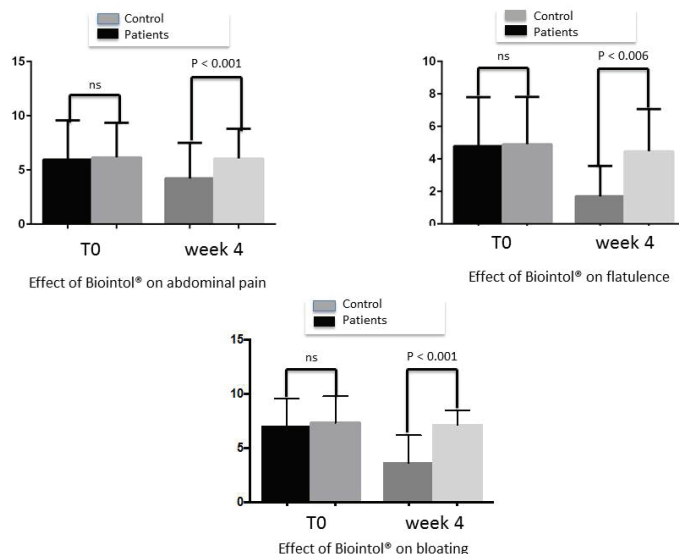
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Background and aim: Symptoms compatible with irritable bowel syndrome (IBS) are frequently present in patients with inflammatory bowel disease (IBD). A recent meta-analysis of patients with inflammatory bowel disease (IBD) demonstrated that 25–46% of those in clinical remission have symptoms compatible with a diagnosis of IBS. To evaluate the effectiveness of the administration of a mixture of beta-glucan, inositol and digestive enzymes in improving GI symptoms in IBD patients on clinical remission.

Material and methods: The study was conducted in the Gastroenterology Unit of the University of Catanzaro. Were enrolled patients with a diagnosis of IBD performed by clinical, endoscopic, histological and radiological criteria. Patients were affected by IBD (CD, RCU) in clinical and endoscopic remission defined by Harvey Bradshaw score <5 for CD and Mayo Score <2 for UC, in treatment only with systemical and topical mesalazine. All patients fulfilling the Rome III criteria for the diagnosis of IBS. Were excluded from the study patients with IBD: UC and CD without strictures, who did not report symptoms of IBS and in treatment by steroids, immunosuppressants and biological agents. The subjects included in the study were randomized to receive Biointol® (one tablet after lunch and after dinner) for four consecutive weeks (Group A), or any therapy (group B). Severity of symptoms at the entry and after four week was evaluated by means of 10 cm Visual Analogical Scales (VAS) in either group.

Results: Were analyzed one hundred patients with IBD. Of these, sixty-two (62%) were in clinical remission: 33 were male (53%), median age of 51 years. 29 (46%) were affected by CD and 33 (53%) by UC. 14 (22%) were smokers. All patients completed the study to four weeks. At enrollment there were no significant differences between the two treatment groups. After four weeks of treatment, in the group A there was a statistically significant reduction compared to the group B in abdominal pain (mean VAS score 2 ± 2 VS 4 ± 3 p <0.001) in bloating (mean VAS score 4 ± 3 VS 1 ± 1 p <0.001) and flatulence (mean VAS score 4 ± 3 VS 7 ± 1 p 0.006).



Conclusions: Few studies have been conducted previously to identify the association between IBS and IBD. For the first time,

in this work, was evaluated the effect of the administration of a mixture of beta-glucan, inositol and digestive enzymes. These findings could pave the way to better characterize the pathogenesis of IBS and IBD. Further studies are needed to clarify the effectiveness of this evidence

P.07.13

FOUR-YEAR EFFICACY AND SAFETY OF AZATHIOPRINE TREATMENT IN THE MAINTAINANCE OF STEROID-FREE REMISSION IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Background and aim: Azathioprine (AZA) and thiopurine are widely used for induction and maintenance of remission in patients steroid-dependent with inflammatory bowel disease (IBD). The treatment must be withdrawn in 5–30% of patients due to the occurrence of adverse events. Aim of this study has been to investigate its efficacy and safety in maintaining steroid-free remission in steroid dependent IBD patients four year after the institution of treatment.

Material and methods: Data from consecutive IBD outpatients referred in our Institution, between 1985–2013, were reviewed and all patients treated with AZA were included in this retrospective study. AZA was administered at the recommended dose of 2–2.5 mg/kg. Blood chemistry was analysed before administration of the drug, every 10–15 days for the first 3 months and then every 1–2 months following the institution of treatment.

Results: Out of 2556 consecutive IBD outpatients visited in the index period, AZA was prescribed to 376 patients, 198 (52.7%) were affected by Crohn's disease (CD) and 178 (47.3%) by ulcerative colitis (UC). One hundred and four patients with a follow-up <48 months were excluded from the study. Two hundred and seventy-two patients were evaluated, 146 (53.7%) with CD and 126 (46.3%) with UC. One hundred and forty-nine (54.8%) were male and 123 (45.2%) female (average age of 33.56 ± 14.34 SD years, range 14–74 y.). Four year after the institution of treatment, 149 (54.8%) patients still were in steroid-free remission (89 CD vs 60 UC, 61% and 47.6%, respectively, p=0.0288), 71 (26.1%) had a relapse requiring retreatment with steroids (42 UC vs 29 CD, 33.4% and 19.8%, respectively, p=0.0130), 52 (19.1%) discontinued the treatment due to side effects (28 CD vs 24 UC, 19.2% and 19%, respectively). Loss of response from 1st to 4rd year of follow-up was low, about 15%.

Conclusions: Four year after the onset of treatment 55% of patients did not require further steroid courses. After the first year loss of response was low in three subsequent years. In the present series the maintenance of steroid-free remission was significantly higher in CD than in UC patients. The occurrence of side effects leading to the withdrawal of AZA treatment has been low.

P.07.14

BIOLOGICAL THERAPY IS ABLE TO MODIFY THE DISEASE PROGRESSION OF CROHN'S DISEASE PREVENTING ITS LONG-TERM ASSOCIATED DISABILITY – A STUDY PERFORMED USING THE LÉMANN SCORE

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Background and aim: Crohn's disease (CD) is a chronic inflammatory bowel disorder characterized by an alternation of remission and relapse phases. Even during periods of clinical remission a subclinical inflammation persists, reflecting a progressive, destructive disease course in the later phases of the disease. Surgical resection of the bowel can be considered the ultimate manifestation of bowel damage. Recently a new score, the Lémann Score (LS), has been proposed in order to assess the cumulative structural damage to the bowel in different CD patients. Limited data are present assessing the value of this instrument in measuring the effect of various medical therapies on the progression of bowel damage. The aim of our study was to evaluate the effect of various medical therapies on the progression of bowel damage using the LS.

Material and methods: In this retrospective study we included 87 CD patients who were followed up at our IBD Unit. All patients underwent clinical assessment with measurement of disease status based on HBI index every three months, and bowel magnetic resonance imaging and a colonoscopy every year, or earlier, in case of disease relapse. Patients were divided on the basis of the drug administered during the follow-up: i) biological mono-therapy; ii) azathioprine; iii) mesalazine, and the LS was calculated both at baseline and at the end of follow-up in each group.

Results: We included 87 patients (49 males, mean age 43.5 years, range 19-79) with a median follow-up of 26 months. Among the 35 (40.2%) patients on biological mono-therapy the median LS was 7.1 (range, 2.5-292.3) at baseline and 9.7 (range, 1.3-292.3) at the end of the follow-up ($P=0.34$). The median LS in azathioprine group (16 patients, 18.4%) was 3.5 (range, 0.6-159.6) and 7.6 (range, 0.6-209.6) at baseline and at the end of follow-up, respectively ($P=0.0017$). In the mesalazine group (36 patients, 41.4%) the median LS at baseline and at the end of follow-up was 3.2 (range, 0.6-202.6) and 4.3 (range, 1-206.5), respectively ($P<0.0001$). As far as the proportion of patients who showed a worsening in the LS is concerned, the azathioprine group showed the highest proportion of patients with increased scores (13/16, 81.3%) followed by the group treated with mesalazine (20/36, 55.6%), and patients treated with biological mono-therapy (8/35, 22.9%) ($P=0.0002$).

Conclusions: Our data suggest that the use of biological therapy rather than azathioprine or mesalazine may change the cumulative structural damage to the bowel and, therefore, is able to modify disease progression in CD patients, preventing its long-term associated disability.

P.07.15

INFLIXIMAB TROUGH LEVELS AND ANTI-DRUG ANTIBODIES AFTER INDUCTION AS PREDICTIVE FACTORS OF LONG TERM CLINICAL REMISSION

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Background and aim: The treatment paradigm of Inflammatory Bowel Disease is dramatically changed in the past decades, thanks to the development of biological drugs. However, approximately 40% of primary responder patients to anti-TNF therapy experience a loss of response (LOR) during the first year of treatment. Recently, drugs trough levels (TL) and anti-drug antibodies (ADA) presence were proposed as useful tools in the management of patients who have a LOR. Currently, one of the most important issue in IBD patients on biological therapy is to timely identify patients at risk of anti-TNF therapy failure. The aim of our prospective study is to evaluate TL and ADA presence after Infliximab (IFX) induction and their correlation with a long term follow up in a series of patients with Inflammatory Bowel Disease.

Material and methods: In this prospective study we included 32 consecutive Inflammatory Bowel Disease patients [20 Crohn's Disease (CD) and 12 Ulcerative Colitis (UC); 17 males, median age 42 years, range 18-69] who underwent IFX therapy and achieved clinical remission after induction (schedule: 5 mg/kg at week 0, week 2, and week 6). Blood samples were drawn at standardized time points (i.e., 0, 2, 6, and 14 week) before IFX infusion. TL and IFX ADA were measured using an homogenous mobility shift assay (HMSA; Prometheus Lab, San Diego, United States). Disease activity was assessed both at week 14 and week 48 by the Harvey-Bradshaw Index (HBI, remission defined by HBI<5) in CD patients and by the Mayo score for UC patients (remission defined by Mayo score <2).

Results: After 48 weeks follow-up, 14 patients (43.8%) experienced LOR. We found significantly lower IFX TL after induction in patients who experienced LOR as compared to patients who maintained remission during the follow up (0.78 mcg/ml, range 0-14.97 mcg/ml versus 10.01 mcg/ml, range 0.00-42.83 mcg/ml; $P=0.0018$). Moreover, IFX TL were significantly lower in ADA positive patients as compared to ADA negative ones (0 mcg/ml, range 0-9.66 mcg/ml versus 11.91 mcg/ml, range 2.00-42.83 mcg/ml; $P<0.0001$). Lastly, ADA concentration after induction was significantly higher in relapsers as compared to patients in remission (3.13 U/ml, range 0-30.52 U/ml versus 0 U/ml, range 0-16.83 U/ml; $P=0.02$).

Conclusions: Patients who experience LOR to IFX during long-term follow-up (48 weeks) have significantly lower IFX TL and higher ADA serum concentrations after IFX induction (i.e., 14 weeks). Therefore, assessment of IFX TL and of ADA serum concentrations after IFX induction can be used as a predictive tool for the long-term clinical response to biological therapy.

P.07.16

PREDICTORS OF BOWEL DAMAGE AND DAMAGE PROGRESSION AS ASSESSED BY THE LÉMANN INDEX IN EVERY-DAY CLINICAL PRACTICE

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Background and aim: Crohn's Disease (CD) shows a gradually and destructive progression, leading to accumulation of structural bowel damage (BD), loss of function and disability. The Lémann Index (LI) is a new instrument to assess the cumulative BD according to stricturing or penetrating lesions as well as surgical resections detected at endoscopic and radiological evaluation [1]. Aim of this study was to evaluate BD progression by LI scoring in patients with CD, in the attempt to identify factors likely to predict its changes.

Material and methods: We retrospectively evaluated all consecutive patients with a diagnosis of CD who received 2 or more serial CT or MR enterographies at at least a 6 months time-distance from 2010 to 2015 at our Hospital. Two radiologists and two gastroenterologists reviewed patients' history, endoscopic examinations and cross-sectional images. Two serial LI evaluations were calculated for each patient and matched with CRP levels, Clinical Disease Activity Index (CDAI), disease location, disease behavior, medical treatments, CD-related hospitalizations and surgeries using the Spearman correlation, the Wilcoxon or the Mann-Whitney tests, as appropriate.

Results: Twenty-eight patients were enrolled (15 men, median age 40.3 years). Most of them had a small-bowel (39%) or ileo-colonic (46%) involvement and a luminal (36%) or a stricturing behavior (43%) at baseline. The median LI was 7.7 (interquartile range [IQR]

= 2.7-17.9) at baseline and 9.1 (IQR = 4.1-17.7) after a median of 20.7 months (IQR = 10-27.5). History of surgical resections ($P < 0.0001$), stricturing or penetrating behaviors ($P = 0.0041$) and a disease duration ≥ 10 years ($P < 0.0001$) were predictive of higher LI value at first evaluation. At follow-up, LI increased in 13, remained unchanged in 9 and decreased in 6 patients. LI was more likely to increase in colonic localizations (median delta LI 2.5 versus 0.0; $P = 0.34$) and in patients with a disease duration < 10 years (median delta LI 0.625 versus 0.0; $P = 0.059$). LI's progression showed no correlation with CRP levels and CDAI. Immunosuppressive or anti-TNF α treatments were associated with slightly higher LIs at baseline (median LI 13.8 vs 6.35, $P = 0.09$), and no improvement at the follow-up evaluation (Delta LI 0.26 vs -0.60; $P = 0.18$).

Conclusions: The newly introduced LI is a feasible tool to assess BD in CD. This study confirms that surgical history, complicated disorders or long duration are independent predictors of BD. These data suggest for the first time that patients with colonic locations or with a recent diagnosis of CD have an increased risk of BD progression, thus suggesting that early therapeutic intervention may reduce damage progression. Further studies should now evaluate the impact of assessing LI in clinical and experimental therapeutic strategies.

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P.07.17

A NEW THERAPEUTIC LASER SYSTEM FOR HEMOSTATIC TREATMENTS IN GI ENDOSCOPY – FIRST RESULTS IN AN ESTABLISHED ANIMAL MODEL

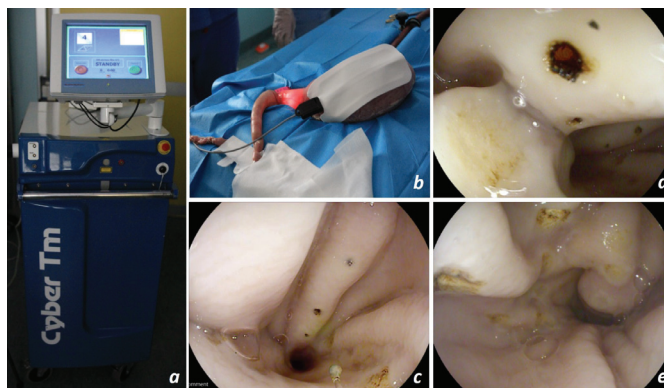
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Background and aim: The Thulium laser system is an established therapeutic technology for surgical resection [1-3; fig. a]. The wavelength of 2 μ m is strongly absorbed by water present in soft organic tissues, thereby providing constant speed of cutting and vaporization (i.e. "vaporesection") regardless of vascularization, with high degree of control on the penetration depth (0.2-0.4mm) to reduce the risk of inadvertent deep injury. However, no study has yet reported its use for achieving hemostasis in the luminal gastrointestinal (GI) tract. We conducted a pilot study in an established animal model (EASIE; fig. b) to test for the first time the safety and efficacy of the Thulium Laser system (Cyber TM®, Quanta System, Varese, Italy) for hemostatic treatment in luminal GI-endoscopy.

Material and methods: Various optical fibers (365 and 550 μ m) were evaluated with different power settings (10, 15, 20, and 25 watts), and diverse configurations (continued laser shaping or pulse modality). Study endpoint was to assess the impact of the device in terms of depth penetration and lateral tissue damage under a laser exposure prolonged for 3, 5 and 7 seconds at fixed distance (0.5-1 cm) from the mucosal surface. Results were compared to the effect of Argon Plasma Coagulation (APC) generated by an established standard electrosurgery system for hemostatic therapy in the luminal GI-tract with a 2.3 mm catheter using 20, 40 and 60 watts. All procedures were performed using a standard video-gastroscope and digitally recorded. Histopathological analysis based on the whole stomach were performed by an expert GI pathologist.

Results: Neither transmural perforation, nor any muscular layer damage was observed with both systems used. A progressive penetration depth and tissue damage was observed with increased laser power and APC settings, as well as with prolonged tissue exposure. Nonetheless, both the fiber diameter and the configuration modality of the laser system were found to have no impact on depth penetration and tissue damage, with only marginal effect on the lateral spread of vaporization. Overall, the laser system was associated with a comparable degree of vertical tissue injury (from 0.1 to 2.0 mm) and a much more precise effect on target according to a lower lateral spreading damage (0.1-0.3 mm and 0.2-0.7 mm using the 365 and 550 μ m fiber, respectively; fig. c-d) compared to APC (1.1-1.6 mm; fig. e).



Conclusions: The Thulium laser system appears to be safe and effective for hemostatic therapy in an ex vivo animal model of the upper GI-tract. In vivo studies should now confirm these initial results in a prospective setting.

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P.08 Esophagus

P.08.1

ABNORMAL INTRA-BOLUS PRESSURE CORRELATES WITH ESOPHAGO-GASTRIC DYSFUNCTION AND ITS AGE-RELATED MODIFICATION – A STUDY USING HIGH-RESOLUTION MANOMETRY

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Background and aim: High Resolution Manometry (HRM) is currently considered the gold standard to assess esophageal peristalsis and esophago-gastric junction (EGJ) function. Indeed, with the use of this technology novel validated metrics have been developed to define esophageal motility abnormalities. In particular, the intrabolar pressure (IBP) has been initially regarded as an indirect measure of bolus transit through the EGJ, although the last iteration of Chicago Classification lacks of its adoption because

of the paucity of data in this regard. We aimed to investigate the role of IBP in consecutive patients with esophageal symptoms.

Material and methods: We included consecutive patients with esophageal symptoms referring to our motility laboratory. Patients with gastro-intestinal surgery, achalasia or scleroderma were excluded. All patients underwent esophagogastroduodenoscopy (EGDS) and HRM with 5-min baseline recording and 10 single water swallows. The diagnostic criteria agreed with the Chicago Classification vers. 2. We stratified these patients according to their IBP value (i.e. normal if lower than 17mmHg) in two groups: patients with and those with abnormal IBP values. Data were expressed as mean and standard deviation. A t-test and x2-test were performed and a p-value <0.05 was considered statistically significant.

Results: Patients with abnormal IBP had a mean age higher than patients with normal IBP (60±13 vs 50±16; p value <0.001), but no difference was found in gender distribution. As to HRM characteristics, patients with abnormal IBP had similar mean Distal Contractile Integral (DCI) than those with normal function (2287±10538 vs. 2100±1497; p=0.9), but a lower LES resting pressure (22±11 vs 33±16; p<0.001) and an increased IRP (22±11 vs 33±16; p<0.001). No differences in terms of distal latency (6.7±1.5% vs 6.4±2.0%; p=0.14), peristaltic swallow (70±34% vs 78±27%; p=0.07) and abnormal type of swallow such as failed, ineffective, and fragmented (p=ns).

Conclusions: Abnormal IBP values correlate more with EGJ dysfunction rather than with vigor of peristalsis suggesting that EGJ compliance plays a major role in its determination. This association is further supported by the increased age of patients with abnormal IBP (i.e. known fibrotic alterations related to aging).

P.08.2

PROXIMAL GASTRO ESOPHAGEAL REFLUX: WHAT'S WRONG WITH GASTRO-ESOPHAGEAL MOTILITY?

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Background and aim: Atypical symptoms are common in gastro-esophageal reflux disease (GERD). Multichannel intra-luminal impedance and pH monitoring (MII-pH) give information about GERD and esophageal activity. Less than 40% of patients with suspected laryngo-pharyngeal reflux has a diagnosis of GERD but little is known about the pathogenesis of proximal extent of GERD.

Aim: to assess the correlation between proximal extent of GERD, esophageal activity and dyspeptic symptoms (nausea, belching, postprandial fullness).

Material and methods: Fifty patients, 26 women, aged between 22 and 83 years old with a diagnosis of NERD and atypical symptoms underwent MII-pH, after a negative upper endoscopy. All patients were PPI-off and H. pylori infection, autoimmune diseases and non-obstructive dysphagia were excluded.

Results: Sixteen patients (32%) had a MII-pH tracing compatible with proximal extent of reflux. There was a positive correlation between number of episodes of reflux and proximal reflux ($\rho = 0.852$). Patients with proximal extent of reflux had a median bolus clearance time delayed (75% vs 41.2%, $p = 0.03$) and the presence of dyspeptic symptoms (56.3% vs 20.6%, $p = 0.01$). No difference was ruled out for acid refluxes ($p = 0.16$), weakly acid refluxes ($p = 0.88$), upper symptoms ($p = 0.73$) and Symptom Association Probability ($p = 0.33$).

Conclusions: Patients with atypical symptoms and proximal extent of GERD had a reduced esophageal clearance associated with a possible delayed gastric emptying. More studies are needed to identify different subgroups of patients for tailoring therapy.

P.08.3

BASILENE IMPEDANCE VALUES CAN REPRESENT A MARKER OF GASTROESOPHAGEAL REFLUX DISEASE AND ARE STRONGLY RELATED WITH THE DURATION OF THE DISEASE

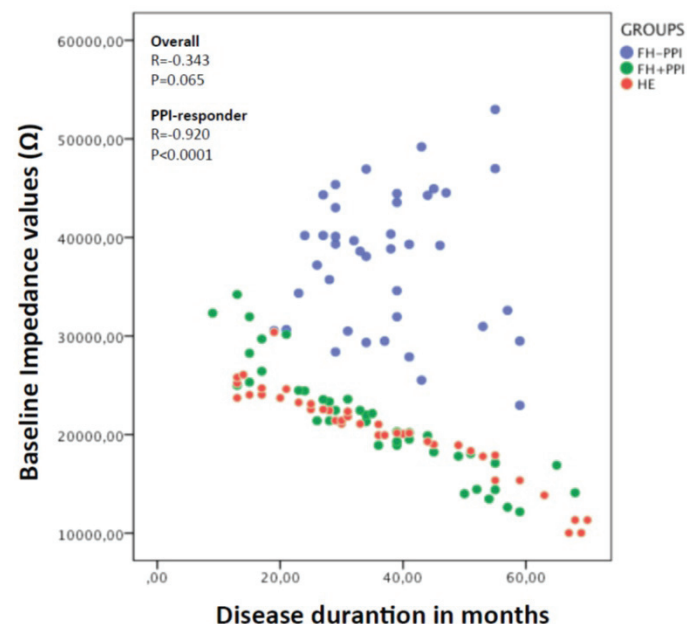
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Background and aim: Recently, it has been described a strong correlation between baseline impedance (BI) values and the symptom relief during proton pump inhibitor treatment. The aim of the study was to evaluate BI levels in patients with heartburn responder and non-responder to acid suppressive therapy (PPI) and to detect the relationship between BI values and number of months of GERD-related symptoms.

Material and methods: NERD patients with heartburn were enrolled and asked to indicate from how long they experienced heartburn (i.e. disease duration in months). All patients underwent 24-h impedance-pH test off-PPI therapy and we selected those with normal acid exposure (AET) and number of reflux events. Thus, 90 patients undertook an 8-week course of PPIs. Sixty of them with >50% symptom improvement were classified as PPI-responders: 30 patients with pathophysiological characteristics of functional heartburn (negative symptom-reflux correlation; FH+PPI) and 30 with hypersensitive esophagus (positive symptom-reflux correlation; HE). The remaining 30 patients with a <50% improvement to treatment and with pathophysiological characteristics of functional heartburn were classified as PPI non-responders (negative reflux symptom correlation; FH-PPI). BI value were calculated manually during overnight rest.



Results: The mean duration of symptoms (in months) was not different between FH+PPI (34.1±15.4), HE (35.7±17.8) and FH-PPI (36.5±15.5); $p=ns$. Patients with FH+PPI showed a higher mean AET (1.9%±1 vs 0.6%±0.6, $p<0.05$), mean reflux number (30.4±9.3 vs 23.5±7.9, $p<0.05$) and acid reflux number (17.1±8 vs 10±6.9, $p<0.05$) compared to FH-PPI. Patients with HE showed mean AET (2.3%±1.8) and total reflux number (34.6±10.4) similar to those recorded in FH+PPI ($p=ns$). Baseline impedance levels were lower in FH+PPI

(1949.6±548.8) and in patients with HE (1839.7±467.6) than in FH-PPI (3812.8±810.2) ($p<0.001$). The overall correlation between BI and disease duration in months was poor ($r=-0.343$; $p=0.065$) but when we evaluated the patients who responded to PPI (HE and FH+PPI) we found a very strong correlation between baseline value and duration of the disease ($r=-0.920$; $p=0.0001$).

Conclusions: Our results showed a very strong correlation between lower BI and response to PPI treatment. BI could represent a marker of GERD. We also found a strong negative correlation between BI values and disease duration in PPI-responder patients, thus corroborating the relevance of this objective marker in evaluating the esophageal mucosal impairment.

P.08.4

INCIDENCE AND MANAGEMENT OF ACHALASIA IN CLINICAL PRACTICE: AN EIGHT-YEAR SINGLE CENTRE EXPERIENCE

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Background and aim: Achalasia is a relatively uncommon primary esophageal motility disorder. Its incidence in clinical practice has not been established yet and the gold standard of treatment is still debated. The aim of this study was to report the incidence of achalasia in our region (Azienda ULSS 12 Veneziana, Veneto Region, North-East of Italy) and to evaluate the modalities and outcome of treatment according to the clinical characteristics of patients.

Material and methods: We retrospectively evaluated our manometric records from January 2008 to September 2015. All patients with a new diagnosis of achalasia were classified into one of the three groups of the Chicago manometric classification. The subsequent modalities and outcome of treatment were recorded. The options of treatment included surgical myotomy (SM), pneumatic dilatation with Rigidflex balloon (PD) or Botox injection (BI). Symptoms relapse after PD was identified by an Eckardt Score >3 , and treated with repeated PD sessions as required.

Results: 46 patients were diagnosed in eight years (M/F 27/19; median age 62, IR 46.75–68.75), with a mean incidence of 2/100000 per year. Type II was the most frequent subtype of achalasia (32 patients, 69.57%) whereas type I and III were rarer (6 patients – 13.04% – and 8 patients – 17.39% – respectively). The manometric presentation was not affected by gender or age class (<50 , 50–70 or >70 years) as confirmed by the Fisher Exact Test ($p=0.955$ and $p=0.905$ respectively).

11 patients were lost after the diagnosis because they were treated in other centres and 4 patients had only mild symptoms which were controlled by dietary and behavioral changes. 7 patients underwent SM as the primary treatment, and 2 after failure of endoscopic techniques (1 BI and 1 PD). None of them had a symptomatic relapse. 22 patients were successfully treated with PD: 10 patients had only one session (45.45%), 8 patients two sessions (36.36%), 3 patients three sessions (13.64%) and 1 patient 4 sessions (4.55%). No complications were reported. A binary logistic model for multiple variables was used to identify any factors related to PD outcome: gender, age class and manometric subtype were tested. Older age was a protective factor for repeated dilatations (OR 0.146, 95% CI 0.025–0.870, $p=0.035$).

Conclusions: The incidence of achalasia in our region is stable in the last eight years and slightly higher than previously reported. Type II is the most frequent subtype, regardless gender and age. PD is a safe procedure which may require repeated sessions, particularly in younger patients.

P.08.5

FEASIBILITY OF HIGH RESOLUTION IMPEDANCE MANOMETRY IN ASSESSING BARRETT'S ESOPHAGUS EXTENSION

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Background and aim: Diagnosis and surveillance of Barrett's esophagus (BE) is performed by means of upper endoscopy with biopsies, which is also important to assess the extension of metaplasia. Several studies demonstrated the risk of dysplasia and adenocarcinoma development in BE is associated to its extension. However, endoscopic evaluation of esophago-gastric junction (EGJ) may be inaccurate, especially in patients with hiatal hernia, reflux esophagitis and abnormal z-line. Recent studies carried out with 24-h impedance-pH testing showed that Barrett mucosa is characterized by very low basal impedance values compared to the normal esophageal epithelium. High resolution impedance manometry (HRiM) is able to localize with more accuracy than upper endoscopy the EGJ and, also, has been recently applied for baseline impedance levels (BI) in patients with reflux disease. We aimed to assess Barrett extension by means of BI assessed by HRiM using upper endoscopy as reference standard. In contrast, HRiM was considered reference for EGJ evaluation.

Material and methods: Consecutive patients with proven BE and a group of healthy volunteers (HVs) were enrolled. Patients underwent endoscopy and HRiM before imp-pHmetry off-PPI therapy was performed. BE extension was endoscopically assessed according to Prague classification. During HRiM, EGJ has been identified by assessing the position of lower esophageal sphincter and diaphragm. BI was recorded every cm above the EGJ. Maximal length (M) at endoscopy was used for comparison.

Results: Ten HVs (4M/6F; 35yy, BMI 23) and 20 BE patients (11M/9F; 46yy, BMI 25.9) were enrolled. Among BE, hiatal hernia (HH) was found in 15 pts (75%) during endoscopy and 12 (60%) with HRiM. Endoscopy overestimated HH of at least ≥ 1 cm in 9 cases. Mean HH was 1.7 vs 0.9cm, respectively (mean error 0.75 cm, median SD: 0.25; $r:0.78$). HVs had no HH. Median BE length was 1.7cm (1.5–2.3) at endoscopy, whereas was 2cm (1.0–3.5) at HRiM (median SD error: 1cm; $r:0.32$). During HRiM BE mucosa showed lower BLI compared to HV ($p<0.01$). Median BI of Barrett segment was lower compared to BI of normal mucosa measured in the same patients (430 Ω vs 650 Ω at 1 to 3 cm above BE, vs 1077 Ω at 4 to 7cm above BE; $p<0.01$). AUC 0.89; BLI of 650 Ω provides Sens 95.6% and Spec 80.0%.

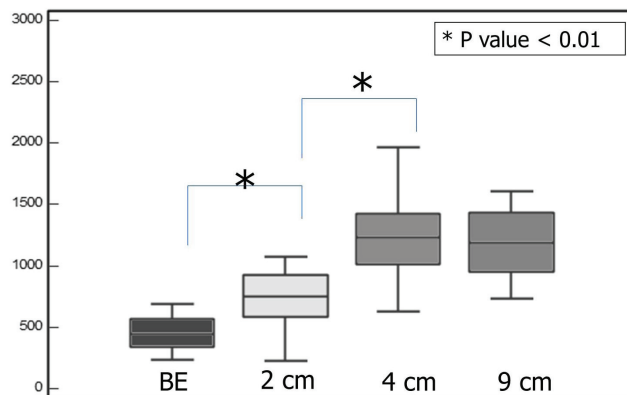


Fig. 1. BLI measured at the site of Barrett's esophagus and at 2–4–9 cm from the upper limit of BE.

Conclusions: Our data showed that HRiM was able to discriminate Barrett mucosa from normal esophageal epithelium. Considering that HRiM is the reference standard to assess EGJ position and borders, this technique might become a useful tool combined with endoscopic examination to assess more precisely BE length.

P.08.6

THE IMPACT OF RHINOLOGIC EVALUATION ON PATIENTS WITH SUSPECTED SUPRAESOPHAGEAL REFLUX DISEASE

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Background and aim: Supraesophageal reflux disease (SERD), defined as reflux proximal to the upper esophageal sphincter, is a common cause of morbidity of the upper aerodigestive tract, including rhinitis, laryngitis, cough, postnasal drip, and throat clearing. There are no unequivocal criteria that reliably demonstrate a causal link between acid reflux and laryngeal symptoms. Results of esophageal pH-testing and response to proton pump inhibition therapy are variable. It is likely that some patients are mistakenly diagnosed with SERD and investigation of the other causes of laryngeal symptoms, including rhinitis, should be considered. **Aim:** To evaluate the impact of the rhinologic evaluation on patients with suspected supraesophageal reflux disease.

Material and methods: Between January 2014 and September 2015 fifty-five patients (28 F) referred to our unit for suspected reflux disease with supraesophageal manifestations and a history of a ENT visit suggesting a suspected reflux cause, were enrolled. An esophageal manometric study and a 24 hour pH-Impedance study were performed in our G.I motility lab and a rhinomanometry, a skin prick test and a nasal cytology were performed in our ENT unit.

Results: Of the 55 patients with suspected SERD, 33 (60%) resulted to have pathological basal pH-Impedance values and 22 (40%) resulted with normal basal values. Of the patients with pathological pH-Impedance, 14 (42.4%) were diagnosed with non allergic rhinitis (NAR), 11 (33.3%) with allergic rhinitis (AR), 2 (6.1%) with both AR and NAR, 1 (3%) with negative rhinologic evaluation whereas 5 (15.2%) were affected of other rhinological pathologies such as sinusitis and sinus polyposis. Of the patients with a normal pH-Impedance, 11 (50%) resulted to have NAR, 9 (41%) AR, 1 (4.5%) NAR and AR and 1 (4.5%) resulted to have a negative rhinologic evaluation.

Conclusions: Our study showed that 40% of the ENT evaluated patients with suggested reflux related ENT symptoms resulted with a normal pH-Impedance. Many patients had associated rhinologic pathologies (allergic and non allergic). There is no statistical correlation between patients affected by rhinologic pathologies and pH-Impedance results. We have concluded that in patients with suspected SERD is necessary a rhinologic evaluation for the frequent and occasional association of rhinitis.

P.08.7

THE USE OF NON-ABLATIVE RF ENERGY (STRETTA) FOR THE TREATMENT OF GERD, WHAT HAPPENS A DECADE LATER

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Background and aim: To date, the Stretta procedure (Mederi Therapeutics Inc., Greenwich, CT, USA), which applies thermal radiofrequency energy to the LES, still remains an available technique for endoscopic treatment of GERD, with documented effectiveness on patient symptom control, quality of life (QoL), oesophageal acid exposure, and LES pressure. From June 2002 to July 2015 a cohort of

158 patients were consecutively treated with the Stretta procedure for GERD; 51 patients (32 females, 19 males) reached to date a ten year follow-up. Primary end point of the study was to verify the durability and efficacy of the procedure at this time.

Material and methods: The primary outcomes of the study were heartburn score, GERD health-related QoL score (HRQL) and general quality of life, using the medical outcome 36-item Short-Form Health Survey (SF-36); GERD HRQL improvement was evaluated as a continuous variable and as a dichotomous variable (responder versus nonresponder). Response was a >50% improvement compared with baseline values. The secondary outcome was the need of medication use.

Results: Out of 158 patients treated with Stretta from June 2002 to July 2015, 98 did not reach at the date of the objective of 10 years of follow-up and nine patients were lost to follow-up. In seven patients the RF treatment lost its efficacy. There here was a significant decrease in both heartburn and GERD HRQL scores as well as a significant increase of QoL scores (mental SF-36 and physical SF-36) and 35 patients out of 51 (68.6%) were completely off PPIs.

Conclusions: The results of our further follow-up study after 10 years confirms the data published by Noar in late 2014 and further sustain the concept that Stretta might represent a viable treatment option for selected patients with symptomatic mild to moderate GERD; this suggestion has been recently stated by the SAGES Guidelines in 2013 and by the ASGE Guidelines in 2015; nowadays it seems reasonable to recommend Stretta, specially to the younger GERD sufferers, as a “bridge therapy” between the continuous medical treatment and the optimal timing for laparoscopic fundoplication.

P.08.8

CAUSAL EFFECT ASSOCIATION BETWEEN GASTROESOPHAGEAL REFLUX DISEASE AND NONALLERGIC RHINITIS WITH NEUTROPHILS

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Background and aim: The role of GERD in causing extra-esophageal symptoms, such as laryngitis, asthma, chest pain and cough is increasingly recognized with renewed interest. Nonallergic rhinitis (NAR) is defined as a compound of nasal symptoms in the absence of an allergic etiology and it is frequently observed in the clinical practice. Nasal cytology allows to identify the different NAR subtypes on the basis of the particular inflammatory cell infiltrate: nonallergic rhinitis with neutrophils (NARNE), NAR with eosinophils (NARES), NAR with mast cells (NARMA) and NAR with eosinophils and mast cells (NARESMA). To date, there are no data about the role of the reflux in rhinitis and in particular in the forms with neutrophils (NARNE). **Aim:** To evaluate the possible association between gastroesophageal reflux disease and nonallergic rhinitis with neutrophils (NARNE).

Material and methods: Between October 2013 and September 2015 thirty-five patients referred to our ENT unit for nasal symptoms such as rhinorrhea, sneezing, and postnasal drip were enrolled. Visual analogue scale (VAS) for nasal obstruction and other NAR symptoms, rhinomanometry, skin prick test and nasal cytology were performed. Exclusion criteria were ambient irritant exposure and/or a positive skin prick test. Of the 35 subjects with NAR, 20 (13F/7M, median age 48 years) showed the presence of neutrophils (neutrophils > 50% with absent spores and bacteria) at nasal cytology (NARNE) and were selected to perform a 24 hour pH-Impedance. Patients with a 24 hour pH-Impedance positive for GERD were treated with a high dose of oral PPI (40 mg x 2/day) for 8 weeks. A second pH-Impedance

was performed during therapy whereas ENT examination and nasal cytology were performed at the end of treatment.

Results: Of the 20 patients with NARNE, 14 (70%) resulted to have pathological basal pH-Impedance values and 6 (30%) resulted to have normal basal values. PH-impedance performed during PPI treatment showed the normalization of the number of refluxes (< 48) and pH values (< 4.2) in nine (64.3%) out of the 14 patients with positive pH-Impedance at enrollment. Ph-Impedance during treatment continued to be pathological in 3 (21.4%) patients with a pathological number of refluxes (2 with acid pH, 1 with normal pH values). Two (14.3%) subjects experienced improvement in symptoms and showed the normalization of nasal cytology but refused to repeat the pH-Impedance during therapy. Seven (77.8%) out of 9 patients with normal pH-Impedance values under treatment showed the simultaneous normalization of nasal cytology whereas two (22.2%) subjects did not show any significant improvement at nasal cytology.

Conclusions: Our study showed a possible causal effect association between GERD and NARNE. Treatment with high dose of oral PPI for 8 weeks seemed to be effective in improving symptoms and in reducing nasal inflammation in a significant number of patients with NARNE. Larger studies are needed to confirm our data.

P.08.9

CORRELATION BETWEEN HIGH RESOLUTION MANOMETRY PARAMETERS AND SYMPTOMS IN TREATED ACHALASIA PATIENTS

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Background and aim: HRM is the gold standard study to follow up achalasia patients after treatment. However, discrepancies between residual achalasia-related symptoms and HRM parameters may occur, thus drifting therapeutic choices in subsets of achalasia patients. Being more physiologic, it has been claimed that a HRM in the upright position may better reflect the clinical condition of these patients. We aimed to examine the effects of body position on HRM parameters and whether they are related to symptoms' persistence.

Material and methods: 40 achalasia patients (20 M, mean age 41 ± 12 ys) were treated with pneumatic dilation according to standardized protocol. In all patients a standardized questionnaire assessing the frequency and the intensity of achalasia-related symptoms (dysphagia for solids and liquids graded from 0: absent to 9: at each meal and precluding daily activities) was administered before and 6 months after pneumatic dilation. A HRM study was performed at the same time points, both in supine and sitting position with at least 10 single 5-mL swallows performed for each series.

Results: In all patients, a significant improvement of dysphagia severity for both solids and liquids was achieved after dilation (1±1.5 vs 6.7±2.2 and 0.6±1.1 vs 5.2±3.2 respectively; all p<0.001). A significant reduction in terms of LES pressure, IRP4 and bolus clearance rate was observed in the sitting as compared to the supine position (32±13 vs 25.4±17 mmHg; 19.8±9.5 vs 14.8±10 and 67.5±36 vs 47.8±43%; respectively, all p<0.05). However, none of the examined values showed a significant correlation with the persistence of dysphagia for solids or liquids both in the upright and supine position.

Conclusions: Here we showed that, despite body position significantly affects HRM parameters, none of these appears to significantly correlate with symptoms' persistence in treated achalasia patients. HRM study, per se, may not predict the clinical outcome of these patients and a number of variables (namely achalasia subtypes, age, sex, presence of megaesophagus) may account for residual symptoms in treated achalasia patients.

P.08.10

ESOPHAGOGASTRIC JUNCTION MORPHOLOGY ASSESSMENT BY HIGH RESOLUTION MANOMETRY IN OBESE PATIENTS CANDIDATE TO BARIATRIC SURGERY

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Background and aim: Obesity is a strong independent risk factor of gastroesophageal reflux disease (GERD) symptoms and hiatal hernia development. Pure restrictive bariatric surgery should not be indicated in case of hiatal hernia and GERD. However it is unclear what is the real incidence of disruption of esophagogastric junction (EGJ) in patients candidate to bariatric surgery. Actually, high resolution manometry (HRM) can provide accurate information about EGJ morphology. Aim of this study was to describe the EGJ morphology determined by HRM in obese patients candidate to bariatric surgery and to verify if different EGJ morphologies are associated to GERD-related symptoms presence.

Material and methods: All patients underwent a standardized questionnaire for symptom presence and severity, upper endoscopy, high resolution manometry (HRM). EGJ was classified as: Type I, no separation between the lower esophageal sphincter (LES) and crural diaphragm (CD); Type II, minimal separation (>1 and <2 cm); Type III, >2 cm separation.

Results: One hundred thirty-eight obese (BMI>35) subjects were studied. Ninety-eight obese patients referred at least one GERD-related symptom, whereas 40 subjects were symptom-free. According to HRM features, EGJ Type I morphology was documented in 51 (36.9%) patients, Type II in 48 (34.8%) and Type III in 39 (28.3%). EGJ Type III subjects were more frequently associated to Symptoms than EGJ Type I (38/39, 97.4%, vs. 21/59, 41.1% p<0.001).

Conclusions: Obese subjects candidate to bariatric surgery have a high risk of disruption of EGJ morphology. In particular, obese patients with hiatal hernia often refer pre-operative presence of GERD symptoms. Testing obese patients with HRM before undergoing bariatric surgery, especially for restrictive procedures, can be useful for assessing presence of hiatal hernia.

P.08.11

THE POSITION WITHIN THE OESOPHAGEAL CIRCUMFERENCE PREDICTS DYSPHASIA IN SHORT SEGMENT BARRETT'S ESOPHAGUS: A 7-YEAR RETROSPECTIVE SERIES OF 341 LESIONS

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Background and aim: A careful endoscopic surveillance of Barrett's esophagus (BE) is essential to prevent esophageal cancer. The aim of this study is to identify the preferred location of short BE and its associated dysplasia within the esophageal circumference.

Material and methods: We retrospectively reviewed a prospectively maintained database of patients with non-circumferential, short-

segment, histologically proven BE who underwent upper endoscopy between January 2008 and February 2015 at our Endoscopy Center. In the case of multiple metaplastic lesions, each tongue was counted individually. The circumferential locations of BE lesions and associated-BE dysplasia lesions were identified as on a clock face and their distributions in the 4 quadrants were compared.

Results: Of a total 435 BE patients, 184 (42%) short-BE patients were eligible for the study purpose. Multiple short BE lesions were diagnosed in 110 (60%) of 184 subjects, for a total amount of 341 metaplastic areas. Short BE lesions were more frequently observed in the posterior wall of esophagus (38.5%), compared with right wall (28.6%), anterior wall (22.4%), or left wall (10.5%) ($P<0.0001$). Twenty eight (8%) of total 341 metaplastic areas were associated with dysplasia, and 1 (0.3%) with adenocarcinoma. Dysplastic lesions were more common in the posterior wall (39.3%) than, respectively, in the anterior wall (35.8%), in the right wall (21.4%), in the left wall (3.5%) ($P=0.03$).

Conclusions: Our results show the posterior wall of esophagus as the preferential location of both short BE and associated-BE dysplasia. Should our findings be confirmed by further, larger experiences, they should be taken into account for the development of future surveillance protocols of Barrett's esophagus.

P.08.12

GERD QUESTIONNAIRE DISTINGUISHES PROTON PUMP INHIBITOR-RESPONSIVE ESOPHAGEAL EOSINOPHILIA FROM EOSINOPHILIC ESOPHAGITIS PATIENTS

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Background and aim: Current studies failed to observe clinical features able to distinguish Eosinophilic Esophagitis (EoE) from Proton Pump Inhibitor-response esophageal eosinophilia (PPI-REE). However, these investigations did not systematically assess reflux symptoms. Recently, GerdQ questionnaire has been validated for the diagnosis of gastro-oesophageal reflux disease (GERD). We aimed to apply GerdQ questionnaire in patients with EoE and PPI-REE to assess whether a prospective and systematic evaluation of reflux symptoms may be helpful to distinguish patients with PPI-REE from those with EoE.

Material and methods: Consecutive patients diagnosed with EoE and PPI-REE according to international criteria [a) presence of at least one typical symptom of esophageal dysfunction; b) at least 15 eosinophils per high-power field at mid/proximal esophagus; c) persisting or nor of eosinophils at mid/proximal esophagus after an 8-week PPI trial] prospectively completed a specific GERD-related questionnaire (GERDQ). GerdQ questionnaire is a simple and self-administered questionnaire including six items. A cut-off value higher ≥ 9 (range of 0–18) was considered diagnostic for GERD. For comparisons, a group of 27 patients with proven reflux disease was used.

Results: Fifty-two consecutive patients with histologically-detected eosinophilic infiltration were enrolled. At the follow-up endoscopy plus biopsy, after 8 weeks treatment with twice-daily PPI, thirty-five (67%) patients were identified as having EoE, whereas 17 (33%) patients were diagnosed with PPI-REE. The two cohorts had similar dysphagia for solids (EoE 74% vs. PPI-REE 76%, $p=1.000$), bolus impaction (66% vs. 70%, $p=1.000$) and chestpain (20% vs. 41%, $p=0.1810$), but different heartburn (26% vs. 58%, $p=0.0315$) and regurgitation (17% vs. 47%, $p=0.0429$). The overall GerdQ score was statistically lower in EoE vs. PPI-REE [1 (0–6) vs. 8 (2.5–11.25),

$p=0.004$]. When compared to control patients with GERD, both EoE and PPI-REE patients showed increased rate in dysphagia parameters, whereas EoE individuals reported less frequently heartburn (26% vs. 85%, $p<0.001$), regurgitation (17% vs. 74%, $p<0.001$) and overall GerdQ scores [1 (0–6) vs. 8 (6–12), $p=0.001$] than control patients with GERD. In contrast, no difference was found comparing PPI-REE and control patients with GERD for heartburn, regurgitation and overall GerdQ score ($p=0.0754$, $p=0.1083$ and $p=1.000$, respectively). Two EoE patients (6%), 8 PPI-REE patients (47%) and 15 control patients with GERD (55%) had a total score equal or above 9 (EoE vs. PPI-REE $p=0.0010$, EoE vs. GERD $p<0.001$ and PPI-REE vs. GERD $p=0.7577$).

Conclusions: GerdQ is a useful complementary tool to distinguish patients with PPI-REE from those with EoE. The implementation of GerdQ could reduce the need for more aggressive therapies (i.e. topical steroids and specialised diets) and improve resource utilisation.

P.08.13

WHICH IS THE BEST CUT-OFF TO DEFINE INEFFECTIVE ESOPHAGEAL MOTILITY?

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Background and aim: The last version (3.0) of Chicago Classification took an arbitrary decision and defined ineffective esophageal motility (IEM) when 50% or more wet swallows (WS) result failed (DCI<100 mmHg/cm/s) or weak (100<DCI<450 mmHg/cm/s) during standard manometric protocol. The aim of this study was to compare patients with different frequency of failed/weak WS, provocative test (MRS, 3ml x 5 times in 10sec) and MRS/WS ratio to better define the IEM diagnosis.

Material and methods: We retrospectively evaluated 59 outpatients who underwent: upper endoscopy, high resolution manometry (HRM) with 5-min baseline recording, 10 single water swallows of 5mL each, and 1 MRS in supine position, and 24-h impedance and pH monitoring for unresponsive heartburn. We excluded patients with achalasia, scleroderma, absent peristalsis and prior surgery. MRS/WS ratio was calculated according to medical literature. All patients were sub-grouped based on the percentage of failed/weak WS as follows: a) $\leq 30\%$; b) 40%; c) 50%; d) 60% and e) $\geq 70\%$ failed or weak WS.

All data were expressed in median and IQR. ANOVA with Bonferroni test has been applied for statistical analysis.

Table 1

The main HRM results and statistical analysis (ANOVA and Bonferroni Test)

	Percentage of failed swallows					p
	Group A (17) $\leq 30\%$	Group B (9) 40%	Group C (10) 50%	Group D (8) 60%	Group E (8) $\geq 70\%$	
Mean age (IQR)	44.5 (16.2)	43.2 (16.8)	51.3 (7.2)	39.8 (13.6)	47.1 (18.1)	0.57 ^a
DCI mean (IQR)	1255.5 (577.8)	1466 (623.5)	1153 (577)	598 (582)	284 (235)	0.0001 ^b
DCI-MRS (IQR)	1653 (541.8)	1578 (502)	1241 (828)	472 (507)	119 (221)	0.0001 ^b
MRS/WS ratio (IQR)	1.3 (0.6)	1.1 (0.2)	1.1 (0.3)	0.6 (0.6)	0.5 (0.3)	0.0001 ^b

^aP > 0.05 for all pairwise comparisons

^bP<0.001 between A vs D; A vs E; B vs D; B vs E; C vs D and C vs E

Results: Male were more represented in groups C (60%), D (75%), E (75%) ($p=0.03$), whereas mean age was similar in all groups ($p=0.57$). Erosive esophagitis was more represented in groups C (70%), D (50%), E (50%) ($p=0.018$). Acid exposure time increased progressively from group A to E (A 4.3[IQR 5.6]; B 8.2[8.4]; C 9[5.7]; D 9.1[11.3]; E 10.2[7.4]; $p=0.014$). Total number of reflux events was higher in C and D groups (A 45.3[IQR 20.7]; B 49[85]; C 96[71]; D 80[37.5]; E 57.5[76.7]; $p=0.008$). Mean DCI during WS, DCI-MRS and MRS/WS ratio were progressively lower from A to E group ($p<0.001$ with ANOVA). The Bonferroni test showed significant differences between A, B, C, versus D and E ($p<0.001$). Details are reported in table 1.

Conclusions: Data on GERD evidence at impedance-pH monitoring demonstrated that IEM should be considered as clinically relevant when the frequency of failed or weak WS is $\geq 60\%$.

P.08.14

A PROSPECTIVE APPLICATION OF THE ESPGHAN GUIDELINES IN A SYMPTOMATIC ADULT POPULATION

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Background and aim: Current adult guidelines require histological confirmation of celiac disease (CD). However, recent pediatric guidelines have proposed algorithms to reduce the need for biopsy in genetically susceptible symptomatic children. We explore the applicability of the current ESPGHAN criteria and assess the accuracy of serology in detecting villous atrophy in a prospective cohort of symptomatic adults.

Material and methods: We recruited 234 consecutive symptomatic adults (mean age=33.9ys) showing EMA positivity and genetic susceptibility. All patients underwent upper endoscopy with multiple biopsy sampling in the duodenum. Histological lesions were graded according to the Corazza-Villanacci classification and considered diagnostic for grades $\geq B$. Anti-tTG titers were assessed with 12 different assays; one ELISA kit (specified Upper Limit of Normal=3.5U/ml) was used in 141 subjects (60.3%), while a second one in 59 (25.2%, ULN=9.9U/ml). Accuracy of anti-tTG testing and optimal cut-off levels were determined by means of a ROC curve. Performance was also calculated for a cut-off 10 times ULN.

Results: Mean anti-tTG levels at inclusion were 71.1 ± 4.4 U/ml, while mean adjusted levels (anti-tTG/ULN) were 14.8 ± 0.9 times ULN (mean \pm SE). Among the 234 patients, 21 (9%) showed no atrophy; partial and total atrophy were present in 85 (36.3%) and 128 (54.7%) respectively. Anti-tTG levels significantly correlated to the degree of villous atrophy ($p<0.001$; $rs=0.397$, $p<0.001$). AUC proved a fair diagnostic accuracy both for unadjusted and adjusted anti-tTG levels (respectively 0.803, 0.807; $p<0.01$). For the ESPGHAN criterion of anti-tTG=10 times ULN, a positive predictive value (PPV) of 97.7% was calculated (sensitivity=59.2%, specificity=86.9%). The optimal cut-off for adjusted anti-tTG levels was 16 times ULN, with a PPV of 98.9% (sensitivity=41.2%, specificity=95.7%). Considering different assays, results were puzzling; although in the first one PPV (=97.14%) seemed to peak at 50U/ml (14.3 times ULN), the second assay proved considerably more predictive: for a cut-off=37.3U/ml (3.7 times ULN) it showed a superior PPV=100% (sensitivity 53.1%, specificity 100%). This persisted after standardization (cut-offs -0.14 vs -1.2).

Conclusions: In adult symptomatic patients with EMA positivity and genetic susceptibility, anti-tTG titers predict severity of duodenal atrophy. Multiples of ELISA cut-off values can be applied to diagnose CD in a subset of adult patients. Measured values are assay-specific, intrinsically difficult to compare and not scale-dependent in our study. Thus, ESPGHAN criteria can be applied in adults but are sub-optimal for the purpose of achieving uniform prediction of

atrophy. Our findings could prove useful when assessing equivocal histological cases, and could help in guiding patient follow-up.

P.08.15

INCREASED INTRA-BOLUS PRESSURE IS ASSOCIATED WITH NON-CARDIAC CHEST PAIN AND NEGATIVE ENDOSCOPY – A STUDY USING HIGH-RESOLUTION MANOMETRY

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Background and aim: High Resolution Manometry (HRM) is currently considered the gold standard to assess esophageal peristalsis and esophago-gastric junction (EGJ) function. Indeed, with the use of this technology novel validated metrics have been developed to define esophageal motility abnormalities. In particular, the intrabolar pressure (IBP) has been initially regarded as an indirect measure of bolus transit through the EGJ, although the last iteration of Chicago Classification lacks of its adoption because of the paucity of data in this regard. We aimed to investigate whether patients with non-cardiac chestpain (NCCP) and reflux-related heartburn (RH) may present different IBP values and which is its pathophysiological role.

Material and methods: We included consecutive patients with NCCP or RH as stand-alone symptom, referring to our motility laboratory. Patients with gastro-intestinal surgery, achalasia or scleroderma were excluded. All patients underwent esophagogastroduodenoscopy (EGDS) and HRM with 5-min baseline recording and 10 single water swallows. The diagnostic criteria agreed with the Chicago Classification vers. 2. Data were expressed as mean and standard deviation. A t-test and χ^2 analysis were performed to compare data. A p-value < 0.05 was considered statistically significant.

Results: Between March 2014 and March 2015, we included 24 patients (9 Male, 56 ± 15 years) with NCCP and 47 patients (50 ± 13 years; 19 M) with RH. No differences in terms of age, sex, BMI, manometry patterns and esophagogastric junction morphologies were found between the two groups ($p=ns$). Patients with NCCP had a mean IBP higher than patients with RH (18.6 ± 6.7 vs. 14.1 ± 4.7 ; $p=0.02$). Mean DCI (79 ± 36 vs. 82 ± 35 ; $p=0.7$) and resting pressure (30 ± 12 vs. 22 ± 11 ; $p=0.06$) were similar between the two groups. Only 1/24 patients (4%) of the NCCP patients had endoscopic evidence of GERD, while in RH group the number was higher (13/47; 28%; $p=0.02$).

Conclusions: The IBP is the only HRM metric that differed between patients with NCCP and those with RH supporting its diagnostic usefulness in distinguishing them and suggesting that NCCP elicitation can be more related to reduced distal oesophageal compliance as a whole (i.e. abnormal bolus transit and EGJ dysfunction) rather than abnormal vigor of peristalsis. Finally, an increased IBP well correlated with a negative endoscopy, thus reflecting a potential role of IBP in contrasting reflux occurrence.

P.08.16**NEW IMPEDANCE-PH PARAMETERS OF GASTRO-ESOPHAGEAL REFLUX DISEASE: A LESSON FROM PATIENTS WITH CHRONIC AUTOIMMUNE ATROPHIC GASTRITIS, NON-EROSIVE REFLUX DISEASE AND FUNCTIONAL HEARTBURN**

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Background and aim: Factors influencing new markers of gastro-esophageal reflux disease (GERD) detected by multichannel impedance monitoring (MII-pH) (i.e., mean nocturnal baseline impedance, MNBI and Post-reflux Swallow-induced Peristaltic Wave, PSPW index (1)) are still to be definitively elucidated.

To evaluate this issue, we included three different groups of patients with a peculiar MII-pH pattern: 1) patients with chronic autoimmune atrophic gastritis (CAAG) and MII-pH evidence of GERD (2) 2) patients with non-erosive reflux disease (NERD) and 3) patients with functional heartburn (FH).

Material and methods: Study design: Multi-center retrospective analysis. Patients: 24 CAAG, 25 NERD and 25 FH patients. MII-pH off PPI: All the tracings were retrospectively reviewed. GERD was defined in presence of: i) increased acid exposure time (AET) and/or ii) increased n° of total refluxes and/or iii) positive symptom index (S.I.) and/or Symptom Association Probability (S.A.P.). Acid and non-acid (i.e., weakly acid + weakly alkaline) as well as proximal refluxes were reported. Normal values were based on (3), MNBI and PSPW index were calculated according to (1). Statistical analysis: mean and standard deviation was calculated. ANOVA was performed to evaluate difference among groups (p significant when < 0.05).

Results: Nineteen/24 CAAG patients (79%) were symptomatic; all NERD and FH patients had heartburn. All data are summarized in Table 1. Females were more prevalent in CAAG and FH groups (p<0.0001), whereas age and body mass index (BMI) was similar among the three groups. As expected, total AET was significantly higher in NERD patients (p<0.0001). Furthermore, CAAG and NERD patients had a higher number of refluxes compared to FH, being acid ones more common among NERD patients and non-acid among CAAG patients. Intriguingly, PSPW index was similar between CAAG and NERD patients but significantly lower compared to FH group (p<0.0001), whereas MNBI decreased progressively in FH (>3000 Ohm), CAAG (> 2000 Ohm) and NERD (< 1000 Ohm) patients (p=0.0046).

Table 1: MII-pH characteristic from the three different groups.

	CAAG (24)	NERD (25)	FH (25)	P
AET tot (% t pH < 4)	1.5±2	10±5.1	0.6±0.6	0.0001
Total reflux (n°)	65.6±19.8	72.8±30.4	23.7±6.9	0.0001
Acid (n°)	11±10.5	47.8±20.3	10.5±5.5	0.0001
Non-acid (n°)	54.4±20	24.9±18.3	13.2±4.7	0.0001
Proximal reflux (n°)	25±13.8	29.6±20	8.7±3.8	0.0001
PSPW index	27.1±8.7	27.2±7.1	70.9±6.1	0.0001
RET	0.9±0.4	5.4±3.3	0.5±0.3	0.0001
MNBI (Ohm)	2227.7±514.7	970.8±180	3888.8±728.3	0.0046

Legend: AET (acid exposure time); PSPW (post-reflux swallow induced peristaltic wave); MNBI (Mean Nocturnal Baseline Impedance); RET= reflux exposure time

Conclusions: Our results showed that both PSPW index and MNBI improve diagnostic accuracy of MII-pH in GERD. PSPW index is a strong marker of GERD and is not affected by AET.

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P.09 Colon 1**P.09.1****HIGHER ADENOMA DETECTION RATE BUT NOT ADVANCED ADENOMA WITH ENDOCUFF-ASSISTED COLONOSCOPY IN A SCREENING POPULATION**

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Background and aim: The Adenoma Detection Rate (ADR) is one of the quality measures in screening colonoscopy. The lower the ADR the higher the risk of cancers after colonoscopy. Endocuff is an endoscopic cap with plastic projections which permits to flatten the colonic fold during withdrawal. Endocuff-Assisted colonoscopy (EAC) is potentially able to ameliorate the ADR which is crucial especially in a screening population. To compare in a screening population: ADR, advanced adenoma detection rate (AADR) and number of adenoma detected between EAC and Standard colonoscopy (SC).

Material and methods: We compared the performance of SC (from January to September 2014) and EAC (from January to September 2015) both in consecutive Fecal Immunochemical Test (FIT) positive and endoscopical Follo-up screening participants. Colonoscopy was performed by the same team of endoscopists in both 2014 and 2015. ADR was defined as the number of colonoscopy with at least one adenoma divided by the total number of colonoscopies; mean number of adenoma per patient was defined as the total number of detected adenomas divided by the number of colonoscopies; AADR as the number of colonoscopy with at least one advanced adenoma (defined as an adenoma of 1cm or greater, or with villous/tubule-villous components or with high grade dysplasia) divided by the number of colonoscopies.

Results: 403 (198 F, mean age: 60.4 years, 49-70) and 445 (186 F, 60.2, 49-70) subjects performed SC and EAC respectively. ADR was 46% in SC and 53% in EAC, p<0.05. Mean number of adenoma per patient who undertook SC and EAC was 0.9 (range: 0-8) and 1.1 (range: 0-13) respectively, p<0.05. Advanced adenoma detection rate was 27% and 23% in SC and EAC respectively, p=ns.

Conclusions: EAC increases both adenoma detection rate and the number of polyps detected. However, it does not ameliorate advanced adenoma detection rate.

P.09.2**COLORECTAL CANCER SCREENING: PRELIMINARY DATA FROM THE CASERTA AREA**

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Background and aim: Italian epidemiological data on colorectal cancer screening programs described a 5.2% of subjects with positive fecal occult blood test (FOBT) in the general population. The same data reported that 80% of these subjects underwent colonoscopy. The cancer detection rate was 2.2 per 1000 people and the detection rate for advanced adenomas was 0.3 per 1000. The aim of our study was to compare the national data to those of the Caserta area in the first 18 months of the screening.

Material and methods: Between January 2014 and August 2015, 70,21% (n=225.907) of eligible 321.765 people who lived in Caserta and aged 45-75 years, were invited to participate in the national population-based screening program. The subjects who agreed to participate received a guaiac-based FOBT and those with positive test were invited to undergo full colonoscopy.

Results: Of the 225.907 participants invited for the screening, 15.08% (n=34.060) agreed to undergo FOBT that resulted positive in 8.08% (n=2.717). Actually, 52.52% (n=1324) of FOBT-positive subjects performed colonoscopy. Colorectal cancer (n=102) was found in 7.7% of FOBT-positive subjects. High grade dysplasia adenomas (n=495) and lower grade dysplasia adenomas (n=219) were found in 37.4% and 16.5% of FOBT positive subjects respectively, whereas in 22% of those investigate other abnormalities (hyperplastic polyps, diverticular disease, inflammatory bowel diseases) were recorded as being present. The cancer detection rate was 3.1 per 1000 people and the detection rate for advanced adenomas was 15 per 1000.

Conclusions: Despite a lower percentage of people who agreed to undergo colonoscopy in our area we found a higher rate of cancers and advanced adenomas compared to the national data. Our results suggest the necessity to continue the screening and increase the awareness of colorectal cancer screening program and its benefits amongst the general population.

P.09.3**COLORECTAL CANCER SCREENING IN EARLY AGE: PRELIMINARY DATA FROM THE CASERTA AREA**

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Background and aim: Several randomized trials suggest that screening for colorectal cancer using guaiac-based fecal occult blood test (FOBT) reduces mortality by 25% in people who undergo the screening. Generally, only people aged 50-74 years are invited. The aim of our study was to evaluate preliminary data on the effects

of FOBT-based colorectal cancer screening in subjects aged 45-49 years.

Material and methods: Between January 2014 and August 2015, 70,21% (n=225.907) of a total of 321.765 eligible people living in Caserta and aged 45-75 years were invited to participate in the national population-based screening program. The subjects who agreed to participate received a guaiac-based FOBT and those with positive test were invited to undergo full colonoscopy.

Results: Among the subjects who accepted to undergo FOBT, 3017 (1.33%) were aged 45-49 years. The FOBT resulted positive in 151 (5%) of this age-group, while 23.1% (n=35) of the FOBT-positive subjects underwent colonoscopy. Colorectal cancer was found in three people aged 45-49 years (8.57%); high grade dysplasia adenomas and low grade dysplasia adenomas were found in 9.27% (n=14) and 4.63% (n=7), respectively. Other diseases were reported in 16% of this age group (hyperplastic polyps, diverticular disease, and inflammatory bowel diseases). Cancer detection rate was 1 per 1000 screened people, while detection rate for advanced adenomas was 4.6 per 1000.

Conclusions: We found a low rate of FOBT positive subjects in the 45-49 age-group, with most of the individuals who agreed to undergo colonoscopy being positive for any lesions. However, a higher numbers of screening in this age group is needed to understand the real benefit of including these subjects in a national screening program.

P.09.4**THREE-DIMENSIONAL HIGH-RESOLUTION ANORECTAL MANOMETRY AND RECTOANAL DELTA CONTRACTILE INTEGRAL FOR THE ASSESSMENT OF FUNCTIONAL DEFECATORY DISORDERS: TOY OR TOOL?**

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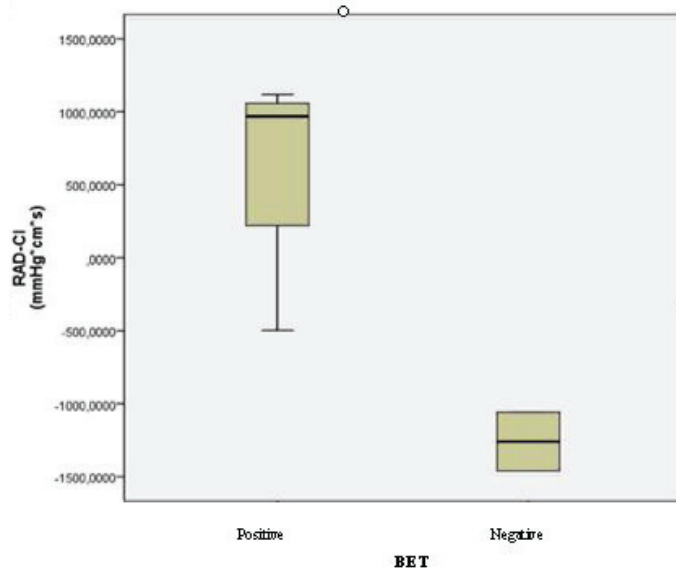
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Background and aim: Conventional water perfused manometry (WPM) identifies functional defecatory disorders (FDD) according to the defecatory patterns suggested by Rao. Unfortunately, manometric data often conflict with clinical data, and the balloon expulsion test (BET) or defecography need to be performed to reach a correct diagnosis. High resolution anorectal manometry (HRAM) and three-dimensional HRAM (3D-HRAM) enable a better evaluation of the endoanal and endorectal pressure and the anorectal dynamics, thus providing better diagnostic accuracy. On the basis of the indexes used by esophageal high resolution manometry we identified a new parameter potentially useful for the evaluation of FDD: the Recto-Anal Delta-Contractile Integral (RAD-CI). The aim of the study was to evaluate: 1) the possible correlation between WPM and 3D-HRAM parameters 2) the anorectal dynamics using RAD-CI and its possible correlation with BET.

Material and methods: Twenty-one FDD (mean age 54.8 ± 17.9 yrs.; 12F), diagnosed by using WPM, BET and/or defecography (15 type I, 6 type II), underwent 3D-HRAM (Manoscan 360TM, Medtronic - USA). Endoanal and endorectal pressure values obtained during the push straining were used to calculate the contractile integral (CI), which is a measure of duration and intensity. Endoanal CI was evaluated on a space including the anal canal for the whole duration of the push straining. By using the function "isobaric contour", pressures lower than mean resting pressure of the anal canal were excluded. Endorectal CI was calculated on a 10 mm space for the whole duration of push straining. RAD-CI was the difference between endoanal CI (proportionally correlated to 10 mm) and endorectal CI.

Results: Correlation between 3D-HRAM and WPM was found regarding maximum pressure ($r=0.53$, $p<0.05$), squeezing pressure ($r=0.85$, $p<0.001$), RAIR ($r=0.76$, $p<0.001$), constant sensation ($r=0.55$, $p<0.05$) and maximum tolerated volume ($r=0.63$, $p=0.005$). Eighteen patients showed a dyssynergic pattern at 3D-HRAM (9 type I, 9 type II). RAD-CI was inversely related to BET ($p<0.05$) (fig.1) and this correlation is stronger than that detected by using the traditional RectoAnal Pressure Gradient (RAPG) (ns, $p=0.17$).

Fig. 1 Balloon Expulsion test



Conclusions: Also in the evaluation of dyssynergic defecation 3D-HRAM shows a substantial agreement with WPM. This study shows that RAD-CI show a correlation with BET better than RAPG. RAD-CI could be an important index for the evaluation of dyssynergic defecation.

P.09.5

DIVERTICULAR DISEASE: ALTERED RESPONSE TO ENTERIC NEUROTRANSMITTERS IN HUMAN COLONIC LONGITUDINAL AND CIRCULAR SMOOTH MUSCLE

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Background and aim: Colonic diverticulosis (CD) represents an asymptomatic condition that may predispose to the development of uncomplicated and complicated diverticular disease (CDD). Several alterations in muscle structure and enteric neural derangement have been reported in both conditions, predisposing to colonic dysmotility. Aim of this study was to investigate the presence of functional and molecular alterations in human colonic muscle in CD and CDD.

Material and methods: Longitudinal and circular smooth muscle cells (SMC) and strips were isolated separately from surgical colon specimen of 9 patients (58<age<80years) affected either by sigmoid CD or CDD and 9 patients (61<age<80years) submitted to surgery for colon cancer. Contraction was tested in response to acetylcholine (ACh 1μM) or carbachol (CCh 1μM), whilst relaxation to vasoactive intestinal peptide (VIP 1μM). qPCR analysis was

performed for transcription of muscarinic M3, VIP-related receptors (VPAC1, VPAC2, NPR-C) and eNOS. qPCR data were normalized to β-actin mRNA. Data are expressed as mean±SE, $p<0.05$ considered significant.

Results: In CD, longitudinal muscle showed a significant decrease in ACh-induced contraction compared to control (cells: 9.8 ± 1.4 vs 16.8 ± 1.8 , strips: 830 ± 54 vs 1664 ± 173 mN/cm² respectively) and in transcripts for M3 receptors (6.8 ± 0.18 vs 7.98 ± 0.45). CD longitudinal muscle did not differ from control in terms of resting cell length, VIP-induced-relaxation and transcripts for VIP receptors and associated signals. In turn, CD circular muscle presented an impaired relaxation in comparison to control (cells: 33.3 ± 8.3 vs 93.2 ± 1.4 , strips: 458 ± 55 vs 1435 ± 242 mN/cm²) associated to a significant decrease of transcripts for VIP-related receptors and signals: VPAC1 (8.7 ± 4.4 vs 15.6 ± 0.1), VPAC2 (9.0 ± 0.4 vs 13.2 ± 1.0), NPRC (9.5 ± 0.03 vs 15.2 ± 0.3) and eNOS (10.3 ± 0.9 vs 14.7 ± 0.2). CD circular muscle did not differ from control in terms of contraction. In CDD, besides the impairment of relaxation, an inhibition of contractile response was observed compared to control (6.5 ± 1.1 vs 17.7 ± 0.7).

Conclusions: In CD and CDD colonic muscle presented an altered response to enteric neurotransmitters associated to different expression of their membrane receptors. These myogenic alterations represent a further element contributing to colonic dysmotility in both conditions.

P.09.6

LONG TERM FOLLOW-UP OF RECURRENT/RESIDUAL COLORECTAL ADENOMAS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION: A SINGLE CENTER EXPERIENCE

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Background and aim: Endoscopic removal of recurrent/residual colorectal polyps (RCP) is a challenging procedure due to low effectiveness in radical resection, technical difficulties and high rates of complications. Some retrospective studies described the performance of endoscopic submucosal dissection (ESD) in this setting, however few data are available on long term outcomes. Aim of this study was to report our data on endoscopic follow-up in this group of patients.

Material and methods: We retrospectively evaluated a group of consecutive patients who underwent ESD from 2011 to 2013 for recurrent/residual colorectal polyps after one or more previous treatments. Data regarding size and site of adenomas, endoscopic technique, complications, histopathological examination and outcomes of the procedure (complications, radicalness of resection, rate of recurrence and need for re-treatment) were evaluated. Data are showed as mean±standard deviation or median with ranges for discrete variables and percentages for continuous ones.

Results: Thirteen patients (mean age 64.4 ± 9.8 years, males 38.4%) were included in the study. Median size of polyps was 20 mm (range 10-50 mm). Three perforations occurred during the endoscopic procedures (23.1%) but were managed conservatively with clips application. En-bloc resection was achieved in 7 patients (53.8%). Histopathologic examination revealed low-grade dysplasia in five cases (38.4%), high-grade dysplasia in seven cases (53.8%) and one case of adenocarcinoma (7.7%). R0 resection was achieved for deep margins in four cases (30.7%) and for lateral margins in 9 cases (69.2%). In one case (7.7%) margins were not evaluable (Rx) because of coagulation artifacts. The patient diagnosed with a malignant polyp underwent surgical treatment for R1 resection evidence. At first endoscopic control in two patients (16.6%) relapse of adenomatous tissue on the post-ESD scar was observed during follow-up, which was successfully removed endoscopically (in one with two sessions

of piecemeal endoscopic mucosal resection + APC and in the other with hot snare polypectomy + APC). In the remaining 10 patients, after a mean follow-up of 26.5±10.3 months, we had no evidence of RCP at the site of endoscopic intervention.

Conclusions: ESD is an efficient technique as salvage treatment of RCP in alternative to surgery. Long term observation revealed low rates of recurrence even when radical resection was not achieved.

P.09.7

PROGNOSTIC SIGNIFICANCE OF CLINICALLY METASTATIC MESORECTAL LYMPH NODES IN LOCALLY ADVANCED RECTAL CANCER TREATED BY NEOADJUVANT CHEMORADIATION: IMPLICATIONS FOR SURGICAL STRATEGIES IN RELATION TO PATHOLOGICAL RESPONSE

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Background and aim: Neoadjuvant chemoradiation therapy (CRT) and radical surgery including total mesorectal excision (TME) reduces the risk of local recurrence, and is considered the standard of care for patients with locally advanced (T3-4 or any N1-2) mid-distal rectal cancer (LARC). Organ preserving strategies have been considered in LARC patients achieving complete pathological response (pCR) after neoadjuvant CRT. Our aim was to explore the value of this approach in cN+ patients.

Material and methods: Data were retrieved from our Institutional prospective rectal cancer data-base. Tumors with mesorectal lymph nodes >5mm by pelvic MRI and/or endorectal US were staged as cN+.

Results: Study population comprised 226 patients (142 men, 84 women; median age 64 yrs, range 25-87) with LARC and no distant metastasis treated by CRT followed by surgery including TME (n. 179), and by full thickness local excision (LE) (n. 47) between 1996 and 2013. At staging 123 (54.4%) patients were cN+. At pathology, pCR in the primary tumor was observed in 65 (28.7%) cases. Median number of examined lymph nodes was 12 (range, 2-37). Metastatic mesorectal lymph nodes (ypN+) were detected in 45 (42.2%) out of 107 cN+ patients compared to 2 (2.7%) out of 72 cN- patients (p<0.01). In cN+ tumors 4 (16.0%) out of 25 cases with pCR were ypN+ compared to 43 (51.8%) out of 83 cases with no-pCR (p<0.01). During a median follow-up of 48 months 30.5% patients had recurrent disease, and 16.3% died of disease. In cN+ patients who underwent TME surgery 5-year DSS and DFS were 100% and 91.6% in pCR patients compared to 71.2% and 58.0% in no-pCR patients (p=0.01). In ypN+ patients with metastatic lymph nodes at pathology 5-year DSS and DFS were both 100% in pCR cases compared to 59.1% and 43.3% in no-pCR patients (p=n.s.). In cN+ patients and pCR 5-year DSS and DFS were 100% and 85.7% in TME patients and 100% and 91.6% in LE patients (p=n.s.). At multivariate analysis pCR was the only independent prognostic factor.

Conclusions: Our findings indicate that in patients with LARC achieving pCR after CRT organ preserving strategies are safe in cN-cases, while the favorable long-term outcome of pCR tumors should be balanced with the risk of metastatic mesorectal lymph nodes in cN+ cases.

P.09.8

BIOFEEDBACK BENEFITS PATIENTS WITH DYSSYNERGIC DEFECATION WITH OR WITHOUT ELECTRICAL STIMULATION

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Background and aim: Constipation is a common disorder but its treatment remains unsatisfactory. A large part of patients affected

by constipation suffers of dyssynergic defecation. Pelvic floor retraining is useful to improve defecatory disorders symptoms but the exercises are not standardized. In particular is not established the utility of functional electrical stimulation (SEF), especially used for urological disorders, in dyssynergic defecation to improve rectal sensation. The aim of the study is to compare biofeedback-guided pelvic floor (BFB) exercise therapy with and without SEF in the treatment of obstructive defecation.

Material and methods: A total of 39 subjects affected by obstructive defecation, diagnosed by clinical history, ano-rectal manometric results and balloon expulsion test, were assigned to BFB (19 pts) and BFB+SEF (20 pts). BFB consists of improving the abdominal push effort together with pelvic floor relaxation followed by simulated defecation training. SEF involves the electrical stimulation of pelvic floor muscles using a probe wired to a device for controlling the electrical stimulation. The Wexner constipation score system (that evaluates frequency of bowel movements, difficult evacuation, digitation necessity, incomplete emptying sensation, laxative dependence, unsuccessful attempts at evacuation, minutes in lavatory per attempt, abdominal pain) was assessed at the beginning and at the end of pelvic floor retraining.

Results: At the end of pelvic floor retraining the symptoms improved in 11/20 pts treated with BFB+SEF and in 11/19 pts with BFB, did not change in 8/20 pts with BFB+SEF and in 8/19 with BFB and worsened in 1/19 pts with BFB+SEF. Patients in both groups referred improvement of incomplete emptying sensation, more of the other symptoms (8 in BFB+SEF and 9 in BFB group). About the efficacy of pelvic floor retraining we showed no differences in patients treated with BFB alone or with SEF.

Conclusions: The pelvic floor retraining is useful for obstructive defecation but electrical stimulation dose not give additional effect in this patient group.

P.09.9

AN APPROACH TO CHRONIC CONSTIPATION BY DIGITAL EXAMINATION + BALLOON EXPULSION TEST IS FEASIBLE IN DAILY CLINICAL PRACTICE AND DECREASES FURTHER ANO-RECTAL INVESTIGATION

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Background and aim: Patients (Pts) affected by chronic constipation are evaluated by general practitioners and, if necessary, by gastroenterologists usually located in primary centers. Both often prescribe many types of laxatives but rarely perform digital examination (DE) focused on motility disorders and/or balloon expulsion test (BET). Only Pts refractory to laxatives are extensively evaluated in tertiary centers. This approach could delay a diagnosis of obstructed defecation syndrome (ODS) and could affect the real prevalence of ODS due to possible selection bias. However it's unclear if an approach to chronic constipation by DE +BET is feasible in daily clinical practice.

In our GE unit we started an open-access medical office focused on chronic constipation. If the patient agrees, we perform DE+BET during the first evaluation. If both tests are negatives we exclude ODS and avoid further ano-rectal tests. If both tests are positives we make a diagnosis of ODS and prescribe a biofeedback therapy or perform AR-manometry (ARM) or defecography (DEF) guided by clinical judgment. If DE+ BET are discordant we prescribe ARM and/or DEF to confirm or not ODS. Obviously we prescribe others investigations (eg. colonoscopy, Rx transit time) if necessary. Our aim was to show that this approach is feasible in daily clinical practice and is able to confirm or exclude ODS, decreasing utilization of others ano-rectal tests.

Material and methods: Data were retrospectively collected. We analyzed data of 206 Pts affected by chronic constipation, previously not evaluated by others gastroenterologists and not affected by secondary constipation. We measured number of Pts studied by DE+BET and concordance between tests.

Results: Pts were 71% females, with an average age of 58 years old and affected by constipation on average by 18 years. DE and/or BET were performed in 157 Pts (76%). Both tests were performed in 119 Pts (57%) and were concordant in 73% of Pts. A concordant (DE+ BET) positive pattern confirming ODS was present in 41% of Pts studied by both tests. A concordant (DE+BET) negative pattern excluding ODS was present in 32% of Pts studied by both tests.

Conclusions: The prevalence of concordant (DE+BET) positive pattern confirming ODS in unselected Pts evaluated in an open access ambulatory was 41%. We were confident to stop other ano-rectal studies in 32% of Pts negatives for both tests. We think that a clinical approach by DE combined with BET is feasible in daily clinical practice, is helpful to guide diagnostic work-up in most of constipated Pts and could prevent further ano-rectal investigation. The prevalence of ODS is elevated in an open access primary center.

P.09.10

CLINICAL USE OF VIDEO CAPSULE ENDOSCOPY FOR SMALL BOWEL SURVEILLANCE IN HEREDITARY COLORECTAL CANCER SYNDROMES

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Background and aim: Patients with Hereditary Colorectal Cancer Syndromes (HCCS) have an increased risk to develop adenocarcinoma of the small bowel (SB) arising from premalignant polyps. In the last fifteen years, the advent of capsule endoscopy (VCE) and balloon enteroscopy allowed to reach a comprehensive exploration of the entire SB and changed the clinical management of these patients (pts). The indications of the International Guidelines for SB surveillance in HCCS are still undefined. The aims of the present study were: 1) to evaluate the prevalence and characteristics of SB neoplasm in pts with HCCS assessed by VCE; 2) to evaluate the safety and diagnostic accuracy of VCE.

Material and methods: From January 2007, pts with a diagnosis of HCCS in follow-up at Regina Elena National Cancer Institute HCCS Clinics were enrolled in the study. All pts were clinically asymptomatic and underwent VCE examination, gastroscopy (with side viewing in FAP cases) and lower endoscopy within one month from VCE examination. Pts with SB neoplasm detected at VCE underwent Push enteroscopy (PE) or Single balloon enteroscopy within 1-3 months from VCE examination.

Results: 86 patients with HCCS (36M/50F, mean age at VCE examination of 40.2 years, range 17-67), were enrolled in the study. VCE detected SB polyps in 48 cases (55.8%), 35/64 FAP (57.8%), 7/8 PJS (87.5%), 4/12 LS (33.3%) and none of the MAP pts. We observed that each HCCS had its typical polyp pattern: low burden (n<5), small size (<5 mm) and most frequently upper SB involvement in FAP; a low burden, large size (> 1 cm), upper SB involvement in LS; a variable number, a large size and the entire SB involvement in PJS. Comparison of VCE with endoscopy (gold standard) showed a low diagnostic accuracy (70.9%; IC 61,33-80,53), sensitivity (71.7%, IC 57,38-86,02) and specificity (69.7%, IC 56,70-82,70). In FAP cases we evaluated the association between Spigelman stage and presence of non duodenal SB polyps and it resulted not significant (Kappa coefficient of concordance=0.402).

Conclusions: In FAP and LS cases, in which upper SB resulted mostly involved (in line with scientific literature), duodenoscopy and upper PE could be adequate and VCE could be performed only in selected cases. In PJS patients, VCE had high performance and allowed to

evaluate the whole SB usually entirely involved. In conclusion, VCE is a safe, well-tolerated, non invasive but expensive tool, its use could be routinary in PJS and limited to selected cases in FAP and LS.

P.09.11

ASSOCIATION BETWEEN COLORECTAL POLYPS AND COLONIC DIVERTICULOSIS

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Background and aim: colonic diverticula and neoplastic colorectal lesions are found in similar ranges of age and populations, but it is unclear whether there is a shared pathway in their development. Their frequency increases with age and seems to be associated with a lack of dietary fibres, increased dietary saturated fats, obesity and a slow colonic transit time. The association of diverticulosis and colorectal polyps has been previously evaluated, reporting conflicting results. Despite common epidemiologic predisposing factors, the association between diverticulosis and colon polyps remains unclear and needs to be better defined, as it could have important implications for the screening of colorectal cancer. The aim is to evaluate the association between colorectal polyps, cancer and colonic diverticulosis.

Material and methods: A one-year prospective study including all consecutive patients undergoing to routine colonoscopy at our GI Unit from September 2014 to September 2015. The presence and location of diverticula, polyps, and cancers was recorded using colonoscopy reports. Types of colorectal neoplastic lesions were defined by histopathological examination. Polyps were classified into adenoma (with low or high dysplasia), hyperplastic or inflammatory polyps. A multiple logistic regression analysis was done to evaluate the association between diverticular disease and colonic lesions.

Results: 447 patients were included in the study (245 M, 202 F, mean age 66 years): 166 (37.1%) patients presented only diverticulosis, 155 (34.7%) patients presented only polyps, and 126 (28.2%) patients presented both the diseases associated.

There was no significant association between adenoma and colonic diverticula, as well as between colorectal cancer and diverticula. On the other hand, colorectal inflammatory polyps showed a significant association with diverticulosis.

Conclusions: The results of the study show no association between adenomas and diverticula nor between cancer and diverticula. Therefore, patients with colonic diverticulosis do not require a different follow-up for the prevention of colorectal cancer than the general population. Inflammatory polyps are frequently associated to colonic diverticular disease probably due to the same pathogenic factors.

P.09.12

ASSESSMENT OF FECAL MICROBIOTA AND FECAL METABOLOME IN SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE OF THE COLON

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Background and aim: Current knowledge on fecal microbiota and fecal metabolome in Symptomatic Uncomplicated Diverticular Disease (SUDD) of the colon is still lacking. We performed a prospective study assessing fecal microbiota and metabolome in those patients.

Material and methods: Stool samples from 52 consecutive female patients (17 with SUDD, 16 with asymptomatic diverticulosis, and 19 healthy) were analysed. Real-time PCR was used to quantify targeted microorganisms. High-resolution proton nuclear magnetic resonance spectroscopy in combination with analysis of variance-Simultaneous Component Analysis model were assessed in determining fecal metabolome.

Results: The overall fecal bacterial quantity did not differ among the three groups ($p=0.449$). The quantitative analysis of bacterial populations showed no difference in the numbers of rRNA gene copies neither for the total bacteria nor for the different types analysed in the three study groups (Akkermansia: $p=0.298$; Bacterioides: $p=0.354$; Bifidobacterium: $p=0.876$; Clostridium: $p=0.463$; Escherichia: $p=0.728$; Lactobacillus: $p=0.633$). Overall, fecal metabolome analysis was not able to detect any significant model. However, methanol, glycine, U1 and U2 was found significantly increased in SUDD.

Conclusions: SUDD does not show any significant quantitative and qualitative alteration of the analysed fecal microbiota. However, increasing expression of some metabolites as expression of different SUDD metabolic activity were found.

P.09.13

ADVANCED ADENOMA IN SCREENING POPULATION AND LIFE STYLE HABITS: A CASE CONTROL STUDY

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Background and aim: Colorectal cancer (CRC) is the most frequent tumor in Italy. Friuli Venezia Giulia Region has higher CRC incidence than in population of Northern Italy (33 vs 21/100,000 men and 21 vs 12.1/100.00 females). Several risk factors may increase the chance of developing CRC. Aim of this study was to evaluate if life-style habits are linked to the development of advanced adenoma in screening population in Trieste area.

Material and methods: In the present single centre, case-control observational study, 50-74 years old asymptomatic subjects participating in an organized CRC screening program based on immunologic fecal occult blood test and undergoing colonoscopy for positive test received a structured questionnaire investigating lifestyle habits. Patients with advanced adenoma were matched on age and sex with patients with negative colonoscopy (controls).

Results: Since January to May 2015, 400 pts were recruited and data on 234 subjects (78 cases and 156 controls) were evaluated. Seven variables were selected for multivariate logistic regression analysis: daily intake of fresh fruit, daily 30' walking, units of alcohol consumption, daily intake of raw vegetables, smoking habits, low dose aspirin and vitamins per day. A protective role for the onset for advanced adenoma was found for the intake of fresh fruit (OR for ≥ 2 vs. 0-1 portions 0.28 CI 0.08-0.78 $p=0.02$) and daily walking (OR 30' or more walking vs. <30' 0.42 CI 0.20-0.87 $p=0.02$).

Conclusions: Daily intake of fresh fruit and regular physical activity are the only significant protective variables towards the onset of colonic precancerous lesions. The results of this preliminary study underline the importance of the implementation of educational interventions for the whole population.

P.09.14

ROLE OF METABOLIC, ATHEROGENIC AND PSYCHOLOGICAL FACTORS IN PATIENTS WITH COLORECTAL ADENOMAS

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Background and aim: Proinflammatory states of large bowel have a multifactorial aetiology, including metabolism, atherogenesis and also psychological determinants. Inflammation is also a key factor for the development of adenoma and colorectal cancer. The aim of the study is investigate the association between pro-atherogenic factors, metabolic status, psychological assessment and the presence of colorectal adenomas.

Material and methods: In our case-control observational ongoing study, patients underwent colonoscopy for positive faecal blood test and/or abdominal symptoms with negative history for neoplasia or inflammatory bowel diseases. We collected waist and hip circumferences, BMI, arterial pressure, fasten serum glycemia, medical and drug history. Patients were analyzed, in blind for the outcome of colonoscopy (adenoma vs no-adenoma), evaluating carotid IMT (QIMT®-Esaote software) and psychometric assessment of anxiety and depression using HADS (Hospital Anxiety and Depression Scale).

Results: From January 2015 we analyzed 18 patients (8 M, 10 F), mean age 62.6 years (range 48-77). 10 patients (M/F 6/4) had at least one adenoma at colonoscopy, 8 (M/F 2/6) had no lesions. Data analysis showed no significant difference between adenoma and no-adenoma group for fasten serum glycemia, arterial pressure, HADS score for anxiety, BMI and waist/hip ratio values. Significant difference between adenoma vs no-adenoma group was found for waist circumference and body weight ($p=0.009$ and $p=0.03$ respectively), carotid QIMT median value ($p=0.037$) and HADS score for depression ($p=0.026$). We observed also an inverse correlation between age and HADS anxiety score ($p<0.05$) and a direct correlation between higher values fasten serum glycemia and carotid QIMT ($p<0.05$).

Conclusions: Despite the small sample size and the preliminary nature of data, the association between waist circumference, body weight, higher values at the QIMT examination and presence of adenomas confirms evidence of literature showing connections between metabolism and risk of development of colorectal cancer. Depression, and not anxiety, seems to be a factor characterizing patients with adenomas versus adenoma-free group. In conclusion our study provides interesting insights into the complex relation between proinflammatory state, evaluated through a multidisciplinary approach, and development of precancerous colorectal lesions.

P.09.15

INCREASED ABUNDANCE OF BENEFICIAL BACTERIA IS ASSOCIATED WITH CLINICAL IMPROVEMENT AFTER RIFAXIMIN TREATMENT

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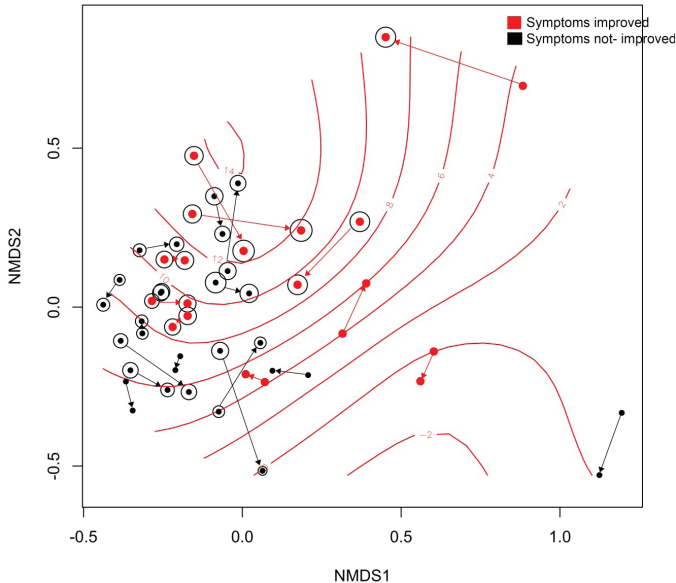
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Background and aim: Rifaximin has been demonstrated to produce a favorable modulation of the gut microbiota. However, whether this beneficial effect is associated with clinical improvement is

still unknown. To explore the correlation between gut microbiota modulation and symptoms improvement in patients undergoing rifaximin treatment.

Material and methods: Rifaximin 1200 mg/daily was administered for 10 days to patients with ulcerative colitis (UC), Crohn's disease (CD), irritable bowel syndrome (IBS), diverticular disease (DD) and hepatic encephalopathy (HE). Inclusion criteria were: no exposure to antibiotics, pre-/pro-biotics and bowel colonoscopy preparation for at least one month, and omnivore normocaloric diet for at least one year. Fecal samples were collected and symptoms were assessed at baseline and at the end of treatment. Clinical improvement was evaluated by Mayo score for UC, CDAI for CD, IBS-SSS for IBS, GSS for DD, and West Haven classification for HE. Fecal microbiota composition was assessed by a metagenomic gene-targeted approach (16S rRNA) using the Roche 454 GS Junior ad Qiime pipeline. Biostatistic analysis was performed using R-statistics packages.

Results: Twenty-five patients were included in the study. Clinical improvement was observed in 10 (40%) patients after rifaximin treatment. Nonmetric multidimensional scaling (NMDS) ordination on Bray Curtis distance highlighted a significant clustering of patients who experienced clinical improvement compared to those who did not ($p=0.047$; PERMANOVA). Differential abundance analysis revealed an increased abundance of *Faecalibacterium prausnitzii* in case of symptoms amelioration after rifaximin treatment (improved post vs pre: $\log_{FC}=1.96$; $p=0.05$; not improved post vs pre: $\log_{FC}=-0.37$; $p=0.810$ Figure 1 and 2). The post-treatment between-groups comparison confirmed a significantly higher abundance of *Faecalibacterium prausnitzii* in those patients whose symptoms improved after rifaximin ($\log_{FC}=4$; $p<0.0001$). Clinical improvement was also paralleled by a significant increase in bacterial alpha-diversity ($p=0.024$).



Conclusions: Beneficial bacteria abundance is increased in patients with gastrointestinal diseases and hepatic encephalopathy who achieve clinical improvement after rifaximin treatment. This mechanism may mediate rifaximin efficacy in different pathologic settings.

P.10 Liver 2

P.10.1

REACTIVATION OF HEPATITIS B VIRUS IN CANCER PATIENTS TREATED WITH CHEMOTHERAPY FOR SOLID TUMORS. IS THE PROPHYLAXIS REALLY REQUIRED?

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Background and aim: Reactivation of hepatitis B virus (HBV) during cancer chemotherapy has become an emerging clinical challenge. High rates of HBV reactivation, 38% to 54%, are now recognized in HBV-positive patients undergoing hematopoietic stem-cell transplantation and treatment for hematological malignancy, especially malignant lymphoma. Less clear is the magnitude of risk for clinically significant HBV reactivation with chemotherapy for non-hematological tumors. Aim of this study is to evaluate the risk of HBV reactivation in carriers and occult carriers of HBV cancer patients treated with chemotherapy for solid tumors.

Material and methods: Two hundred sixty-seven patients with solid tumors were consecutively enrolled, between March 2013 and February 2014 at two Oncological Division in the Campania Region in Southern Italy. Before beginning the study, as a screening procedure, all patients underwent viral marker status (HBsAg/HBsAb, HBeAb, anti-HCV), liver function test with alanine aminotransferases (ALT), and liver ultrasonography.

In HBsAg positive patients we evaluated hepatitis B e-antigen/antibody (HBeAg/HBeAb), HBV-DNA (with real-time fluorescent PCR).

HBV carriers were followed every 3 months by ALT, HBV DNA; occult carriers of HBV were followed every 3 months by ALT and HBsAg. Patients with hypertransaminasemia and HBV-DNA positivity were treated with tenofovir (245 mg/day).

Results: Out of the 267 patients, 13 (4.8%) were HBsAg positive, of whom 6 were documented inactive carrier and 7 had chronic liver disease (1 compensated cirrhosis). Thirty-two patients (12%) were HBsAg negative/HBeAb positive and were classified as potential occult carriers of HBV.

Among patients with HBsAg positive, 12/13 were anti-HBe positive and 1 patient was HBeAg positive. All patients with chronic liver disease had an HBV-DNA level >2000 IU/mL and carried genotype D of HBV. Six occult carrier and one inactive carrier patients were also anti-HCV positive.

None of the patients undergo therapy with one of the following drugs: corticosteroids at high dose (>10 mg/day) for long time, cyclophosphamide, methotrexate. None of the patients had a reactivation of HBV over 18 months (range 2-24) of observation. The patient who was HBeAg positive at the enrolment seroconverted to anti-HBe during the course of treatment with tenofovir after 6 months. The antiviral agents were well tolerated and were not associated with any unexpected or additional toxicities to chemotherapy.

Conclusions: Our study showed that none of the patients presented an HBV reactivation. Thus, it appears reasonable to avoid HBsAg and anti-HBe screening in these patients since anti-HBe result is not relevant to clinical decision. Clearly, screening strategy should be revised periodically, according to survey results on HBsAg prevalence in cancer patients.

P.10.2**EFFECTS OF SILYBIN ADMINISTRATION ON THE REDOX STATE AND OXIDATIVE STRESS RESPONSE OF HUMAN ENDOTHELIAL CELLS IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS**

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Background and aim: Nonalcoholic fatty liver disease (NAFLD) has been identified as independent risk factor for the development of cardiovascular diseases, because of oxidative stress induction.

Literature data documented that silybin presents a marked antioxidant activity both in vitro and in vivo.

The aim of this study was: 1) to compare the levels of oxidants and antioxidants in sera collected from patients with nonalcoholic steatohepatitis (NASH) treated with Silybin conjugated with phosphatidilcholine and vitamin E (Realsil®, R, IBI-Lorenzini, Italy) or placebo (P) at time 0 and after 12 months of treatment; and 2) to investigate the effects of these sera on endothelial cells exposed or not exposed to oxidative stress.

Material and methods: Twenty-seven patients with histological diagnosis of NASH were recruited (11 P and 16 R).

We evaluated peroxidative damage with the Thiobarbituric Acid Reactive Substances (TBARS) method, Superoxide dismutase (SOD) and catalase (Cat) activities in sera and cell lysates.

Human Umbilical Vein Endothelial Cells (HUVEC) were used for the in vitro experiments, exposed or not to oxidative stress with hydrogen peroxide H₂O₂.

Results: We stratified patients (both P and R) in two groups on the basis of the trend in the TBARS serum levels: the first group patients showed a reduction of TBARS at T12 and second group patients showed an increase of TBARS at T12. No differences in the activity of SOD between T0 and T12, both in P and R groups were found. Cat activity decreased exclusively in the R-II group ($p < 0.01$) after 12 months of R administration. A significant reduction of procollagen I after 12 months of R administration in both group R-I ($p = 0.018$) and R-II ($p = 0.030$) was found. In the R-II group we also recorded a significant reduction of ALT ($p = 0.041$) and transforming growth factor (TGF)- β ($p = 0.015$) after 12 months of R administration.

In RI-ECs, an increase of Cat activity at T12 when compared with T0 ($p < 0.05$) was detected, and in RII-ECs we recorded a drastic increase of Cat activity at T12 ($p < 0.02$) when compared with levels at T0.

The treatment with H₂O₂ induces a drastic increase of Cat activity between T0 and T12 in both RI-ECs and RII-ECs (both, $p < 0.01$).

Conclusions: The use of R, which has anti-inflammatory, antioxidant and anti-fibrotic properties, determines a slowdown of the liver damage and could help contribute to the reduction of the incidence of cardiovascular diseases in patients with NAFLD at least in part, through perturbation of the redox state homeostasis.

P.10.3**COUPLED PLASMA FILTRATION ADSORPTION (CPFA) REDUCES BILIRUBIN. CASE REPORT WITH A SYSTEMATIC REVIEW OF THE LITERATURE**

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Background and aim: Severe hyperbilirubinemia frequently occurs in liver failure and may rapidly progress to kidney and neurologic

damage leading to death. While looking for definitive treatments of liver disease, hyperbilirubinemia can be treated by means of artificial liver support devices. The most appropriate artificial liver support device is considered to be Molecular Adsorbent Recirculating System (MARS). However MARS is generally available only in Liver Transplant Unit.

Material and methods: We describe the case of a patients affected by portal cavernoma cholangiopathy who developed acute severe hyperbilirubinemia and that, due to unavailability of MARS, was treated with 2 cycles of coupled plasma filtration adsorption (CPFA). Bilirubin was reduced by 40% after each cycle. CPFA resulted effective in lowering the concentration of bilirubin and allowed to refer the patient to a Liver Transplant Unit.

Results: A systematic literature search was performed using PubMed with the aim to identify studies on the treatment of hyperbilirubinemia using CPFA. Only four papers were retrieved, and they describe, overall, 15 cases of hyperbilirubinemia due to acute liver failure treated using CPFA; in all cases bilirubin promptly decreased.

Conclusions: Summarizing, this is the fifth literature report describing the use of CPFA in a patient with acute hyperbilirubinemia. Each treatment cycle lowered the initial plasma level of bilirubin by about 40%. CPFA is a effective tool in hyperbilirubinemia following acute liver failure.

P.10.4**SPLEEN ELASTOGRAPHY WITH ACOUSTIC RADIATION FORCE IMPULSE IMAGING IN CIRRHOSIS WITH PORTAL HYPERTENSION**

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Background and aim: Spleen elastography is a promising non-invasive method for the characterization of portal hypertension in cirrhotic patients.

We assessed diagnostic performance of spleen stiffness using acoustic radiation force imaging impulse (ARFI) for diagnosing portal hypertension and oesophageal varices.

Material and methods: Our study included 60 subjects (33 healthy volunteers, 27 cirrhotic patients with portal hypertension). All patients were prospectively enrolled from April 2014 to May 2015; they were submitted to liver function blood tests, upper gastrointestinal endoscopy and spleen stiffness measurement with ARFI elastography (IU22 Philips) to determine a cut-off value for the presence of portal hypertension. We performed 10 measurements in each patient expressed in kiloPascal, mean and median values were obtained.

Results: We only experienced patients with portal hypertension above 41,39 kPa, whereas only healthy volunteers were below 12,74 kPa. Nevertheless an overlap of values of the two subjects' classes was observed for the intermediate values (22,1 < kPa < 32,88). For a cut-off value of >20,9 kPa of spleen stiffness, ARFI had 84.9% Se, 71.4% Sp (AUROC=0,833) for detection of oesophageal varices.

Conclusions: Spleen stiffness showed promising results for the detection of oesophageal varices but is not yet sufficiently robust for clinical practice owing to overlap of values.

P.10.5**BERBERINE, TOCOTRIENOLS AND GREEN DECAFFEINATED COFFEE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE: EFFECT OF FULL AND HALF DOSE TREATMENT. SINGLE-CENTRE OBSERVATIONAL STUDY**

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Background and aim: Clinical and epidemiological studies showed a correlation between hypercholesterolemia and non-alcoholic fatty liver disease (NAFLD). Recently, it has been described that a synergistic action of Berberine, Tocotrienols and green decaffeinated Coffee (Trixy® – Nathura) is able to regulate several physiological pathways to achieve a balanced hepatic metabolism. The aim of this study was to observe the effects of Trixy® in reducing cholesterol, triglycerides, glycemia, aspartic-transaminase (AST), alanine-transaminase (ALT), and gamma-glutamyl-transferase (GGT) in overweight and obese patients with NAFLD.

Material and methods: We enrolled 70 consecutive patients with NAFLD, presenting moderate to severe grade of hepatic steatosis, abnormal hepatic-necrotic indexes (AST, ALT, GGT), and abnormal values of metabolic parameters (cholesterol, triglycerides, glycaemia), albumin and platelets count. No patients had acute or chronic hepatic viral infections. All patients give their consensus to undergo 6-month therapy with Trixy® (1 tab per day before overnight rest). Hematological examinations (metabolic parameters and hepatic-necrotic indexes) have been performed after 6 months. Eco-tomography was performed after 6 months. After 6-months 25 patients continued a full dose treatment (Group A), 24 patients halved their dosage (Group B) and 20 stopped their treatment (Group C).

Results: Male/female ratio was 0.63 (29M and 46F). Mean age was 53.4±10.2yrs. All parameters showed a significant reduction compared with baseline: Glycaemia (114.9 to 106.2; p=0.01); Cholesterol (278.4 to 211.3; p=0.01); Triglyceride (263.7 to 178.5; p=0.01); ALT (49.1 to 29.7; p=0.01); GGT (97.2 to 51.8; p=0.01) and NAFLD score (0.41 to -0.56; p=0.01). There were no differences in mean age and sex between 3 sub-group. In Group A we did not observe any change after 6 and 9 month of full dosage treatment. In Group B we found minimal but not significant differences between 6 and 9 months. In Group C, all metabolic parameters increased after treatment interruption. All data are reported in Table 1.

Table 1

Details of all evaluated parameters (all data are expressed in median and IQR)

	Glycaemia	Cholesterol	Triglyceride	ALT	NAFLD score
Group A					
Basal	112.1±11.3	277.3±17.5	267.1±15.5	49.3±11.4	0.7±0.1
6 months	104.5±7.5	210.5±13.4	183.5±12.8	30.1±6.7	-0.8±0.2
9 months	102.8±9.6	209.3±9.9	181.4±16.9	29.1±5.5	-0.6±0.1
Group B					
Basal	115.1±13.7	278.9±19.1	264.7±17	51.5±10.6	0.8±0.1
6 months	106.2±9.8	208.7±21.6	179.2±14.6	28.7±8.4	-0.6±0.1
9 months	108.5±7.7	211.5±17.8	188.5±17.2	29.9±6.1	-0.6±0.1
Group C					
Basal	114.8±14.6	279.5±15.9	262±18.3	50.3±12	0.9±0.1
6 months	107.1±10	221.1±11.5	177.4±11.8	29±9.9	-0.5±0.1
9 months	113.2±9.4	277.5±19.4	253.5±17.2	48.8±11.7	0.8±0.1

P < 0.05 for all values at basal versus 6 months, and basal versus 9 months.

P > 0.05 between 6 and 9 months

Conclusions: The results of our single-center observational study showed that Trixy® (Nathura) therapy is able to reduce cholesterolemia, triglyceridemia, glycaemia after 6 mths. Half dose

is enough to maintain the effect of a full dosage treatment. The interruption of the treatment was associated with an increase of all metabolic parameters.

P.10.6**MICROWAVE ABLATION OF LARGE HCCS USING A NEW DEVICE: A CASE SERIES**

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Background and aim: Evaluation of a new device designed to achieve large volumes of necrosis in hepatocellular carcinoma (HCC) by synchronous insertion and activation of multiple Microwave (MW) antennae.

Material and methods: 10 consecutive patients with a single large HCC nodule (diameter range: 3.5-6.5 cm; mean diameter: 4.6 cm) underwent ultrasound (US) guided percutaneous MW ablation by synchronous insertion of multiple MW antennae (SynchroWave 915 MHz antennas - MicroThermX® microwave ablation system, Terumo, Belgium, Europe). In general anesthesia, a single insertion of 2 antennae in 3 cases, and 3 antennae in 5 cases were performed. 2 insertions of 3 antennae in the same session were performed in 2 cases. Treatment efficacy was assessed by three-phase contrast-enhanced computed tomography (CT) and bimonthly US follow-up.

Results: Post-treatment CT showed complete necrosis in 8/10 HCC nodules (80%). 2 patients with incomplete ablation underwent an additional MW ablation session. CT showed complete necrosis in both of them. Several major complications occurred: anaerobic infection of the treated necrotic area in 2 cases, severe right pleural effusion in one case, jaundice from transient liver failure. All complications recovered with medical treatment. Follow-up in 10 patients ranges from 12 to 20 months. All patients are alive. In 6/10 (60%) cases, intrahepatic recurrence occurred within 6-14 months (mean 10 months). Recurrences could be successfully treated with ablation in 3 cases. The other 3 patients started chemotherapy with Sorafenib.

Conclusions: The MicroThermX microwave ablation system seems an effective and relatively safe device for treatment of large HCC.

P.10.7**MICROWAVE ABLATION VERSUS RADIOFREQUENCY ABLATION FOR THE TREATMENT OF HEPATOCELLULAR CARCINOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background and aim: Radiofrequency ablation (RFA) and Microwave ablation (MWA) are the two main percutaneous techniques for the treatment of unresectable hepatocellular carcinoma (HCC). However, to date, studies comparing the two therapies have provided discordant results. Aim of this meta-analysis is to evaluate the efficacy and safety of the two treatments for HCC patients.

Material and methods: Computerized bibliographic search was performed on PubMed/Medline, Embase, Google Scholar and Cochrane library databases. The rates of complete response (CR), local recurrence (LR), 3-year survival (SR) and major complications were analyzed.

Results: One randomized-controlled trial (RCT) and six retrospective studies with 774 patients were included in the meta-analysis (Table 1). A non-significant trend of higher CR rates in the patients treated with MWA was found [Odds Ratio (OR) = 1.12, 95% Confidence Interval (CI) 0.67-1.88, p=0.67]. Overall LRR was

Table 1 (abstract P.10.7)

Characteristics of the included studies

Study	Arm	Sample size	Recruitment period	Study design	Region	CP (A/B/C)	Tumorsize (cm) mean (range)	Number nodules*	Quality
Ohmoto 2009 (20)	RFA	34	2002-2006	R	Japan	20/11/3	1.6 (0.7-2)	1.08	H
	MWA	49				31/14/4	1.7 (0.8-2)	1.14	
Lu 2005 (22)	RFA	53	1997-2002	R	China	49/4/0	2.6 (1-6.1)	1.35	M
	MWA	49				39/10/0	2.5 (0.9-7.2)	2	
Shibata 2002 (25)	RFA	36	1999-2000	RCT	Japan	21/15/0	1.6 (0.7-2)	1.08	M
	MWA	36				19/17/0	1.7 (0.8-2)	1.14	
Ding 2013 (26)	RFA	85	2006-2010	R	China	49/36/0	2.38 (1-4.8)	1.15	H
	MWA	113				75/38/0	2.55 (0.8-5)	1.15	
Zhang 2013 (27)	RFA	78	2006	R	China	78/0/0	NA	1.24	H
	MWA	77				77/0/0	NA	1.36	
Abdelaziz 2014 (28)	RFA	45	2009-2013	R	Egypt	24/21/0	2.95±1.03	1	M
	MWA	66					2.9±0.97	1	
Vogl 2015 (29)	RFA	25	2008-2010	R	Germany	NA	NA	1.28	M
	MWA	28				NA	NA	1.28	

* Number of nodules per patient; + Expressed as mean ± standard deviation. Abbreviations: RFA, Radiofrequency Ablation; MWA, Microwave Ablation; RCT, Randomized-controlled trial; R, retrospective; CP, Child-Pugh; M, Moderate; H, High

similar between the two treatment groups (OR=1.01, 0.53-1.87, $p=0.98$) but MWA outperformed RFA in cases of larger nodules (OR 0.46, 0.24-0.89, $p=0.02$). 3-year SR was higher after RFA without statistically significant difference (OR=0.95, 0.58-1.57, $p=0.85$). Major complications were more frequent, although not significantly, in MWA patients (OR=1.63, 0.88-3.03, $p=0.12$).

Conclusions: Our results indicate a similar efficacy between the two percutaneous techniques with an apparent superiority of MWA in larger neoplasms.

P.10.8

PREVALENCE AND RISK FACTORS OF METABOLIC SYNDROME AFTER LIVER TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

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Background and aim: Metabolic syndrome (MS) is a condition affecting more than half of liver transplanted recipients, resulting in an increased mortality and morbidity in the long term after transplantation. However, only few studies have evaluated the short and long-term prevalence of the MS after liver transplantation (LT) and its potential risk factors. The aim of this study was to evaluate the short and long-term prevalence of MS after LT and to identify potential risk factors for its development.

Material and methods: Patients who underwent LT at the Padova Liver Transplant Center between January 2000 and March 2013 (retrospective cohort) and between April 2013 and April 2014 (prospective cohort) and who were regularly followed-up at Multivisceral Transplant Unit were included in the study. Patients <18 years, who underwent multiorgan transplantation or re-LT and who had a diagnosis of MS at the time of LT were excluded from both cohorts. For each patient general and metabolic (pre- and post-LT) variables, donor characteristics, transplant variables were recorded.

Results: One-hundred-sixty-one patients (120 male) were included in the retrospective cohort. Mean±SD age at transplant was 52.5±9.5 years. The most common indication to liver transplantation was HCV-related cirrhosis (49.1%). A post-LT significant increase in BMI values (27 ± 4 vs. 25.1 ± 3.4 , $p<0.001$), in diabetes mellitus and systemic hypertension prevalence (38.5% vs. 11.8%, $p<0.001$ and

57.1% vs. 11.2%, $p<0.001$, respectively) and in total cholesterol and triglyceride levels (176.8 ± 51.1 vs. 123.5 ± 62.2 , $p<0.001$ and 146.7 ± 81.1 vs. 93.9 ± 61.2 , $p<0.001$, respectively) was found compared to pre-LT values. At a mean post-transplant follow-up of 6.9 ± 4.2 years 81/161 (50.3%) patients developed MS. Recipient male sex (OR 2.36, 95%CI 0.94-5.85; $p=0.045$), a higher pre-LT BMI (OR per unit 1.14, 95%CI 1.01-1.28; $p=0.03$), and the presence of pre-LT diabetes mellitus (OR 5.98, 95%CI 1.48-32.55; $p=0.04$) were found to be associated with the development of post-LT MS. Fifteen patients were included in the prospective cohort (10 male), with a mean±SD age of 52.2 ± 5.8 years (range: 46-65). One third of patients (5/15) were transplanted for HCV-related cirrhosis. At 3, 6 and 12 months after LT a significant increase in BMI, diabetes and hypertension prevalence and in cholesterol and triglycerides levels was found compared to pre-transplant values and 5/15 (33.3%), 3/11 (27.3%) e 4/10 (40%) patients developed MS.

Conclusions: In conclusion, these data show that post-LT MS is affecting nearly half of LT patients, starting early after LT. Recipient male gender, pre-transplant diabetes and increased BMI are risk factors for MS after LT. Lifestyle modifications, especially in overweight LT-recipients should be recommended starting in the early post-LT period. This would reduce the incidence of post-LT MS and the related cardio-vascular events.

P.10.9

ACCURACY OF INTESTINAL PERMEABILITY IN PREDICTING THE DEVELOPMENT OF COMPLICATIONS IN PATIENTS WITH LIVER CIRRHOSIS

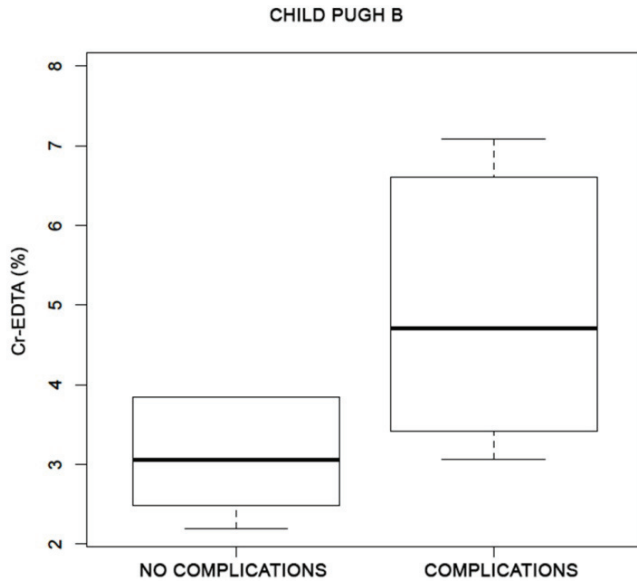
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Background and aim: Liver cirrhosis complications are often associated with increased intestinal permeability (IP), which is in turn common in the advanced stages of the disease. However, at what extent IP could be useful to predict the development of complication is still unknown. To evaluate the accuracy of IP in predicting the development of hepatic encephalopathy (HE) and spontaneous bacterial peritonitis (SBP) in comparison with Child-Pugh and MELD score.

Material and methods: Cirrhotic patients without concomitant diseases or medications potentially altering IP and with no evidence of active alcohol consumption were prospectively evaluated; IP was

measured by the (51)Cr-EDTA permeability test. Only patients at the first episode of SBP and HE were included.



Results: Thirty-two cirrhotic patients (Child-Pugh A 10/B 11/C 11; median MELD score 15) were included in the analysis, 16 of them experiencing a complication (4 HE, 7 SBP, 5 both) and 16 who did not being controls. According to receiving operator curve (ROC; Figure 1), the accuracy in predicting the development of complications was: IP 84.4% (95%CI 0.672–0.947), MELD 89.5% (95%CI 0.735–0.975), CHILD 79.5% (0.616–0.916), without any statistical difference (IP vs MELD $p=0.450$; IP vs CHILD $p=0.190$).

Although median IP was directly correlated with MELD (Spearman's ρ 0.564, $p<0.0001$) and Child-Pugh scores (Spearman's ρ 0.637, $p<0.0001$), in case of moderate liver impairment (Child-Pugh B) it was able to discriminate between patients who developed a complication and those who did not (Figure 2). As expected, all patients with Child-Pugh C showed a high IP independently of complications.

Conclusions: IP accuracy is comparable to Child Pugh and MELD scores in predicting the development of liver cirrhosis complications. However, among patients with moderate liver impairment, high values of IP allow to identify those more prone to develop complications.

P.10.10

FEASIBILITY OF HCV INFECTION SCREENING IN BABY BOOMERS WITH A RAPID, NON-INVASIVE POINT-OF-CARE TEST IN ORAL FLUID

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Background and aim: The overall prevalence of anti-HCV positivity in Italy is about 3.2% with a remarkable north-south gradient, depending on the age of the population being analyzed. In some southern region where the prevalence of anti-HCV is over 12% overall, the rate among persons younger than 30 years of age is only 1.3% compared to 33.1% in subjects older than 60 years. According to the U.S. Department of Health and Human Services most cases of HCV infection worldwide are currently undiagnosed. People born from 1945 through 1965, so called "Baby Boomers", are five times more likely to have HCV. The longer people live with HCV the more likely they are to develop serious liver disease like cirrhosis and liver cancer. Furthermore HCV related complications represent a major item of expenditure for the National Health Service. In recent years

you can notice a growing demand to launch a nationwide quality-assured HCV screening program targeted especially at individuals born between 1945 and 1965. The aim of the current pilot study was to screen a group of 50 asymptomatic individuals born between 1945 and 1965 with a non-invasive rapid antibody test for the detection of IgG HCV antibodies.

Material and methods: We used the OraQuick/HCV Rapid Antibody Test (OraSure Technologies), a rapid immunoassay for the detection of IgG HCV antibodies in oral fluid, whole blood, serum and plasma specimens, giving results in 20–40 minutes. To reduce patient discomfort we choose to take oral fluid samples from buccal mucosa. According to recent studies sensitivity and specificity of the oral fluid test version are 97.8%. The test has been offered for two weeks, costless, to all our outpatients between 50 and 70 years of age attending for endoscopic procedures. Volunteers with known HCV infection were excluded a priori.

Results: 52 volunteers (med age 61.7 years) without known HCV infection have been tested for IgG HCV antibodies during our 2-week screening program; 29 were female (med age 61.4 years) and 22 male (med age 62.0 years). 3 tests, all in patients with atrophic gingiva, had to be interpreted as invalid since no control line appeared in the test window. All participants have been found non-reactive for the presence of IgG HCV antibodies in oral fluid.

Conclusions: Even though all evaluable 49 participants were found to be negative for HCV antibodies in oral fluid, we consider the performance of a national HCV screening program useful to identify patients with asymptomatic infection. The progression of HCV disease usually occurs over decades and HCV complications represent a significant item of expenditure for the National Health Service. A screening program can help to identify the disease at an early stage and get people into lifesaving treatment. We consider the use of a rapid, non-invasive point-of-care test, which can be used either with venous blood, finger stick blood, serum, plasma or oral fluid, a good screening tool to realize HCV screening, especially in non-clinical settings.

P.11 Endo/EUS 2

P.11.1

EUS-GUIDED PANCREATICOGASTROSTOMY AFTER GASTRIC SURGERY WITH ROUX-EN-Y RECONSTRUCTION: A BRIEF CASE SERIES

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Background and aim: Although surgical drainage of the pancreatic duct is considered more effective than endoscopic treatment in patients with obstruction of the pancreatic duct due to severe chronic pancreatitis, surgery is not always eligible. In these cases, endoscopic procedures can be chosen in order to resolve the symptoms.

Material and methods: Three patients presented with upper abdominal pain due to chronic pancreatitis. All patients underwent gastric surgery with Roux-en-Y reconstruction. Transpapillary access was not possible and EUS was used to perform pancreaticogastrostomy (PGS).

Results: EUS-guided PGS was performed in all cases. No technical complications were recorded. The postoperative course was characterized by mild abdominal pain and hyperamylasemia in the patient with previous pancreaticoduodenectomy; it was uneventful

in the other two cases. Patients were found symptoms-free at follow-up. One patient underwent a second stent placement.

Conclusions: The present method results a safe alternative endoscopic procedure in very selected patients when surgery is not indicated.

P.11.2

ENDOSCOPIC ULTRASONOGRAPHY IN THE DIAGNOSIS AND STAGING OF NEUROENDOCRINE TUMORS

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Background and aim: Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are nosological entities, whose incidence has dramatically increased during the last decades.

Endoscopic ultrasonography (EUS), associated to FNA and harmonic contrast-enhancement (CH-EUS), has been reported to be extremely useful for the diagnosis and the staging.

The objective of this study is to evaluate the accuracy of EUS in the diagnosis and the staging of GEP-NETs.

Material and methods: From January 2010 to September 2015, all NET's patients referred for EUS in our center were enrolled in this study.

According to the localization of the tumor, the patients also underwent laboratory tests and imaging techniques such as CT, MRI, SRS Octreoscan or DOTATOC. EUS procedures were performed using radial or linear echoendoscopes Pentax EG-3670URK–EG-3870UTK (Pentax Hamburg, Germany) with a Hitachi – Aloka Avius processor (Hitachi, Hamburg, Germany).

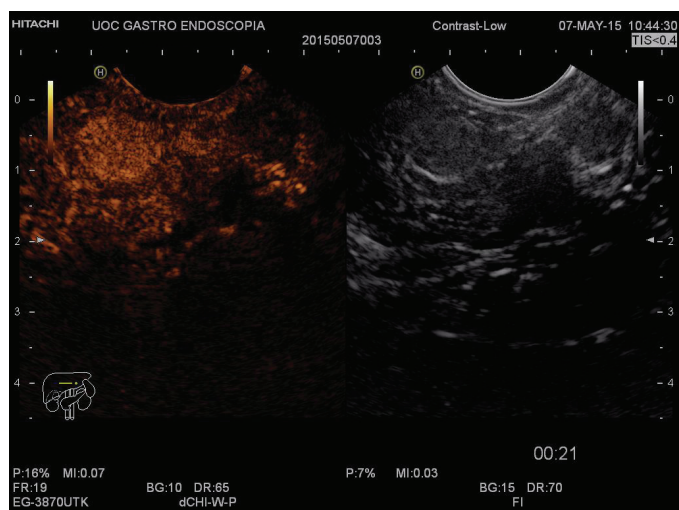
FNA procedures were performed with 25G FNA biopsy needles (EchoTip, Wilson-Cook Medical Inc, Winston-Salem, NC) and SonoVue (Bracco, Milano, Italy) was used for CH-EUS.

Results: 26 patients were enrolled in the study (17 m, 9 f) with median age of 56.9 years (range 10 - 87).

NET's were located in upper GI tract in 9 patients (6 stomach, 3 duodenum), in the rectum in 7 patients and in the pancreas in 10 patients.

In the patients with upper GI NET's, found at bioptic sampling, EUS confirmed endoscopical resection in 1 patient; surgical resection in 4 patients because of an invasion of the deeper layers; medical treatment in 4 patient with advanced disease.

In the patients with rectal NET's, found at bioptic sampling in colonoscopy, EUS permitted to choose the mucosectomy in 6 patients, and in 1 case surgical approach.



In pancreatic localization, CH-EUS showed a fast enhancement with a homogeneous pattern lesion in 3 patients with recurrent

hypoglycemias. FNA confirmed the diagnosis of insulinoma in all cases.

CT suspected a pancreatic NET in the other 7 patients, EUS+FNA confirmed the presence of neuroendocrine tumor. FNA was performed with a mean of 2.0 passages per patient.

Three patients underwent surgery, while the others underwent medical therapy for the advanced disease.

Neither major or minor complications showed up during or after the procedures.

Conclusions: This study highlights the diagnostic accuracy, safety of EUS in the evaluation and management of GEP-NETs. In particular, EUS was necessary to define whether the lesion could be managed endoscopically or surgically.

P.11.3

THE ROLE OF COMBINED USE OF EUS-FNA AND BILIARY BRUSHING IN CYTOLOGICAL DIAGNOSIS OF PANCREATOBILIARY MALIGNANCIES

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Background and aim: Fifteen percent of patients with suspected pancreatobiliary malignancy that undergo surgery without a cytological assessment have a benign lesion. Cytological or histological diagnosis of pancreatobiliary malignancies before surgery is desirable in order to avoid unnecessary interventions.

We conducted a study in order to assess whether the combined use of biliary brushing and endoscopic ultrasound-guided fine needle aspiration (EUS–FNA) has greater accuracy than the individual procedures in diagnosing pancreatobiliary malignancies.

Material and methods: Study was conducted at the Gastroenterology Unit of Academic Hospital "S. M. della Misericordia", Udine, Italy. Twenty five patients with probable pancreatobiliary malignancy were subjected both to biliary brushing and EUS-FNA and collected material was sent for cytological analysis. The results of cytology were compared to the results of histology from surgical specimen.

Results: Histology of surgical specimen confirmed the diagnosis of pancreatobiliary malignancy in 24 of 25 patients, benign lesion caused by chronic pancreatitis was identified in one patient. Cytology from biliary brushing provided a correct diagnosis in 9 patients, with diagnostic accuracy of 36%. For the remaining 16 patients (54%), cytological diagnoses were as follows: indeterminate because of poor quantity or quality of the specimen in 15 patients, negative in one case (1 false negative). EUS-FNA provided a correct diagnosis in 18 patients with diagnostic accuracy of 72%, including the patient with a benign lesion. In 7 patients (28%) EUS-FNA didn't provide any result because of the poor quality of the specimen. The combined diagnostic accuracy of both methods was 80% as they together provided a correct diagnosis in 20 patients. The additional diagnostic gain derived from the joint use of biliary brushing and EUS-FNA was +44% compared to biliary brushing alone and +8% cases compared to EUS-FNA alone.

Conclusions: The combined use of the EUS-FNA and biliary brushing results in increased accuracy of cytological diagnosing in pancreatobiliary malignancies. The biliary brushing as an addition to EUS-FNA should be considered in patients undergoing the endoscopic retrograde cholangiopancreatography (ERCP) in therapeutic purposes.

P.11.4**CLINICAL IMPACT OF ENDOSCOPIC ULTRASOUND–FINE NEEDLE ASPIRATION (EUS-FNA) OF LEFT ADRENAL GLAND (LAG)**

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Background and aim: A left adrenal gland (LAG) mass is found at the initial diagnosis of non small cell lung cancer (NSCLC) in 5 to 16% of the patients and malignancy preclude surgery. Adrenal gland is a metastatic site of other malignant neoplasms too. Sensitivity and specificity of imaging techniques are currently insufficient to differentiate benign from malignant lesions. Adrenal masses are traditionally sampled by percutaneous biopsy, but endoscopic ultrasound (EUS) through the esophagus is superior to transabdominal ultrasound or CT scan for imaging the LAG. We investigate the clinical impact of EUS-FNA of LAG in patients with an established or suspected diagnosis of cancer.

Material and methods: EUS with or without fine needle aspiration (FNA) was performed in 10 patients with enlarged LAG or focal left adrenal lesion (9 suspected adrenal metastasis from lung cancer and 1 suspected adrenal and pulmonary metastasis from renal cancer). We performed EUS FNA both in lung mass and focal lesion of LAG in one patient with history of renal cancer and in four patients with suspected lung cancer; in 3 patients with suspected lung cancer we performed EUS FNA both in station #7 enlarged lymph nodes and focal lesion of LAG. In 2 suspected lung cancer patients with station #7 enlarged lymph nodes and enlarged LAG with preserved shape we performed EUS FNA only on MLN (mediastinal lymph node). We used a 22 Gauge needle with a median of 3 passes of the needle.

Results: The patient with a history of renal cancer had negative LAG but pulmonary metastasis from renal cancer (sent to pulmonary metastasectomy); one case with diagnosis of adenocarcinoma both in lung mass and in LAG was sent to chemotherapy; in other 2 cases LAG was negative and MLN biopsies were diagnostic for adenocarcinoma (sent to neoadjuvant chemotherapy); in 1 case both LAG and MLN were diagnostic for neoplasia (sent to chemotherapy); in 3 cases lung mass biopsies were diagnostic for cancer and LAG negative (sent to surgery).

Conclusions: These results suggest that EUS FNA of left adrenal gland is a safe procedure with a high diagnostic yield in the diagnosis of left adrenal gland. FNA of LAG and enlarged MLN have a real clinical impact on management of disease and avoiding futile surgery.

P.11.5**THE USE OF A POCKET MOBILE ULTRASOUND DEVICE IN THE EVALUATION OF PATIENTS WITH SUSPECTED BILIARY DISEASE**

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Background and aim: The accuracy of a physical examination for patients with a suspected biliary disease is often poor and it requires further tests to assess the diagnostic hypotheses. Adding the use of pocket mobile ultrasound devices (PUDs) to physical examinations could lead to an incremental benefit in the evaluation of patients with biliary disease. We assessed whether the use of PUD should be recommended, in the evaluation of a patient presenting suspect of biliary disease, to improve the diagnostic accuracy of a physical examination and to assess the appropriateness of further testing.

Material and methods: We conducted a prospective study for eight months from February to September 2015 involving 31 patients, which were evaluated in the emergency room for suspected biliary disease. All the patients were submitted to evaluation with PUD (V-Scan GE) looking for dilation of the biliary tract or biliary stones.

The images were collected by a physician, who is an expert in abdominal ultrasound.

We then monitored the following diagnostic of these patients without affecting it, and evaluated the correlation between the test and results of gold standard methods (Eco /RMN/TC).

Results: Of the 31 patients, in 77% of the cases the PUD's examination confirmed the suspected diagnosis. The correlation with the standard ultrasound was equal to 87%, 91% with TC and 90,5% with MRI. It was also possible to assess the sensitivity and specificity, respectively equal to 88,2% and 100%.

Conclusions: PUD can be used in combination with physical examination in the first assessment of a patients presenting suspected biliary disease. In fact, this tool presents good sensitivity and specificity in identifying the presence of stones and / or dilatation of the bile ducts. Its use could then optimize the demands of subsequent investigations, by reducing waiting times and costs.

P.11.6**ECHOENDOSCOPIC ETHANOL ABLATION OF TUMOR COMBINED TO CELIAC PLEXUS NEUROLYSIS IN PATIENTS WITH PANCREATIC ADENOCARCINOMA**

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Background and aim: Endoscopic ultrasonography (EUS) guided-celiac plexus neurolysis (EUS-CPN) is effective in relieving pain in pancreatic cancer (PC) patients, but with often suboptimal and transient results. This study is aimed at comparing the efficacy and safety of EUS-guided tumor ethanol ablation combined to CPN with respect to EUS-CPN alone for pain management in PC patients.

Material and methods: Among 123 unresectable PC patients referred to our Institution between 2006 and 2014, 58 treated with EUS-CPN (group 1) and 65 with the combined approach (group 2) were compared. Logistic regression models were applied to identify predictors of pain relief, while time-to-event data were compared by means of log-rank test.

Results: The two groups presented similar baseline clinical and tumoral parameters. Pre-procedural visual analogue scale (VAS) score was 7 in both groups (p=0.8) and tumor max diameter was 38 mm (range 25-59) in group 1 and 43 mm (22-59) in group 2 (p=0.4). The combined treatment increased the pain relief and the complete pain response rate (p=0.005 and 0.003, respectively). Median duration of pain relief was 10 (7-14) and 18 (13-20) weeks in the two groups, respectively (p=0.004). At multivariate regression, initial VAS score and EUS technique adopted resulted significantly associated to pain relief. No severe treatment-related adverse events were reported. Median overall survival was 6.5 months (5.1-8.6) in group 1 and 8.3 (6-11.4) in group 2 (p=0.05).

Conclusions: EUS-guided tumor ablation combined to CPN appears to be superior to standard EUS-CPN in terms of pain control and overall survival.

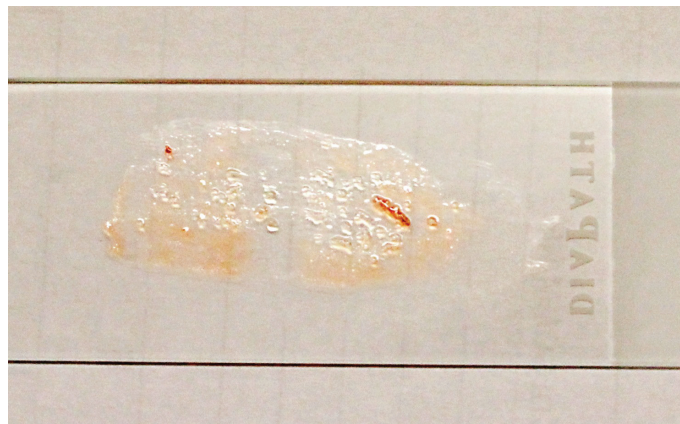
P.11.7**PANCREATIC FNA: CAN WE GET RID OF THE MICROSCOPE?**

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Background and aim: EUS-FNA is an essential procedure for obtaining a tissue confirmation of solid pancreatic malignancy but at least 5 to 7 needle passes are generally needed to have a good accuracy. In this study we checked if the real-time macroscopic

inspection of the slides by the endosonographer, in the absence of a microscopic rapid on-site evaluation (ROSE), can increase FNA adequacy, thus allowing to complete the procedure with a limited number of needle passes.



Material and methods: We retrospectively evaluated our FNA procedures on solid pancreatic lesions when the cytopathologist was absent and the endosonographer smeared, observed and fixed the slides by himself. A standard 22G or 25G needle was moved in the target lesion without suction and the aspirated material was expelled on slides by blowing air. The slides were smeared and observed with oblique white light: when thin granular or filamentous whitish or pink material was visible and blood was poor, the slides were considered adequate and they were fixed with alcohol. When blood or clots were predominant the smears were eliminated. When no material was present in the needle, suction was applied in the next needle passes. The procedure was closed, regardless of the number of needle passes, when 5 slides were judged satisfactory. For each case the number of needle passes and the final microscopic adequacy were recorded.

Results: Overall 100 patients entered the study. A mean of 4.1 (range 1–7) needle passes were effected. Microscopic adequacy was achieved in 95 cases (95.0%): 74 pancreatic adenocarcinoma, 3 neuroendocrine tumor, 3 atypical pancreatic cells, 11 benign pancreatic cells, 2 lymphoma, 2 benign lymphocytes. Most procedures were ruled out with a 22G needle, which got an adequate sample in 79 out of 84 (94.0%) cases; the 25G needle was used only 16 times, all resulting adequate (100%) ($p = n.s.$). No complications occurred.

Conclusions: Although the best technique for improving the performance of pancreatic FNA still seems ROSE, either its cost or its low diagnostic gain in centers with an already high accuracy limits its availability. We suggest a simple, rapid and cheap alternative to ROSE; the visual inspection of the smeared slides could help choosing those with abundant diagnostic material, hence increasing FNA adequacy and reducing the number of needle passes.

P.11.8

THE ROLE OF EUS-FNA IN THE DIAGNOSIS OF PANCREATIC NEUROENDOCRINE TUMORS

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Background and aim: One of the most controversial issue in the diagnosis of pancreatic neuroendocrine tumors (NET) is the accurate prediction of their clinical behaviour. According to the ENETS and WHO 2010 criteria the grading for pancreatic NET has to be expressed by using the mitotic index and the Ki67 proliferation index. The aim

of this study was to evaluate the of the EUS-FNA in the diagnosis and grading of pancreatic NET.

Material and methods: We retrospectively reviewed all consecutive patients referred to our Unit with a radiological finding suspicious for NET. A computerized system was used to extrapolate the list of patients with NET in the field of pancreatic EUS between May 2014 and Oct 2015. EUS was performed with the linear array Olympus GF-UCT-180 series echoendoscopes in combination with the echoprocessor EU-ME2. FNA was performed with Beacon or Boston Scientific 25G or 22G needles. Forty-nine patients undergoing EUS were identified with 24 having also FNA. Adequacy of the aspirated material was assessed by Rapid On Site Evaluation (ROSE) and fragments observed on slide at macroscopic evaluation were placed in formalin for histology evaluation. In patients undergoing surgery the EUS-FNA results were compared with final histological diagnosis.

Results: Patients population included 9 women and 15 male (mean age 58 years). Fourteen patients (58%) had an incidental finding of pancreatic mass, 2 (9%) had genetic syndrome and the others (33%) had symptoms like pain, weight loss or jaundice. All the cases were non-functioning. Clinical and technical data are summarized in the Table. In 2 cases the procedure was interrupted before the adequacy was obtained because of a mild self-limited bleeding. The combination of cytology and histology reached an adequacy of 92% (the 2 inadequate cases were those in which a bleeding was observed) and gave a ki67 result in 15 cases (62.5%). The final diagnosis was obtained with EUS-FNA in 22 cases (92%). Six patients underwent surgery (25%): 4 distal pancreatectomy, one enucleation, and one Whipple resection; 8 patients are waiting for surgery; 4 are in follow up, 1 had chemotherapy, 5 are lost at follow up. In 3 patients who underwent surgery who had a ki67 result on the EUS-FNA report, there was a 100% correspondence between FNA and resected specimen.

Conclusions: The combination of cytology and histology from EUS-FNA is an effective method for the diagnosis of pancreatic NET and ki67 index grading for WHO 2010 classification.

P.12 Coeliac Disease 2

P.12.1

GLUTEN-FREE DIET DOES NOT INFLUENCE THE OCCURRENCE AND THE TH1/TH17-TH2 NATURE OF IMMUNE-MEDIATED DISEASE IN PATIENTS WITH COELIAC DISEASE

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Background and aim: Even though coeliac disease (CD) is considered to be the most common lymphocyte T helper-1 (Th-1) mediated enteropathy in Western countries, it seems that Th1- and lymphocyte T helper-2 (Th-2)-mediated diseases could co-exist in CD patients. The aims of the study were: 1) to establish the prevalence of immune-mediated disorders at time and after CD diagnosis; 2) to evaluate a possible change in immune response after starting gluten free diet (GFD); 3) to investigate the potential role of GFD in reducing and/or preventing immune-mediated disorders in adult CD patients.

Material and methods: We carried out a database-driven study including all consecutive adult CD patients followed-up at our Gastrointestinal Unit. CD diagnosis was made in accordance with the

Oslo classification. All patients were investigated for the presence of Th1/Th17 and/or Th2-mediated disorders at time of CD diagnosis. The search for Th1/Th17 and/or Th2 diseases were reassessed after a 5-years follow-up period.

Results: Finally, 1255 CD were enrolled (M/F 258/997). 257 patients out of 1255 (20.5%) suffered from immune-mediated diseases at time of CD diagnosis, with 150 of them (58.4%) presenting a Th1/Th17-predominant disease vs 107 (41.6%) with Th2-mediated diseases ($p=0.7$). After a 5-years follow-up period, 682 out of 1255 patients (54.3%) showed an immune-mediated disease even if following a restrict GFD; among them, 391 subjects (57.3%) presented a Th1/Th17-related condition vs 291 (42.7%) with a Th2-mediated disease ($p=0.8$). When comparing the prevalence of immune-mediated diseases before and after CD diagnosis, no significant “switch” from Th1/Th17 to Th2-response or vice versa was seen (58.4% and 41.6% before CD vs 57.3% and 42.7% after CD diagnosis, respectively; $p=0.9$). The number of patients with a Th1/Th17- and/or a Th2-mediated disease increased during the GFD period (20.5% vs 54.3%; $p<0.01$; OR 1.9). The most frequent CD-related immune-mediated diseases were: Hashimoto's thyroiditis (8.2% before vs 24% after CD diagnosis; $p<0.01$; OR 1.6); psoriasis (0.7% before and 2.7% after CD diagnosis; $p<0.01$; OR 1.5), type 1 diabetes mellitus (1.8% before vs 0.2% after CD diagnosis; $p<0.01$; OR 0.08). No correlation was found between the developed immune-mediated diseases and age at the time of CD diagnosis, clinical symptoms, a-tTG serum levels and Marsh grade.

Conclusions: The prevalence of immune-mediated diseases at time of CD diagnosis, particularly as regards with Hashimoto's thyroiditis, psoriasis and type 1 diabetes mellitus, is high and it seems to increase in the follow-up period despite GFD. GFD does not influence and/or reduce the prevalence, the occurrence and the Th1-Th17/Th2 nature of immune-mediated diseases in CD.

P.12.2

DIAGNOSIS OF CELIAC DISEASE IN ADULTS WITHOUT DUODENAL BIOPSY IN THE PRESENCE OF POSITIVE ANTI-ENDOMYSIUM ANTIBODIES AND ANTI-TRANSGLUTAMINASE ANTIBODIES

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Background and aim: The latest ESPGHAN guidelines for the diagnosis of coeliac disease (CD) allow to avoid duodenal biopsy sampling in symptomatic children with genetic predisposition to CD who show immunoglobulin A (IgA) antitransglutaminase antibody titers >10 times the upper limit of normal range after confirmation of anti-endomysium antibodies (EMA) positivity. In adults, however, tTG IgA is the preferred single test for detection of CD, and upper endoscopy and small-bowel biopsy are still requested for the diagnosis of CD. Our aim was to evaluate if the presence of EMA can predict villous atrophy (Marsh 3) in tTG-positive adult subjects.

Material and methods: We performed a retrospective analysis of data from all consecutive adult subjects without IgA deficiency who underwent dosage of EMA and tTG on a gluten-containing diet between 2004 and 2014. Patients who had not undergone duodenal biopsy sampling were excluded from the study and contacted to offer them a re-evaluation and upper endoscopy. Then we assessed the positive predictive value of a combination of EMA and tTG for predicting villous atrophy (Marsh 3).

Results: The study included 167 patients with positive tTG. Of them, 103 showed also positivity for EMA. Histology showed Marsh 1 in

5%, Marsh 2 in 2%, Marsh 3 in 79% of subjects. The combination of EMA and tTG had a positive predictive value of 96% for villous atrophy (Marsh 3).

Conclusions: Our preliminary findings suggest that CD can be diagnosed without the need of biopsy sampling in adult patients with positive EMA and tTG. Should our results be confirmed by further, larger studies, the diagnosis of CD based only on serology, without duodenal biopsy, may become a reasonable approach.

P.12.3

IDENTIFICATION OF A SERUM ANTI-TRANSGLUTAMINASE THRESHOLD VALUE FOR THE NONINVASIVE DIAGNOSIS OF CELIAC DISEASE IN ADULTS

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Background and aim: Celiac disease (CD) diagnosis is based on duodenal histology, with the exception of children showing anti-tissue transglutaminase (anti-tTG) serum levels exceeding ten times the cutoff.

Our aim was to reproduce this simplified approach in adults, identifying an anti-tTG threshold value useful to diagnose CD without endoscopic procedures.

Material and methods: 671 adult CD patients were subjected to blood sampling to determine anti-tTG serum levels, as well as to endoscopy with biopsy to perform duodenal histology. The anti-tTG serum levels/cut-off ratio was compared with the degree of duodenal lesions.

Results: Anti-tTG serum levels/cut-off ratio determined in patients with type IIc was significantly higher than that measured in patients with type IIb ($p<0.001$), IIIa ($p<0.001$), II ($p<0.05$) and 0 ($p<0.001$) of Marsh-Oberhuber histological classification. A significant correlation ($r = 0.297$, $p<0.0001$) was found between the anti-tTG serum levels/cut-off ratio and the degree of duodenal lesions. The anti-tTG serum levels/cut-off ratio was classified as an accurate parameter (AUC = 0.715, $p<0.0001$), with the best diagnostic performance obtained considering the threshold value >3.6 (sensitivity = 76.8%, PPV = 97.2%).

Conclusions: The anti-tTG serum levels/cut-off ratio correlates with the degree of duodenal lesions and, if used with the threshold value >3.6, could avoid endoscopy with biopsy in about 75% of seropositive adults waiting for CD diagnosis. However, since this procedure could also imply CD diagnosis in almost 3% of seropositive patients with normal villous architecture, a consensus opinion is needed to suggest its use in the diagnosis of adult CD.

P.12.4

MACRONUTRIENT INTAKES IN OBESE SUBJECTS WITH OR WITHOUT SMALL INTESTINAL BACTERIAL OVERGROWTH: AN ALIMENTARY SURVEY

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Background and aim: Obesity is a multifactorial disorder with a possible microbiota derangement in its pathogenesis. Moreover, in obese patients the likelihood of small intestinal bacterial overgrowth (SIBO) is greater than in controls, although few studies are currently available. This study investigates the prevalence of SIBO and the possible role of dietary macronutrients in obesity.

Material and methods: Sixty obese patients and normal lean controls were enrolled for SIBO detection. Diagnosis of SIBO was performed by a glucose breath test. A 24-hour recall questionnaire was administered to investigate macronutrient daily intake between the two obese patient subgroups (with/without SIBO).

Results: The presence of SIBO in obese and controls was respectively 23.3% and 6.6% ($p=0.02$, $OR=4.26$, 95% Confidence interval=1.31-13.84). Obese patients with SIBO ingested more carbohydrates (252.75 ± 30.53 versus 201 ± 70.76 g/day, $p=0.01$), more refined sugars (104.15 ± 28.69 versus 73.32 ± 44.93 g/day, $p=0.02$) and less total and insoluble fibers (9.6 ± 1.97 versus 14.65 ± 8.80 g/day - $p=0.04$ and 4.7 ± 1.11 versus 8.82 ± 5.80 g/day - $p=0.01$, respectively). There were no significant differences in lipid and protein intake between the two groups.

Conclusions: SIBO is widespread in obese subjects. Carbohydrates might promote the development of SIBO in obesity and fibers provide a protective function. Our results suggest a close relationship between diet and SIBO in obesity, thus supporting a possible role for intestinal microbiota.

P.12.5

EXOCRINE PANCREATIC INSUFFICIENCY IN ADULT CELIAC DISEASE IS ASSOCIATED WITH SYMPTOM SEVERITY AND READILY RESPONDS TO GLUTEN EXCLUSION

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Background and aim: Exocrine pancreatic insufficiency (EPI) has been described in children with celiac disease (CD), variably correlating with symptom severity at presentation. Different mechanisms have been proposed, although etiology could be multifactorial. In adults, EPI has been associated to symptom persistence, although data are scarce.

Aims of this study were to explore the prevalence of EPI in a cohort of adult celiacs and the clinical/laboratory response to gluten-free diet (GFD).

Material and methods: We recruited consecutive adults, showing antiTG positivity and villous atrophy. As controls we recruited consecutively: a) asymptomatic celiacs under adequate GFD for ≥ 24 months; b) Romelli D-IBS patients; c) healthy subjects.

Results: Among celiacs ($n=43$, mean age (ma)=42.9ys) prevalence of EPI was highest at diagnosis (overall 47%, severe 12%). At 6 months, EPI remained higher (4.7%) compared to patients on GFD=24 months ($n=54$, ma=48.9ys) and healthy controls ($n=64$, ma=51.5ys), respectively 1.9%, 1.6%. Mean FE-1 was lowest at diagnosis ($188.6\pm81.9\mu\text{gr/gr}$), showing a significant improvement already after 3 months (248.9 ± 78.5 , $p<0.001$), alongside symptoms when present. At 6 months, mean FE-1 levels (362.8 ± 76.4) were comparable to healthy controls and celiacs in GFD=24 months (respectively 376.5 ± 68.0 , 422.4 ± 82.7 ; $p>0.5$). Overall, FE-1 was significantly lower in subjects with diarrhea ($p<0.001$), showing a strong inverse correlation to symptom severity ($rs=-0.51$, $p<0.001$). At CD diagnosis mean FE-1 or EPI status did not significantly differ based on symptoms. Statistical significance for FE-1 levels and EPI association with diarrhea was attained at 3 months (respectively, $p=0.02$; $p=0.04$). At diagnosis, FE-1 and EPI severity strongly correlated to symptom severity ($rs=-0.59$, $p<0.001$; $rs=0.81$, $p<0.001$). One healthy control showed severe EPI without symptoms. Among IBS patients ($n=28$, ma=38.3ys) EPI prevalence was 14%; mean FE-1 (310.5 ± 144.1) was comparable to titers of celiacs at 6 months ($p>0.5$). FE-1 levels did not correlate to sex or age.

Conclusions: In newly diagnosed adult celiacs, EPI (FE-1 <200) was frequent; FE-1 and EPI showed correlation to severity but not

to presence of diarrhea, probably owing to the multifactoriality of the initial presentation. In most patients EPI recovered after 3-6 months, alongside symptoms, without need for additional treatment. Subjects with persisting diarrhea at 3-6 months showed significantly lower FE-1 levels and higher EPI prevalence, suggesting a more direct causality. EPI in celiacs under long-term GFD has a comparable prevalence to healthy controls. It is frequent in Romelli D-IBS patients, probably due to inadequate screening. Symptom presentation of CD should guide pancreatic function testing and early treatment, in an effort to reduce symptom severity and fat malabsorption where needed.

P.12.6

GENETIC VARIANTS ASSOCIATED WITH ANAEMIA IN ADULT COELIAC PATIENTS: THE ROLE OF TMPRSS6 AND HFE

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Background and aim: Coeliac disease (CD) is a chronic, immune-mediated disease occurring in genetically predisposed individuals who assume gluten. Iron deficiency anaemia (IDA) is very common in CD and has been reported in up to 46% of cases of subclinical CD. Even though the link between malabsorption and anaemia is well known, the role of genetic factors remain unexplored. We speculated that common SNPs of iron metabolism genes would be associated with anaemia of CD patients.

Material and methods: From October 2011 to July 2015 we prospectively assessed the frequency of TMPRSS6 variant rs855791 and HFE variants rs1800562 and rs1799945 in both anemic and non-anemic CD patients at time of CD diagnosis. We also estimated the association of these variants with some hematological and iron parameters (Hb, MCV, serum iron and serum ferritin). Statistical analysis was performed by using T-student and X-square test when indicated; all differences were considered significant when $p<0.05$.

Results: Finally, 491 patients were enrolled: 266 with IDA (mean age 31.2; females 88%), 225 with non-IDA (mean age 32.4; females 65%). TMPRSS6 variant rs855791 and HFE variant rs1799945 were found higher in non-IDA than IDA CD patients (52.2% vs 47% and 27% vs 24.5%, respectively), although not statistically significance ($p=0.1$). Conversely, HFE variant rs1800562 was found to be significantly higher in IDA than non-IDA CD patients (3.4% vs. 0.8%, $p=0.03$). Furthermore, CD subjects with TMPRSS6 variant rs855791 showed higher Hb and serum ferritin and lower MCV and serum iron level compared to CD subject with TMPRSS6 WT variant. IDA subjects with HFE variant rs1800562 showed increased serum iron and ferritin values in comparison with CD subject carrying the wild type variant.

Conclusions: In CD patients, HFE variant rs1800562 appeared to be more frequent in IDA than in non-IDA and it associated with higher iron status, so conferring a protective role regarding IDA in CD.

P.12.7

OUTCOME OF PATIENTS WITH POSITIVE BREATH TEST FOR SIBO SIX MONTHS AFTER COMBINED TREATMENT WITH RIFAXIMIN AND PROBIOTICS

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Background and aim: SIBO is a frequent condition, the diagnosis of which is commonly carried out by lactulose or glucose breath test, or both. The treatment of this condition is largely empirical and based on antibiotics and probiotics. The aim of the study is to assess, in a group of patients who had a positive lactulose breath test for SIBO, the medium-term response to a three month treatment with a combined regimen of nonabsorbable antibiotics and probiotics.

Material and methods: 123 patients (87 females, 78%), with a mean age of 43 yrs, all presenting with symptoms suggestive of SIBO (abdominal bloating, abdominal pain, diarrhea, constipation) and a positive lactulose breath test for SIBO (defined as >10–20 ppm after ingestion of 85 ml of water, containing 66 g of lactulose), were treated with rifaximin at a dose of 200 mg, 2 tablets 3 times a day, for one week each month, for 3 months and followed by a probiotic, namely *Genefilus F19*, 1 sachet a day during the next 2 weeks.

Results: At baseline, patients complained of the following symptoms: bloating in 88 cases (71.5%), abdominal pain in 62 (50%), diarrhea in 64 (52%) and constipation in 14 cases (11.4%). Six months after the end of therapy bloating was still present in 32.5% of subjects, abdominal pain in 23.6%, diarrhea in 21.1%, and constipation in 5%, whereas the majority of patients (54.5%) had a complete resolution of symptoms, as opposed to 22% who showed only a partial improvement, and 23.5 who did not respond to therapy. No correlation between symptoms response and body weight change was observed.

Conclusions: In this prospective, uncontrolled study, we found that patients with SIBO defined on the basis of a positive lactulose breath test might be treated successfully with nonabsorbable antibiotics and probiotics in more than half of cases. Whether the partial or complete refractoriness to this regimen is due to persistent SIBO or not was not tested in our study.

P.12.8

INTESTINAL FERMENTATION IN SELF-REPORTED NON-CELIAC GLUTEN SENSITIVITY: A COMPARISON WITH IRRITABLE BOWEL SYNDROME AND HEALTHY VOLUNTEERS

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Background and aim: The presence of non-celiac patients claiming a strict correlation between gluten ingestion and intestinal and/or extraintestinal symptoms is an increasingly frequent occurrence in outpatient clinics. This clinical condition has been named non-celiac gluten sensitivity (NCGS) (Sapone, BMC Medicine 2012) and many doubts have been raised about the algorithm for its identification. In our experience, the administration of gluten in a double-blind, placebo-controlled protocol in non-celiac patients claiming severe gluten-related symptoms showed that this condition has a low frequency (Di Sabatino, CGH 2015). A simplified diagnostic test, based on symptom monitoring during a period of gluten withdrawal from diet according to an unblinded protocol and configuring a sort of self-reported NCGS, was recently proposed

(Fasano, Gastroenterology 2015). The clinical presentation of this condition overlaps the irritable bowel syndrome (IBS), a condition characterized by an impairment of intestinal sensorimotor activity. In both NCGS and IBS, many abdominal symptoms may occur and all these symptoms could share the same pathophysiological mechanism. Therefore, we focused on breath hydrogen excretion after oral administration of lactulose, in self-reported NCGS subjects compared to a group of IBS patients and healthy volunteers (HV).

Material and methods: Eighteen consecutive self-reported NCGS patients (14 F, 4 M, mean age 34±8 yrs) complaining of severe symptoms after gluten ingestion took part in the study. The presence of organic gastrointestinal and systemic disorders was ruled out in all subjects. Twenty-seven IBS patients diagnosed according to Rome III criteria (17 IBS-C and 10 IBS-D) and a group of 20 HV, both matched for gender and age, were considered for the comparison of results. All the subjects underwent breath hydrogen excretion measurement after oral lactulose administration. Ten grams of lactulose in 400 mL water solution were administered orally in fasting condition and air samples were then collected every 15 min for a 7-h period. Parameters of interest were cumulative H₂ excretion and peak of H₂ excretion.

Results: None of the measured parameters showed a significant difference between the three groups of subjects. Cumulative H₂ excretion was 9109±4800 ppm x min in self-reported NCGS, 11325±9282 ppm x min in IBS and 10376±7572 ppm x min in HV (ANOVA=NS). Peak of H₂ excretion was 55±28 ppm in self-reported NCGS, 65±43 ppm in IBS and 36±25 ppm in HV (ANOVA=NS).

Conclusions: Breath hydrogen excretion after lactulose did not show any difference between self-reported NCGS, IBS and HV. Accordingly, it seems that no differences of intestinal fermentation occur among these subjects. The definition of this disorder based only on self-reporting does not, however, seem correct: a more objective diagnostic test should be adopted for the diagnosis of NCGS.

P.12.9

INTENSIVE COMBINED TREATMENT IN REFRACTORY MORBID OBESITY: OUR EXPERIENCE WITH A GROUP OF PATIENTS NOT ELIGIBLE FOR BARIATRIC SURGERY

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Background and aim: Morbid obesity is difficult to treat. Often conventional outpatient diet therapy is not effective and bariatric surgery not eligible. We thus examined the effects of an intense combined treatment (diet, psychological, peer group support, physical exercise) in a group of refractory morbid obese patients.

Material and methods: From June 2014 to July 2015, 14 severe obese pts (7M, 7W, mean age 49yrs), not eligible for surgery, were selected for a nutritional rehabilitation programme as twice weekly daily sessions in groups of 3–4 pts, for a mean time of 8.9 months. At the beginning/periodically during the treatment, weight, BMI,

Table (abstract P.12.9)

	Basal		N.	At 3 months		N.	At 6 months		N.	At 9 months	
	Weight kg	BMI kg/m ²		Δ kg	Δ %		Δ kg	Δ %		Δ kg	Δ %
Group	136.6±30 (97 to 182)	47.9±9 (40 to 68)	14	-11±7 (-0.5 to -26)	-8±5 (-0.4 to -19)	11	-20.5±11 (-3 to -37)	-14±7 (-3 to -25)	7	32.2±17 (-16 to -64)	-22±9 (-9 to -36)
Men	151.6±24 (126 to 182)	47.7±7 (40 to 57)	7	-11.9±7 (-0.5 to -21)	-8±5 (-0.4 to -13)	5	-26.1±9.6 (-14 to -37)	-17±7 (-8 to -25)	4	-37.8±20.4 (-16 to -64)	-25±12 (-9 to -36)
Women	121.5±28 (97 to 172)	48.1±11 (40 to 68)	7	-10.1±8 (-1 to -26)	-8±6 (-1 to -19)	6	-15.8±9.8 (-3 to -29)	-12±6 (-3 to -17)	3	-24.8±7.9 (-17 to -32)	-19±4 (-16 to -24)

Values are shown as mean ± SD (range)

resting metabolism (REE; indirect calorimetry, Sensor Medics), body composition (BIA Akern), food intakes/eating disorders (kcal/macronutrients; 24 hr recall history), nutritional blood exams were registered and recorded. Each patient followed a personalized program: -medical checks, nutritional counseling, meal planning and assistance at meals by an expert dietician; -individual psychiatric/psychological sessions (to identify and treat core personality traits/disorders in relation to obesity); -physical exercise planning. Results were divided per sex.

Results: Results on weight loss at 3, 6 and 9 months: see table.

Most patients lost a lot of weight; 7 obtained a mean loss of >20% initial weight at 9months, but the programme is still in progress. 2 diabetics significantly reduced insulin therapy; one suspended the treatment. All improved eating behaviour, reduced glucides/lipid intakes. A better psychological well being was achieved also due to peer group support and more physical exercise.

Conclusions: Our experience on a difficult population of morbid obes, with a combined intensive nutritional rehabilitation program was successful in terms of weight loss, eating behaviour and subjective well being. With a patient targeted approach (personalized dietetic and psychological therapy together with the peer group support) patients developed a better insight on the mechanisms underlining the development and maintenance of morbid obesity

P.12.10

SMALL INTESTINAL BACTERIAL OVERGROWTH IS LINKED TO VASCULAR DISEASE VIA VITAMIN K2-DEPENDENT MECHANISMS

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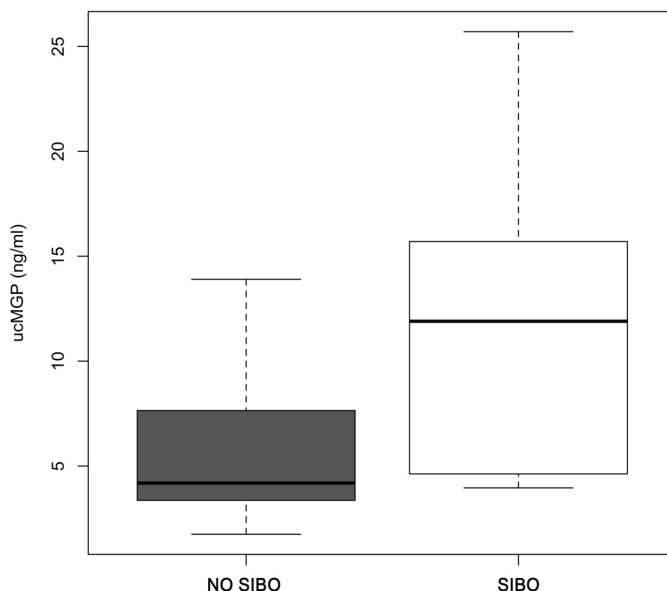
Background and aim: Matrix Gla-protein (MGP) is a vitamin K2 carboxylation-dependent enzyme with inhibitory activity on vascular calcification. MGP inactive form (undercarboxylated MGP, ucMGP) has been recognized as a marker of cardiovascular disease and is associated with increased arterial stiffness.

In Western populations, vitamin K2 request is mainly supplied by gut bacteria since dietary intake is minimal. To investigate if ucMGP levels may be reduced in patients with SIBO and if this could be associated with increased arterial stiffness/presence of vascular calcifications.

Material and methods: Consecutive patients with very low/low Framingham risk score evaluated for gastrointestinal symptoms suggestive for SIBO underwent abdominal aorta and peripheral arteries doppler ultrasound to assess arterial stiffness (carotid artery distensibility (mm)/pulse wave velocity, PWV (cm/sec)) and the presence of vascular calcifications; vitamin K2 daily intake was investigated by a nutritional questionnaire and a blood sample was performed to quantify circulating levels of ucMGP. Patients with conditions potentially affecting ucMGP levels were excluded (e.g. diabetes mellitus, renal insufficiency). A glucose breath test was used to confirm the diagnosis of SIBO. Statistics was performed using r statistics package v. 3.1.2; data are expressed as median (range) and frequency (%).

Results: Thirty-nine patients were included in the analysis; median age was 57 (41-50) years, 14 (35.9%) male, median K2 intake 29.6 (8-103) mcg/day. SIBO diagnosis was confirmed in 12 (30.8%) patients. As expected, circulating ucMGP levels were increased in patients with vascular calcifications (6.7 vs 4.6 ng/ml) and indirectly correlated with arterial distensibility (Spearman's rho -0.596 p=0.05) and directly with PWV (0.535 p=0.0004). Although vitamin K2 daily intake was lower in patients with SIBO (18.9 vs 32.5 mcg/day p=0.05), as expected circulating ucMGP levels were independent of it (p=0.725). ucMGP levels were higher in

patients with SIBO (11.9 vs 4.2 ng/ml, p=0.003 Figure 1), who presented vascular calcifications in 66.7% of cases (vs 51.8%) and an increased arterial stiffness (distensibility 210 vs 255 mm, PWV 9.8 vs 8.2 cm/sec Figure 2).



Conclusions: Dysbiosis may contribute to increase the risk of vascular calcifications and increased arterial stiffness in patients with SIBO, by increasing circulating levels of ucMGP due to reduced vitamin K availability.

P.13 Colon 2

P.13.1

SPLIT-DOSING REGIMEN FOR BOWEL PREPARATION BEFORE COLONOSCOPY: LOW-VOLUME PEG (POLYETHYLENE GLYCOL) SOLUTIONS VERSUS LARGE-VOLUME PEG SOLUTION IN CLINICAL PRACTICE

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Background and aim: Colonoscopy is the current gold standard for the diagnosis and treatment of large-bowel pathologies and for colorectal cancer screening. High quality colonoscopy is largely dependent on the quality of bowel preparation, that has a large impact on adenoma detection rate (ADR), caecal intubation rate (CIR). Split dosing of large volume preparations seems to improve efficacy of bowel preparation, improve ADR and patients acceptance but there is no clear evidence in literature about split dosing applied to low-volume formulations. Primary endpoint was to assess efficacy of split-dose low-volume PEG solutions (PEG+BIS or PEG-ASC) versus split-dose large-volume bowel preparation (PEG-ELS) in unselected outpatients population; secondary endpoints were to assess the acceptance, compliance, tolerability, safety profile.

Material and methods: We retrospectively analyzed data from our patients' registry. Procedures from 5/12/2014 to 1/04/2015 have been considered, including 427 patients using split-dose preparation. Evaluation of efficacy was performed by using the Ottawa Bowel Preparation Scale.

Results: Efficacy of bowel preparation was 76.8% for subjects in the PEG-ELS group, 74.6% for subjects in the PEG+BIS group and 72.6% for PEG-ASC group. No statistical difference was found with regard to efficacy ($p=0.727$). Also with regard to CIR (91.85, 87.9% and 89.4%, respectively) and to ADR (28%, 35.7% and 28.3%, respectively) no statistically significant difference was observed in the inter-group analysis. Moreover, no statistical difference between groups emerged in respect to compliance, acceptance, tolerability and safety.

Conclusions: Split-dose bowel preparations is effective even when applied to low-volume PEG solutions. Low volume preparation compared to large volume preparation administered in split dose did not demonstrate significant difference in term of patients' acceptance, compliance tolerability and safety profile.

P.13.2

DO WE REALLY NEED BIOPSY TO DIAGNOSE COLORECTAL CANCER?

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Background and aim: Colorectal cancer (CRC) is a frequent finding during colonoscopy and endoscopic biopsies are generally performed to confirm the diagnosis. Aim of our study was to evaluate the accuracy of endoscopic biopsy compared to the macroscopic appearance in the diagnosis of colorectal cancer.

Material and methods: We prospectively collected all the colonoscopies in which the endoscopists have suggested a diagnosis of colorectal cancer; 8 skilled endoscopists were asked to describe the macroscopic aspect of the lesions, the size, the presence of bleeding and the site of the lesions. Then they performed biopsy with standard endoscopic forceps. The endoscopic diagnosis of CRC were compared with the results of the histological analyses or with surgical specimens when available.

Results: We included in the study 71 patients with an endoscopic diagnosis of CRC (44 males, mean age 70.2 yr). The lesions were located in 24 cases in the right colon (34%), in 15 cases in the transverse (21%), in 23 cases in the sigmoid colon (32%) and in 9 cases in the rectum (12%). The macroscopic description of the lesions were protruding mass in 27 cases (38%), annular involvement in 24 (34%), stenotic in 10 (14%) and ulcerated in 10 (14%). The lesions were bleeding in 28% of the cases. The sizes were over 4 cm in 66% of the cases. We found concordance between macroscopic appearance and histology in 63 cases (89%); in the remaining cases the biopsy results showed tubulovillous adenomas (5 cases) and aspecific inflammation (3 cases). Nonetheless the analysis of surgical specimens revealed a diagnosis of adenocarcinoma in 4 cases (5.6% histological false negative). The overall accuracy of endoscopic appearance was 95.8% with 3 cases of false positive diagnosis (4.2%).

Conclusions: Endoscopy is highly accurate in diagnosing CRC and the confirmation by biopsy is probably unnecessary.

P.13.3

EFFICACY OF OSTEOPATHIC MANIPULATIVE TREATMENT ON FUNCTIONAL CONSTIPATION: PILOT STUDY OUTCOME RESEARCH

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Background and aim: The American College of Gastroenterology defines constipation as "unsatisfactory defecation, characterized by infrequent bowel movements and/or difficult passage of stool for at least three months" (Brandt et al, 2005). An Italian study (Cottone

et al, 2009) showed that about one third of the patients referred to the clinics of family doctor considering suffering from constipation. This percentage drops to 20% if the family doctor use ICD diagnostic definitions. Laxatives are among the drugs most commonly used the treatment. Only 2 studies in the literature show the application of the Osteopathic Manipulative Treatment (OMT) for disorders of constipation: a case report of a woman diagnosed with colonic inertia and indication for surgery (Cohen-Lewe, 2013) and a pilot study on the impact of OMT on secondary constipation in children neurologically (Tarsuslu et al, 2009). The aim of our study is to verify the effectiveness of OMT on patients with functional constipation.

Material and methods: 30 subjects, 9 males and 21 females, with diagnosis of functional constipation were included in one treatment group. Have been used as an outcome the scale of quality of life SF-12, the Patient Assessment of Constipation Quality of Life (PAC-QOL) and the Cleveland Clinic Constipation, these were detected at enrollment (t0) and after the last sitting of OMT (t1). All subjects were submitted to three sessions of OMT at a distance of one week between the first and the second and two weeks between the second and the third. The OMT was applied to each subject individually and different techniques were used depending on the Somatic Dysfunction (SD) that was found. For each session of OMT it was assessed the prevalence of somatic dysfunction and a comparison was made between the sessions.

Results: It was found, in all sessions of OMT a higher prevalence of SD to sigma: 53% in the first session and 43% in the other two. Between sessions of OMT was observed a reduction in SD that showed a significant reduction of total dysfunctions in second ($p=0.00$) and third ($p=0.00$) treatment, of the SD in the Musculoskeletal system ($p=0.02$ and $p=0.00$), in the visceral system ($p=0.00$ $p=0.00$) and those of the craniosacral system to the third treatment ($p=0.04$). Were observed at t1 significant results (t-student test) on the SF-12 for mental health ($p=0.00$) and physical ($p=0.02$) and all score outcomes of PAC-QOL and the Cleveland Clinic Constipation produced a statistically significant with p-value = 0.00.

Conclusions: The results of this study of outcome research we can observe how the OMT of somatic dysfunction in patients with functional constipation can be effective on improving the quality of life and act on the characteristic symptoms of constipation. The authors would like to lay the foundations and turns the invitation to structure more relevant methodological trial (RCT) to study the somatic treatment of functional disorders.

P.13.4

A LOW FODMAP DIET IN IRRITABLE BOWEL SYNDROME IMPROVES SYMPTOMS WITHOUT AFFECTING BODY COMPOSITION AND EXTRACELLULAR BODY WATER

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Background and aim: FODMAPs, poorly absorbed in the small intestine, enter the colon, where they are fermented, producing gas responsible for bloating, abdominal discomfort and pain, symptoms frequently complained of also by patients affected with irritable bowel syndrome (IBS). A low FODMAP diet is frequently suggested to IBS patients even if the evaluation of possibly significant nutritional concerns remains to be clarified. The aim of this study was to test the effects of a low FODMAP diet on body composition, abdominal symptoms, quality of life, anxiety/depression and sleep disturbances of IBS patients.

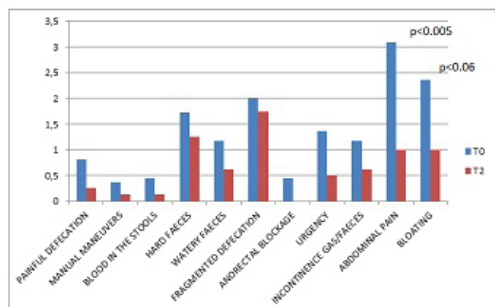
Tab.1 IBS-SSS

	Time 0	Time 2	
Global score	305.8 ± 77.4	98.9 ± 55.5	P<0.002
Abdominal pain (0-100)	49.2 ± 34.2	16.7 ± 16.6	p< 0.05
Days with abdominal pain/10 days	6.8 ± 1.9	1.7 ± 1.6	p< 0.05
Abdominal bloating (0-100)	65.0 ± 24.3	22.2 ± 16.2	p< 0.05
Bowel habits satisfaction (0-100)	74.2 ± 21.9	30.0 ± 22.9	p< 0.05
Interference with daily life activities	47.5 ± 19.1	24.4 ± 20.1	p< 0.05

Tab.2

SF 36	Time 0	Time 2	
Physical activity	79.5 ± 27.2	82.2 ± 25.5	ns
Physical role limitations	59.1 ± 45.1	72.2 ± 42.3	ns
Pain	53.7 ± 18.9	70.6 ± 22.4	p<0.05
General health	61.4 ± 22.4	63.7 ± 21.9	ns
Vitality	50.0 ± 23.4	53.9 ± 16.9	ns
Social activities	63.4 ± 26.5	81.8 ± 20.0	p<0.005
Emotional role limitations	57.4 ± 45.0	70.2 ± 39.0	ns
Mental health	59.6 ± 16.5	71.1 ± 10.9	p<0.02
Physical health index	44.8 ± 11.7	46.8 ± 12.9	ns
Mental health index	40.4 ± 13.4	46.8 ± 8.0	ns

Fig.1 Bowel Habits



Tab.3 Bioelectrical impedance analysis

	Fluids/Hydration				Soft tissue/Nutrition		
	TBW	ECW	ICW	FFM	FM	BCM	PA
T0	20.6 ± 2.6	0.5 ± 0.04	0.5 ± 0.04	27.7 ± 3.8	11.4 ± 5.2	14.1 ± 2.9	5.4 ± 0.8
T2	19.8 ± 1.8	0.5 ± 0.03	0.5 ± 0.03	26.5 ± 2.6	12.2 ± 5.5	13.4 ± 1.7	5.4 ± 0.6
	ns	ns	ns	ns	ns	ns	ns

Material and methods: Twelve IBS patients, diagnosed according to Rome III criteria (11F; mean age 44.2±15.5 yrs.: 2 constipation-predominant, 3 diarrhea-predominant and 7 with mixed IBS) were treated with a low FODMAP diet, adequate in macro/micronutrients, for 8 weeks. When entering the study (T0) and after 8 weeks (T2) several assessments were carried out. These were an IBS-SSS questionnaire referring to IBS symptom severity, a questionnaire evaluating bowel habits using a scale from 0 (no symptom) to 4 (symptom present ≥75%), SF36 for quality of life, HADS for anxiety and depression, Pittsburgh questionnaire for sleep disorders and a bioelectrical impedance analysis to assess body composition.

Results: At T2 IBS-SSS improved (global score: 305.8 ± 77.4 vs 98.9 ± 55.5; p<0.002) (tab.1) together with bowel habits (fig.1) and quality of life (tab.2). No change in sleep quality (6.0 ± 4.8 vs 5.0 ± 2.1), anxiety (6.5 ± 3.6 vs 6.0 ± 3.5) and depression (5.6 ± 4.3 vs 6.6 ± 4.6), BMI (23.6 ± 4.2 vs. 23.6 ± 4.5), body composition and extracellular body water (Table 3) was noticed. The degree of relief using a scale from 0 (total relief) to 7 (no relief) was 1.2 ± 1.0.

Conclusions: The low FODMAP diet greatly improved IBS symptoms as well as quality of life in IBS patients, without affecting BMI, body composition and extracellular body water. Patients were highly satisfied with their clinical improvement.

P.13.5

COLONIC FLAT LESIONS DETECTION USING 64-MDCT COLONOGRAPHY, AND A COMPUTER AIDED DETECTION (CAD) SYSTEM. RADIOLOGICAL-ENDOSCOPICAL CORRELATION

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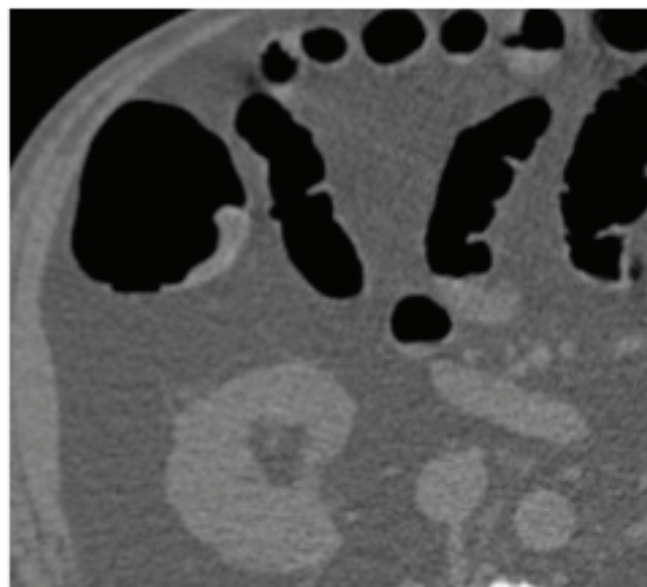
Background and aim: To evaluate the ability of computer aided detection (CAD) software to detect morphologically flat “non polypoid” lesions at CT colonography. To correlate CT colonography Examination with Endoscopy.

To create a hit list of top ten difficult lesion with Radiological and Endoscopic correlation

Material and methods: The CTC datasets of a total of 61 patients with 74 endoscopically proven flat lesions were loaded onto a workstation with CTC viewing software and reviewed with and without CAD system by two radiologists experienced in CTC interpretation, fully unaware of the colonoscopic report.

A total of 61 patients underwent fecal tagging preparation before CTC. Mean reading time with and without CAD, sensitivity and number of false positive were evaluated. Colonic localization as well as histology of all lesions was provided.

Finally an expert reader put flat lesions under magnifying glass creating a top ten list of most difficult lesions discovered on CT Colonography with endoscopic correlation.



Results: 21 of 74 lesions were missed by reading CTC examination without CAD. CAD alone detected 58 of 74 flat lesions. Two radiologist in consensus using CAD software detected 62 of 74 lesions and two lesions detected by CAD was not reported as flat lesions due to low conspicuity. 39 lesions were of 3 mm in height, and 18 ranging in

height between 1 and 2 mm. 12 lesions with the height of 1 mm or less were not seen on CT Colonography. 5 lesions are larger than higher, representing a cancerized lesion.

Concerning the localization of those non polypoid flat lesions, 68/74 lesions were located within right colon. 28 within caecum, 33 within ascending colon and 7 within transverse colon whilst the remaining 6, 5 were located within rectum and 1 within sigmoid colon.

From the histological point of view 44/74 lesions were adenoma with LGD. 21/74 lesions were HDG. 5/74 are flat cancer and 4/74 are hyperplastic.

Mean reading time using primary 2D approach and 3D as problem solving was 4' 28 sec; using CAD has required 52 sec additional

Conclusions: In conclusion, 28% of flat lesion in our population was missed by radiologists without CAD that improved flat lesion detection from 70 to 82% of proven lesions. Visualized flat lesions were 3 mm or lower in height and 6 mm or greater in diameter. Lesions with a height of 1 mm or less were not seen on CT colonography.

Also if the use of CAD did not improve mean reading time of the exam, this software could be very helpful for surveillance, together endoscopy, of high risk patients (like those with cancer history or familiarity for colon cancer, or long history of ulcerative colitis).

P.13.6

A PRIMARY CARE INTERVENTION MODEL ON THE DIVERTICULAR DISEASE

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Background and aim: In routine colonoscopy, diverticulosis is the most commonly found pathology, a great part of it presents signs of diverticular disease. The epidemiological data and the pharmacological approach from the literature do not, exhaustively reflect, real life and daily practice.

Material and methods: From June 2014 to December 2014 we enrolled prospectively 178 patients (M/F=0.47, mean age 71.7±11.5 years, min 41-max 95 years) from 15 GPs' lists, distributed in two different regions of Northern Italy (Emilia Romagna and Veneto). All patients symptomatic, diagnosis was confirmed by a colonoscopy. Patients with acute diverticulitis were excluded.

Based on the predominant symptom patients were addressed to four different therapeutic approaches:

A) Rifaximin 400 mg b.i.d for 10 days/month;

A1) Rifaximin 400 mg b.i.d for 10 days/month followed by supplementation with 2 g of Plantago Ovata husk and 24 billions of different strains of probiotics (a consortium of different species of Lactobacillus and Bifidobacterium) for 20 days once a day;

B) Mesalazine 800 mg b.i.d for 10 days/month;

B1) Mesalazine 800 mg b.i.d for 10 days/month followed by supplementation with 3.40 g Plantago ovata husk for 20 days once a day.

All treatments lasted 3 months.

Statistical analysis was performed blindly from the statistician by means of univariate analysis (ANOVA + Tukey post-hoc test); multivariate analysis was performed through a GLM in order to evaluate the effects of covariates on continuous variables and a regression analysis for categorical variables.

Results: Sixty-three patients were enrolled in group A, 43 in group A1, 23 in group B, 31 in group B1.

Eighteen patients dropped out lasting the 3 months of observation (respectively: 5 in group A, 3 in group A1, 2 in group B and 2 in group B1). ANOVA suggested a statistically significant difference ($p < 0.003$) among groups at T1, with Group A1 and B1 showing higher number of bowel movement/week. GLM confirmed the role of treatment as a significant factor ($F = 2.858$; $p = 0.039$), associated with BMI ($F = 6.972$; $p < 0.009$). Relatively to the bloating, B1 treatment was also associated with non statistically significant lower levels ($p = 0.097$; OR 0.419 95%CI 0.150-1.1710.150-1.171).

Conclusions: In accordance with the baseline clinical presentation, the supplementation of fiber (Plantago Ovata Husk) and/or 24 billions of different strains of probiotics (in a consortium of different species of Lactobacillus and Bifidobacterium) are associated with the statistical significant improvement in the clinical pattern of symptoms in patients with diverticular disease in primary care / family physician setting.

P.13.7

CORRELATION BETWEEN GUT PATHOGENS AND FAECAL LACTOFERRIN LEVELS IN CHILDREN WITH ACUTE DIARRHEA

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Background and aim: In developing countries, children are more often exposed to intestinal pathogens, in this case bacteria that caused acute diarrhea. Difficulties often experienced is the diagnosis in distinguishing between bacterial and non-bacterial causes of acute diarrhea. In children for the benefit of antimicrobial administration, increased level of faecal lactoferrin as a marker of neutrophil migration in the intestinal lumen and it is associated with intestinal inflammation.

To analyze the correlation between gut pathogens and faecal lactoferrin levels in children with acute diarrhea.

Material and methods: An analytic observational with cross sectional study. This study conducted at general hospital in Manado. Sampling was conducted consecutively and 43 children suffer from acute diarrhea, age 7-60 months. The results analyzed with descriptive analysis for children characteristic and laboratory datas and also logistic regression analysis. Datas were counted using SPSS version 21, with levels of significance $p < 0.05$.

Results: This study obtain the relationship between gut pathogens and faecal lactoferrin levels in children with acute diarrhea ($p < 0.0001$).

Conclusions: These results suggest that positive intestinal pathogens in this group of pathologic intestinal bacteria have faecal lactoferrin levels higher than the negative intestinal pathogens non bacterial.

P.13.8

IRRITABLE BOWEL SYNDROME: EFFECT OF A LOW FODMAP DIET ON SYMPTOMS AND NUTRIENT INTAKE

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Background and aim: Background: Patient with irritable bowel syndrome (IBS) often refer adverse reaction to food, and amelioration of symptoms after exclusion-diets. Beneficial effects of diets with reduced intake of substances poorly-incompletely absorbed (such as fermentable oligosaccharides, disaccharides, monosaccharides

and polyols - FODMAPs) have been shown, but is unclear if such diet modification could impact adequate nutrient intake. Aim of the present study was to evaluate the effect of a low FODMAPs diet on symptoms, quality of life and nutrient intake in patients with irritable bowel syndrome.

Material and methods: 29 IBS pts (21-67 yrs, 24 females) underwent nutritional evaluation and counseling: T0 instruction for low FODMAPs diet, symptoms and quality of life evaluation; T1, instruction for reinserting previously withdrawn food, symptoms and quality of life evaluation; T2 symptoms and quality of life evaluation. Patients completed an alimentary diary during the entire duration of the study.

Results: Low-FODMAPs diet was well tolerated by the majority of patients, although was judged frustrating and boring. 9 patients (31%) interrupted the study (3 worsening of symptoms, 2 no beneficial effect, 3 no compliance), while 61% completed the protocol.

During low FODMAPs diet significant amelioration of intestinal and extraintestinal symptoms was observed, except for constipation: abdominal symptoms overall [T0 5.9±2.2 vs t1 3.2±2.5 M± DS, p 0.001], discomfort [t0 7.7±1.4 vs t1 3.3±2.5; P 0.000], pain [T0 5.7±2.9 vs t1 2.8±2.6; p 0.001], bloating [t0 7.1±1.7 vs t1 3.3±2.3; p 0.000], diarrhea [t0 4.7± 3.2 vs t1 2.1±2.2; p 0.003], urinary symptoms [t0 2.0±2.2 vs t1 0.7±1.3; p 0.003], fatigue [t0 5.6±3.1 vs t1 3.6±3.2; p 0.003], headache [t0 3.8± 3.0 vs t1 2.0±2.2; p 0.008], constipation [t0 3.3± 2.7 vs t1 2.6±2.2; p 0.147]. A persistent amelioration of symptoms was also observed after dietician-guided reintroduction of previously withdrawn foods and in some patients after.

Furthermore, quality of life improvement in both physical and mental environment was observed (respectively [PCS-12 t0 43.5; t1 48.2; t2 47.7. MCS-12 t0 39.3, t1 45.4, 48.9]).

However, alimentary diaries showed, during low FODMAPs diet, reduced intake of fibers, calcium, folate, vit D compared to suggested levels.

Conclusions: Low FODMAPs-diet ameliorates both intestinal and extraintestinal symptoms and quality of life in IBS patients. However, since it could be associated with inadequate intake of several nutrients, nutritional counseling and follow-up are recommended.

P.13.9

A PREDICTIVE ROLE OF ANORECTAL MANOMETRIC DIAGNOSIS OF CHRONIC REFRACTORY CONSTIPATION

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Background and aim: Anorectal Manometry (AM), fundamental in the correct diagnosis of patients with Chronic Refractory Constipation (CRC), is described as a test operator-dependent. The aim of this study was to evaluate the predictive value and sensitivity of the AM and the Ballon Expulsion Test (BET) in the diagnosis of CRC, comparing the experience of two Centers of Digestive Pathophysiology of second level.

Material and methods: From September 2014 to September 2015 they were submitted in total in the two Centers in AM, 187 patients with CRC, following criteria Roma III. Among these, 164 were performed to complete a diagnostic imaging exam: 84 TransPerineal Ultrasonography (S.Camillo Hospital) and 80 patients defecated-NMR (S.Giovanni-Addolorata Hospital). After AM, the doctor performer, on the basis of the results associated with the medical examination thorough history and the Digital Rectal Exploration, expressed a suspected diagnosis which was then compared with the result of the Imaging exam not known previously.

Results: A) patients with CRC secondary to pelvic floor dyssynergia (TEP and phase straining altered, paradoxical contraction of the

pubo-rectal muscle) is forecasted to 41/164 (25%) and then it has been confirmed in 38/41 = 92% sensitivity, accuracy 92.6%;

B) patients with SCR secondary to anorectal anatomical changes (prolapse, intussusception, rectocele, descending perineum etc) without dyssynergia (normal phase of straining, alteration of the TEP, squeeze and sensitivity thresholds) is forecasted to 98/164 (60%) and then it has been confirmed in 90/98 = 91% sensitivity, accuracy 91.8%;

C) patients with dyssynergia and anorectal anatomical changes (all changes described above) is forecasted to 25/164 (15%) and then it has been confirmed in 23/25 = 92% sensitivity, accuracy 92%.

Conclusions: This study demonstrates that the AM performed in Centres diagnostic of a second level is not an examination operator-dependent and it has a predictive value with high sensitivity, and accuracy greater than 90% in the diagnosis of patients with SCR.

P.13.10

NON-ELECTIVE SURGERY FOR ACUTE COMPLICATED DIVERTICULITIS. PRIMARY RESECTION-ANASTOMOSIS OR HARTMANN'S PROCEDURE? A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and aim: The use of Primary Resection-Anastomosis with or without protective ileostomy (PRA) or Hartmann's Procedure (HP) in the surgery of complicated acute diverticulitis is still an open question. The latest published meta-analyses were limited to the most severe stages (Hinchey III and IV).

Our systematic review aimed to compare PRA with the HP in all non-elective surgical patients with complicated acute diverticulitis (perforation or obstruction).

Material and methods: A computerized literature search was performed on Medline databases until July 2014. The studies included in the meta-analysis were 24 with a total of 4,062 patients. Study outcomes included postoperative surgical complications, reintervention, 30-day mortality, overall mortality as well as the length of stay as secondary outcome. The pooled effects were estimated using a fixed effect model or random effect model based on the heterogeneity test. Results were expressed as odds ratio (OR) and 95% confidence interval (CI) for dichotomous outcomes and as mean difference (MD) with 95% CI for continuous outcomes. Subgroup analyses by study type were performed.

Results: The PRA group had a lower rate of postoperative surgical complications (OR=0.525, 95% CI 0.387-0.713), reintervention (OR=0.688, 95% CI 0.525-0.902), 30-day mortality (OR=0.389, 95% CI 0.259-0.586), overall mortality (OR=0.467, 95% CI 0.272-0.803) and length of stay (MD=9.129, 95% CI 2.391-15.867) compared to the HP group.

Conclusions: Our meta-analysis shows that the PRA technique is better than HP for all considered outcomes. Due to the high variability of the included studies, further randomized controlled trials would be required to confirm these results.

P.13.11

KAPLAN-MEIER CUMULATIVE SURVIVAL CURVES: A SIX YEAR EXPERIENCE OF A LARGE VOLUME COLONOSCOPY COLORECTAL CANCER SCREENING CENTER

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Background and aim: Colorectal cancer (CRC) in West Countries is the third cause for incidence and mortality of malignant tumors in the man after lung and prostate tumors and the second cause in the women after breast tumors. The CRC screening is now recommended in the general population. The aim of our study is to assess the patients' cumulative survival in CRC lesions diagnosed during routine colonoscopies (RC) and in those found during the colorectal cancer screening colonoscopies (SC).

Material and methods: We retrospectively reviewed the files of 17587 colonoscopies (8343 RC and 9244 SC) performed in our Endoscopy Unit from July 2009 to January 2015 and extracted all the CRC. Statistical analysis were assessed using SPSS software: student T test for unpaired data, Pearson X2 test, Breslow test (generalized Wilcoxon) for cumulative survival.

Results: In 65 months CRC was diagnosed in 605 pt, 329 (54%) during SC and 276 (46%) during RC. The median follow up was 38 months. CRC prevalence was 329/9244 in SC (3,5%) and 276/8343 (3,3%) in RC (Pearson X2= 0,83, p=0,362). Mean±SD patients age at CRC diagnosis, disease free survival and days of hospitalization after surgery were respectively: 62,5±5,6 yr for SC group and 63,4±32,9 yr for Rc group (p=0,673), 34,3±18,6 days for SC group and 24,1±21,5 days for RC group (p<0,0001), 10,2±5,7 days in SC group and 14,2±8,5 in RC group (p<0,0001). CRC prevalence in the right colon was significantly higher in RC 28,6% vs 16,5% of SC (p<0,001), there was no difference in the other colon tracts between the two groups. In SC CRC group until 1st January 2015 314/329 pt (95,4%) were still alive vs 162/242 pt (67%) of RC CRC group, the survival curves showed a significant difference between the two groups (p<0,0001). Kaplan-Meier curves were then performed selecting only patients aged between 50 and 70 yr, 220 pt in SC CRC group and 52 pt in RC CRC group, and the survival estimate was respectively 98% and 81% maintaining the statistical significance (p<0,001). Cumulative survival for male and female were respectively 97% in SC CRC group vs 82% in RC CRC group (p<0,001) and 100% in SC CRC group vs 79% in RC CRC group (p<0,001).

Conclusions: Data from controlled retrospective and prospective studies have generally shown that sigmoidoscopy and colonoscopy are associated with a significant reduction in CRC incidence and CRC mortality. Instead the data on their impact on cumulative survival are much more limited, with most studies unable to report a reduction in cumulative survival. Although our study is a retrospective analysis, we were able to demonstrate the effectiveness of SC in modifying CRC patients cumulative survival comparing them with CRCs diagnosed during routine endoscopies, with a dramatic advantage in terms of mortality, disease free survival and time of hospitalization after surgery.

P.13.12

OMEGA-3 SUPPLEMENTS FOR RECTAL PATIENTS IN NEOADJUVANT CHEMORADIOTHERAPY

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Background and aim: Clinical studies have reported beneficial effects of Fish oil (FO) rich in Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in patients undergoing chemotherapy and/or radiotherapy on different outcomes. The aim of our study is to assess the effects on nutritional and inflammatory parameters in specific rectal cancer population.

Material and methods: We conduct a randomized controlled clinical trial comparing the administration of 2,2g DHA and EPA with standard of care (SOC; no intervention) on rectal cancer. All patients with a diagnosis of rectal cancer clinically staged as cT3-4 and/or N(+) treated on AC Camargo Cancer Center with neoadjuvant chemoradiation followed by radical surgery are eligible. The sample

size calculated is 76 patients, to be recruited by December, 2016. We are presenting an interim analysis. From January to October, 2015, twenty patients concluded neoadjuvant chemoradiation until this date and had biochemical (inflammatory, hematological) and nutritional (anthropometric, subjective global assessment, bioelectrical impedance, handgrip strength) measured in baseline (pretreatment antineoplastic, M1) and post-chemoradiation (M2).

Results: Were tested variables general, clinical, nutritional and inflammatory. There is no difference in all variables between the SOC and FO group at baseline (p>0.05). Patient Generate Subjective Global Assessment (PG-SGA) shows that chemoradiation implicate in nutritional deterioration: in M1 40,1% of individual was well-nourished (PG-SGA-A) and M2 only 5%; no was difference in SOC and FO group. FO group presents average caloric intake and right hand grip strength greater than the SOC in M2 (p<0.05). The cachexia in M1 was present in 15% of patients and in 30% in M2; none of these with caquexia in M2 was supplemented with FO during chemoradiation. When Delta values (final less initial) was analyzed, a significant increase of fat mass (Kg) in the FO group vs. decrease in SOC group was observed (2,83 vs. -2,66; p=0,014); concerning inflammation, Delta C-reactive protein decreased in FO group and increase in SOC (-4,26 vs. 13,98; p=0,046). There wasn't difference about FO and SOC group for muscle mass (kg), muscle mass index (Kg/m2), body mass index (Kg/m2), albumin (g/dL).

Conclusions: These preliminary results show the anti-inflammatory action of omega-3 fish oil (EPA and DHA) and ability to prevent the development of cachexia during chemoradiation. Was observed preservation of muscle strength by FO even without difference in muscle quantity.

P.13.13

DYNAMIC TRANSPERINEAL ULTRASOUND FOR THE EVALUATION OF PELVIC FLOOR DISORDERS: WHICH IS THE BEST POSITION?

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Background and aim: Dynamic transperineal ultrasound (DTPUS) is gaining increasing interest for the study of pelvic floor pathophysiology. It is very useful to evaluate pelvic floor dynamics and morphological changes. Unlike defecography, it is usually performed in a left lateral position, an unnatural position for straining and squeezing maneuvers. This study was aimed at evaluating if body position affects the assessment of puborectalis muscle length (PRL) and anorectal angle (ARA).

Material and methods: Twenty eight consecutive females (mean age: 50.6±16.6 yrs) referred for the presence of chronic non organic constipation were enrolled. According to the Rome III criteria they were separated into functional constipation (FC) (14 pts) and functional defecatory disorder (FDD) (14 pts) by using anorectal manometry, Rx defecography and the balloon expulsion test. Control subjects were 12 asymptomatic non-constipated females (mean age 49.7±11.9 yrs). Transperineal images were obtained using a 3.5-6 MHZ convex probe by the same operator in three different positions: left lateral (LL), supine (SP) and sitting (ST). For each position, the ARA and the distance between the symphysis pubis and the posterior limit of anorectal junction (expressing the PRL) at rest and during push straining and squeezing were evaluated. The emptying of the rectal ampulla was assessed after filling the rectum with 120 cc of ultrasound gel.

Results: Tab. 1 shows mean basal values of ARA and PRL in the different positions. Tab. 2 and 3 show mean changes of ARA and PRL during push straining and squeezing, respectively. n basal conditions PRL values in HV were significantly different in ST in comparison

with LL and SP. PRL values were lower in FDD than in HV and FC because of contraction or lack of relaxation of PR. During push straining in HV and FC, PR relaxation was better in ST than in SP and in LL a trend toward a less paradoxical contraction of PR was seen in FDD. During squeezing in HV and FC, contraction is less effective in SP than in ST and LL.

Tab.1	ARA° (LL)	ARA° (SP)	ARA° (ST)	PRL mm (LL)	PRL mm (SP)	PRL mm (ST)
FC	108±5.5 #	107.7±7.1 #	102.3±14.6	66.7±8.4 #	67.3±6.0 §	74.3±4.4 *§
FDD	91±5.1	95.7±12.7	95.1±11	59.8±5.4	57.8±6.8	61.0±4.1
HV	104.2±4.6 #	105±5.1 #	108.3±8.0 #	62.7±4.4	62.2±5.8	68.3±6.0 #

*p<0.05 vs SP and LL; § p<0.05 vs HV and FDD; #p<0.05 vs FDD;

Tab. 2	ARA (%) (LL)	ARA (%) (SP)	ARA (%) (ST)	PRL (%) (LL)	PRL (%) (SP)	PRL (%) (ST)
FC	15.3±3.9 §#	5.6±11.7 #	12±3.1 #	15.1±7.3 §#	5.7±7.8 #	13.7±6.5 §#
FDD	-12.4±14.1	-12.8±14.2	-12.6±11.7	-6.3±9.7	-4.6±4.9	-1.1±7.5
HV	9.0±2.8 #	8.0±4.7 #	12.5±2.3 #	8.6±4.6 #	7.2±3.3 #	13.3±4.7 #

*p<0.05 vs SP and LL; § p<0.05 vs SP; #p<0.05 vs FDD; *p<0.05 vs HV

Tab. 3	ARA (%) (LL)	ARA (%) (SP)	ARA (%) (ST)	PRL (%) (LL)	PRL (%) (SP)	PRL (%) (ST)
FC	17.4±7.5*	17.8±12.4 #	15.3±6.0	15.4±6.1	12.7±4.5	16.3±5.4 §#
FDD	13.7±8.2 §	8.1±4.0	13.7±7.5 §	14.1±6.0	10.6±5.4	11.6±6.1
HV	10.6±4.2	10.5±5.0	16.5±5.9*	16.6±4.7 §	11.2±5.5	18.8±3.9 §#

§ p<0.05 vs SP *p<0.05 vs SP and LL; #p<0.05 vs FDD *p<0.05 vs HV

Conclusions: ST is the most effective position to study the pelvic floor dynamics and FDD.

P.14 IBD 2

P.14.1

EVALUATION OF BONE METABOLISM DURING ANTI-TNF THERAPY IN INFLAMMATORY BOWEL DISEASES

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Background and aim: Inflammatory bowel diseases (IBD) are associated with increased risk of developing osteopenia or osteoporosis. This is due to many factors some of which related to disease activity, such as increased concentration of pro-inflammatory cytokines, and some related to the specific therapies. In particular, in addition to its role in the pathogenesis of intestinal inflammation, the TNF- α has direct, detrimental effects on osteoblast activity. Osteoblast are responsible for bone formation, whereas osteoclast are responsible for bone resorption, the two phases are coupled in bone remodeling. Aim of the study was to examine short-term changes in biomarkers of bone formation, serum procollagen type I N propeptide (PINP), and bone resorption, serum collagen type I C-telopeptide (CTX), as recommended by IOF/IFCC, following initiation of anti-TNF- α therapy (Infliximab, IFX) and the association with disease activity over 54 weeks of IFX therapy.

Material and methods: Serum samples for bone markers were collected at baseline (T0), before starting the therapy, and every two months. At T0 patients underwent (1) clinical evaluation, (2) endoscopic evaluation, (3) inflammatory laboratory test (reactive protein C (RPC) and fecal calprotectin, and (4) measurement of bone mineral density using dual energy x-ray absorptiometry (DEXA). Every two months patients underwent through the steps 1) and 3).

All the patients (pts) showed no sign of osteopenia or osteoporosis at DEXA.

Results: A preliminary analysis of the first 5 enrolled pts, after two months of IFX therapy, showed: 2 pts with baseline levels of CTX within reference interval (RI) and elevated levels of PINP had an increase of CTX and a decrease of PINP; 3 pts with baseline levels of both CTX and PINP within RI had unmodified CTX levels but increase of PINP. Almost all pts showed biochemical inflammation and endoscopic-clinical moderate activity at T0 and a clinical response and normalization of RPC at T2.

Conclusions: Our findings indicate a modulation effect of IFX therapy on osteoblast in all pts, but a heterogeneous effect on osteoclast activity. These results represent preliminary but promising data that could expand knowledge of the interactions between cytokines and bone in the bone-remodeling process.

P.14.2

IS TOPICAL THERAPY UNDERUSED IN PATIENTS WITH ULCERATIVE COLITIS? OUR EXPERIENCE

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Background and aim: Rectal administration of 5-ASA/steroids is the treatment of choice for ulcerative colitis (UC), particularly for left-sided/distal forms. Little is known about the adherence rates to rectal therapies, and some studies demonstrated an adherence as low as 30% in patients with UC. We aim to quantify the prevalence of non-adherence to rectal therapies in UC patients recruited for the first time in 2 dedicated IBD unit in Legnago Hospital (Verone) and Alto Vicentino Hospital (Santorso, Vicenza).

Material and methods: We retrospectively collected demographical and clinical variables of patients admitted for the first time in the IBD outpatients units from august 2012 to september 2015.

Results: 135 ulcerative colitis patients were recruited. Demographical and clinical variables are summarized in table 1 and 2. 46 pts (34%) had pancolitis, 20 (15%) left sided colitis, 45 (33%) procto-sigmoiditis and 24 (18%) proctitis. Topical therapy with 5-ASA or steroids was given in 6 (9%) pts with proctitis/proctosigmoiditis, a combined systemic and topical treatment was given in 28 pts (41%), whereas systemic treatment with 5-ASA alone was given in 31 (45%) patients. Proportions of topical drug use decreased with respect to disease extension from 34 (49%) pts for proctitis/proctosigmoiditis to 12 (26%) pts for pancolitis (p=0,01). There was no association between disease activity and the use of topical therapy.

Table 1

Patients	
Males	71 (53%)
Females	64 (47%)
Age	49.7 (18-89)
Disease duration	8.8 (0.1-53)
Disease extension	
Pancolitis/extensive colitis	46 (34%)
Left-sided colitis	20 (15%)
Proctosigmoiditis	45 (33%)
Proctitis	24 (18%)
Disease activity	
Remission (Mayo < 2)	61 (45%)
Mild (Mayo 2-4)	56 (42%)
Moderate (Mayo 5-7)	13 (9%)
Severe (Mayo > 7)	5 (4%)

Table 2

	Proctitis	Proctosigmoiditis	Left-sided colitis	Extensive/ Pancolitis
Disease activity				
Remission	7 (29%)	21 (47%)	13 (65%)	20 (43%)
Mild	12 (50%)	22 (49%)	5 (25%)	17 (37%)
Moderate	4 (16%)	1 (2%)	1 (5%)	7 (15%)
Severe	1 (5%)	1 (2%)	1 (5%)	2 (5%)
Therapy				
Oral	7 (30%)	24 (53%)	17 (85%)	35 (76%)
Topical	3 (12%)	3 (7%)	0	0
Combined	12 (50%)	16 (35%)	2 (10%)	10 (22%)
Other*	3 (12%)	15 (33%)	1 (5%)	21 (46%)
No therapy	2 (8%)	2 (8%)	1 (5%)	1 (2%)

* Other therapies: Steroids, Immunosuppressors or anti-TNF antibodies

Conclusions: Topical therapy is underused in our cohort of patients, especially in patients with pancolitis. A dedicated IBD outpatients unit may help to ameliorate the rate of adherence to medical topical treatment. Further studies are needed to evaluate factors affecting adherence and possible strategies to improve topical therapy use.

P.14.3

CORRELATION BETWEEN CLINICAL RESPONSE AND ANEMIA RESOLUTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASES TREATED WITH ANTI-TNF INHIBITORS

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Background and aim: Iron deficiency anemia (IDA) represents a frequent and undertreated finding in IBD patients. Oral iron supplementation is considered as effective as intravenous iron for treating IBD-associated IDA, even if active intestinal inflammation may limit iron enteral absorption. However, response to oral iron supplementation in IBD with respect to inflammatory status is still largely unknown. Present retrospective study was aimed at determining whether the effectiveness of anti-TNF therapy is associated with response to iron supplementation in IBD-related IDA.

Material and methods: Patient series included 174 IBD patients with IBD-related IDA, examined at the enrolment and after long term anti-TNF regimen given at a single UK center (Royal Free Hospital, London). Primary response was defined as the combination at least two of the following: absence of symptoms, steroid withdrawal, and C reactive protein normalization. Primary non-response was defined as one or none of the above.

Results: In the present cohort, 155/174 patients (89%) had Crohn's disease and 85/174 (49%) were anaemic at anti-TNF initiation, with a mean [SEM] haemoglobin level of 10.89[0.144] g/dl. At baseline, 51/85 (60%) had iron deficiency anaemia, 15/85 (18%) anaemia of chronic disease, 4/85 (5%) vitamin B12/folate deficiency and 15/85 (17%) undefined. Overall, 35 out of the 51 IDA patients (69%) were treated with oral iron. In this set of patients with iron supplementation (28 with CD and 7 with UC), there was no difference in baseline mean haemoglobin levels in responders as compared with nonresponders to anti-TNF treatment (11.04[0.158] vs 10.59[0.282]), $p=0.14$. Notably, responders had a slightly greater increase in haemoglobin levels at 14 weeks (11.04 to 12.05 vs. 10.59 to 11.16 in non-responders) even if no significant difference in mean change in haemoglobin was

observed (responders +1.01[0.179]; non-responders +0.60[0.299]), $p=0.21$.

Conclusions: Our data suggest that oral iron supplementation is effective in increasing haemoglobin levels in IBD patients, regardless to their response to anti-TNF therapy which does not impair oral iron absorption and could be used at the same time. These results suggest that oral iron should be considered in all IBD patients with active inflammation.

P.14.4

ESCHERICHIA COLI NISSELE 1917 IN ULCERATIVE COLITIS TREATMENT: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and aim: Escherichia coli Nissle 1917 (EcN) has been advised as a therapeutic tool for Ulcerative Colitis (UC) treatment. However, to date, no meta-analysis has been performed on the topic.

Material and methods: We performed a literature search on PubMed, MEDLINE, Science Direct and EMBASE. We evaluated success rates for induction of remission, relapse rates and side effects, expressed as Intention-To-Treat. Odd ratios (OR), pooled OR and 95% confidence intervals (CI) were calculated, based on the Mantel-Haenszel method. Heterogeneity was assessed by using the χ^2 and I² statistics and, if present, a random-effects model was adopted.

Results: We selected six eligible trials, with 719 patients, 390 assigned to the study group and 329 to the control group. EcN induced remission in 61.6% of cases, while in the control group (mesalazine) the remission was achieved in 69.5% of cases, with a mean difference of 7.9%. The pooled OR was 0.92 (95% CI 0.15-9.66, $p=0.93$). A single study showed a better performance of EcN than placebo. A relapse of the disease occurred in 36.8% in EcN group and in 36.1% in control group (mesalazine), with a mean difference of 0.8%, OR=1.07, with a 95% CI of 0.70-1.64 ($p=0.74$). Side effects were comparable (OR=1.44, 95% CI 0.80-2.59, $p=0.22$).

Conclusions: EcN is equivalent to mesalazine in preventing disease relapse, thus confirming current guidelines recommendations. EcN seems to be as effective as controls in inducing the remission; therefore, its use cannot be recommended as in one study the comparison was performed against placebo despite further studies may be helpful for this topic.

P.14.5

METASTATIC CUTANEOUS CROHN'S DISEASE OF THE FACE TREATED WITH INFlixIMAB: CASE REPORT AND FOLLOW UP

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Background and aim: MCD is a rare extraintestinal manifestation of active CD. Only a few cases of facial involvement have been reported. Diagnosis can be difficult and treatment is largely anecdotal. Sometime improvement has been reported with drugs used for CD. We describe a patient with intestinal CD disease in remission but active MCD refractory to usually drugs used for CD, that improved after infliximab (IFX).

Material and methods: In 2008 a 58-y-old female was referred to Dermatology Department for evaluation of painful erythematous purple papulas, nodules and plaques on her face, she referred in 2006 a ileocecal resection for stenosing and fistulizing CD and since then in clinical and endoscopy remission. Empiric treatment with topical and systemic antibiotics and steroids and azathioprine was ineffective, cutaneous biopsy was performed; histologic examination

showed focal cronic follicular dermatitis with non caseating granulomas; periodic PAS and ZiehlNielsen and Gram stains reaction were negative. A diagnosis of MCD was made, although the patient refused colonoscopy, we decided to treat with IFX.

Results: IFX (5 mg/kg of body weight) was administered at weeks 0 (first dose 09/2010), 2 and 6 and every 8 weeks, after 3th infusion we observed marked improvement and after 5th infusion complete resolution of the lesions. The treatment was continued to 18 months and 3.2012 was interrupted. A follow-up was started, we revised the patient every 12 weeks and after 42 months non relapse was observed.



Conclusions: MCD is a rare cutaneous manifestation of active CD of variable clinical appearance remote from bowel. Diagnosis is difficult and must be differentiated from infectious and non infectious skin's disease; skin biopsy should be performed to assess characteristic granulomas of CD and rule out infection or other etiologies; the treatment is not standardized. Our experience suggest that: 1) MCD can be not related to active intestinal CD; 2) IFX can be a effective and well tolerated treatment; 3) efficacy of IFX is very fast; 4) the effect of IFX remains long after discontinuation of therapy.

P.14.6

PREVALENCE AND CLINICAL SIGNIFICANCE OF HYPERGAMMAGLOBULINEMIA IN INFLAMMATORY BOWEL DISEASE PATIENTS: A RETROSPECTIVE CROSS-SECTIONAL STUDY

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Background and aim: Hypergammaglobulinemia (HGG) is an alteration commonly described in patients with autoimmune, infective or inflammatory disorders where an increment of antibodies production is observed. No data are available for the prevalence and clinical significance of HGG in inflammatory bowel disease (IBD) patients. Aim of the present study was to evaluate the prevalence and clinical significance of HGG in IBD patients in a retrospective cross-sectional study.

Material and methods: We included IBD patients referred at S. Andrea Hospital in Rome, Italy, in outpatient visit, between January 2013 and December 2014. Inclusion criteria were: firm diagnosis of IBD [ulcerative colitis (UC) or Crohn's disease (CD)], and complete records of clinical [age, sex, localization, comorbidities, extra-intestinal manifestations (articular, dermatologic or ocular IBD-related diseases), disease activity, presence of flare at 1 year of follow-up] and biochemical [hemoglobin, C reactive protein, presence of HGG (defined as polyclonal increment of the gammaglobulins

level above the normal lab-reported value)] parameters. Exclusion criteria were: uncertain diagnosis, presence of monoclonal HGG, hematologic or autoimmune disorders. From a total of 388 IBD patients, 81 patients were excluded (uncertain diagnosis=12, lack of data=64, monoclonal HGG=3, multiple myeloma=1, autoimmune thrombocytopenia=1). 307 patients were included (UC=212, CD=95). Prevalence of HGG was calculated. Clinical and biochemical features in patients with and without HGG were compared by t-test and chi-squared test for parametric and non parametric data, respectively. Multivariate analysis was performed with presence of HGG set as independent variable. Odd Ratio (OR) and 95% Confidence Interval (CI) were calculated.

Results: HGG was found in 46/307 (15%) of IBD patients [CD: 11/84 (13%), UC: 35/177 (20%)]. IBD patients with HGG had significant higher prevalence of UC (76% vs. 68%, p=0.05) and extra-intestinal manifestations (28% vs. 14%, p<0.05). At the multivariate analysis, UC (p<0.05) and extra-intestinal manifestations (p<0.005) were independently associated with presence of HGG. UC patients with HGG had significant higher association with presence of extra-intestinal manifestation than UC patients without HGG (OR 4.5, 95%CI 1.6 to 12.1, p=0.0032), while CD patients with HGG did not displayed significant difference (OR 2.3, 95%CI 0.7 to 8.5, p=0.19).

Conclusions: In the present retrospective study, HGG was quite frequent in IBD patients, and it was associated with higher prevalence of extra-intestinal manifestation in UC patients.

P.14.7

DRUG ADHERENCE IN IBD PATIENTS

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Background and aim: Therapeutic adherence to multiple drugs has become one of the major issues in the management of inflammatory bowel disease (IBD), especially in remission periods. A recent review showed that non-adherence rates ranged from 7 to 72%, and a scarce adherence has been associated with frequent relapses, more complications and increased social costs. Aim of the present study was to investigate the rate of non-adherence among our IBD patients.

Material and methods: Patients were recruited at a IBD referral centre of the University Hospital in Salerno (Italy). All patients with a scheduled office visit were asked to fill in a self-administered and anonymous questionnaire available online on a specific website. The questionnaire explored in the long-, middle- and short-period (months, weeks and days, respectively) the adherence to the 4 major class of drugs used as long term therapy (mesalazine, immunosuppressors (IMM), steroids and biologic). Also, the presence of confounders (travels, harassment of taking drugs in social contexts, being worried of adverse events) and the severity of the disease were considered.

Results: Complete data are available on 37 IBD patients (63,4% male, age 21-30 years, 48% Crohn's disease, 52% RCU). 62% were in clinical remission, 80% were on mesalazine, 32% on mesalazine plus an IMM drug, and 21% on mesalazine plus a biologic drug. About half of the patients (46%) were totally compliant to the prescribed therapy, while mesalazine was the most frequently forgotten drug among non-adherent patients. The patients showed a good adherence to IMM, steroids and biologics in the long, middle and short term period. When adherence was evaluated according to disease activity, 12 (30%) of the patients admitted to forget mesalazine when in clinical remission, 7% forgot IMM and 10% forgot to inject biologics or to show up at clinical appointment for anti-TNF infusion. When outside home, patients tended to forget mesalazine (10%), but none

skipped the other drugs, and 10% were non-adherent to mesalazine or to IMMs because of worries about adverse events.

Conclusions: IBD patients of our series showed a scarce compliance to long term therapy particularly when in clinical remission or when they consider a drug less effective than other (mesalazine). More work is required to increase the cohort and to investigate the reasons for non-adherence.

P.14.8

DO ULCERATIVE COLITIS PATIENTS TREATED WITH CORTICOSTEROIDS AT DIAGNOSIS REALLY HAVE A MORE AGGRESSIVE DISEASE COURSE?

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Background and aim: Ulcerative colitis (UC) is a chronic relapsing disease usually treated with mesalazine. In non-responders and in the more severe cases, corticosteroids (CS) are needed. The need for CS therapy at diagnosis is generally considered as a poor prognostic factor. The aim of our study was to assess whether patients treated with CS at diagnosis have more clinical relapses and/or disease progression in a 5-year follow up.

Material and methods: We retrospectively evaluated consecutive patients who had received diagnosis of UC from 1990 to 2010. According to NICE Classification, UC was classified as proctitis (P), proctosigmoiditis (PS), left-side colitis (LC) or extensive colitis (EC). Relapse was defined as a worsening of symptoms requiring an increase of medical treatment. Patients were divided in 4 groups according to the number of relapses in 5 years: Group A (0), Group B (1-2), Group C (3-4) and Group D (5 or more). Moreover, to evaluate disease progression, the sub-population of P, PS, LC at diagnosis was investigated. Progression of disease was defined as the proximal extension of mucosal involvement.

Statistical analysis was performed by Fisher Exact Test.

Results: We recruited 195 UC patients (115 M), 96 (49%) treated with CS at diagnosis. In 5 years, 25/96 (26%) patients had more than 5 relapses with a significant difference if compared to CS-untreated patients at diagnosis ($p<0.001$). Results are shown in Table 1. Out of 137 patients without EC at diagnosis, 53 (38%) showed disease progression (19 P, 22 PS, 12 LC), of whom 32 (60%) were treated with CS at diagnosis, in comparison with 21 (40%) treated only with mesamine ($p<0.001$). Results are shown in Table 2.

Table 1: Relapses

	CS YES	CS NO	<i>p</i>
Group A	7	16	<0.001
Group B	31	57	
Group C	33	21	
Group D	25	5	

Table 2: Disease progression

	CS YES	CS NO	<i>p</i>
Disease Progression YES	32	21	<0.001
Disease Progression NO	25	59	

Conclusions: Our results showed that the use of CS at diagnosis is strongly correlated with a higher number of relapses during a long-lasting follow up. Moreover, we demonstrate the correlation between the need of CS at diagnosis and the proximal extension of

mucosal involvement. These data provides evidence that the need of CS at diagnosis is associated with a worse clinical outcome.

P.14.9

JEJUNAL CROHN'S DISEASE: CHARACTERISTICS, OUTCOME, NEED OF SURGERY AND IMMUNOMODULATORS IN A RETROSPECTIVE SINGLE-CENTER STUDY

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Background and aim: The natural history of Crohn's Disease (CD) involving the jejunum is undefined. In a retrospective, single-center study, we aimed to characterize clinical characteristics and outcome of all patients (pts.) with jejunal CD referring at our tertiary IBD center. Whether the frequency of jejunal lesions in CD is increased during the last years was also investigated.

Material and methods: Clinical records of all CD pts. with complete data, followed up from 2000-2015 (for ≥ 1 yr) were retrospectively reviewed. All clinical characteristics were prospectively recorded, including: gender, age and CD behavior (at diagnosis, current): B1=non-stricturing non-penetrating; B2= stricturing; B3=penetrating; CD duration (yrs), CD-site (ileum, I:L1; colon, C: L2; I+C: L3; jejunum+ I with/without C), surgery (Y/N/ ≥ 1), familial IBD, smoke (Y/N/ex), perianal (PA), appendectomy, comorbidities, EIM, cancer, steroid-(CS) dependence (Y/N), immunosuppressors (IS; AZA/6MP/ MTX), biologics (IFX, ADA). Statistical analysis: Data expressed as median (range), Fisher exact, Chi square tests

Results: From 2000 to 2015, 57 pts. with jejunal CD were identified (23 [40.3%] M; 34 [59.7%] F; age 44 [17-71]; age at diagnosis of CD (27 [12-66] CD duration 12 yrs [1-36]). Lesions at diagnosis of CD involved: jejunum+I: n=34; jejunum+C n=3; I with/without C: n=20). Current lesions involved: jejunum+I: n=41; jejunum+C: n=6; I with/without C, no jejunum n=10. Overall, 42/57 (73.7%) pts required any intestinal resection and 21/57 (36.8%) jejunal surgery. Behaviour in jejunal CD was: B1 n=13; B2=36; B3=8, being B2 correlated with the need of any intestinal surgery ($p=0.016$ and $p=0.023$ for 0 vs ≥ 1 and \leq vs ≥ 1 surgery), but not of jejunal surgery ($p=0.10$). Perianal CD was observed in 18 (31.6%) pts, being correlated with the need of any intestinal surgery ($p=0.025$), but not of jejunal surgery ($p=0.71$), familial IBD ($p=0.07$), smoke ($p=0.97$). Age at diagnosis of CD was correlated with IS use ($p=0.0018$), while the relation between IS and CD behavior was at limit of significance ($p=0.055$). The diagnosis of jejunal lesions (but not of CD) significantly increased during the follow up (1979-89; 1990-9; 2000-2009; 2010-5; $p<0.0001$) (Fig.1a) being significantly more frequent after vs before 2000s ($p=0.001$) (Fig.1b). Jejunal CD was correlated with the need of surgery ($p=0.0016$ surgery \leq vs >1 ; $p=0.022$ surgery 0 vs ≥ 1). Therapies: CS in 50/57 (87.7%) (B1 n=12; B2 n=31; B3 n=7), IS in 24/57 pts. (42%) (B1 n=2; B2 n=17; B3 n=5), anti-TNFs in 17/54 (29.8%) jejunal CD pts. (B1 n=4; B2 n=11; B3 n=2).

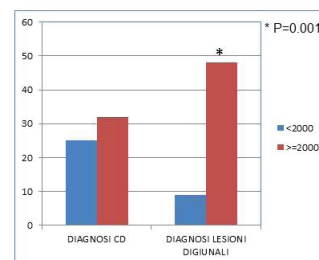


Figure 1a

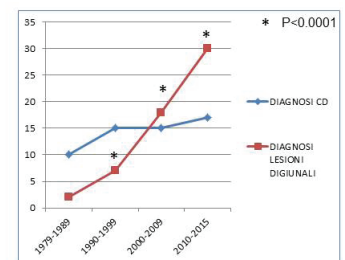


Figure 1b

Conclusions: In a cohort of CD pts., the diagnosis jejunal lesions (but not of CD) significantly increased during the last decades. The

new imaging techniques may be involved in this finding. Two/third of pts. required intestinal surgery, including jejunal surgery in one/third of cases.

P.14.10

QUANTIFICATION OF FODMAPS INTAKE IN PATIENTS WITH QUIESCENT INFLAMMATORY BOWEL DISEASE

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Background and aim: Ongoing troublesome bowel symptoms despite quiescent inflammatory disease are a frequent management challenge when caring for patients with Inflammatory Bowel Disease (IBD). Even when active disease has been excluded, the prevalence of residual gastrointestinal symptoms is surprisingly high and the cause often obscure. Fermentable, short chain carbohydrates (FODMAPs) have been identified as triggers for functional gastrointestinal symptoms. Dietary restriction of FODMAPs has been shown to reduce symptoms of bloating, gas, and diarrhea, with placebo-controlled re-challenge confirming the role of FODMAPs in symptom induction. The aim of our study was to evaluate the FODMAPs intake in the usual diet of patients with IBD in quiescent phase.

Material and methods: A total of seventy patients with quiescent IBD (40 with Ulcerative Colitis, 30 with Crohn's Disease) were enrolled in the study, and compared with a control group of forty healthy patients. All IBD patients were in remission and on stable treatment for at least 6 months. In all patients lactose and/or fructose intolerance was excluded. FODMAPs intake (g/day) was evaluated by 1-week food records. All patients with IBD were asked if they suffered from irritable bowel syndrome (IBS) symptoms according to Rome III Diagnostic Criteria.

Results: We observed that IBD patients had a FODMAPs intake significantly lower than healthy patients (20.29 ± 3.85 vs 30.91 ± 6.25 ; $p < 0.05$). According to Rome III Diagnostic Criteria, twenty-nine (41%) of patients with quiescent IBD had IBS-like symptoms. IBD patients without IBS-like symptoms had a FODMAPs intake significantly lower than those with IBS-like symptoms (18.42 ± 3.56 vs 23.42 ± 3.65 ; $p < 0.05$).

Conclusions: Our data showed that patients with quiescent IBD had a low intake of FODMAPs in their usual diet. Moreover, patients without IBS-like had a FODMAPs intake significantly lower than patients with IBS-like symptoms. These results lead us to assume that these patients tend spontaneously to exclude FODMAPs-rich foods which could cause bowel symptoms despite quiescent inflammatory disease.

P.14.11

METABOLIC SYNDROME: AN UNRECOGNIZED RISK FACTOR IN IBD

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Background and aim: Metabolic Syndrome (MS) is a combination of biochemical and anthropometric disturbances closely associated to diseases spanning from myocardial ischemia, thrombosis and cancer. It has been scarcely investigated and mainly in non-caucasian patients with inflammatory bowel diseases (IBD) in spite of the high prevalence of these complications in such patients. Yet, similarly to what observed in other chronic inflammatory diseases, it may be a factor affecting the prognosis and therapeutic outcome of IBD patients. Aim of this study was to assess the prevalence of MS

in a group of IBD patients, and its association with disease activity and therapy.

Material and methods: 125 consecutive IBD patients and 250 controls, age and sex-matched with a 2:1 ratio were enrolled during a 1-year period. MS was diagnosed according to recent criteria (Circulation 2009) as the presence of >3 criteria among waist circumference, blood pressure, blood glucose, HDL, triglycerides levels. All IBD patients underwent ileocolonoscopy (activity was defined according to SES-CD and Mayo scores), CRP and fecal calprotectin (FC) were also measured (positivity cut-off respectively >0,50 mg/dl and >150 µg/gr).

Results: We enrolled 41 CD, 84 UC (48 M/77 F; mean age 49 ± 17 ys) and 250 controls (96 M/154 F; mean age 49 ± 17 ys). MS prevalence was higher in IBD patients than in controls (37% vs 22%, $p < 0.001$), slightly higher in UC than in CD (respectively 27% and 10% p -ns), with no differences between sexes. In a multivariate logistic analysis MS was associated with IBD (OR: 4.8; 95% CI: 2.1–12.1), even in subjects younger than 50 years (OR: 2.3; 95% CI 1.2–4.5). According to disease activity, we found no difference in SM prevalence according to endoscopy and FC; SM was significantly associated with CRP positivity (72% vs 28%, $p = 0.006$). No difference in SM prevalence during therapy with steroid, mesalazine or immunodulator (respectively $p = 0.15$, $p = 0.35$ and $p = 0.2$); SM prevalence was lower in patients treated with biological therapy (21% vs 44%, $p = 0.018$), although this effect appears to be lower in those with BMI > 30.

Conclusions: MS should be considered in patients with IBD and treated in terms of prevention of SM-associated diseases. In this context a multimodal therapy which includes biologic agents seems to be the most effective.

P.14.12

ADHERENCE TO OUTPATIENT FOLLOW-UP VISIT IN IBD PATIENTS

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Background and aim: IBD are chronic relapsing-remitting medical conditions requiring lifelong treatment. Non adherence to treatment is detrimental. Improvement of pts adherence is crucial in IBD since non-adherence has been shown to increased risk of relapse. To date, non adherence to follow-up is poor known. The aim was to evaluate factors that modulate non-adherence to outpatient follow-up in IBD pts referring to a tertiary center.

Material and methods: 250 non-adherent to outpatient visit IBD pts (NAP) for 2yrs were identified and compared with 132 pts in regular follow-up. A structured phone interview was administered to participants, investigating epidemiological and organizational aspects, clinical data on disease activity, adherence to medical therapy using the Morisky Scale (score <6=low, 6-7=moderate, 8= high adherence). In NAP group we evaluated quality of care patients' perception and the reasons for non-adherence to scheduled visits.

Results: 250 non-adherent pts (M/F 137/113; mean age $49,92 \pm 26,53$) were included. Of those 136 (45.6%) were authentic non-adherent pts (NAP-A) while 114 (36.8%) were considered false non-adherent pts as actually in follow-up in peripheral centre (NAP-B). 132 pts (M/F 76/56, mean age $41.72 \pm 12,92$ yrs) were included in the adherent Group (AD). In NAP-A 97% were poorly symptomatic, 10,8% followed other treatment plan, 6,8% reported social related reasons. NAP-B pts chose peripheral centre for similar care and less wasting of time (44%), for logistic reasons (34%) or for a more familiar approach (22%). Most of NAP-A pts have UC (59,56%), while AD and NAP-B have more frequently CD (respectively 57,58% and 46,49%, $p < 0,05$).

Concerning UC, NAP-A are older (51,12±15,1yrs) than NAP-B and AD (respectively 46,18±17,87 and 44,30±13,86 yrs, $p<0,05$); NAP-A pts have lower educational level than AD pts (primary education 47,78% Vs 26,79%). Therefore, NAP-A CD pts are older than AD pts (46,59±14,44yrs Vs 39,82±12,00, $p<0,05$) but no differences were found in epidemiological- disease features. MoriskyScale showed a low adherence to therapy (<6) in 59,56% of NAP-A pts and 63,16% of NAP-B, while 50% of AD pts had a Morisky Scale >7 , $p<0,05$. Care satisfaction was positive in both.

Conclusions: We unexpectedly found a false non-adherent pts cohort who chose other centers for regular follow-up. High prevalence of non-adherence to therapy was found among patients not attending regular follow up visits in tertiary centre. However, no differences in disease activity was found within the groups. NAP are most likely UC pts and >50 yrs old. Non-adherence to follow-up is strictly related with low adherence to therapy either. Moreover we can focus the importance of a network of collaboration between secondary and tertiary centers in order to ensure the best assistance to chronic pts, which will probably have benefit from a multidisciplinary and complex approach. More studies are required to understand how to reinforce adherence to follow-up

P.14.13

ENDOSCOPIC ACTIVITY EVALUATION IN ULCERATIVE COLITIS: STILL AN UNSOLVED ISSUE

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Background and aim: The relevance of the endoscopic evaluation in ulcerative colitis (UC) management has been recognized from long time. Nonetheless, the modalities of reporting the endoscopic activity still represent an unsolved issue. To this purpose, several endoscopic scores have been proposed, but very few have been properly validated and the use of such tools remains sub-optimal and mainly restricted to clinical trials. In the last years, the growing emphasis of the concept of 'mucosal healing' as prognostic marker and therapeutic goal, has reproposed the need of a more accurate definition of endoscopic activity in UC.

Material and methods: We performed a review of the literature of UC endoscopic scores. The evolution of the problems related to the endoscopic scores have been analyzed, with particular attention to the renewed relevance that endoscopic activity has gained in recent years. The most frequently used scores, and in particular the very last ones proposed, have been critically examined.

Results: More than 30 scores have been described in literature, and we focused on 5 scores (Modified Baron, Mayo Endoscopic Subscore, UCEIS, UCCIS and Modified Mayo Endoscopic Scores) that represent the most commonly used or the most recently proposed ones. Crucial unsolved issues remains the definition of mucosal healing, the possible evaluation of disease extension, the dualism between simplicity and accuracy of the scores, inter-observer agreement, and the implementation of the utilization of the scores.

Conclusions: At present, despite the growing relevance of the issue of endoscopic activity, confirmed by the very recent proposal of novel endoscopic scores, the issue of the evaluation of the endoscopic activity in UC is still open, and the implementation of the use of efficacious endoscopic scores, and the better definition of the absence of activity (mucosal healing), should be improved in the next years.

P.14.14

EXPLORING THE EPIDEMIOLOGICAL ASPECTS OF IBD: PRELIMINARY DATA FROM EPIMICI STUDY IN SAN MARINO

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Background and aim: IBD, including Ulcerative Colitis (UC) and Crohn's Disease (CD), are chronic relapsing conditions with an increasing worldwide incidence. San Marino is the third smallest country of the world with peculiar epidemiologic aspects and can represent an ideal population for studying IBD pathophysiological basis.

Material and methods: To study the epidemiological aspects of IBD in San Marino population. This is a study population including all San Marino persons diagnosed with IBD between 1980 and 2014. Information on socio-demographic and clinical characteristics of cases were obtained via linkage to administrative databases. The principal variables evaluated were age at diagnosis, family history of IBD, disease localization, extra-intestinal manifestations, therapies and their outcome, and need for surgery.

Results: Among all San Marino inhabitants, the overall IBD prevalence was 610/100.000, 350/100.000 for UC and 260/100.000 for CD. The incidence of IBD progressively increased, especially for CD, during the studied period. 15% of patients for CD and less than 10% for UC had a family history of IBD. At gender stratification, 52% UC and 51% CD patients were males. Average age at diagnosis was 38 for UC and 35 for CD. The time lapse between onset of symptoms and diagnosis was less than 1 year for UC and 1-2 years for CD. Extra-intestinal manifestations were observed in 10% of patients with UC and in 30% with CD. Of note, 1 UC patient had sclerosing cholangitis and 1 CD patient had ankylosing spondylitis. Disease localization for UC was: rectum (33%), sigma-rectum (28%) and pancolitis (27%); while for CD was ileum (43%), ileo-colon (41%). Colectomy was needed for 2 UC patients; while 20% of CD patients with ileal stenosis underwent surgery and 80% of these experienced a disease recurrence after 5 years. Immunosuppressive drugs were needed in less than 10% of UC patients and in 17% of CD patients. Biologics were used only in 5 CD patients with achievement of remission.

Conclusions: Our preliminary data demonstrated that IBD prevalence is increased and gender distribution is different in San Marino population when compared to Italian and European data. Early diagnosis and treatment could explain the overall good outcome of the patients evaluated. Further data are needed to confirm and better clarify these findings.

P.14.15

EFFICACY AND SAFETY OF INFLIXIMAB AND ADALIMUMAB IN CROHN'S DISEASE PATIENTS IN A SINGLE IBD CENTER: A RETROSPECTIVE REAL-LIFE STUDY

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Background and aim: Anti-TNF α biologic therapy [infliximab (IFX) and adalimumab (ADA)] are considered a safe and efficacious option for Crohn's disease (CD) patients. Safety profile and efficacy of the two drugs are considered similar, but comparative studies are lacking. Moreover, the most of the data come from registrative and randomized clinical trial performed in tertiary referral centers and in ideal condition, that may not reflect the real clinical scenario of many inflammatory bowel disease (IBD) centers. Aim of the study

was to evaluate clinical efficacy and safety of IFX and ADA in a single IBD center in a real-life study.

Material and methods: Clinical records of CD patients, that underwent anti-TNF therapy (who started from January 2011 to October 2014 and performed at least 3 infusions) at S. Andrea Hospital in Rome, Italy, were retrospectively collected. Baseline characteristics of patients before the start of biologic therapy were recorded. For the biologic therapy, the duration, side effects, and interruption rate, were considered. Finally, clinical remission (defined as the complete absence of clinical symptoms) and clinical response (amelioration of clinical symptoms from baseline) rate, at 1 year of follow-up, in intention-to-treat (ITT) and per protocol (PP) analysis, was recorded.

Results: A total of 30 patients (16 treated with IFX and 14 with ADA) were included. Baseline characteristics between the two groups did not differ except for the rate of biologic naïve patients, that was significantly higher in IFX than in ADA group (94% vs. 57%, $p < 0.05$). Four patients stopped the therapy before 1 year, two in IFX (1 primary non response, 1 prostate cancer diagnosis) and two in ADA group (1 death unrelated to therapy, 1 extensive psoriasis onset). Adverse events that require postponement of therapy schedule occurred in 5 (31%) and 2 (14%) of patients in IFX and ADA group, respectively. At 1 year, clinical remission was observed in 50% (44% and 57% in IFX and ADA group) and clinical response in 70% of patients (63% and 79% in IFX and ADA group, respectively) at the ITT analysis, and in 58% (50% and 67% in IFX and ADA) and 81% (71% and 92% in IFX and ADA group, respectively) at the PP analysis.

Conclusions: The present retrospective single center real-life study confirms that infliximab and adalimumab are safe and effective therapies in CD patients. Prospective multi-center head-to-head studies would better clarify specific profile of the two anti-TNF α drugs.

P.14.16

A NEW THERAPEUTIC LASER SYSTEM FOR ENDOSCOPIC ABLATION OF ESOPHAGEAL LESIONS – FIRST RESULTS IN AN ESTABLISHED ANIMAL MODEL

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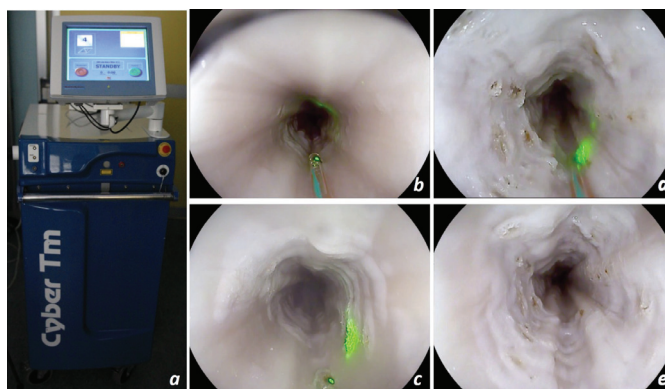
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Background and aim: The Thulium laser system is a novel therapeutic technique for open surgery and endourological treatments [1; fig. a]. To date, the experience on the use of this therapeutic device in gastrointestinal (GI) endoscopy is very limited [2]. Recent experience on animal models showed that the wavelength of 2 μ m allows for ablation and vaporessection of the superficial GI layer providing high control on penetration depth (0.2-0.4 mm) and tissue damage [3]. We conducted a pilot study in an established animal model (EASIE) to test for the first time both feasibility and safety of the Thulium Laser system (Cyber TM®, Quanta System, Varese, Italy) for endoscopic ablation of pre-neoplastic esophageal lesions, such as Barrett esophagus.

Material and methods: According to previous experience [3] and the need of lateral ablative effect, we used a dedicated 600 μ m side fiber with a line beam that emerges at 45 degrees with soft power settings (5-10 watts) and continued laser modality. For safety, the study endpoints was the impact of the laser ablation in terms of depth penetration and lateral tissue damage after having vaporesected circumferentially a 3 cm-length luminal esophageal

surface. All procedures were performed using a high-definition video-gastroscope and digitally video-recorded.

Results: Neither transmural perforation, nor any submucosal layer damage was observed. Two endoscopists completed a circumferential ablation of a 3cm-length luminal esophageal surface within 1 minute each. Overall, each laser ablation on target produced mucosal vaporessection with only a diminutive lateral spreading of epithelial injury (1-3 mm), depending on the distance between the fiber's tip and the esophageal target (fig. b-e).



Conclusions: The Thulium laser system appears to be safe, effective, and very easy to use for the ablation of superficial esophageal lesions in an ex vivo animal model. In vivo studies should now confirm these initial results in a prospective setting.

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P.15 Endoscopy 1

P.15.1

ENDOSCOPIC RESECTION OF DUODENAL NEUROENDOCRINE TUMORS: A CASE SERIES OF A SINGLE INSTITUTION

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Background and aim: Duodenal neuroendocrine tumors (dNETs) represent 1-3% of all primary duodenal tumors. dNETs not located in the periampullary region are suitable for endoscopic treatment if limited to the submucosal layer, without metastases and with size <10 mm. Nevertheless, few data are available about the efficacy of this approach. We reviewed our data about dNETs treated with endoscopic resection (ER).

Material and methods: From 2012 to 2014, 11 dNETs were diagnosed during upper GI endoscopy (UGIE). Five of them were considered suitable for ER. The endoscopic procedure was performed with a high definition single-channel endoscope (EG29i series, Pentax) and the resection technique was chosen according to endoscopist's preference, morphological characteristics, site and endosonographic features of each lesion.

Results: En-bloc resection was obtained in all cases. Endoscopic mucosal resection (EMR) was used for 3 bulb tumors and endoscopic submucosal dissection (ESD) for one bulb tumor. One tumor of distal duodenum was treated with Hybrid-ESD (HESD). In 4 cases the resection site was closed with metal clips. The mean size of resected specimens was 14 mm (range 7-22 mm); histologically the tumor

mean size was 9 mm (range 5–12 mm). The invasion depth was limited to the submucosal layer. R1 resection was present in 2 cases (one after EMR and one after HESD). All lesions were G1–G2 tumors with <1–2 mitosis per high power field. Ki67 proliferation index was 2–4% in 4 tumors and 16% in one. One immediate perforation occurred and was treated conservatively. During the mean follow-up period of 17 months (range 6–31) no local recurrence was observed. A liver metastasis was diagnosed one year after ER in one patient.

Conclusions: Duodenal ER has a higher incidence of complications than in other sites of gastrointestinal tract because of the thickness duodenal wall. Despite en-bloc resection was performed, R0 resection was present in only 60% of cases. We suppose that such result is due to the paucity and laxity of submucosal duodenal tissue, which is destroyed during ER. In fact, because of the narrow duodenal lumen, to avoid excessive burning of peritumoral submucosal duodenal tissue may be technically difficult. To support this hypothesis we did not observe any local recurrence at follow-up UGIE. Our experience, although limited and retrospective, confirms the safety and efficacy of ER for the treatment of dNETs limited to the submucosal layers. However, additional studies with longer follow up are needed.

P.15.2

NEO-ENDOSCOPIC CUL DE SAC OTSC MADE IN DELAYED SURGICAL COMPLICATION

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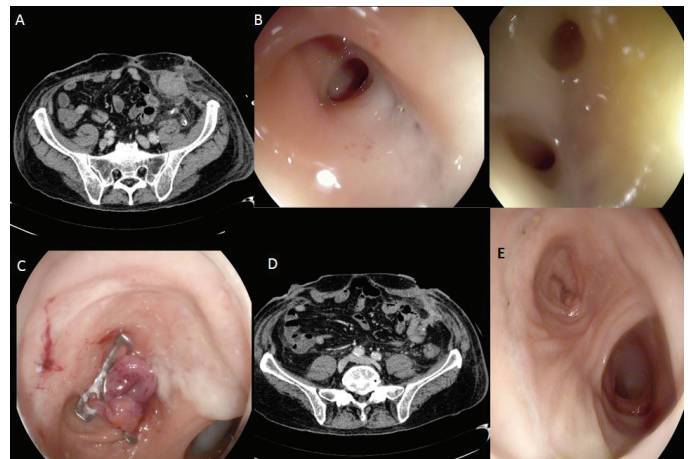
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Background and aim: Anastomotic leakage, the most feared complication of colorectal surgery, is associated with increased morbidity and mortality, prolonged hospital stay, and additional health-care costs. Its reported prevalence varies widely from 1 to 39%, but clinically relevant leaks probably occur in 3–6% of cases, depending on the definition and the type of resection. Where indicated, operative endoscopy to achieve wound healing may be a viable alternative, allowing minimally invasive treatment. We report a case of successful endoscopic closure of chronic double cul de sac fistulas modifying OTSC application and deployment.

Material and methods: A 67-year-old man underwent left hemicolectomy for sigmoid colon cancer. A colocolonic end-to-side anastomosis was performed. Five months later the patient was admitted to the intensive care unit because of worsening clinical status. An anastomotic dehiscence was diagnosed by use of a CT scan (Fig 1 A). Air was also present in the retroperitoneum. Endoscopy was immediately performed, and two areas of anastomotic dehiscence of approximately 5 and 10 mm of colocolic fistula occurred in the cul de sac (B). The cap was applied against the fistula, and aspiration was performed to remove a large amount of collected fluid and debris outside the colon. The anchor probe was introduced through the fistula and the grasped tissue firmly pulled inside the cap. Continuous suction was applied to assist traction of the anchor probe. It was impossible to correctly deploy the OTSC due to insufficient grasping and suction caused by fibrosis, scarred and hardened postsurgical tissues at the edges of the lesion. Such, to allows to capture a large amount of soft tissue above the leakage, we positioning the device at medial tract of the cul de sac and without using any grasper. Healthy mucosa were fully pulled and suctioned into the cap, then the clip was deployed (C).

Results: The patient was allowed to have a full diet 24 hours later, after a Gastrografin enema confirmed sealing. The patient was discharged from the hospital 1 week later. CT scan performed 1

month after hospital discharge confirmed that the leakage was sealed (D). Endoscopy confirmed a new cul de sac, with healthy mucosa without OTSC (E).



Conclusions: Endoscopic OTSC (Over-the-Scope Clip (OTSC®; Tübingen, Germany) application is an especially attractive option for the treatment of small leakages and fistulas. It allows the closing of defects by grasping much larger amounts of tissue with a high compression force. Some studies reported a lower efficacy for treatment of chronic fistulas. In a recent case series including 9 patients, the overall success rate of OTSC application was 55%; it was impossible to correctly deploy the OTSC due to insufficient grasping of the tissue caused by fibrosis at the edges of the lesion. In our case, we overcome these limitation aspirating soft and healthy mucosa above the scarred and fibrotic tissue, creating a new endoscopic cul de sac.

P.15.3

INCREASED PERFORMANCE OF AN UPDATED ROCKALL SCORE IN ACUTE NON VARICEAL UPPER GASTRO INTESTINAL BLEEDING: A PROSPECTIVE MULTICENTRE ITALIAN STUDY

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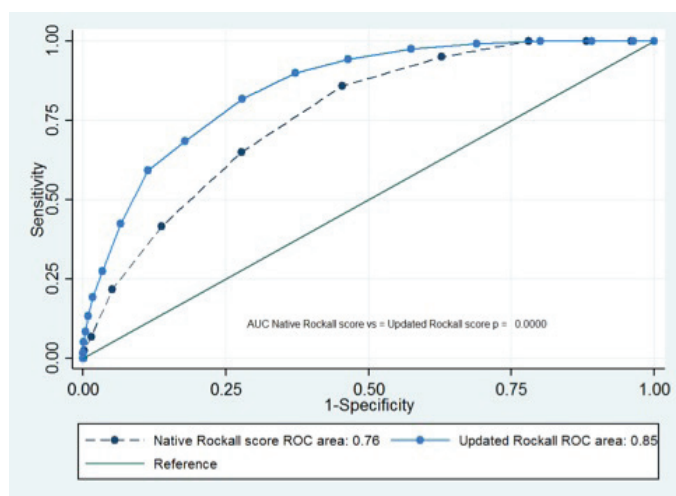
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Background and aim: Patients with acute non-variceal upper gastro intestinal bleeding (ANV-UGIB) have a wide range of clinical severity, ranging from patients needing of diagnostic procedures to patients at death risk. Triaging and differentiating patients in correct classes of risk could impact on clinical outcomes and on resource saving. The Rockall score is a widely used and validated score addressing these issues on hospital admission. In the last years, factors other than those included in the Rockall score were studied. Our aim was to evaluate the prognostic value of an updated Rockall score compared with the traditional one.

Material and methods: Data on patients admitted for ANV-UGIB were collected from January 2014 to September 2015. Primary

outcome was 30-day mortality. We integrated the traditional risk factors for mortality considered in the Rockall score with those more recently recognized in the literature, e.g. inpatients bleeding, endoscopic treatment failure, comorbidities severity (evaluated by American Society of Anaesthesiologists physical status classification, or ASA score), rebleeding and need for surgery. Statistics: the performance yield of prognostic scores was assessed by comparing the ROC curves

Results: A total of 2,191 patients with ANV-UGIB were included (mean age 69.2, 67.1% male). Comorbidities were present in 75.8% and were judged as severe (ASA score 3–4) in 34.7% patients. At admission, 7.2% of the patients had hemodynamic instability and inpatient bleeding occurred in 410 (19.9%). Rebleeding and need for surgery occurred respectively in 124 (5.6%) and 90 (4.1%) patients with an overall mortality of 5.8%. In those patients, the native Rockall score had a performance of 76% [AUC= 0.76 (0.73 to 0.80)], while when we integrated additional risk factors, the updated Rockall provide a better performance [AUC= 0.85 (0.82 to 0.88) $p < 0.000$, Figure 1]. Compared the native score, the new Rockall has a better sensitivity for death risk between 5 to 7 points (94.2% vs. 65.0%) and an implemented sensitivity for score ≥ 8 points (81.7% vs. 21.7%, $p < 0.000$).



Conclusions: In ANV-UGIB patients, different events could occur during hospital stay, which in turn can increase the death risk. Unfortunately, those are not considered during the initial clinical triage of those patients. Our data show that when the traditional Rockall score is implemented with new risk factors, the accuracy and sensitivity are implemented, thus allowing a better identification of patients with a higher mortality rate.

P.15.4

BLACK ESOPHAGUS: AN UNCOMMON CAUSE OF NON VARICEAL UPPER GI BLEEDING

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Background and aim: Black esophagus or acute esophageal necrosis (AEN) is a rare cause of acute upper gastrointestinal bleeding (AUGIB) characterized by circumferential black appearance of distal esophageal mucosa that stops abruptly at gastroesophageal junction (GEJ). It is diagnosed in elderly men with multiple comorbidities and younger adults with history of alcohol consumption. Etiology take into account an initial ischemic damage and a topical injury that can lead to diminished mucosal defense and compromise of the intrinsic repair mechanisms. We report a case of AUGIB due to AEN.

Material and methods: A 67-year-old man presented to the emergency department with hematemesis after three days of fever, right hypochondriac pain and vomiting. He reported moderate recent alcohol consumption but no NSAIDs abuse. Laboratory evaluation revealed conjugated hyperbilirubinemia with cholestasis, hemoglobin 15.6 g/dL which decreased to 13 g/dL six hours later; glycemia 467 mg/dL; BUN 241 mg/dL. On presentation, he was given an iv bolus of proton pump inhibitor (PPI) 80 mg followed by an iv PPI drip at 8 mg/h. A CT scan showed gallbladder, common bile duct and intrahepatic gallstones with dilation of biliary tree.

Results: An urgent upper endoscopy (EGD) revealed striking diffuse circumferential black discoloration of the middle and distal esophagus with abrupt interruption at the GEJ and no active bleeding. Endoscopic biopsies were deferred and no further endoscopic intervention was required. The patient was kept nil-per-os with iv hydration, insulin and antibiotic therapy. Three days after admission a second endoscopic look revealed white-yellow circumferential exudates in the middle and distal esophagus. After ERCP and cholecystectomy he progressively recovered without any complication. He started soft diet at day 7 and was discharged in good clinical conditions one week later.

Conclusions: AEN is a rare cause (prevalence 0.001-0.2%) of AUGIB with multifactorial etiology. Endoscopic appearance is diagnostic and histologic confirmation is not warranted unless other etiologies are suspected. Management consists of treatment of the underlying diseases, fasting and high dose PPI. Antimicrobial therapy is indicated only when infections are suspected. Mortality ranges from 13 to 35% and esophageal perforation is reported up to 7% of cases. About 40% of patients develop progressive dysphagia due to esophageal strictures. In conclusion, although AEN is a rare condition it should be considered and mentioned on international guidelines as a possible cause of AUGIB.

P.15.5

GUIDE WIRE ASSISTED CANNULATION OF MINOR PAPILLA IN PANCREAS DIVISUM: OUR EXPERIENCE

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Background and aim: The minor papilla cannulation is a challenging procedure with an high rate failure in literature (20%)*. We describe our experience of endotherapy in patients with pancreas divisum affected by symptomatic pancreatic diseases.

Material and methods: From April 2012 to October 2013 14 patients with pancreas divisum affected by symptomatic diseases underwent ERCP using a minor papilla approach. We retrospectively evaluated technical results at first attempt and early complications as well.

Results: In patients with a diagnosis of pancreas divisum (11/14) we approached directly to the minor papilla with a double lumen sphincterotome (Mini-Tome, Cook) and a 0.018 fr hydrophilic guide wire without contrast injection (WIRE-GUIDE CANNULATION), then we performed sphincterotomy and plastic stent placement (calibre 5, 8.5 or 10 Fr).

The minor papilla cannulation was achieved in 13 of 14 patients (92.8%) at first attempt, in one case, after unsuccessful pre cut, we repeated ERCP the next day and we got a successful cannulation after secretin's injection for a better visualization of duct's opening. Endoscopic minor papillotomy (EMP) was performed in 13 of 14 patients using a sphincterotome (Mini-Tome, Cook). Pancreatic stent was placed in 92.8% of cases. In 3 cases we need to remove the stent repeating the endoscopy, in the others we observed a spontaneous migration.

An intraprocedure bleeding after EMP occurred in 3 patients and was successfully treated with adrenalin injection or endoclip. No pancreatitis or bleeding occurred.

Conclusions: Our minor papilla approach, guide wire assisted without contrast injection, is safe, and effective when the procedure is performed in a high-volume referral center by experienced endoscopists.

P.15.6

THE ACCURACY OF ACETIC ACID CHROMOENDOSCOPY (AAC) FOR THE DIAGNOSIS OF SPECIALIZED INTESTINAL METAPLASIA (SIM) AND EARLY NEOPLASIA (EN) IN PATIENTS WITH BARRETT'S OESOPHAGUS (BO). SYSTEMATIC REVIEW AND META-ANALYSIS

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Background and aim: Barrett's Oesophagus (BO) surveillance with a random biopsy protocol has many limitations. It is time consuming, invasive, and can lead to sampling error. Chromoendoscopy with acetic acid (AAC) and targeted biopsies has been proposed as an effective alternative to address these limitations. The aim of this study was to assess the diagnostic accuracy of AAC for the detection of SIM and EN (High Grade Dysplasia and Early Cancer) in patients with BO.

Material and methods: We performed a meta-analysis of all primary studies which compared AAC-based diagnosis (index test) with histopathology as the reference standard. The data were extracted both on a "per patient" and "per area" and "per procedure" basis wherever available.

Results: Thirteen studies met the inclusion criteria. For diagnosis EN, the pooled sensitivity and specificity for all included studies were 0.92 (95% CI 0.83-0.97) and 0.96 (95% CI 0.85-0.99), respectively. The positive and negative likelihood ratios (LR's) were 24.97 (95% CI 5.92-105.3) and 0.08 (95% CI 0.04-0.18) respectively. No statistically significant different results were obtained considering only studies with a per-patient analysis. For the characterization of SIM, the pooled sensitivity and specificity for all the included studies were 0.96 (95% CI 0.83-0.99) and 0.67 (95% CI 0.51-0.79), respectively. The positive and negative LR's were 2.9 (95% CI 1.9-4.4) and 0.06 (95% CI 0.02-0.28), respectively.

Conclusions: AAC has a high diagnostic accuracy for diagnosing early neoplasia in patients with BO. AAC has high sensitivity but poor specificity for characterizing SIM, suggesting that histological confirmation is mandatory when AAC is positive.

P.15.7

GUIDELINES ON THE MANAGEMENT OF ANTITHROMBOTIC THERAPY (ATT) FOR ENDOSCOPIC PROCEDURES AND CLINICAL PRACTICE: PRELIMINARY REPORT

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Background and aim: Perioperative management of ATT occurs frequently and requires considerations of the patients (pts), the procedures, and the antithrombotic agents. ATT with antiplatelet agents is widespread and is indicated for the management of

primary and secondary prevention of atherosclerotic thrombotic disease. The most frequently used agents (aspirin and clopidogrel) need to be withheld (7-10 days before) or not depending on the risk of bleeding of the procedures and the thromboembolic risk of the pts according to the guidelines recommendations.

Aim of the study is to verify the adherence to the guidelines on the management of the ATT pts for endoscopic procedures in our endoscopic unit.

Material and methods: 117 consecutive outpatients (56 male, 61 female) taking ATT for the prevention of atherosclerotic thrombotic disease and referred to our endoscopic unit for gastroscopy (48/120) or colonoscopy (72/120) from January 2015 to March 2015.

The endoscopists were blinded about the ongoing study and decided autonomously to perform or not biopsies. Nurses collected data after endoscopy.

Results: 20/117 pts had the discontinuation of the ATT (16/20 aspirin, 2/20 ticlopidine, 2/20 clopidogrel) from the general practitioner (GP) before endoscopy (4/20 egdsco, 16/20 colonoscopy) ranging from 1 day to 15 days. 93/117 pts did not stop the treatment before endoscopy. 30/95 pts had endoscopic indication for biopsy (23/30 colonoscopy, 7/30 egdsco). Biopsies were performed during endoscopy in 8/30 pts taking aspirin (6/8 colonoscopy, 2/8 egdsco). The other pts were surprisingly asked to suspend ATT 7-10 days before to repeating the procedure. No complications were reported in biopsied pts.

Conclusions: Our preliminary data show that clinical practice is very far from the clinical guidelines with few differences between GP and specialists. The final aim of this observational study is to improve the knowledge in GP and gastroenterologists for the best management of the ATT pts and reduce risks of periprocedural bleeding and thromboembolic complications.

P.15.8

POOR OUTCOME FROM ACUTE UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH LIVER CIRRHOSIS: A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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Background and aim: Acute upper GI bleeding (AUGIB) frequently occurs in patients with liver cirrhosis, the main source usually being esophago-gastric varices or portal hypertensive gastropathy. However, the epidemiology of UGIB in cirrhotic patients appears to be changing, with a decrease in the incidence of variceal bleeding. On the other hand, data on cirrhotic patients with a non-variceal source of bleeding are scarce and mainly retrospective. Aim of the study was to assess the rebleeding, surgery and death risk in cirrhotic patients with AUGIB from a variceal or a non-variceal source.

Material and methods: Data on patients admitted for AUGIB were collected from January 2014 to September 2015. Primary outcomes were 45-day mortality, recurrent bleeding, need for surgery, use of transjugular intrahepatic portosystemic shunt (TIPS), and length of

hospital stay in variceal bleeders (VB) vs. non-variceal bleeders (NVB). Pre specified death causes were registered.

Results: A total of 2,628 patients were included, of which 549 (20.9%) had liver cirrhosis. The bleeding source was variceal in 404 (73.6%) and non-variceal in 145 (26.4%) patients. Characteristics of the 2 groups are described in table 1. Among the VB, the source of AUGIB was oesophageal in 304 (80.2%) and gastric in 66 (16.3%), while among the NVB the source was portal hypertensive gastropathy in 33.1%, a gastric or duodenal ulcer in 20%, a vascular lesions in 14.5% or a gastroduodenal erosions in 13.1%. 265 (65.6%) VB patients were transfused vs 81 (55.9%) of the NVB ($p < 0.04$). Six patients in VB group and one in NVB group were treated with TIPS (1.5% vs. 0.7%). Overall, recurrent bleeding, need for surgery, 45-day mortality did not differ between groups. The most frequent causes of death were liver failure (34%), multi organ failure (24%) and respiratory insufficiency (12%) among the VB, and multi organ failure (42.8%) respiratory insufficiency (14.3%) and sepsis (7.4%) among the NVB. The death causes were judged not directly linked to the blood loss in 77% and in 82% of VB and NVB.

Table

	Variceal bleeders (VB, n = 404)	Non-variceal bleeders (NVB, n = 145)	P
Gender (male, %)	68.5 %	67.5 %	0.24
Age (mean \pm SD)	63.6 \pm 12.1	62.2 \pm 14.8	0.35
Child score (mean \pm SD)	8.1 \pm 3.06	7.8 \pm 2.2	0.21
Haemoglobin value (mean \pm SD)	8.9 \pm 2.0	9.3 \pm 2.4	0.08
Hemodynamic instability (%)	8.9%	7.3%	0.56
Use of aspirin (%)	6.9%	6.2%	0.77
Use of NSAIDS (%)	5.7%	8.3%	0.27
Hematemesis as clinical presentation (%)	81.7%	51%	< 0.0001
Hepatocellular carcinoma (%)	28.3%	20.8%	0.08
Transfusion (%)	65.6%	55.9%	0.02
Rebleeding (%)	9.2%	5.5%	0.17
Death	12.4%	11.7%	0.84

Conclusions: Recurrent bleeding, need for TIPS or surgery are infrequent events in our cohort. Transfusions are more frequently prescribed in variceal bleeders. Mortality due to variceal or non-variceal bleeding is similar, as the great majority of mortality was unrelated to blood loss per se.

P.15.9

TRANSFUSION STRATEGY AND DEATH RISK IN PATIENTS WITH ACUTE NON VARICEAL UPPER GASTRO INTESTINAL BLEEDING (NV-UGIB) IN ITALY: A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY

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Background and aim: Acute non-variceal upper gastrointestinal bleeding (NV-UGIB) is a frequent indication for hospital admission and blood transfusions. A liberal use of blood supplies may affect the mortality, but studies on the correct strategy for transfusion of patients with hemoglobin between 7 and 9 g/dL are inconclusive.

Aim: we evaluated the impact of transfusion strategies on death risk in patients with NV-UGIB.

Material and methods: Prospective data on patients admitted for NV-UGIB were collected from January 2014 to September 2015. 30-day mortality and transfusion strategy were the primary outcomes. Transfusion strategy definitions: "restrictive" if the patient was transfused for hemoglobin (Hb) levels ≤ 7 g/dL; "not justified" for Hb levels from 7 to 9g/dL; "liberal" for Hb levels ≥ 9 g/dL; "not indicated" for Hb levels ≥ 10 g/dL.

Results: 2,191 NV-UGIB patients were included (mean age 69.2, 67.1% males). Comorbidities were present in 75.8%. At admission, mean Hb value was 9.3 ± 2.6 and 7.2% of the patients had hemodynamic instability. Overall, half of the patients (56.4%) were transfused, receiving a mean of 3.1 blood units, with a mortality rate of 5.8%. Need for transfusions impacted on mortality, being statistically different between transfused and non-transfused patients (8.1% vs. 2.9% $p < 0.000$), and the death risk varies considerably within the Hb value (tab.1). 43% of the patients had a restrictive transfusion strategy while 7.8% received a liberal. In the restrictive group, mean infusion of 3.8 RBCs units increased Hb value from ≤ 7 g/dL to 7.8 gr/dL in 98% of patients; in those with persistent low Hb levels, death occurred in 58%. In the not justified group, after the administration of a mean of 2.6 units, the Hb did not change substantially in 65 pts and 16.9% of them died. Both in the restrictive and in the not justified group, when Hb increased over 9 g/dL, we observed a substantial decrease in mortality rate, fluctuating between 5.8% and 8.6% ($p < 0.13$).

Before transfusion			Transfusion			After transfusion			Mortality according to Haemoglobin value after transfusion		
Strata	Pts. nr.	Hemoglobin	Number			Strata	Pts. nr.	Hemoglobin			
Hb/dL		Mean (S.D.) ^a		Mean (S.D.) ^a		Hb/dL		Mean (S.D.) ^a		Nr.pts	Dead Nr.
≤ 7	535	6.0 (.9)		3.8 (2.2)		≤ 7	12	6.5 (.7)		12	7
7-8	396	7.6 (.3)		2.6 (1.9)		7-8	65	7.8 (.3)		65	11
8-9	210	8.5 (.3)		2.6 (2.2)		8-9	315	8.7 (.3)		315	27
9-10	63	9.6 (.3)		2.7 (2.8)		9-10	430	9.6 (.3)		430	25
≥ 10	34	11 (.6)		2.3 (1.7)		≥ 10	416	10.9 (.7)		416	30

Conclusions: The "restrictive" transfusion strategy was adopted in 43% of patients with NV-UGIB while the liberal was adopted only in a minority of patients with no effect the mortality rate. Reassessing Hb concentration during transfusions and an appropriate transfusion strategy could reduce an over-utilization of RBC as a substantial number of transfusions were administered without indication.

P.15.10

ENDOSCOPIC TREATMENT OF ANASTOMOTIC STENOSIS AFTER INTESTINAL RESECTION FOR DEEP ENDOMETRIOSIS: A SINGLE CENTER'S EXPERIENCE

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Background and aim: Endometriosis is a very complicated multivisceral disease. Intestinal resection for deep endometriosis is associated with many complications, the most frequent is anastomotic stenosis. Our experience shows that for this kind of complication endoscopic approach is safe and feasible.

Material and methods: We collected from our database the single center experience about deep endometriosis surgery (data from 2010 until 2014).

Of the 1548 female patients who underwent intestinal resection for deep endometriosis, we studied the patients affected by post-operative anastomotic stenosis. We evaluated the surgical features

of these patients and above all the clinical outcome of the chosen treatment of the stenosis.

All the strictures were treated by endoscopic use of Savary's dilators. Clinical success of endoscopic treatment of the stricture was defined as regular bowel movement and absence of re-intervention.

Results: Of the 1548 female patients who underwent intestinal resection for deep endometriosis (mean age 34 years old) stenosis was observed and treated by Savary dilation in 85 patients (5.5%), after a mean post-operative period of 90 days. A protective colostomy was performed in 30/85 patients. No significant statistical correlation was seen between presence of anastomotic stenosis and stapler's size (mean size 29), length of intervention (mean operative time 291 minutes), resection level (mean distance from anal verge 10,3 cm), and preoperative stenosis, evaluated by barium enema (mean preoperative stenosis mildly higher in the studied group vs other patients: 30% vs 26%).

The number of Savary dilations was different between patients (mean number 2 dilatations, minimum 1 and maximum 13) but the endoscopic performances were made by the same endoscopist. We recorded only one complication of the endoscopic treatment: a microperforation showed by CT, treated in a conservative way. In another patient endoscopic dilation was not effective, so we decided for rectal stent placement.

No patients underwent a new intervention for anastomotic stenosis.

Conclusions: Anastomotic stenosis after intestinal resection for deep endometriosis is not a rare complication, but endoscopic treatment by Savary dilation seems to be effective, safe and feasible. At the moment we lack pre-operative predictive factors for this kind of complication.

P.15.11

HIGH DOSE VERSUS NON HIGH DOSE OF PROTON PUMP INHIBITORS IN PATIENTS WITH PEPTIC ULCER BLEEDING AFTER ENDOSCOPIC TREATMENT: A META-ANALYSIS

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Background and aim: Treatment with proton pump inhibitors (PPIs) improves clinical outcomes in patients with peptic ulcer bleeding after endoscopic treatment but the optimal dose remain controversial. In clinical practice high dose after endoscopic treatment are used according to International guideline. However there are no evidence showing that high dose of PPI are superior to non high dose. To compare the high versus non high dose of PPI in patients with peptic ulcer bleeding after endoscopic treatment a meta-analysis was performed.

Material and methods: A computerized medical literature search was performed by using MEDLINE, EMBASE, Cochrane Library, from 1980 to March 2015, aimed at identifying available studies that assess clinical outcomes of high vs non high dose of PPI. We finally analyzed 11 RCTS, involving 1854 patients. Outcomes were: rebleeding, surgery, mortality, hospital stay and blood transfusion.

Results: There was no difference between high dose and non high dose PPI in rebleeding rate (OR 1.3595%CI 0.93-1.97), need for surgery (OR 1.14 95%CI 0.60-1.20) and mortality (OR 1.03, 95%CI 0.60-1.75). Hospital stay and blood transfusion were equivalent in both group (MD 0.27 95%CI -0.44,0.98); MD 0.41;-0.22-1.03).

Conclusions: High dose of PPI is not superior to non high PPI in reducing rebleeding rate, need for surgery or mortality after endoscopic treatment. Furthermore High dose did not reduce the hospital stay or need for blood transfusion.

P.15.12

POST-POLYPECTOMY BLEEDING: RISK FACTORS AND ROLE OF ANTIPLATELET AND ANTICOAGULANT AGENTS

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Background and aim: Post-polypectomy bleeding (PPB) is a known adverse event that can occur following colon polypectomy in 0.3-6.1% of cases. Several factors that depend on patient and technical removal may impact the occurrence of PPB, but antiaggregant and anticoagulation drugs' assumption during polypectomy represent still a major debate. Suspension of the drugs prevent may PPB but arise the risk of potential ischemic events. Aim of this study was to establish the risk factors of PPB and the role of antiplatelet/anticoagulant drugs.

Material and methods: 15,946 medical records from 2007 to 2015 were retrospectively reviewed to find cases of immediate (within 1 day from polypectomy) and delayed (within 15 days from polypectomy) PPB. The control group was a cohort of patients that underwent to consecutive polypectomy from January to April 2014. Following informations were collected: age, sex, assumption of antiplatelet/anticoagulant drugs 5 days before and after polypectomy, comorbidity, dimension, location and morphology of polyps, technical of removal and use of preventive measures for bleeding. Analysis was conducted "per patient".

Results: 118 cases (279 polyps) and 539 controls (966 polyps) were included in this case-control study. 50 patients experienced immediate bleeding while 72 patients had delayed bleeding (4 patients had both immediate and delayed). Mean time from polypectomy to bleeding was 3.5 days. According to univariate analysis the two groups (cases vs controls) differ for assumption of any type of antiplatelet/anticoagulant drugs (41% vs 15%, p<0.0001), LWMH somministration (23% vs 1%, p<0.0001), any comorbidity (69% vs 40%, p<0.0001), number of polyps per patient (27% vs 18%, p=0.02), dimensions > 10 mm (78% vs 33%, p<0.0001) and sessile morphology of polyps (68% vs 82%, p=0.02). Multivariate logistic regression analysis shown that PPB was associated significantly with somministration of LWMH, any comorbidity and polyps with dimensions ≥10mm. Preventive measures as clip did not reduce the risk of PPB.

Conclusions: PPB is mainly associated with with polyp ≥10 mm and comorbidity of the patients. LWMH not discontinued is an important risk factor for bleeding.

P.16 Endoscopy 2

P.16.1

FIRST NATIONAL REGISTRY ON A NEW DISPOSABLE CHOLANGIOSCOPE FOR SINGLE OPERATOR CHOLANGIOSCOPY

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Background and aim: The new single-operator cholangioscopy (SOC) system (SpyGlass Direct Visualization System, Boston Scientific Corp, Natick, Mass) has been designed to overcome previous technological limitations. The aim of this study was to describe the first reported Italian experience in the management of biliary disease using SpyGlass DS in order to assess the technical

success, clinical success, diagnostic yield, therapeutic yield, and safety of the SpyGlass system for biliary diagnostic and therapeutic procedures in tertiary care centers.

Material and methods: The present study was a retrospective analysis of data collected from all consecutive patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) with SpyGlass between April 2015 and October 2015 for biliary disease in four tertiary care centers. The components of the modular SOC system include the disposable SpyScope (Boston Scientific Corp) 10F access and delivery catheter with a 1.2-mm diameter working channel, 2 dedicated irrigation channels and 4-way tip deflection for enhanced steerability. All patients were treated under deep sedation with propofol. All the procedures were performed by expert operators.

Results: 13 SpyGlass cholangioscopy procedures were performed in 12 patients: 33.3% female, mean (\pm SD) age was 67.3 years \pm 15 (range from 26 to 82 y). The indications for SpyGlass were diagnostic (indeterminate biliary strictures) in 9 patients (4 of the common bile duct, 1 cystic duct and 3 of the intrahepatic biliary duct, 1 PSC to exclude carcinoma), therapeutic (stone disease) in the remaining 3 patients. 100% of the patients had undergone ERCP at least once with sphincterotomy. In biliary strictures overall accuracy of SpyGlass for visual and tissue diagnosis was 93% and 87%, respectively. Successful electrohydraulic lithotripsy with stone clearance was achieved in 100% of the 3 patients who failed previous conventional therapy. One patient received two cholangioscopy procedures due to technical problems with one cholangioscope. The mean (\pm SD) procedure time was 37 \pm 18 min (range 15 min to 60 min). No major complications occurred during the procedure and at follow up.

Conclusions: Our result confirmed the high diagnostic and therapeutic success rates of SpyGlass in biliary disease. The system demonstrated to be safe, easy to use and not time consuming in expert hands. Further studies are needed to evaluate the diagnostic and therapeutic yield of cholangioscopy in biliary disease.

P.16.2

SMALL BOWEL CAPSULE ENDOSCOPY IN PATIENTS WITH LYNCH SYNDROME. A CASE REPORT

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Background and aim: Hereditary nonpolyposis colorectal cancer, or Lynch syndrome (LS), is an autosomal dominant genetic disorder responsible for 2-5% of all colorectal cancers (CRC), linked to DNA mismatch repair gene defects and characterized by predominantly right-sided CRC in early age with an increased risk for extracolonic tumors. These include endometrial, biliary, urinary and small bowel cancers. Small bowel tumors are rare in the general population accounting for 1-3% of all primary gastrointestinal neoplasms. In LS the lifetime risk of developing small bowel cancer is estimated to be around 4% with a relative risk of over 100 compared with the general population. The diagnosis is often delayed because symptoms are unspecific and tests may be inconclusive.

Video capsule endoscopy (VCE) is recommended in the suspect of small bowel tumors when obscure gastrointestinal bleeding and iron-deficiency anemia are not explained otherwise (strong recommendation, moderate quality evidence).

At the present time the usefulness of VCE screening in asymptomatic LS patients is discussed.

Material and methods: We report the case of a LS 56-year-old man, undergone 15 years before right hemicolectomy for a well-differentiated adenocarcinoma of the ascending colon without lymph node metastasis, who presented unspecific abdominal pain

and iron deficiency anemia with negative fecal occult blood test and normal CEA value.

The patient underwent VCE after negative esophagogastroduodenoscopy and colonoscopy.

Results: VCE detected a metachronous jejunal tumor, which was not reached by a following push enteroscopy. Computed tomography scan revealed a jejunal wall thickening.

Surgical exploration confirmed a jejunal tumor which was resected. By microscopic examination, the tumor consisted of a poorly-differentiated adenocarcinoma with lymph node metastasis (T3N1M0).

Conclusions: Although VCE has not been included in guidelines for surveillance of families with LS, its role should be considered in selected patients with unspecific symptoms.

P.16.3

IMPROVEMENT OF APPROPRIATENESS AND REDUCTION OF WAITING LISTS CONCERNING UPPER GI ENDOSCOPY OUTPATIENTS: A SINGLE-CENTRE PROSPECTIVE STUDY

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Background and aim: Increasing the appropriateness of use of upper GI endoscopy is important to improve quality of care while at the same time containing costs. Aim of this study was to evaluate the reduction of waiting lists concerning upper GI endoscopy outpatients through a strict selection of endoscopy prescriptions, Gastropanel introduction and endoscopic activity reorganization.

Material and methods: We conducted a prospective study from July 2013 to July 2015. The upper GI endoscopy reservation was managed by our Endoscopy Unit and all the prescriptions were evaluated by an endoscopist. All the requests are evaluated within 24 hours. The endoscopist evaluated if the prescription was appropriated and decided the priority. In some cases the endoscopist could either cancel the request or chose a less invasive examination (i.e. Gastropanel) which evaluates serum Pepsinogen I (PGI) and II (PGII), gastrin 17 (G17) levels and Helicobacter pylori (Hp) antibodies.

Results: From July 2013 to July 2015 a total of 5192 upper GI endoscopy requests were evaluated. 539 (age 50 years, range 14-91) were judged inappropriate, 105 of which performed an upper GI endoscopy within 2 years (range 1-22 months). The indication of the 539 cancelled requests were: 66 cases dyspepsia, 307 cases gastroesophageal reflux disease (GERD), 34 cases absence of written indication, 113 cases wrong follow-up, 20 cases other. 282/539 patients were submitted to Gastropanel giving the results: 94 normal, 48 patients normal but in PPI therapy, 56 Hp infection and 30 Hp eradicated, 50 GERD, 4 atrophic gastritis. In the last 4 cases a upper GI endoscopy was performed immediately after Gastropanel reporting. 71/105 (67.5%) performed endoscopies were normal. No cancer was found in upper GI endoscopies judged inappropriate.

Conclusions: This strategy, based on a strict control of the prescription, is effective to reduce waiting lists without any additional public cost. The use of Gastropanel improves patient selection for upper GI endoscopy.

P.16.4**ENDOSCOPIC ULTRASOUND-GUIDED TRANSMURAL STENTING FOR GALLBLADDER DRAINAGE IN HIGH RISK PATIENTS WITH ACUTE CHOLECYSTITIS: A SYSTEMATIC REVIEW AND POOLED ANALYSIS**

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Background and aim: Endoscopic ultrasound-guided transmural stenting for gallbladder drainage is an emerging alternative for the treatment of acute cholecystitis in high risk surgical patients. A variety of stents have been described, including plastic stents, self-expandable metal stents (SEMSs), and lumen-apposing metal stents (LAMSs). LAMSs represent the only specifically designed stent for transmural gallbladder drainage. A systematic review was performed to evaluate the feasibility and efficacy of EUS-guided drainage (EUS-GBD) in acute cholecystitis using different type of stents.

Material and methods: A computer-assisted literature search up to September 2015 was performed using two electronic databases, MEDLINE and Embase. Search terms included MeSH and non-MeSH terms relating to acute cholecystitis, gallbladder drainage, endoscopic gallbladder drainage, endoscopic ultrasound gallbladder drainage, alone or in combination. Additional articles were retrieved by hand-searching from references of relevant studies. Pooled technical, clinical and adverse event rates were estimated using all included studies.

Results: Twenty-one studies met the inclusion criteria and the eligible cases were 166. The overall technical success rate, clinical success rate and frequency of adverse events were 95.8%, 93.4% and 12.0%, respectively. The technical success rate was 100% using plastic stents, 98.6% using SEMSs and 91.5% using LAMSs. The clinical success rate was 100%, 94.5% and 90.1% after the deployment of plastic stents, SEMSs and LAMSs respectively. The frequency of adverse events was 18.2% using plastic stents, 12.3% using SEMSs and 9.9% using LAMSs.

Conclusions: Among the different drainage approaches in the non-surgical management of acute cholecystitis, EUS-guided transmural stenting for gallbladder drainage appears to be feasible, safe and effective. LAMSs seem to have high potentials in terms of efficacy and safety, although further prospective studies are needed.

P.16.5**TRANSORAL OUTLET REDUCTION FOR THERAPY OF WEIGHT REGAIN AFTER GASTRIC BYPASS**

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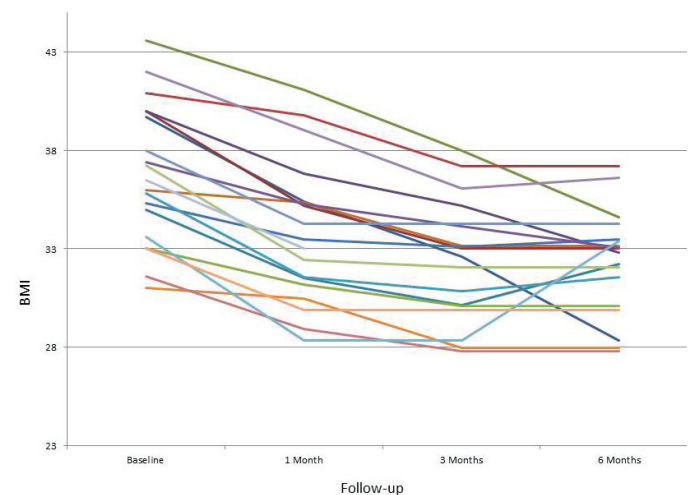
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Background and aim: Enlargement of gastrojejunal anastomosis aperture is associated with weight regain in patients with Roux-en-Y gastric bypass (RYGB). Endoscopic transoral outlet reduction (TORe) has proven safe and effective for treatment of weight regain. The objective of this study was to evaluate the results of endoscopic outlet reduction in single Italian center.

Material and methods: The series included consecutive post-RYGB patients with weight regain and enlarged gastrojejunal anastomosis aperture (>15 mm). Endoscopic reduction was performed with a full-thickness endoscopic suturing device at our endoscopy unit.

Results: Nineteen patients who had regained weight after gastric bypass (BMI > 35) underwent TORe from January to September 2015. Baseline mean BMI was 36.8 (range 33–43.6) and weight was 104.5

kg (range 85–131). The procedure was done with the Overstitch device (Apollo Endosurgery) and Olympus double channel operative endoscope. An Overtube (US Endoscopy) was placed before the procedure in all patients. Before suturing the outlet rims were cauterized with pulsed Argon Plasma (ERBE Vio 200) on 40 Watts in all patients. Mean procedure time was 35 minutes (range 15–60) and a mean number of 2.3 stitches per patient were placed (range 2–4) on the level of the gastric outlet. After suturing the patency of the new redone outlet was tested with standard gastroscope. There were three (15.7%) complications of which two were mild (one intraoperative bleeding that arrested spontaneously and fever due to small retrogastric collection treated with antibiotics), while one patient (5.2%) had gastric perforation that required urgent surgery. Mean hospital stay was 2.8 days (range 2–10). Telephonic follow-up was done at 1, 3 and 6 months. Mean BMI at 1 month follow-up was 33.8, at 3 months was 32.4 while at 6 months was 32.3. Figure 1 shows the BMI during follow-up for each patient.



Conclusions: In our experience TORe was safe and effective procedure in patients with weight regain after RYGB. Longer follow-up is needed to establish the durability of these results. Further studies are however needed to better understand the role of TORe after RYGB and the proper selection of patients.

P.16.6**ENDOSCOPIC TREATMENT WITH SELF EXPANDABLE METAL STENT OF NEOPLASTIC COLONIC STRICTURES**

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Background and aim: To evaluate the clinical efficacy of endoscopic treatment of neoplastic colonic strictures with self expandable metal stents (SEMS) positioned with palliative intent or “bridge to surgery”.

Material and methods: We placed SEMS for the treatment of neoplastic stenosis from July 2009 to April 2015 c/o the Digestive Endoscopy and Surgery Rooms of AOU Careggi in Florence.

Results: We placed 90 SEMS for the treatment of neoplastic stenosis from July 2009 to April 2015 c/o the Digestive Endoscopy and Surgery Rooms of AOU Careggi in Florence.

Patients were 85, including 42 women and 43 men with an average age of 76 years.

45 stents were placed as “bridge to surgery” and elective surgery was performed after 30 days (range 9–180 days), 45 stents were placed with palliative intent.

The seat of stents was: 33 in rectum, 29 in sigmoid, 14 in descending, 7 at the level of the left flexure, 6 in the transverse, 1 at the right colic flexure.

89 of 90 stents were not covered and one partially covered; 87 N-type and D-stent-stent (Taewoong Medical), 1 and 2 type Wallflex Ultraflex (Boston Scientific).

Technical success was achieved in 90/90 patients (100%), while the clinical success was achieved in 88/90 patients (97.8%).

Early complications (within 72 hours) were 2 dislocations of the stent. Late complications (after 72 hours) were represented by two cases of ingrowyh tumor 10 months after the procedure and one case of dislocation after about six months.

In none of the patients in which the stent has been positioned as a “bridge to surgery” it has been necessary to pack a stoma protection during surgery.

Conclusions: SEMS use is considered a therapeutic alternative to surgery in the treatment of neoplastic stenosis of the colon.

In patients with neoplastic disease in advanced stage or where surgery is contra-indicated, endoscopic therapy may be palliative.

In the case of intestinal obstruction tumors amenable to surgery, the goal of stenting is to enable the ideal timing of surgery definitive, reducing the high rate of morbidity and mortality related to surgery in emergency.

P.16.7

WIRELESS CAPSULE ENDOSCOPY FOR THE DIAGNOSIS OF OBSCURE GASTROINTESTINAL BLEEDING IN VON WILLEBRAND DISEASE: A RETROSPECTIVE CASE SERIES

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Background and aim: Von Willebrand disease (VWD) is the most common inherited bleeding disorder characterized by deficiency/dysfunction of von Willebrand factor. Recurrent gastrointestinal bleeding is a severe manifestation, mainly related to angiodysplasia. In these patients, diagnosis and management of obscure bleeding is challenging, often requiring hospitalization. A recommended diagnostic and therapeutic management has not been codified yet. In particular, the role of capsule endoscopy (CE) needs further validation.

Material and methods: Among 675 subjects affected by VWD and followed at the A.B. Bonomi Hemophilia and Thrombosis Center, we retrospectively collected data about patients affected by obscure recurrent GI bleeding referred to our Gastroenterology and Endoscopy Unit for small bowel evaluation between January 2010 and June 2015. Demographic data, VWD natural history, diagnostic tests, treatment and clinical follow-up were analyzed.

Results: Six patients (3 F; median age 66 years, range 48-81) underwent CE to investigate anaemia in recurrent GI bleeding. They were affected by type 1 VWD (2 patients), type 2A (2), type 2B (1), type 3 (1). Overall, 9 procedures were performed; seven positive findings were detected: small bowel angiodysplasia (3 patients, one with active bleeding), bright red blood in small bowel lumen (2) and in stomach (2). Anterograde double-balloon enteroscopy was performed to successfully treat the active bleeding. Argon plasma coagulation and clipping were applied. The other patients were all conservatively managed with VWF/FVIII concentrate, tranexamic acid, oral iron and blood transfusions. In 2 cases, secondary long-

term prophylaxis with VWF/FVIII concentrates was started to prevent new bleeding episodes. Surgical resection and second-line treatments such as hormonal therapy or thalidomide were not necessary in any case.

Conclusions: Obscure gastrointestinal bleeding is a challenging complication in VWD. Endoscopic procedures such as capsule endoscopy and double balloon enteroscopy seem to be a successful and well-tolerated tool to diagnose and treat small bowel bleeding. However, the effectiveness highly depends on the timing of procedure and the presence of active bleeding. A positive finding can crucially modify the management of the patient, usually requiring a multimodal therapeutic approach.

P.16.8

UTILIZATION OF OBSERVATION UNIT IN EMERGENCY DEPARTMENT FOR THE FINDING OF OBSCURE GASTROINTESTINAL BLEEDING THROUGH CAPSULE ENDOSCOPY: A PILOT STUDY

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Background and aim: Overcrowding and hospital admission is a serious and ongoing challenge in Italian emergency departments (EDs), due to the continuous constriction of beds in the hospitals.

As a consequence, brief observation units (BOU) have been introduced in Italian EDs, aimed at reducing inpatient hospital admission by allowing rapid access to diagnostic techniques and therapy. Gastrointestinal (GI) bleeding is one of the causes of admittance to EDs, and obscure gastrointestinal bleeding (OGIB) remains a major clinical challenge since it usually requires hospital admission.

The scene was revolutionized by the availability of the capsule endoscopy (CE), which is noninvasive and well tolerated by patients. ED-based short-stay units can lessen ED overcrowding by influencing outcomes such as ED wait times and hospital costs.

The aim of our study was to assess the feasibility of a new approach based on performing CE directly from BOU instead of inpatient hospital admission, thus reducing hospitalization.

Material and methods: We enrolled 19 (6M/13F; mean age 60.5 +/- 11 years) consecutive patients accessing our ED from July 2014 to July 2015, with both upper and lower gastrointestinal endoscopy with negative results and with an active gastrointestinal bleeding and/or a significant sideropenic anemia (Hb lower than 9 gr/dl).

All patients were admitted to the BOU, and underwent CE with the PillCam capsule endoscopy system (Given Imaging, Yoqneam, Israel), according to the standard protocols.

A positive CE was defined as the presence of CE findings that may account for the clinical bleeding (angiodysplasia, ulcers or erosions, tumor, Crohn's disease, and active bleeding with no identifiable source), whereas a negative CE was defined as the absence of abnormalities on CE.

Results: 84% (16 out of 19 pts) resulted positive to OGIB.

Eight showed angiodysplasias, 1 colon diverticulosis actively bleeding, 1 ileal erosion from drug abuse, 1 duodenum-ileal ulcers, 1 suspected Meckel's diverticulum, 1 erosive gastroduodenitis, 1 duodenal neoplasia, 1 Gastrointestinal Stromal Tumor and 1 active bleeding in the jejunum.

The day after the CE pts were submitted to enteroscopy for endoscopic treatment.

All patients were finally discharged, while only 2 were referred for emergency surgery.

Conclusions: Performing CE in patients with OGIB in BOU instead of hospital admission is feasible and cost effective, since the daily cost of BOU is 275 Euro compared to 1000 Euro of regular hospital admission. This approach decreases unnecessary inpatient

admission, reduces timing of procedures actuation and allows a faster and appropriate therapy.

P.16.9

DOES URGENT COLONOSCOPY FOR LOWER GASTROINTESTINAL BLEEDING NEED ORAL BOWEL PREPARATION?

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Background and aim: Acute Lower Gastrointestinal Bleeding (LGIB) represents a quarter of all bleeding events with a progressive increased annual incidence. Colonoscopy is recommended in the early evaluation of LGIB. It is suggested that bowel preparation improves endoscopic visualization, diagnostic yield and safety of the procedure. In clinical practice, it can be difficult to perform bowel preparation in emergencies, maybe delaying times for colonoscopy. **Material and methods:** From July 2014 to October 2015 we analyzed retrospectively data from patients (pts) affected by LGIB undergoing urgent colonoscopy in our Endoscopic Unit. Pts characteristics, endoscopic diagnostic/therapeutic results and clinical outcome were submitted to statistical analysis.

Results: Overall, 40 pts with LGIB (F/M ratio 1:1, mean age 70 years) were included in the analysis. As expected, 65% of pts were on antiplatelet or anticoagulation therapy. All the pts performed colonoscopy within 24 hours.

The 77,5% of colonoscopy (31/40 pts) had a early and satisfactory diagnostic yield. The diagnostic ability was superior for the left colon compared to the right colon lesions (20 vs 7 lesions). In the left colon were found 24 bleeding lesions: 6 rectal ulcers, 4 diverticula, 4 ischemic colitis, 3 post-polypectomy bleeding, 2 other colitis, 2 polyps/neoplasia, 2 radiation proctitis, 1 hemorrhoids while only 7 bleeding sources were found in the right colon (2 diverticula, 2 post-polypectomy bleeding, 3 small bowel bleeding). Where the bleeding source was not identified (9/40 pts; 22,5%), complete colonoscopy after bowel preparation showed 3 right colon angiodysplasias and 2 right diverticular bleeding self-limited.

Overall, 35,5% (11/31) of pts had active bleeding endoscopically treated (clips or clips plus epinephrine). Two pts were referred to surgical treatment (ischemic colitis), while the other pts received medical treatment.

Conclusions: In our experience, peristaltic water pump cleaning use during urgent colonoscopy without bowel preparation, is effective in the diagnosis and endoscopic treatment of acute LGIB. The diagnostic ability of this procedure seems to be superior for the left colon compared to right colon lesions. This approach enables to suggest bowel preparation and subsequent colonoscopy just to pts with suspected right colon bleeding.

P.16.10

DOUBLE BALLOON ENTEROSCOPY IN DETECTING SMALL BOWEL NEUROENDOCRINE NEOPLASMS (SB-NENS)

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Background and aim: Small bowel neuroendocrine neoplasms (SB-NENS) are usually difficult to diagnose, given their nonspecific presentation and poor accessibility of the distal small bowel. The diagnosis of small bowel tumors has been hugely improved with the advent of small bowel endoscopy allowing a direct visualization of the entire small bowel. Data describing the effectiveness of double-balloon enteroscopy (DBE) in the detection of SB-NENS are scanty,

due to the low frequency of NENS and the still limited use of DBE in clinical practice. Accordingly, present series was aimed at reporting the experience at a single referral centre for NENS.

Material and methods: All consecutive patients with a suspected SB-NEN selected for diagnostic DBE were enrolled at our Institution.

Results: Between January 2011 and September 2015, 45 patients with suspected SB-NEN or affected with NEN from unknown primary were referred to our Centre. SB-NENS were suspected on the basis of clinical presentation, elevated neuroendocrine biomarkers and the presence of histologically confirmed neuroendocrine metastases (two patients), positive video capsule endoscopy (VCE) (four patients) or positive nuclear imaging (one patient). After an extensive work-up, six patients (4 M, 2 F, median age 50 years) underwent DBE (three antegrade, two retrograde, one both; median time: 60 min; median insertion 200 cm). DBE was positive in two patients with evidence of an ileal lesion of 1 and 2 cm in diameter, respectively (histologically G1 NEN), these findings being superimposable to those of VCE. Both patients underwent uneventful surgical resection of the SB-NEN. Of the four other patients with negative DBE, two had metastatic NENS of unknown primary, one had primary jejunal NEN revealed by Gallium68-PET and then surgically removed and the last patient resulted a true negative as NEN was not confirmed at long-term follow-up. Overall, in absence of falsely positive results, DBE showed a sensitivity of 33%. No complications were observed during the procedure.

Conclusions: In line with data from literature, present series showed that DBE is a safe procedure in the diagnosis of SB-NENS. Further studies are needed to better clarify the diagnostic role of DBE in the neuroendocrine tumor setting and its relationship with other techniques, i.e. VCE and nuclear imaging.

P.16.11

SIMULTANEOUS ONE-PIECE ENDOSCOPIC SUBMUCOSAL DISSECTION FOR TWO POORLY DIFFERENTIATED EARLY GASTRIC CANCER IN ELDERLY PATIENT

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Background and aim: Incidence of early gastric cancer (EGC) is higher in Eastern than in Western countries and endoscopic submucosal dissection (ESD) is actually a feasible treatment since extended indications have been developed.

EGC presents with simultaneous multiple lesions in 5.8% to 15% cases and only few Eastern papers describe their simultaneous treatment with ESD.

Material and methods: An 81 year-old woman was referred to our unit from another hospital to treat two adjacent but separated mucosal lesions of the antrum greater curvature. According to the Paris Classification lesions were 0-IIa and 0-IIc, about 18mm and 6 mm wide respectively and histological examination of biopsy specimens showed high grade dysplasia and intramucosal adenocarcinoma in the large one and high grade dysplasia in the small one. Endoscopic ultrasound (EUS) described mucosal and only first level submucosal invasion. CT scan was negative. We performed ESD under general anesthesia using Olympus Hook-Knife (Olympus Medical System, Tokyo, Japan).

Results: As our video material shows, both adjacent lesions were simultaneously completely removed in one piece. No bleeding or other complications occurred. Every visible vessel was coagulated with hemostatic forceps (Coagrasper Olympus Medical System, Tokyo, Japan) and hemoclips were used for bleeding prophylaxis. Histological examination revealed single specimen of 4.2 x 3.8 cm with 2 lesions: a 0.6cm and a 2cm lesions. Both were poorly

differentiated adenocarcinoma (PDA) with signet-ring cells (SRC) cancer component (PDA was predominant), no lymphatic or vascular invasion was detected, depth of submucosal invasion was < 500 micron, vertical and horizontal margins were negative and there was no ulceration. Given the patient's age and histological criteria that met expanded indications for endoscopic resection (ER), after multidisciplinary discussion ESD was considered curative and scheduled a 3-month follow up.

Conclusions: EGC diagnosis is more common in Eastern (70%) than in Western (15%) countries and histologically undifferentiated-type is less common than differentiated-type. Only very recently have European guidelines shared the expanded indications for ER of the Japanese guidelines.

In conclusion, simultaneous ESD (same day- one piece-same time) for synchronous EGC was a feasible and safe option for our elderly patient. The single procedure for the two EGC reduced hospital stay, avoided patient risks and discomfort, with lower costs compared with separate procedures. To our best knowledge, in Western countries no papers have dealt with "one piece en bloc ESD " for simultaneous resection of two poorly differentiated adjacent but separated EGC in elderly patient.

P.16.12

CAP-ASSISTED MUCOSECTOMY OF COLORECTAL LESIONS: EXPERIENCE OF 59 CASES BY THE GASTROENTEROLOGY AND ENDOSCOPY UNIT – TRENTO

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Background and aim: CAP-assisted endoscopic mucosal resection (C- EMR) is a well codified procedure to treat superficial esophageal and gastric lesions (also reported in the technical file of the device). However the use of these techniques for the resection of colorectal lesions is not regulated. There are few studies on C-EMR for colorectal lesions and few centers perform this type of technique. The main limitation of the use of CAP in colonic lesions is the increased risk of entrapment of the muscle layer in the loop with secondary perforation.

The advantages are a better view of the lesion, the opportunity to remove lesions in difficult sites and to obtain deeper histological sample.

The Gastroenterology and Endoscopy Unit of Trento performs C-EMR since many years, not only for upper gastrointestinal lesions but also for colorectal lesions.

The main aim of the present study was to evaluate usefulness, effectiveness and safety of C-EMR in the treatment of colorectal lesions, compared to piecemeal resection.

Material and methods: we retrospective collected all C- EMR for colorectal lesions performed at the Gastroenterology and Endoscopy Unit of Trento, between January 2012 and September 2014.

The results were compared with a control group represented by the endoscopic piecemeal resection of colorectal lesions larger than 20 mm performed during same period.

Results: 59 lesions underwent C-EMR.

41 were lateral spreading tumours (69%) and 18 sessile polyps (31%). Complications were recorded in 4 cases (6.8%): 1 "early" bleeding, 2 "delayed" bleeding and 1 "early" bleeding + perforation. None of them underwent surgery.

Post procedure follow up was available in 47 lesions with a median of follow-up of 10 months (range 2-28). Disease recurrence was described in 9 cases (19%).

Complications and recurrence rate were compared with the control group (47 piece-meal removed lesions). No differences between the two groups were not statistically significant (complication rate: 6.8% vs 2.1%, p: 0.26; recurrence rate: 19% vs 32.5%; p: 0.07).

Conclusions: The present study shows that the efficacy and safety of C-EMR of colorectal lesions is comparable to the piecemeal resection.

Furthermore C-EMR is characterized by a better visualization of the lesions allowing treatment in difficult sites and by deeper histological sections.

P.16.13

THE INCIDENCE OF POST-ERCP PANCREATITIS IS NOT REDUCED IN PATIENTS GIVEN INTRAVENOUS KETOROLAC FOR POST-PROCEDURAL ABDOMINAL PAIN

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Background and aim: Non-steroidal antiinflammatory drugs (NSAIDs) such as indomethacin and diclofenac, administered rectally, are effective in reducing post-ERCP pancreatitis (PEP). This effect seems lost when they are injected intramuscularly or intravenously. The aim is to assess whether intravenous ketorolac given as an analgesic to patients with post-procedural abdominal pain reduces the rate of PEP.

Material and methods: We retrospectively evaluated all hospital in-patients who had undergone therapeutic ERCP in a one-year period, comparing the rates of PEP in those who developed post-ERCP abdominal pain and those who did not. Patients with pain received ketorolac as analgesic NSAID (group A), patients without pain did not (group B). Patients with post-ERCP abdominal pain who were given ketorolac were also compared with those treated with non-NSAIDs because of contraindications.

Results: A total of 587 patients underwent ERCP: 277 had post-procedural abdominal pain (47%), 310 had none. Among patients with pain, the rates of PEP were 7.8% for those given ketorolac and 8.5% for those taking non-NSAIDs (p=0.79). Comparing groups A and B, the rates of PEP were not significantly different considering both all the patients (respectively 7.8% and 4.2%, p=0.08) and those at high risk (3.8% and 6%, p=0.6). In multivariate analysis, age was the only factor significantly associated with PEP (p=0.03); ketorolac was not (p=0.16).

Conclusions: Intravenous ketorolac to patients with post-ERCP abdominal pain seemed not to reduce the rate of PEP in either the whole group or in patients at high risk for this complication, compared to patients with no post-ERCP pain and no treatment.

P.16.14

BILIARY FULLY COVERED SELF EXPANDABLE METAL STENTS: EXPERIENCE IN A SINGLE CENTER

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Background and aim: Fully covered self-expandable metal stents (FCSEMS) have been used for the management of malignant biliary strictures as well as non malignant various biliary conditions including fibrotic distal bile duct stenosis, difficult choledocolithiasis and post-sphincterotomy bleeding. We describe a series of fully covered self expandable metal stents displaced for the treatment of different diseases involving the common bile duct in a single center. Feasibility, short and long term efficacy and adverse events were evaluated.

Material and methods: We retrospectively reviewed all the patients treated in the period between January 2014 to June 2015, receiving a fully covered self expandable metal stent as first choice procedure

or as a secondary option after plastic stent disfunction. Short and long term efficacy was ascertained after one and three months on the basis of clinical and laboratory findings.

Results: 57 patients were included (M: 28, mean age: 72.3 years). 48 were affected by malignant and 7 by benign biliary stenosis, 2 were treated for difficult choledoco-lithiasis. In 16 patients, CSEMS were deployed after dysfunction of plastic stent.

Short term (1 months) efficacy was obtained in 53/55 patients; other two patients were lost to follow-up. Early (within one week) complications included: bleeding (3), cholangitis (1), distal migration (1), pancreatitis (1), retroperitoneal perforation (1). Late complications were: migration (2), clogging (2), cholecystitis (2). Clinical success after three months was obtained in 45/50 patients (3 patients lost to follow-up). Among these patients we observed: 1 stent dysfunction due to clogging after one month, 2 cholecystitis and 2 distal migrations.

Conclusions: In our experience biliary FCSEMS appeared safe and efficient especially for the treatment of biliary stenosis. We achieved a high success rate with low early and late complications, both when used as first line treatment or after plastic stent disfunction.

P.16.15

FAMILIAL ADENOMATOUS POLYPOSIS SMALL BOWEL SURVEILLANCE: COULD INDICATORS FOR VIDEO-CAPSULE ENDOSCOPY BE ASCERTAINED?

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Background and aim: Familial adenomatous polyposis (FAP) is a genetic disease characterized by multiple colonic adenomas. Small intestinal polyps (SIPs) may occur in FAP with possible malignant transformation. However, conventional endoscopy cannot explore the whole small bowel. Only videocapsule endoscopy (VCE) could be used for this purpose. Aim of the study was to evaluate, by VCE, prevalence and possible indicators of SIPs in FAP patients.

Material and methods: Twelve FAP patients underwent VCE and upper endoscopy for duodenal polyposis staged by Spigelman score. Mutational analysis was additionally performed. Fisher's and t test were used for statistical analysis.

Results: Eight patients showed SIPs at VCE (66.6%) as well as eight patients had duodenal polyposis (1 patient with SIPs did not demonstrate duodenal polyps). Patients with SIP had higher Spigelman score than those without. The presence of SIP directly correlated with the Spigelman score.

Conclusions: VCE could be proposed as SIPs surveillance in FAP patients with particular clinical/endoscopic features.

P.17 Endoscopy 3

P.17.1

COMPARISON BETWEEN DIFFERENT BOWEL PREPARATION REGIMENS FOR COLONOSCOPY: A SINGLE-CENTRE OBSERVATIONAL STUDY

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Background and aim: Adequate bowel preparation is the key of a successful colonoscopy. The aim of this study was to analyse and compare different bowel preparation regimens and clinical characteristics of patients referred for colonoscopy to our centre.

Material and methods: We conducted a retrospective study from January 2014 to September 2015. Data were collected from colonoscopies reports and included sex, age, body mass index (BMI), comorbidities, type of bowel preparation, dosage and split vs single administration. Bowel cleansing was evaluated using the 5-point Aronchick rating scale for each colonic segment, where overall quality of A or B were considered a criterion of successful bowel preparation. Deep sedation was routinely offered to patients.

The bowel preparation were: 4L PEG (Isocolan®), 4L PEG + simethicone (Selgesse®), 2L PEG + Asc (MoviPrep®), 2L PEG with citrate and simethicone plus bisacodyl (LoVOL®-esse), 2L Phospholax and 2L Citrafleet.

Results: Of the 6,720 patients evaluated 6,135 (M=3164, F=2971, mean age=60.3 ± 12.9 years, range=18-92) were included in the analysis.

Successful bowel cleansing was achieved in 5189 of 6135 pts (92.0%) without significant differences for high and low volume (p=0.548). Split-dose is significantly effective respect to single administration (p=0.0001).

In 5838 pts (95.2%) was achieved the cecal intubation. Detection rates for polyps was 32% and for neoplasm was 1.6%.

The table shows the main characteristics of patients divided according to bowel preparation.

	4L-PEG Isocolan® n.3044		4L-PEG Selgesse® n.2439		2L-PEG MoviPrep® n.376	2L-PEG LoVOL®-esse n.205	2L Phospholax® n.36	2L Citrafleet® n.35
	4L	Split	4L	Split	Split	Split	2L	2L
Number	78	2866	96	2343	376	205	36	35
Gender (%) F	53.8	44.1	60.4	49.7	59.8	60.0	63.9	74.3
Age (Mean ±SD, years)	64.7±14.4	61.0±11.1	62.1±15.6	59.8±14.4	58.3±12.7	58.4±14.7	56.8±12.8	59.3±12.8
BMI (mean)	25.6	26.3	26	25.3	24.9	25	24.8	24.6
Caecal intubation (%)	85.9	95.2	90.6	95.7	95.7	94.1	91.7	94.3
Detection rates for polyps (%)	24.4	37.8	25.0	27.1	25.8	26.3	27.8	14.3
Bowel cleansing (%)								
A	29.5	67.8	44.8	75.2	66.0	64.9	27.8	22.9
B	47.4	24.1	40.6	17.5	24.7	24.9	33.3	57.1
C	16.7	3.6	7.3	3.8	5.9	4.9	27.8	17.1
D	1.3	0.9	3.1	0.5	0.8	2.0	5.6	2.9

Conclusions: According to International Guidelines, in our cohort the split-dose, but not high or low volume, was judged more effective than one single-dose bowel preparation and was significantly associated with the indicators of quality.

P.17.2

USEFULNESS OF PROPHYLACTIC HEMOCLIPS PLACEMENT IN MINIMIZING DELAYED POST-ENDOSCOPIC MUCOSAL RESECTION BLEEDING IN GASTRIC SUPERFICIAL LESIONS: RETROSPECTIVE STUDY

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Background and aim: Bleeding events are one of the potential severe complications after endoscopic polypectomy, occurring immediately or delayed. At the present time, there are no existing data in literature about the prophylactic placement of hemoclips after gastric endoscopic mucosal resection (EMR) in minimizing delayed post-endoscopic mucosal resection bleeding (pEMRb). However, with the availability of endoscopic hemoclips their prophylactic placement is spreading. Our aim was to evaluate the usefulness of this practice after gastric EMR in reducing the rate of delayed pEMRb in a retrospective study.

Material and methods: A retrospective analysis of consecutive operative gastroscopies with a hot-snare en-bloc EMR at our Unit between 04/2008-02/2015 was performed. Single-use Olympus standard clip were applied. Hemoclips prophylactic placement was

defined as the use of hemoclips in the absence of acute bleeding, on a clean cutting base (no active bleeding, no visible vessel). Delayed pEMRB (bleeding that required endoscopic consultation) at 30 days from the EMR was reported. We compared the rate of delayed pEMRB in patients with and without hemoclippping. Good correlation in age, use of anticoagulant/anti-platelet drugs and lesions type. Median lesion dimension was higher for the group with hemoclips than the other (table 1). About statistical analysis, a Fisher's exact test was used.

Table1	Prophylactic hemoclip	No prophylactic hemoclip
EMRs	14	32
Mean age (years)	74	70
Site (%)	Body 7 (50 %) Others 7 (50%)	Antrum 17 (53%) Others 15 (47%)
Median lesion dimension (mm)	15	10
Lesion type (%) according to Paris-Kyoto classification	0-1s 9 (64) Others 5 (32)	0-1s 19 (59) Others 13 (41)

Results: Among all the EMRs, we identified 14 EMR with prophylactic hemoclippping and 32 with no hemoclips. Delayed pEMRB occurred one time in both the groups (7,1% vs 3,1%; $p=0,5$) with no differences in the bleeding extent managed endoscopically.

Conclusions: According to this retrospective single center study, the risk seems higher in the group where hemoclips were applied. Although, no significative difference in the occurrence of delayed pEMRB was found between the two groups of patients. The paucity of data and the difference in median lesion dimension allow us only to underline the need for a prospective study to assess the cost-effectiveness of this prophylactic approach.

P.17.3

COLONOSCOPY IN ELDERLY MORE THAN 80 YEARS OLD: OUR EXPERIENCE

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Background and aim: Colonoscopy (CS) is recognized as the gold standard for diagnosis of colorectal cancer (CRC) and represents the diagnostic and therapeutic procedure to more effectively detect and treat pre-neoplastic lesions. The incidence of CRC increases with age, and therefore in the elderly population, CS plays a decisive role in the detection of these cancers, although advanced age can be a deterrent for its execution. We reviewed our colonoscopy experience over the last 8- years, in patients beyond 80 years of age, by assessing the diagnostic yield, effectiveness and safety.

Material and methods: A descriptive, retrospective study including 1278 CS performed from January 2008 to September 2015 in 1123 inpatients and outpatients (508 males and 615 females) was conducted. The mean age was 86,3 years (range 80-98 years). Of these, 291 patients were subjected to abdominal CT colonography (virtual colonoscopy). Data recorded included age, indication for examination, co-morbidities, bowel preparation, colonoscopy report and therapeutic maneuvers if performed (polypectomies, EMR, and

metallic stent placement). Bowel preparation was made as our unit's standard protocol, using PEG lavage solution. CS were considered complete upon reaching the caecum, and were performed according to various conscious sedation protocols, and in the presence of severe co-morbidities with anesthesiologist care.

Results: The main indications for CS were anemia and gastrointestinal bleeding, followed by change in bowel habits, abdominal pain and weight loss. CS was performed completely in 77% (984/1278) of all procedures. Poor bowel preparation (216/294), intolerance to endoscopic procedure for excessive discomfort (46/294) and presence of insuperable colonic strictures both benign and malignant (32/294) precluded complete bowel examination in 23%. Elderly patients have been more likely than younger to have an abnormal colonoscopy finding. CS revealed a normal bowel in 427 patients (38%), in 265 patients (23,6%) a CRC was diagnosed. Diverticular diseases and various polyps were observed in 58%, colitis and vascular diseases in 8%. The risks of CS are generally associated with the bowel preparation, sedation and the procedure itself. There were no CS-related deaths, serious complications and no severe adverse events within 72 hours after the procedure.

Conclusions: CS is a practicable, effective and quite safe endoscopic procedure, with an acceptable complications rate, in patients aged 80 years or older, whereas often represents the only therapeutic option available for these patients. The most common reason for unsuccessful CS was inadequate bowel preparation. The completion rate of CS has been good, the diagnostic yield proved high, and there is a potential benefit for therapy.

P.17.4

PEG IN VERY ELDERLY PATIENTS WITH DEMENTIA: A SAFE PROCEDURE

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Background and aim: Percutaneous endoscopic gastrostomy (PEG) is usually performed for patients with different types of dysphagia that occurs more frequently in elderly people (> 65 years). Because of ethical considerations other than procedural and clinical risks in elderly as well as very elderly people (>80 years), clinicians may deal with a difficult decision choosing PEG for artificial enteral nutrition. **Material and methods:** We retrospectively analyzed 211 PEG procedures performed from January 2010 to September 2015. All procedures were carried out with deep sedation (combination of intravenous sedative/analgesic anesthesia given by the anesthetist). Seventy-three patients were older than 80 years (very elderly people). Major indications for PEG positioning were: non-Alzheimer non-Parkinson neurogenic dysphagia (37 pts), Parkinson's disease (20 pts), head and neck cancer (11 pts), Alzheimer's disease (1 pt), miscellaneous (4 pts).

Results: Pulmonary disease was the most common comorbidity observed, but did not limit the procedure. No PEG-related complications were observed, in particular no major complications, such as buried bumper syndrome, perforation, or bleeding. Only minimal subcutaneous hematoma were observed in the site of fistula of a single case, probably due to patient low platelet count.

Conclusions: The number of very elderly patients with dementia conditioning dysphagia has increased dramatically over the past few decades and it could be a medical, ethical and economic problem. Despite these implications, in our experience PEG is frequently required for artificial enteral feeding in very elderly people, due to neurogenic dysphagia. Our data show that in this category of patients PEG performed under deep sedation is a safe procedure.

P.17.5

FIBRIN SEALANT (EVICEL®): ENDOSCOPIC INTERVENTIONAL MANAGEMENT OF BLEEDING GASTROINTESTINAL LESIONS: PROSPECTIVE, SINGLE-ARM, PILOT STUDYStaiano T.^{*3}, Martinotti M.¹, Rispo A.², Buffoli F.⁴

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Background and aim: The mortality and morbidity rates for gastrointestinal bleeding lesions are higher in patients with spurting bleeding, oozing, or a non bleeding visible vessel on endoscopy. The prognosis of patients presenting with major peptic ulcer bleeding is improved by endoscopic injection therapy. A high success rate of 70 – 100% has been reported using various agents, such as ethanol, polidocanol, cyanoacrylates. Evicel® is a fibrin sealant consisting of two components, human clottable fibrinogen and human thrombin. It is indicated as supportive treatment in patients undergoing surgery when control of bleeding by standard surgical techniques is ineffective. It is a new formulation of the previously available fibrin sealant. Evicel is easy to use and don't contain synthetic or bovine aprotinin, reducing potential for hypersensitivity reactions. The aim of this study was to evaluate the clinical outcomes of patients with GI bleeding lesions treated with Evicel.

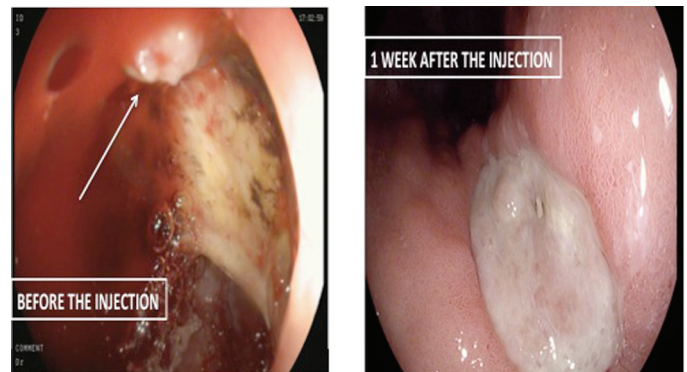
Material and methods: Between September 2014 and August 2015, a total of 10 patients with major hemorrhagic lesions (Non Variceal Upper and Lower Gastrointestinal Bleeding Lesion (NV-ULGIBL)) with active bleeding or a nonbleeding visible vessel were enrolled. The pts were well matched for age, sex, initial hemoglobin values, ulcer size and location, and bleeding stigmata.

7 of 10 patients were female (median age 82.9 y). Patients who underwent Evicel injection the fibrin sealant was injected submucosally at the bleeding site. We opted for the sequential single lumen injection technique to facilitate injection and diffusion of the diluted fibrin into the submucosa followed by the thrombin activator to maximize hemostasis within the target area and avoid early superficial clot formation. Patients, lesions characteristics and outcomes are summarized in Table 1 (Fig 1).

Results: Initial hemostasis was achieved in all cases (100%). Rebleeding occurs in one case (duodenal ulcer with active arterial bleeding) and was treated with selective transarterial embolization. No early or late rebleeding occurred during the follow-up. No complications or instrument lesions related to Evicel injection were recorded.

Conclusions: In our series, fibrin sealant injection was found to be a potentially safe and effective endoscopic haemostatic treatment modalities in controlling bleeding from NV – UL GIBL with major hemorrhagic stigmata. Due to the the small number of patients and the absence of randomisation, in our study, no definitive conclusions

could be drawn concerning the use of the Evicel in the treatment of severe NV ULGIBL bleeding.



P.17.6

QUALITY OF LIFE AFTER GASTRIC BANDING AND GASTRIC BY-PASS FOR MORBID OBESITY: A PROSPECTIVE COMPARISONMarchesi F.¹, Forlini C.^{*1}, De Sario G.¹, Tartamella F.¹, De Lorenzis G.³, Generali I.⁴, Ricco' M.², Dall'Aglio E.⁵, De Panfilis C.⁴

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Background and aim: Among bariatric surgery evaluation criteria, improvement in quality of life (QoL) surely represents the most important. However, the lack of reliable evaluation models has significantly limited the research in this field. The aim of this study is to prospectively compare QoL after Roux-en-Y gastric bypass (RYGB) and laparoscopic adjustable gastric banding (LAGB).

Material and methods: 35 patients submitted to RYGB at "Parma Hospital" and 35 patients submitted to LAGB at the "Clinica Città di Parma" were enrolled in the study. Patients were prospectively submitted to one preoperative and 4 postoperative (1, 3, 6 and 12 months) clinical evaluations including two psychodiagnostic tests: the Short Form 36 (SF-36) testing the quality of life and the Bariatric Surgery Satisfaction Questionnaire (BSSQ) assessing the satisfaction for the intervention. At the same times, comorbidity (i.e glucidic tolerance, degenerative joint disease etc.) and biometric changes (i.e weight, height and BMI), have been evaluated. The two groups have been compared relatively to change in BMI and comorbidities and the outcome of the two questionnaires.

Results: Both interventions produced a significant amelioration of biometric data, significantly higher for RYGB (p=0.05). While at early controls no significant difference in SF-36 was detected among the

Table 1 (abstract P.17.5)
Characteristics of patients and outcome

Patient (case)	Sex	Age	Site of bleeding	Hemorrhagic Stigmata	Successful Hemostasis	Additional Treatments	Rebleeding	Outcome
1	F	89	J-jejunal anastomosis	Ia	Yes	No	No	Favorable
2	F	87	Duodenal ulcer	Ib	Yes	No	No	Favorable
3	F	72	Duodenal ulcer	Ib	Yes	No	No	Favorable
4	M	87	Gastric ulcer (fundus)	Iia	Yes	No	No	Favorable
5	F	78	Duodenal ulcer	Ia	Yes	Yes: clip	Yes: Tae	Favorable
6	F	85	Rectal ulcer	Spurting vessel	Yes	No	No	Favorable
7	F	82	Gastric ulcer (antrum)	Iia	Yes	No	No	Favorable
8	M	37	Gastric ulcer (body)	Ia	Yes	No	No	Favorable
9	M	68	Rectal cancer	Oozing bleeding cancer floor area	Yes	No	No	Favorable
10	F	66	Colo-anal anastomosis	Spurting vessel	Yes	No	No	Favorable

groups; at 12-month control QoL resulted significantly better for RYGB patients, particularly for SF-36 domains: Role Limitation PH ($p=0.045$), Energy Fatigue ($p=0.017$), General Health ($p=0.017$), Pain ($p=0.014$). Satisfaction for surgery was higher for LAGB at early controls (6 month), but not statistically significant ($p=0.355$) and significantly higher for RYGB at 12 month ($p<0.001$). Comorbidities improves both procedures, better in RYGB ($p=0.002$) especially for degenerative joint disease ($p < 0.0001$), similar in LAGB ($p = 0.460$). Food dissatisfaction was significantly higher for LAGB, at early controls (6 month, $p<0.0001$) and late controls (12 month, $p<0.0001$). Satisfaction for surgery was dependent to food dissatisfaction ($p<0.001$).

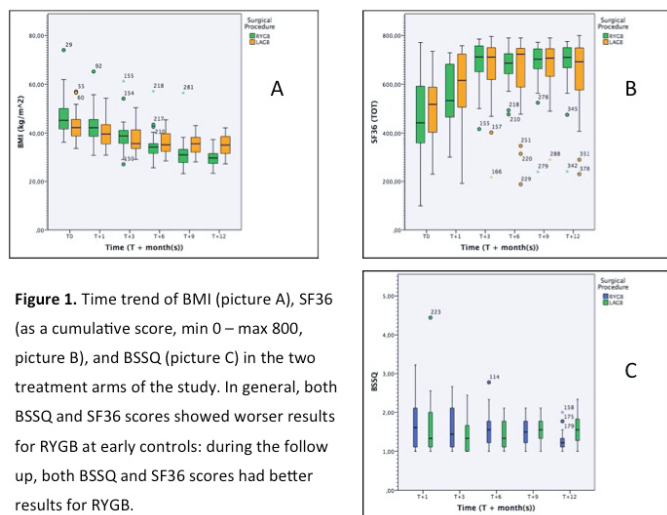


Figure 1. Time trend of BMI (picture A), SF36 (as a cumulative score, min 0 – max 800, picture B), and BSSQ (picture C) in the two treatment arms of the study. In general, both BSSQ and SF36 scores showed worse results for RYGB at early controls: during the follow up, both BSSQ and SF36 scores had better results for RYGB.

Conclusions: RYGB, compared to LAGB, produces, along with a higher weight loss and comorbidity resolution, a higher QoL, more evident starting from 6 month postoperative and more significant at 12 month. The change of QoL, is dependent on type of intervention (RYGB), independent from BMI preoperative and from changes of comorbidities during the follow up. Satisfaction intervention, appears greater in patients undergoing RYGB, directly proportional to reduction of BMI, negatively to SF-36 and independent from resolution of comorbidities. An additional parameter for assessing the effectiveness of the intervention of RYGB, is the best food dissatisfaction compared to LAGB.

P.17.7

DIGESTIVE BLEEDING IN PEDIATRIC AGE: A SINGLE CENTER EXPERIENCE

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Background and aim: Digestive bleedings are important endoscopic urgencies in paediatric age, with severe morbidity and mortality if not adequately treated.

They can be divided in high and low, above or under Treitz ligament. The first ones represents 20% of all gastrointestinal (GI) bleedings in children, can be variceal or non variceal. In this context, diagnostic and therapeutic endoscopy is increasingly used.

Aim of this study is to assess clinic, endoscopic presentation, therapy and complications in children, submitted to endoscopy for acute GI bleeding.

Material and methods: In the period 2009-2015, 123 pediatric patients with acute or acute-recurrent bleeding have been recruited in our Unit.

After clinic evaluation, patients were stabilized if necessary and submitted to endoscopy. Active bleedings were treated endoscopically, otherwise medical therapy was started or surgical approach was required.

In case of negative upper and lower endoscopy, videocapsule was applied; histology and clinical evaluation for follow up was scheduled.

Results: Sixty-three patients were males, median age 4,7 years (range 2 days-18years). Clinical presentation was: 55 (45%) hematemesis, 22 (18%) melena, 3(2%) rectal bleeding.

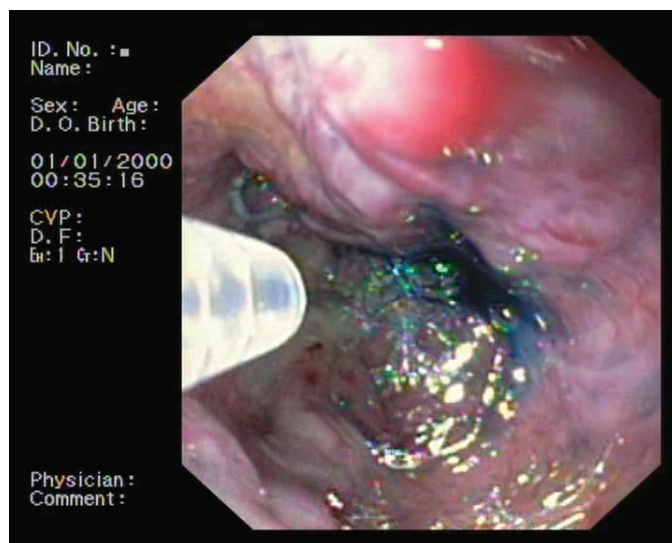
One hundred eleven patients had macroscopic lesions at endoscopy; 78 had sign of recent/active bleeding, of which 1 above superior oesophageal sphincter, 47 in the upper GI tract (5 variceal, 42 non variceal), 28 in the lower tract, 2 in both sites.

Endoscopic therapy was necessary in 11 patients (14,1%): 7 had an upper bleeding, 5 lower. Among variceal bleedings, 2 were band ligated, 3 were sclerotized with atosisclerol; non variceal bleedings were treated 1 with adrenaline injection, 1 with adrenaline injection and clip application.

Lower bleedings were treated endoscopically with: 1 clip application, 1 adrenaline injection, 3 polypectomy.

Percentages of relapse of bleeding were: 18% for low, 2% for upper non variceal, 100% for upper variceal, due to the underlying cause.

Considering all the patients, 90 (73,2%) underwent medical therapy, 2 (1,6%) needed surgery.



Conclusions: Diagnostic and therapeutic endoscopy demonstrated to be the gold standard for the management of GI haemorrhages, with good clinical outcomes if used by expert paediatric endoscopists experienced in urgencies in Tertiary Care Centers, reducing life threatening complications.

P.17.8

ENDOSCOPIC SUBMUCOSAL DISSECTION LEARNING CURVE: EXPERIENCE OF A LARGE VOLUME COLONOSCOPY CRC ITALIAN SCREENING CENTER

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Background and aim: Endoscopic submucosal dissection (ESD) is an advanced endoscopic technique that allows for curative resection of superficial neoplasms in GI tract. The vast majority of experience and guidelines for ESD resection comes from Japan,

where this technique was developed more than 10 years ago. In East countries the training curve is done on gastric GI lesions with expert supervision before starting on esophageal and colon lesions. In West countries EGC is a rare disease and expert guidance is not commonly available, so the learning curve of this technique has to be developed in a different way. **Aims:** To demonstrate that the ESD learning curve performed on rectal lesions is a good way to practice on these difficult procedures in European countries.

Material and methods: We retrospectively included in the study all the ESD performed in our Endoscopy Unit in Padua from February 2012 to April 2015 on 10552 colonoscopies. None neoplastic lesions come from other endoscopy units. We considered the learning curve of a single dedicated endoscopist that before starting on humans performed 10 ESD on in vivo animal models under expert guidance. All the dissections were performed using Hybridknife needle and ERBEJET2(ERBE®). Complications after procedure were managed with hemoclips, OTSc clips and hemostatic forceps. ESD was performed if the neoplastic lesion was considered susceptible to ESD regardless to the size. T test for unpaired data and Pearson chi-test were used for statistical analysis.

Results: 48 ESD were performed, 27M(56%) and 21F(44%), mean age 63yr. 31 rectum (64%), 12 sigmoid tract (26%), 1 transverse colon (2%), 4 ascending colon (8%). The neoplastic lesions were: 35 laterally spreading tumors (73%), 5 polypoid lesions 0-Is (11%), 4 recurrent tumor on scar (8%), 4 polypoid lesion 0-Isp (8%). Mean polyp area was 13,74 cm² (range 1-70). Mean intervention time 99 min (range 20-240). En-bloc dissection was successful in 33/48 (68%) and R0 was reached in 24/33 (72%). Polyps histological features were: 10 LGD (20%), 27 HGD (57%), 6 pT1 (17%), 3 pT2 (6%). Procedural complications occurred in 13/48 (27%): perforation in 9/48(18%), delayed bleeding 2/48(4%), rectal stenosis 2/48(4%). No deaths or surgical interventions followed the procedural complications. From the 12th procedure onwards the en-bloc performance became acceptable 22/27(81%) vs 3/12(25%) (p<0,001). From the 30th procedure onwards the en-bloc performance became good 17/18 (94%, p<0,001) and the mean execution time was significantly lower 55 vs 122 min (p<0.0001) with no significant difference in the mean area of the lesions 16,6 vs 18,2 cm² (p=ns).

Conclusions: In our experience to reach an acceptable confidence with ESD procedure starting the training from in vivo animal model (at least 10 procedures) and then to colo-rectal neoplasms (no size limit) no less than 12 procedures had to be performed, but we still probably haven't yet reached the learning curve plateau also after 40 procedures.

P.17.9

VIDEOCAPSULAR ENDOSCOPY IN OCCULT OBSCURE GASTROINTESTINAL BLEEDING: REPORT OF FIVE YEARS EXPERIENCE OF A REFERRAL TERTIARY CENTRE

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Background and aim: Gastrointestinal bleeding is still a frequent challenge in daily practice and one of the most frequent issue requiring specialist evaluation. It is defined occult when the bleeding is not visible, and obscure when both oesophagogastrroduodenoscopy (OGDS) and colonoscopy (CS) are negative for lesions or potential source of bleeding. Videocapsule endoscopy (VCE) is the first choice in the evaluation of patients with obscure occult gastrointestinal bleeding (OOIGB). The aims were to report a five years of experience in a tertiary referral centre for VCE in case of OOIGB and to identify whether factors exist, able to predict presence of lesions at VCE.

Material and methods: Consecutive patients with OOIGB from 1st of January 2010 to 31st December 2014 were included. A systematic

register for VCE was created in 2010 including demographic and clinical data of patients, indication to VCE and endoscopic findings.

Results: Out of 1159, 412 VCE were performed for OOIGB. Particularly, there were 209 male patients with a median age of 67.04+/-15.48 yrs, and 203 female pts with a median age of 63.78+/-15.48yrs. 176 (43%) pts were taking NSAIDs, anticoagulant or antiplatelet agents. Basal hemoglobine (Hb) was 8.62+/-1.82 g/dL. 10 examinations (2,4%) were incomplete, 146 (35,2%) were negative for lesions, 256 were positive, of whom 43 (10,4%) with active bleeding. Not bleeding lesions detected by VCE were: 107(25,9%) angiodysplasia, 59(14,3%) ulcers, 18(4,3%) polyps, 13(3,2%) ulcers and angiodysplasia, 9(2,2%) petechiae, 4(0,97%) cancer and 3(0,7%) signs of portal hypertension. In case of bleeding active source was identified in 24 cases (55,8%), mostly angiodysplasia (37,2%) and ulcers (13,9%). Among these latter pts 16(39%) were taking NSAIDs or anticoagulant/antiplatelets agents. At univariate analysis, there was no difference between pts with a positive and negative VCE for gender, age, mean basal value of Hb, NSAIDs and anticoagulant/antiplatelets agents.

Conclusions: VCE is useful but not exhaustive method for identification of bleeding or lesions in OOIGB, identifying lesions in 2/3 of performances: in 10% of cases it is able to identify lesions previously missed by OGDS and CS. However, we failed to predict the results of VCE based on clinical features of the patients at baseline.

P.18 Endoscopy 4

P.18.1

SMALL BOWEL TUMORS IN PATIENTS UNDERGOING CAPSULE ENDOSCOPY: A SINGLE CENTER EXPERIENCE

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Background and aim: Small bowel tumors (SBT) are a rare disease but their incidence is increasing. Until recently, the diagnosis of SBT is difficult and often delayed. Video capsule endoscopy (CE) seems to be the ideal tool for diagnosis of SBT; however, the data from clinical studies are different in terms of diagnostic yield, clinical and pathological features. The aim of this study is to report a single center experience regarding small bowel tumors in patients undergoing capsule endoscopy in order to analyze the clinical items, endoscopic findings and clinical management of these patients.

Material and methods: We retrospectively analysed the charts of 606 consecutive patients who underwent CE (Pillcam Given M2A video capsule system; Given Imaging Ltd, Yoqneam, Israel) between October 2008 and November 2014 in order to identify those with CE findings consistent with SBT and subsequent histological confirmation. Capsule ingestion was performed in the morning after an overnight fast. The day before the exam bowel preparation with 2L of polyethylene glycol solution was administered. All the patients gave their written informed consent.

Results: Of 606 patients undergoing CE, 17 (2.8%) had primary SBT; 13 (76.5%) were males, with a mean age of 69.7 years. Among these patients, indications for CE were obscure gastrointestinal bleeding (OGIB) in 14 (82.3%, overt type and occult type in same proportion); follow up of Peutz Jeghers syndrome in 1; radiological suspect in 1 and Octreoscan suspect in 1. The main SBT type found was adenocarcinoma (7 cases, 41.2%); followed by carcinoid (29.4%) and gastrointestinal stromal tumor (GIST) in 29.4%. No secondary SBT were found. Capsule retention occurred in a single case (5.9%), without onset of symptoms; in this case the capsule was retrieved

by double balloon enteroscopy (DBE). After CE, 7 patients (41.2%) underwent other diagnostic procedure on small bowel (DBE in all the cases). 16 patients underwent surgical treatment (1 patient refused it).

Conclusions: According to previous findings, our data suggest that CE identify SBT in a small proportion of patients undergoing this procedure. However, in our series the mean age of patients with SBT is higher than expected and the main histological type of tumor is adenocarcinoma, in contrast with previous experiences.

P.18.2
UPPER AND LOWER GASTROINTESTINAL LESIONS OVERLOOKED AT CONVENTIONAL ENDOSCOPY AND FURTHER DIAGNOSED WITH SMALL BOWEL CAPSULE ENDOSCOPY: THE CRUCIAL ROLE OF ENDOSCOPIC EXPERIENCE IN PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING

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Background and aim: The role of small bowel capsule endoscopy (CE) in the investigation of obscure gastrointestinal bleeding (OGIB) is well established, with a mean diagnostic yield of 60%. However, in up to 20% of patients the cause of OGIB is located within the reach of upper and lower endoscopy. No data are available regarding the impact of endoscopic experience on the rate of lesions missed by previous esophagogastroduodenoscopy (EGDS) or ileocolonoscopy (ICS) and further found with CE. The aim of this series is to clarify if the experience of the endoscopy units could influence the rate of overlooked lesions.

Material and methods: We retrospectively reviewed the charts of 584 patients who underwent CE at Endoscopy Unit between October 2008 and March 2015 for OGIB. The CE-derived data are recorded and analyzed in terms of non-small-bowel CE findings (gastric, duodenal and colonic lesions) overlooked at previous upper and lower endoscopy. The type of endoscopic units who performed the conventional endoscopy (tertiary referral centres or primary level centres) and the respective lesions miss rate was recorded. The Given M2A video capsule system (Pillcam; Given Imaging Ltd, Yoqneam, Israel) was used.

Results: 547 patients were enrolled for the final investigation (41 cases were excluded from further analysis because of the capsule did not reach the colon). In 35 patients (6.4%) one or more lesions previously missed by conventional endoscopy were diagnosed at CE. 20 of these 35 cases were males. The mean age was 72.8 years (range 51-89). 77.1% of lesions were overlooked at primary level endoscopy units; 22.9% at tertiary level units (p<0.01). The overlooked lesions are reported in the table according to the type of endoscopic centre. The most frequently missed lesions were located in stomach and duodenum (66.6%); primary centres missed lesions mostly during EGDS (71.4%); tertiary centres miss lesions during EGDS and ICS equally. Both types of centres can miss neoplasias (66.6% at primary centres): tertiary centre overlooked a gastric GIST (gastrointestinal stromal tumor); primary centres overlooked a non invasive intraepithelial gastric haemorrhagic neoplasia and an ascending colon adenocarcinoma.

	Gastric angiodysplasia	Small intestinal angiodysplasia	OGIB	Gastric neoplasia	Esophageal haemorrhagic neoplasia	Gastro ulcer	Gastric Dieklysis lesion	Duodenal angiodysplasia	Duodenal Dieklysis lesion	Duodenal ulcer	Esophageal haemorrhagic neoplasia	Colon Angiodysplasia	Colon polyp	Colon neoplasia
Primary Endoscopy	1	2	2	1	1	1	1	2	2	1	1	6	1	1
Tertiary Endoscopy	1	-	-	1	1	-	-	1	-	-	-	4	-	-

Conclusions: Our results suggest that endoscopic experience, in terms of number of referral patients, can significantly reduce the miss rate of lesions located in upper or lower gastrointestinal tract, avoiding unhelpful CE.

P.18.3
EARLY WAKE UP, ONE DAY LOW FIBER DIET: SPLIT BOWEL EVEN FOR PATIENTS UNDERGOING COLONOSCOPY EARLY IN THE MORNING. A REAL LIFE EXPERIENCE

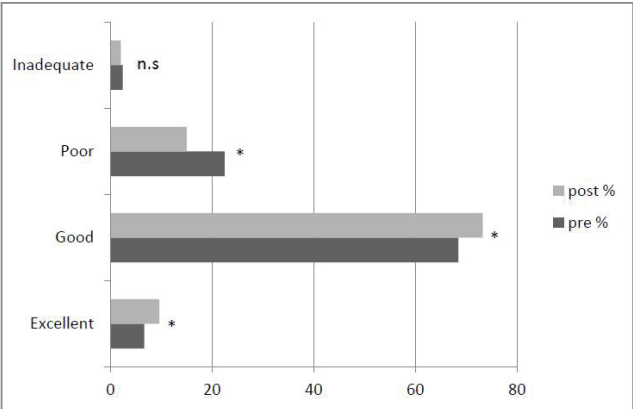
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Background and aim: Bowel preparation is crucial for colonoscopy outcome. Split preparation is the gold standard but its application among subjects undergoing colonoscopy during the first part of morning endoscopy sessions is still object of discussion for reasons of compliance.

Since 1st January 2015 we have extended split prep with just one day of low fiber diet also to subjects undergoing colonoscopy before 11.00 AM despite the need for an early wake up the day of colonoscopy. Previous version included low fiber diet for 3 days and 4 l prep the day before colonoscopy without the need for night-time bowel cleaning. Aim of this study was to compare colonoscopy per outcome before and after data sheet update.

Material and methods: The 9 months before the new regimen introduction (Pre) and the 9 months after new regimen introduction (Post) were compared. Inpatients were excluded. Data of bowel preparation were prospectively collected and colonoscopies were performed by the same team of five gastroenterologists. A modified Aronchick scale including 4 grades was used to assess bowel preparation. Chi square test was used when appropriated. Significance was set at p<0.05.

Results: Pre period included 1608 colonoscopies, and post 2134. After extension of the split regimen to all colonoscopies, the rate of excellent preparations increased by/to 45% (206/2134; 9.65% vs 107/1608 6.65% p<0.005); the rate of good preparations increased by/to 6% (1563/2134; 73% vs 1101/1608 68.4%; p<0.05); the rate of poor preparation decreased of by/to 32% (321/2134; 15% vs 361/1608 22%; p<0.05) but the difference among rates of inadequate preparation wasn't significant (44/2134; 2.0% vs 39/1608 2.4% n.s.). The rate of repeat colonoscopies due to inadequate preparation was significantly lower (400/1608; 24.8% vs 365/2134 17.1% p<0.001). Data suggest that compliance was good even if early wake up was necessary. The rate of subjects with completely inadequate preparations was the same maybe because of general non acceptance of preparation procedure.



*p<0.05

Conclusions: New regimen including split regimen for all subjects undergoing colonoscopy despite scheduled time of examination was a successful strategy in terms of quality of bowel preparation. Further studies are necessary to identify which subgroup of subjects showed a better improvement.

P.18.4

CLINICAL OUTCOMES OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN ELDERLY PATIENTS WITH DEMENTIA

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Background and aim: There is no clinical evidence supporting the use of percutaneous endoscopic gastrostomy (PEG) in elderly patients (pts) with dementia. Many studies have shown that feeding tubes are rarely effective in improving nutrition, maintaining skin integrity by increased protein intake, extending life or preventing aspiration pneumonia. Despite this, PEG continues to be performed extensively on these pts. The aim of this study was to evaluate the clinical outcomes after placement of the PEG in elderly pts with dementia.

Material and methods: We evaluated retrospectively 58 pts with dementia and more than 75 years old that underwent the placement of a PEG during the period from 01/01/2008 to 31/12/2013. Mean age was 85,5 years (range 75–96), 19 were male. Mean follow up was 4,5 years (range 2–7). 30 pts had vascular, 17 Alzheimer, 2 fronto-temporal, 1 Lewy's bodies and 8 mixed form dementia. All the pts with advanced psycho-organic decay with low level of activities of daily living (measured through the ADL scale) had abnormalities of swallowing and episodes of inhalation. After PEG placement, 29 pts lived at home and 29 in nursing homes.

Results: We divided pts into 2 groups by age (more or less than 85 years old) and by serum albumin concentration (more or less than 3 gr/dl). We evaluated survival, complication rate, serum albumin concentration, episodes of aspiration pneumonia (AP) at T0 (PEG placement), T1 (6 months later) and T2 (1 year later) in 49 pts. 9 pts did not follow up. At the time of evaluations, 10 pts were alive, 23 pts (59%) had died within a year (16,33% within a month) and 16 (41%) after a year. The mean survival rate was 600,7 days. There was no difference in survival rate between pts with serum albumin concentration more or less than 3 gr/dl at the moment of PEG placement. The incidence of AP was 51% (25/49) before PEG placement, 16% (8/49) at T1 (p-value = 0,00048, statistically significant) and 45% at T2 (14/31). Only 26% of pts died from complications related to AP. The mean values of albumin levels were 2,9 g/dl at T0, 3,2 at T1, 3,0 at T2 and there were no significant differences.

Complication rate at T1 was 45,5% (25/55) and at T2 87,5% (28/32): the most frequent complication was AP; there was no difference between pts living at home or in nursing homes.

Conclusions: In our survey, PEG placement does not improve nutritional status in elderly pts with dementia, but allows the maintenance of the main biochemical parameters. In the short term, there is a reduction of aspiration pneumonia, but this trend is lost after six months. There is no difference in the complication rate between pts living at home or in nursing homes.

P.18.5

CLINICAL MANAGEMENT AND LONG TERM FOLLOW UP OF PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING AND UNCERTAIN SUBMUCOSAL MASSES AT SMALL BOWEL CAPSULE ENDOSCOPY

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Background and aim: The role of small bowel capsule endoscopy (CE) in the diagnosis of small bowel tumours (SBT) is well established. More than 50% of SBT (neuroendocrine and mesenchymal tumours, lymphomas) arise from small bowel extramucosal layers and their endoscopic typical appearance is consistent with a bulge protruding into the lumen, often indistinguishable from innocent bulges due to prominent normal folds, intestinal loops or compressions. The major concern for capsule endoscopy is to discriminate between benign and malignant bulges. The aim of this series is to report the clinical management and the long term follow up of patients with capsule endoscopy finding of uncertain submucosal mass.

Material and methods: We retrospectively reviewed the charts of 584 patients who underwent CE at Endoscopy Unit between October 2008 and March 2015 for obscure gastrointestinal bleeding (OGIB). Only patients in whom an uncertain bulge was described at CE were enrolled for further analysis. Their clinical management was reported in terms of type and number of subsequent endoscopic or radiological procedure performed and new diagnoses obtained with these procedures. All the patients are still following a clinical follow up. The Given M2A video capsule system (Pillcam; Given Imaging Ltd, Yoqneam, Israel) was used. The day before the exam bowel preparation with 2L of polyethylene glycol solution was administered. Capsule ingestion was performed in the morning after an overnight fast.

Results: A submucosal uncertain mass was reported in 20 of 584 patients (3.4%) referred for OGIB. The mean age was 67.1 years (range 30–93); 14 were males. The mean follow up was 26.4 months (range 1–72 months). Two patients were excluded from further analysis because they are still waiting for new diagnostic procedure. In the remaining 18 patients a total number of 25 procedures were performed: 15 CT enterography (CTE); 7 device-assisted enteroscopy (DAE), two second-look CE and 1 MR enterography (MRE). 11 patients had radiological procedure only; 3 patients had DAE only, 2 cases had both endoscopic and radiological procedures, 2 patients had radiology and CE. In 5 patients (27.8%) the presence of a submucosal mass was confirmed by these further investigations: 2 patients had gastrointestinal stromal tumours; 2 had neuroendocrine tumours and 1 patient had a jejunal lipoma; in another patient (5.5%) CTE was consistent with suspected lymphoma but the histological confirmation was not reached. In a patient with recurrent OGIB a duodenal Dieulafoy's lesion was found at further upper endoscopy. In all the 11 remaining patients the follow up is free from recurrent bleeding or cancer-related symptoms.

Conclusions: Our results suggest that the CE finding of uncertain submucosal mass should lead to further radiological or endoscopic investigation because in almost a third of the patients the suspected submucosal mass is confirmed and is related to a neoplastic lesion.

P.18.6

ERCP OUTCOMES IN PRESENCE OF A PERIAMPULLARY DIVERTICULUM

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Background and aim: The presence of a periampullary diverticulum (PAD) ranges from 9% to 32% of patients who undergo an ERCP;

this anatomical setting can hamper the cannulation of the major papilla, although a higher incidence of complications has not been demonstrated. To overcome this issue different tricks have been proposed, for example the use of a biopsy forceps to change the position of the papilla in a more favorable position. We reviewed the outcomes of ERCP in patients with a PAD.

Material and methods: A single center retrospective analysis from January 2014 to August 2015. According to its position, the major papilla was classified in: PED (papilla on the edge of the diverticulum), PID (papilla in the diverticulum), or NVP (papilla in the diverticulum but not directly visible). If the standard attempt of cannulation with the sphincterotome and the guidewire failed, a pediatric biopsy forceps was passed in the working channel of the duodenoscope, parallel to the sphincterotome. Using two devices at the same time, the mucosa inside the diverticulum was grasped, shifted or pulled with the forceps in order to get an easier cannulation with the sphincterotome. We calculated the cannulation rate and number of complications when the standard technique and the forceps were used.

Results: 397 ERCPs were reviewed. In 42 cases (11%) a PAD was identified: 31 patients (74%) had PED, 10 patients (24%) had PID, 1 patient (2%) had NVP. The standard technique was successful in 35 cases (83%), while it failed in 7 (17%); the successive use of the biopsy forceps get the cannulation in 5 out of 7 patients (2 with PED, 3 with PID); in 2 cases of PED both methods were unsuccessful. After the standard cannulation a mild post-sphincterotomy bleeding was seen in 11 out of 35 cases (31%), 2 of which required epinephrine injection; on the contrary no complications occurred after the manipulation of the duodenal diverticulum with the forceps.

Conclusions: The evidence of a PAD during an ERCP is not rare and this can prolong or hinder the cannulation of the papilla. In this study, when the standard technique failed, the use of a biopsy forceps to change the position of the papilla increased the cannulation rate from 83% to 95% without additional complications.

P.18.7

ENDOSCOPIC PAPILLARY LARGE BALLOON DILATION FOR THE REMOVAL OF LARGE STONES IN ELDERLY PATIENTS (80 YEARS OLD OR OVER)

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Background and aim: Endoscopic papillary large balloon dilation [EPLBD] is considered a possible alternative to endoscopic sphincterotomy [ES] for the treatment of large bile duct stones (>10mm). This technique can be used in alternative to ES or following a limited sphincterotomy [EPLBD + ES] to perform a dilation assisted stone extraction [DASE]. A recent meta-analysis has shown that ES + EPLBD technique is a safe technique, with a lower rate of adverse events than traditional ES. However, little information is available in elderly patients because of the improved risks of complications, mainly bleeding or perforation. Particularly, in literature, only one study investigated the feasibility of EPLBD for large common bile duct [CBD] stone extraction in elderly patients. We aimed to evaluate the efficacy and safety of DASE for CBD stone extraction in elderly patients of 80 years of age or older.

Material and methods: A total of 22 DASE (EPLBD + ES) procedures effectuated on elderly patients with evidence of large CBD stones who underwent ERCPs from January 2014 to September 2015 were analyzed.

Results: Median age of patients was 84 (81-93) years, 7 males and 15 females. Thirteen patients had a concomitant duodenal diverticula. Mean size of stones was 14.07±4.12mm. Cannulation

rate and complete stone extraction rate were 95% (21/22). Wirsung was cannulated in five procedures and a pancreatic stent (Advanix Boston Scientific) was placed in two cases. ML was never performed and use of Dormia was avoided in 31% of cases. Spontaneous stones expulsion occurred in 7 cases. One patient presented a mild bleeding. No severe or fatal outcomes were observed. No differences were observed in procedure results regarding papilla location with respect to dilation time (30" or 60").



Conclusions: This is one of the first studies evaluating efficacy and safety of DASE for CBD large stones extraction in elderly patients. Despite the small number of patients, this technique seems to be safe and effective in patients of 80 years of age or over.

P.18.8

FAMILIAL ADENOMATOUS POLYPOSIS AND EXTRAINTestinal MANIFESTATIONS WITH MALIGNANT POTENTIAL: DIAGNOSTIC AND THERAPEUTIC APPROACH

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Background and aim: Familial Adenomatous Polyposis (FAP) is characterized by numerous polyps with high malignant potential in the intestinal tract and high risk of extraintestinal malignancies. Clinical variants are classic, attenuated (AFAP), MUTYH associated (MAP) and Gardner syndrome.

Typical extraintestinal manifestations are: Congenital Hypertrophy of the Retinal Pigment Epithelium, papillary thyroid carcinoma, osteomas, surrenal glands adenomas, hepatoblastoma, soft tissues tumors, nasal polyposis.

This study underlines the importance of a multidisciplinary approach to FAP to allow early detection of malignancies.

Material and methods: Sixty-three patients were recruited at Gastroenterology and Endoscopy Unit of University Hospital of Parma in the period 2004-2015.

Every patient was diagnosed and/or followed up with laboratory tests (full blood count, liver-, thyroid- and kidney function, tumor markers), genetic test, abdominal, thyroid, pelvis, testicular ultrasonography, dermatologic, eye and otolaryngologic exam, panoramic radiography.

Besides the endoscopic follow up, the protocol for extraintestinal manifestations varied based on clinical and family history.

Ultrasonography of thyroid, abdomen, pelvis, testes and dermatologic exam were repeated annually.

Results: The cohort included 63 patients (32M, 8–80 years, median age 32.8 years).

Fifty-nine had classic FAP, 1 Gardner Syndrome, 1 AFAP, 2 MAP.

The follow up protocol allowed to detect malignant lesions: among classic FAPs, 1 manifested hepatoblastoma (1.7%), 3 surrenal adenomas (5%), 3 osteomas (5%) and 4 disodontiasis (6.7%), 2 nasal polyposis (3.4%), 7 retinal pigmented lesions (11.8%), 3 desmoids (5%), 3 papillary thyroid carcinomas (5%), 1 testicular carcinoma (1.7%), 1 ovarian adenocarcinoma (1.7%).

The patient affected by Gardner Syndrome manifested 1 retroperitoneal neurofibroma, 1 surrenal adenoma and disodontiasis; among MAP and AFAP patients, none manifested malignancies.

All the lesions were detected at early stage and followed up or treated with good prognosis, complete resolution and without relapse.

Conclusions: FAP is a complex syndrome with multiorgan involvement. The diagnostic and follow up protocol detected typical and non typical associated malignancies at early stage. Further research is requested to optimize dedicated diagnostic-therapeutic protocols, which have to be performed in specialized tertiary care centers.

P.18.9

ENDOSCOPIC PIECEMEAL RESECTION OF SESSILE OR FLAT COLONIC LESIONS > 2 CM: LONG-TERM RESULTS

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Background and aim: Evaluate the efficacy of endoscopic piecemeal resection of sessile or flat colonic lesions > 2 cm.

Material and methods: We selected all the sessile or flat colonic lesion > 2 cm underwent endoscopic piecemeal resection.

Results: We selected 109 sessile or flat lesions > 2 cm of 104 patients (41 women and 63 men).

The average size of polyps was 37 mm (range 21–80 mm). 18 were located in ceco, 16 in the ascending colon, 6 at the right colic flexure, 5 in the transverse, 2 in the left colic flexure, 3 in the descending colon, 17 in sigmoid and 42 in the rectum.

Histological examination showed 94 adenomas tubule-villous, 2 tubular adenomas, 2 villous adenoma. High-grade dysplasia was in 48 lesions; 9 lesions had areas of intramucosal cancer with clear surgical margins and 2 had areas of cancer infiltrating the submucosa and engaging margins. These last two patients underwent surgery. Additional treatment with APC was performed in 96 of 109 lesions. We observed a statistically significant correlation between the presence of invasive carcinoma and the seat rectal and size > 5 cm. Complications occurred in 13 cases: 8 bleeding treated endoscopically, 4 perforations treated with medical therapy and 1 post-polypectomy syndrome. We observed a statistically significant correlation between the onset of complications and the size > 5 cm lesion.

In six cases we observed endoscopic recurrence at 3 months after resection. After endoscopic treatment of relapse in this case no further relapses occurred.

We observed a statistically significant correlation between the loss of use of the APC and the onset of relapse and between the size > 4 cm and the onset of relapse.

Conclusions: Endoscopic piecemeal resection can be considered a valid alternative as ESD because it is a safe and simple technique, with a low complication rate, low cost and requesting a lower execution time.

P.18.10

SAFETY AND EFFICACY OF UNDILUTED N-BUTYL-2 CYANOACRYLATE INJECTION AS ENDOSCOPIC RESCUE THERAPY FOR REFRACTORY ACUTE NONVARICEAL UPPER GASTROINTESTINAL BLEEDING

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Background and aim: Nonvariceal upper gastrointestinal bleeding (NVUGIB) remains one of commonest medical emergencies associated with a relevant proportion of refractory hemorrhage. Novel technique, such as hemostatic powder, over-the-scope clip and endoscopic suturing, have been recently used to treat refractory NVUGIB. Cyanoacrylate glue (CYA) injection is an "old" technique that has been shown to be very effective for control of variceal bleeding, but its role in NVUGIB remains unclear. For CYA, the most significant concern is the risk of distal embolization. Glubran 2® (GEM; Viareggio, Italy) is a preparation of N-butyl-2 cyanoacrylate plus methacryloxysulfolane (NBCM) with a longer polymerization time than pure CYA and does not usually require dilution with lipiodol. This could lead to a minor rate of adverse events. Aim of this study is to report author's experience about the safety and efficacy of NBCM injection for emergency control of refractory acute NVUGIB.

Material and methods: A retrospective chart review was performed on patients who underwent NBCM injection for severe recurrent NVUGIB when conventional endoscopic techniques have failed. Main outcome data for the procedure included achievement of initial hemostasis, rate of early rebleeding (within 7 days), procedure-related complications, and mortality.

Results: From January 2010 to May 2015, 29 patients (19 men; mean age 84, range 28–96) with refractory acute NVUGIB were treated with NBCM. At the time of NBCM injection the patients were treated previously with hemoclip placement (72.4%), local epinephrine injection (68.9%), and argon plasma coagulation (3.4%). A bleeding lesion was identified in the esophagus in one (3.4%) patient, stomach in 14 (48.2%) patients, and duodenum in 14 (48.2%) patients. Hemorrhage was secondary to 23 peptic ulcers (79.3%), 2 Dieulafoy lesions (6.8%), 1 GIST (3.4%), 1 polypectomy (3.4%), 1 submucosal dissection (3.4%) and 1 PEG placement (3.4%). Immediate hemostasis was achieved in 27 patients (93.1%). Early rebleeding occurred in two patients (6.8%); one of these was successfully treated with a second NBCM injection. A total of 3 patients (10.3%) underwent salvage treatment (surgery). No procedure-related adverse events and no mortality were observed during the follow-up in any of the patients. No instrument damage were reported.

Conclusions: NBCM injection appears to be a safe, effective, economic and easily performed endoscopic rescue therapy for refractory acute NVUGIB. NBCM may offer endoscopists an alternative therapeutic strategy for severe bleeding when conventional endoscopic techniques have failed.

P.18.11**USE OF PILLCAM COLON 2 IN PATIENTS AT ELEVATED RISK OF COLONOSCOPY ASSOCIATED ADVERSE EVENTS**Spada C.^{*1}, Rex D.², Eliakim R.³, Costamagna G.⁴¹Fondazione Policlinico Universitario Gemelli, Rome, Italy, ²Indiana University Hospital, Indianapolis, United States, ³Sheba Medical Center, Rama-Gan, Israel, ⁴Italy

Background and aim: Optical colonoscopy (OC) is considered as the leading tool to visualize the colon and has a good safety profile. However, select patients are at elevated risk of OC associated adverse events (AEs) (referred to as “at risk”). Colon capsule endoscopy (CCE) with PillCam® COLON 2 is intended to provide visualization of the colon using a less invasive method, which may limit AEs in such patients. The goal of this study was to assess the safety and accuracy of CCE in an at risk cohort vs. those at standard risk.

Material and methods: A post-hoc analysis was performed using the combination of four prospective, multicenter trials to assess the CCE AE rate, exam completion rate, and accuracy in at risk vs. standard risk patients. At risk patients were defined as those with chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), those on prescription antithrombotics (ATs), and the elderly (≥ 70 YO). OC was performed after CCE, and OC AEs were excluded. OC-CCE lesion matching was previously described (Rex et al., Gastroenterology, 2015).

Results: A total of 1208 subjects enrolled, 86 (7.1%) of whom were at risk. Of these 86, 18 (21%) possessed COPD/OSA, 15 (17%) were on ATs, and 57 (66%) were ≥ 70 YO. No CCE related serious adverse events occurred. In the combined at risk group, AEs occurred in 3/86 patients (3.5%) vs. 94/1122 (8.4%) in the standard risk ($p=0.15$). The CCE exam was complete in 76/86 (88.4%) of the at risk population vs. 1026/1122 (91.4%) of those at standard risk ($p=0.32$). 999 subjects were included in the accuracy analysis. CCE sensitivity for detecting subjects with any polyp ≥ 6 mm in the at risk group was 88% (95% CI, 71-97) vs. 82% (95% CI, 78-86) in the standard risk group ($p=0.79$) with specificities of 80% (95% CI, 64-91) and 92% (95% CI, 89-94), respectively ($p=0.10$). CCE sensitivity for detecting subjects with any polyp ≥ 10 mm in the at risk group was 83% (95% CI, 59-96) vs. 82% (95% CI, 75-88) in the standard risk group ($p=1.0$) with specificities of 94% (95% CI, 85-99) and 97% (95% CI, 96-98), respectively ($p=0.40$).

Conclusions: CCE possessed an equivalent low AE rate, high exam completion rate, and good accuracy in patients at elevated risk of colonoscopy associated AEs vs. those at standard risk. This suggests that CCE could be used effectively and safely in patients with these risk factors if they are considered poor candidates for OC.

P.18.12**HEMOSPRAY IN TREATMENT OF ACUTE BLEEDING DUE TO UPPER GASTROINTESTINAL TUMORS: PRELIMINARY RESULTS**Arena M.^{*1}, Luigiano C.¹, Viaggi P.¹, Morandi E.¹, Fanti L.², Granata A.³, Traina M.³, Testoni P.A.², Masci E.⁴¹A.O. San Paolo, Milano, Italy, ²Ospedale San Raffaele, Milano, Italy, ³ISMETT, Palermo, Italy, ⁴Istituto Nazionale dei Tumori, Milano, Italy

Background and aim: Acute bleeding can complicate upper gastrointestinal (UGI) tumors. Endoscopic treatment in these cases is associated to a lower success rate than in case of bleeding due to other causes. Initial endoscopic hemostasis with traditional methods ranges from 67% to 100%, but re-bleeding rate is about 30%. Hemospray is a new hemostatic powder that is revealing successful in GI bleeding conditions. Aims of this study is to assess the Hemospray's efficacy to stop neoplastic UGI bleeding and to evaluate re-bleeding rate after initial hemostasis with Hemospray.

Material and methods: Prospective, multicenter, not randomized study on consecutive patients with acute bleeding from UGI

neoplastic lesions. Hemospray was used as single therapy or in association to other endoscopic hemostatic treatments. We evaluated initial hemostatic efficacy with Hemospray and any re-bleeding defined as early (until 3 days) or late (> 3 days). We defined effective hemostasis as stop of bleeding after 5 minutes or more from the end of treatment and re-bleeding as reduction of hemoglobin > 2 g/dl and endoscopic signs of bleeding.

Results: We enrolled 13 consecutive patients with UGI neoplastic bleeding. One patient presented with melena, hematemesis and shock, six patients with anemia and melena, three with anemia, and two with melena. Hemoglobin values ranged from 4 to 11 g/dl. Seven patients had gastric cancer, five patients had duodenal cancer, and one had a duodenal metastases due to melanoma. All patients showed endoscopic oozing bleeding. Hemospray was used as single therapy in 9 patients with immediate outcome in 100%. One of these patients presents early re-bleeding, treated successfully with Hemospray without further bleeding. Four patients were treated with Hemospray in association with other endoscopic methods (2 with injection therapy; 1 with mechanic therapy and 1 with thermic and mechanic therapies. Among these four patients, two had successful hemostasis without re-bleeding; one presented early and late re-bleeding after initial hemostasis and finally he died from causes related to bleeding; one patient failed initial endoscopic hemostasis, so he underwent surgery and died after few hours.

Conclusions: In this case series we found that initial hemostasis with Hemospray in patients with UGI neoplastic bleeding is about 92%, and re-bleeding rate is about 17%. According with these preliminary results Hemospray is a useful endoscopic treatment in acute bleeding due to UGI tumors.

P.18.13**HEMOSPRAY AS FIRST-LINE AND RESCUE THERAPY FOR GASTROINTESTINAL BLEEDING**Pigò F.^{*}, Bertani H., Manno M., Caruso A., Mirante V.G., Barbera C., Mangiafico S., Conigliaro R.L.

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Background and aim: Among devices employed for gastrointestinal bleeding (GIB), Hemospray (Cook Medical, Winston-Salem, North Carolina, USA) is a new promising tool because of its efficacy, safety and simple use. Hemospray is an hemostatic inorganic agent that becomes adhesive in contact with blood, creating a mechanical barrier. In Europe, Hemospray is licensed for upper gastrointestinal bleeding. The current use in the lower gastrointestinal tract is “off-label”. We present a prospective case series pointing the use of Hemospray in daily routine for the treatment of GIB at our tertiary endoscopy center.

Material and methods: Patients treated with Hemospray between January 2014 and July 2015 were involved in this study. Informations as age, sex, ASA class, antithrombotic/anticoagulant use, presence of shock, cause of bleeding, previous interventions, additional modalities of hemostasis, rebleeding and mortality to 30 days were collected. In every case the technique was feasible and it was administered a maximum of 20 g of the powder. In 1 case Hemospray was used “off-label”.

Results: 13 patients were treated with Hemospray as first line therapy in 7 cases and as rescue therapy in 6 cases. In 8 cases (3 gastric neoplasia, gastrojejunal anastomosis, ischemic colitis, 1 post-sphincterotomy bleeding, esophageal ulcer) no more bleeding episodes occurred. In 3 cases of duodenal ulcers angiography and/or surgery were necessary to stop bleeding. 3 patients died within 30 days from admission (2 gastric neoplasia and 1 duodenal ulcer). No adverse events were registered.

Table (abstract P.18.3)

Patient	Age	Sex	ASA class	Anticoagulant/ antithrombotic drugs	Shock	Site/cause of bleeding	Previous interventions	Additional modalities	Rebleeding	Mortality (30 days)
1	66	M	3	Heparin	yes	Post-sphincterotomy bleeding	Adrenalin	no	no	no
2	56	M	4	Heparin	yes	Duodenal ulcer (Ib)	Adrenalin + clip	no	Angiography and surgery	no
3	74	M	4	Heparin	yes	Gastro-jejunal anastomosis	Clip+ cianoacrilate	cianoacrilate	no	no
4	78	M	3	Heparin	yes	Gastric adenocarcinoma	no	no	Surgery for curative purpose after 7 days	no
5	72	M	3	Heparin	yes	Duodenal ulcer (Ia-Ib)	Adrenalin + OTSC	OTSC	yes	yes
6	91	F	3	ASA	yes	Gastric adenocarcinoma	no	no	yes	yes
7	80	M	3	Warfarin	yes	Duodenal ulcer (Ib)	no	adrenalin	angiography	no
8	72	F	4	Heparin + ASA	yes	Ischemic pancolitis	Right emicolectomy	no	no	no
9	74	M	3	Ticlopidin	no	Metastatic gastric adenocarcinoma	no	no	no	no
10	37	F	1	none	no	Post-sphincterotomy bleeding	no	adrenalin	no	no
11	56	M	4	ASA	yes	Metastatic gastric adenocarcinoma	no	adrenalin	no	yes
12	57	M	4	Heparin	yes	Duodenal ulcers (Ia)	Adrenalin+clip+OTSC	no	angiography and surgery	no
13	93	F	2	Clopidogrel + ASA	no	Esophagel ulcer (Ib)	no	Adrenalin	no	no

Conclusions: Hemospray, from these preliminary results, has been effective for diffuse site of bleeding as gastric neoplasia, anastomosis and ischemic colitis.

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