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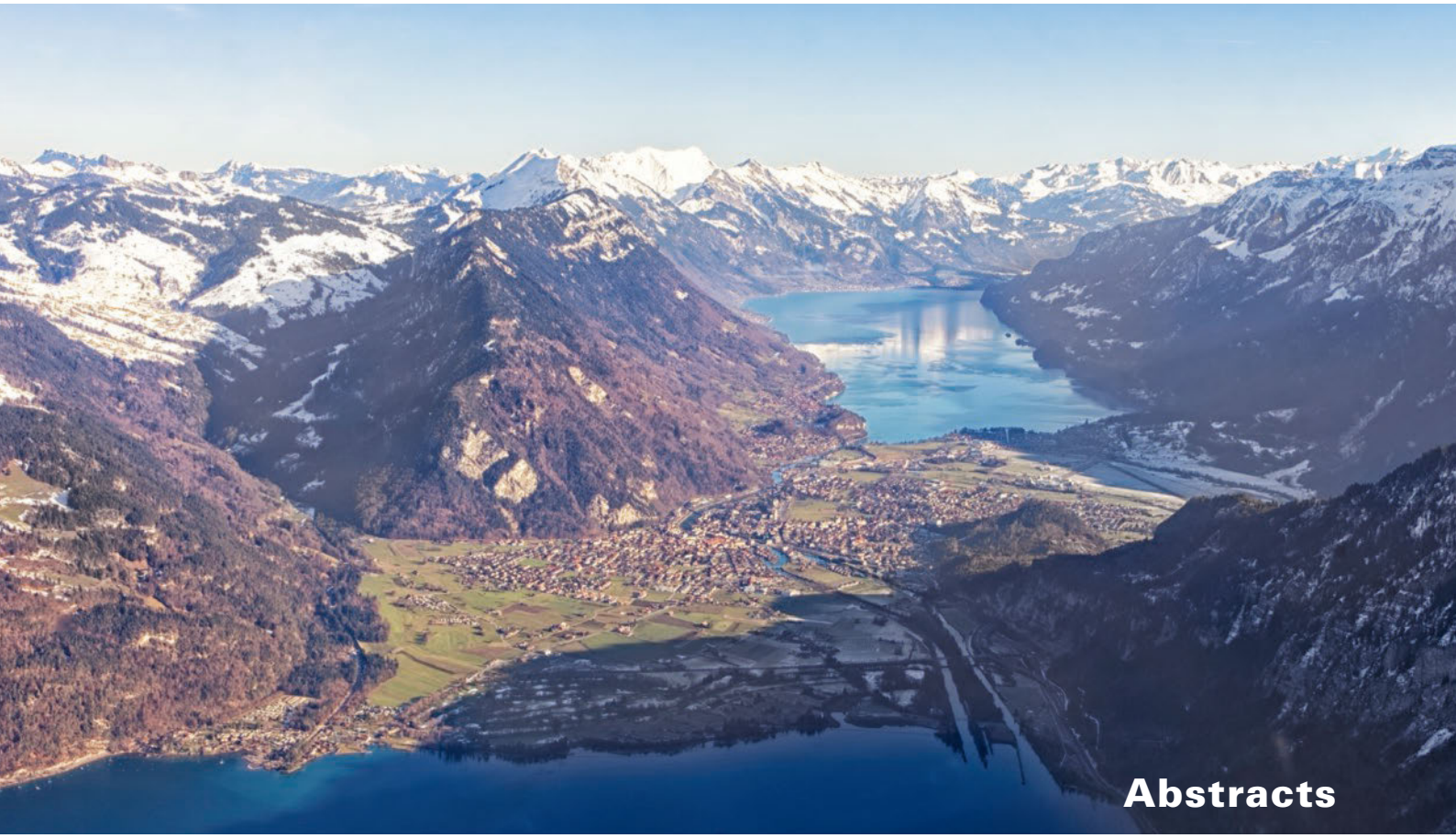

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The intra-individual Variability of Fecal Calprotectin in patients with GI-symptoms

O1

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Background: Fecal Calprotectin (FC) is used to distinguish between functional and organic gastrointestinal disease. So far only single analyses were performed. Since we have observed a great variability of FC measurements that were performed in the same patient in a short amount of time, we wanted to investigate this variability in our pts.
Methods: We searched our data base for pts with GI disorder who had at least three documented FC values within 10 days.
Results: 404 pts were included (284 female (70%), range 11-92y, mean 45.8y). First we applied the usual cut-off of 50 µg/g. 110 pts (28.1%) showed normal and elevated values. These 110 pts showed ranges: 48 pts (43.6%) <50; 33 pts (30%) 50-99; 11 pts (10%) 100-199; 9 pts (8.2%) 200-500; 8 pts (7.3%) > 500. The 150 pts with three elevated values showed even higher ranges: 21 pts (14%) with a range <50; 25 pts (16.7%) 50-99; 33 (22%) 100-199; 38 pts (25.3%) 200-499; 19 pts (12.7%) 500-1000; 14 pts (9.3%) >1000. Age and gender had no statistically significant influence. Comparable variability was shown in the subanalysis of patients with organic disease (232 pts, 57.4%), non-organic disease (153 pts, 37.9%) and uncertain diagnosis (19 pts, 4.7%). With a cut-off of 100µg/g 92 pts (22.6%) had normal and elevated values, with a cut-off of 150 µg/g 62 pts (15.4%).
Conclusions: The data showed that more than ¼ of the patients (28%) showed values deemed normal as well as pathological, as well as high ranges. This raises the question if a single measurement is sufficient to base clinical decision on. To definitely formulate recommendations for everyday clinical practice, a large protective study is needed.

OBESITY IS FREQUENT IN INFLAMMATORY DISEASE PATIENTS AND ASSOCIATED WITH HIGHER DISEASE ACTIVITY IN CROHN`S DISEASE, BUT NOT IN ULCERATIVE COLITIS

O3

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BACKGROUND: Obesity is common among patients with inflammatory bowel disease (IBD). Weight changes after bariatric surgery result in higher rates of de-novo IBD. However, the impact of obesity, weight changes over time on IBD disease activity has yet to be determined. METHODS: Data on obese IBD patients (body mass index (BMI) of ≥30 kg/m^2) included in the Swiss IBD cohort study were analyzed cross-sectionally and compared to normal weight IBD controls (BMI 18.5-24.9). The two groups were compared with respect to clinical disease activity (such as the Crohn`s disease (CD) activity index CDAI), CRP levels, fecal calprotectin, quality of life (QoL) and presence of extraintestinal manifestations (EIM). Subsequently, data on obese IBD patients were analyzed longitudinally with regards to development of complications according to whether they lost (minus >1kg/m^2), gained (plus >1kg/m^2) weight or remained stable. RESULTS: A total of 325 obese patients (194 CD, 131 ulcerative colitis (UC)) and 1725 normal weight controls (977 CD, 748 UC) were analyzed. Compared to normal weight controls, obese patients were older at diagnosis (median 32 vs. 26y, p<0.001) and reported higher rates of EIM (56.0 vs. 49.6%, p=0.035,), particularly arthritis/arthralgia (51.4 vs. 40.6%; p<0.001). These differences were seen in both CD and UC. Obese CD patients had higher median CDAI scores (33 vs. 20, p=0.001), with increased soft stool frequency compared to normal weight controls (8 vs. 4/week, p=0.001) and higher CRP levels (5 vs. 3mg/L, p<0.001). QoL was partially affected (decrease in the systemic, social IBDQoL and SF36 physical score, but not IBDQoL global score). In obese UC patients, there was no difference in disease activity scores compared to normal weight IBD controls. Nevertheless, high numbers of bowel movements per day were more frequently seen (p=0.021) and CRP levels were higher (4 vs. 2mg/L, p=0.008). In addition, QoL was only decreased in terms of the IBDQoL systemic score. Subsequent longitudinal analyses revealed that development of complications was not increased in obese patients except for fistula/abscess surgery in CD (HR 1.845 (95% CI 1.077-3.162). Within the subgroup of obese patients, increase or decrease in BMI over time did not result in higher or lower rates of complications except for fistula/abscess surgery in CD. Both decrease and increase of BMI compared to stable obese BMI showed a trend towards higher rates of fistula/abscess surgery (HR 2.566 (95% CI 0.932-7.065) and HR 2.418 (95% CI 0.870-6.723)). CONCLUSION: In a large, nation-wide IBD cohort, obese BMI was frequently identified. Association between BMI and disease activity scores as well as impaired QoL was seen in CD, but not UC. Obesity and weight changes may increase the need for CD surgery. BMI and weight changes over time should be considered when caring for IBD patients.

Isoproterenol activates gut-liver-axis: effects on intestinal mucus and vascular barrier as entry sites.

O2

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Background: The gut-liver-axis presents the pathophysiological hallmark for multiple liver diseases and has been proposed to be modulated during stress and shock. Access to the gut-liver-axis needs crossing of the mucus and gut-vascular barrier (GVB). The role of β-adrenoreceptor-activation for both barriers has not been defined and is characterized here.

Methods: Isoproterenol or vehicle (sterile saline) were applied via osmotic pump intraperitoneally for 7 days. Ileal intestinal loop experiments were utilized in-vivo for assessment of extravasation of size-defined FITC-dextran (i.v.) and their translocation from the lumen to the liver. Whole ileum was analysed by immune-histochemistry for plasmalemma-vesicle (PV)-1, a marker of vascular permeability as well as RNA-sequencing.

Results: Healthy mice lack translocation of 4kDA-FITC-dextran from the small intestine to the liver whereas isoproterenol-treated mice demonstrate pathological translocation. Mucus layer is reduced in thickness with loss of goblet-cells and Muc2-staining and -expression in isoproterenol-treated animals under standardized gnotobiotic conditions. GVB is likewise altered by isoproterenol-treatment with pathological extravasation of large-sized 70- and 150 kDa-FITC-dextran in ileal microvasculature. This pathological endothelial permeability and accessibility induced by isoproterenol associates with an augmented expression of PV1.

Conclusions: Isoproterenol impairs the intestinal muco-epithelial and endothelial-vascular barrier promoting pathological trans-location to the liver. This barrier dysfunction on multiple levels potentially can contribute to liver injury induced by catecholamines during states of increased β-adrenergic drive.

Efficacy of Etrolizumab in patients with moderate to severe UC who had failed TNF Antagonist Therapy (HICKORY)

O4

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Background: Patients (pts) with moderate-severe ulcerative colitis (UC) and intolerant or refractory (IR) to TNF antagonists (aTNFs) are a difficult-to-treat population. HICKORY evaluates the safety and efficacy of etrolizumab open label induction via centrally read endoscopy, patient-reported outcomes (PROs) and inflammatory biomarkers in these pts.
Methods: 130 aTNF-experienced UC pts receiving etrolizumab 105 mg s.c. q4w in a 14-week induction period were assessed at baseline (BL) and week 14 (endoscopic scores (ES), patient-reported rectal bleeding (RB), stool frequency (SF)). Clinical response: ≥3-point + 30% reduction of Mayo Clinic score (MCS) vs BL + ≥1-point decrease in RB or RB≤1. Remission: MCS≤2 (subscores ≤1) + RB=0. Endoscopic improvement: ES≤1; RB remission: RB=0; SF remission: SF≤1 (≥1-point reduction vs BL).
Results: At week 14, etrolizumab treatment was associated with clinical response in 50.8%, remission in 12.3%, ES≤1 in 23.9%, RB remission in 52.3% and SF remission in 35.4% of pts. 43.9% of pts had ≥1-point ES improvement from BL, and improved ESs were associated with increased rates of RB and SF remission. Among pts with ES=0, 100% reported RB≤1 and 90% SF≤1.
Conclusions: aTNF-experienced pts with moderate-severe UC and high disease burden treated with open-label etrolizumab for 14 weeks achieved clinically meaningful clinical response, remission, and endoscopic improvement. Pts who had a decline in ES≥1 achieved higher rates of RB and SF remission and greater reductions in inflammatory biomarkers. Study recruitment continues, a randomised maintenance phase is also ongoing.

Previously presented: Peyrin-Biroulet L et al. UEGW 2017

LPA-induced GPR35 signaling in macrophages resulted in reduced TNF production associated with decreased intestinal corticosterone synthesis

O5

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Background: Host-or microbial derived metabolites drive the development of inflammatory bowel disease (IBD) through G protein-coupled receptors (GPCR). Polymorphism in GPR35 are associated with ulcerative colitis (UC), but the function of GPR35 in mucosal immunity is rather understudied.
Methods: In order to study GPR35 in the intestine the mouse lines GPR35tdTomato, GPR35Ko and GPR35$^{\Delta CX3CR1}$, in which GPR35 can be deleted in macrophages by tamoxifen-induced Cre-mediated recombination have been generated. Potential ligands were screened in *Gpr35.2*-deficient zebrafish (ZF).
Results: *Ex vivo* imaging of GPR35tdTomato / CX3CR1-GFP mice confined GPR35 expression to intestinal epithelial cells and CX3CR1^{+} macrophages, which can be distinguished in GPR35^{+} and GPR35^{-} macrophages with higher *Tnf*, *Il1b* and *Il23* expression by GPR35^{+} macrophages. Potential ligands were screened with a Chinese Hamster Ovary (CHO)-K1 human GPR35 overexpressing cell line. Lysophosphatidic acid (LPA) and CXCL17 but not kynurenic acid (KNA) inhibited forskolin-induced cAMP production. LPA induced *Tnf* expression in ZF and in mouse macrophages in a GPR35-dependent manner. Deletion of GPR35 in macrophages resulted in increased DSS severity associated with reduced TNF production by macrophages. The treatment of GPR35$^{\Delta CX3CR1}$ mice with TNF attenuated colitis and restored *CYP11B1* expression required for intestinal corticosterone synthesis. **Conclusion:** LPA-mediated GPR35 signaling may induced TNF production by macrophages associated with intestinal corticosterone synthesis.

Is *iBDialog monthly* a helpful tool in daily clinical practice?

O6

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Background: *iBDialog monthly* pledges to help doctors and IBD nurses to stay up-to-date with their patients by giving them access to tools that track their disease activity[1] and monitor treatment adherence[2]. The aim of the present analysis is to evaluate the feasibility in daily clinical practice.
Methods: Patients were asked whether they wished to take part and use *iBDialog monthly*. Their records were regularly controlled. Interviews were conducted with the nursing staff and physician in order to assess the feasibility and benefits of the *iBDialog monthly* platform.
Results: **81** patients with IBD have been contacted: 38 patients (20 women, 18 men) with Crohn's disease (CD) and 43 (19 women, 24 men) with ulcerative colitis (UC). In total, 39 patients accepted to participate, implying a participation rate of 48.1%. 1 patient lost interest and dropped out, partly due to technical problems with the App; 4 patients were passive participants: they constantly forgot their monthly record. 6 patients with a significant increase of disease activity were discovered: 3 of them already had a consultation date set for the next days, while the other 3 didn't undergo regular medical care. These 3 patients were contacted without delay to set up an appointment.
Conclusion: The survey confirmed that *iBDialog monthly* is a feasible and helpful tool in a gastroenterology practice. IBD nurses used the tool and followed up on patient data much more frequently than physician. In 6 cases the reporting had a direct influence on patient management. Nevertheless, the follow-up period has been too short and the number of patients too small in order to adequately estimate whether *iBDialog monthly* has a relevant impact on the quality of care.

[1] Simple clinical colitis activity Index: SCCAI
[2] Partial Harvey Bradshaw Index
Source: https://www.ibdialog.ch/

Aspirin suppresses age-associated and colon cancer relevant DNA methylation changes in the healthy colon

O7

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Background The protective effect of aspirin against colon cancer (CC) is well described, but the underlying molecular mechanisms preventing tumor initiation and progression are poorly understood.
Methods In a longitudinal study including 31 screening females, we performed Illumina Infinium MethylationEPIC array profiling DNA methylation over 850,000 CpGs in healthy colon biopsies obtained at baseline and a median follow-up of 10 years.
Results Principal component analysis revealed colon location (51.4%) and time (4.5%) as top two components explaining the variability in the data. Differential methylation analysis showed that aspirin use suppresses methylation gain over time. Out of 753630 CpGs analyzed, 26170 (3.5%) showed hyper- and 8774 (1.2%) hypomethylation in nonusers compared to 1286 CpGs (0.2%) with hyper- and 7188 (1.0%) with hypomethylation in users over time in proximal colon (P<0.05). In distal colon, 10108 CpGs (1.3%) showed hyper- and 6005 (0.8%) hypomethylation in nonusers compared to 3360 CpGs showing hyper- (0.4%) and 18869 (2.5%) hypomethylation in users over time (P<0.05). Median methylation change over time was increased in nonusers (prox 3.6%, dist 2.0%), but reduced in users (prox 2.9%, dist 3.2%). Aspirin use suppressed hypermethylation selectively at non-CGIs (P<0.0001) and at intergenic regions (P<0.001). Pathway-based gene set enrichment analyses showed aspirin suppresses methylation at genes involve in metabolism, primary immune deficiency, NF-kappa B signaling, platelet activation etc.
Conclusions Aspirin use modulates DNA methylation stability in the healthy colon and we propose this to be a major molecular mechanism underlying its anti-neoplastic effect.

Liver fibrosis screening in patients undergoing a screening colonoscopy (FIB-SCREEN): feasibility and preliminary results of a prospective study

O8

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Background: Advanced liver disease is one of the main causes of morbidity and mortality worldwide however diagnosis is rarely made at early stages as no feasible and practical screening strategy have been developed. We aimed to assess the feasibility and preliminary results of non-invasive liver fibrosis screening in all patients aged 50 or more undergoing a screening colonoscopy.
Methods: From November 2018 to April 2019, patients aged ≥ 50 years admitted for screening colonoscopy at our institution were prospectively recruited for liver fibrosis screening. Screening was performed using transient elastometry (TE) with Fibroscan M or XL probe with values ≥ 8kPa considered as significant fibrosis. We excluded patients with known liver disease and severe comorbidities.
Results: 49/52 (95%) screened patients consented to participate in the study. Our cohort was composed of 33 men (67%), median age was 57 y [53-62y] and 7 patients (14%) had TE ≥ 8kPa (**Table 1**). Patients with TE ≥ 8kPa were more often obese (57% vs 19%, p=0.031), diabetic (43% vs 19%, p=0.178) and had a higher proportion of at-risk alcohol consumption (43% vs 4%, p=0.017). ALT and AST were significantly higher in the TE ≥ 8kPa group. FIB4 was non-significantly higher in the TE ≥ 8kPa group.
Conclusion: Preliminary results indicate that liver fibrosis screening in the context of screening colonoscopy is feasible and acceptable to patients. 14% of subjects had raised TE underlining the potential significant burden of undiagnosed liver fibrosis in this population.

Table 1: Patient characteristics

Variable	All cohort n=49	Fibrosis (TE ≥ 8kPa), n=7 (14%)	No fibrosis, n=42 (86%)	p-value
Clinical				
Age (median, IQR)	57 (53-62)	58 (56-60)	56 (52-62)	0.753
Male sex n (%)	33 (67%)	6 (86%)	27 (64%)	0.402
Diabetes n (%)	11 (23%)	3 (43%)	8 (19%)	0.178
Obesity n (%)	12 (24%)	4 (57%)	8 (19%)	0.031
Biological				
ALT (median, IQR)	27 (21-35)	60 (18-82.5)	25 (20.25-31.5)	0.009
Non-invasive fibrosis assessment				
FIB4 (median-IQR)	1.15 (0.83-1.54)	1.7 (1.1-2.06)	1.1 (0.7-1.4)	0.056
TE (median-IQR)	4.7 (2.5-6.7)	12.6 (10.5-19)	4.3 (3.5-5.4)	0 017

Abbreviations: BMI, body mass index; ALT, alanine aminotransferase; AST, Aspartate aminotransferase; FIB4, FIB4 score; IQR, interquartile range; TE, transient elastography

Drug-induced liver toxicity in a prospective cohort of cancer patients receiving immune checkpoint inhibitors

O9

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Background: Drug-induced liver injury (DILI) by immune checkpoint inhibitors is a frequent but poorly understood adverse event. In this study, we characterize liver immune-related adverse events (irAEs) in a prospective cohort.

Methods: We examined DILI in melanoma and non-small cell lung cancer patients during checkpoint inhibitor treatment. We investigated for presence and dynamics of antibodies associated with autoimmune liver diseases at three timepoints: before treatment start, at the onset of liver irAE, and two months later.

Results: There were 11 cases of liver irAEs among 142 patients (7.7%); 5/11 showed CTCAE grade 3/4 liver toxicity. Viral hepatitis was excluded in all individuals. 6/11 required treatment with steroids. Interestingly, 7/11 liver irAE patients (63.6%) showed positive autoantibody titers already prior to treatment start. 9/11 patients (81.8%) developed additional irAEs compared to 20/73 controls (27.4%) with multiple irAEs (p=0.0001). There were no deaths due to hepatic irAEs.

Conclusions: Liver irAEs are frequent and are often associated with additional irAEs of other organs. Pre-existing autoantibodies may predispose patients to immune-related hepatitis.

Endoscopic full-thickness resection for early colorectal cancer

O10

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Background: Current international guidelines recommend endoscopic resection for T1 colorectal cancer (CRC) with low-risk histology features and oncologic resection for those at high risk of lymphatic metastasis. Exact risk stratification is therefore crucial to avoid under-treatment as well as over-treatment. Endoscopic full-thickness resection (EFTR) has shown to be effective for treatment of non-lifting benign lesions. In this multicenter, retrospective study we aimed to evaluate efficacy, safety and clinical value of EFTR for early CRC.
Methods: Records of 1234 patients undergoing EFTR for various indications at 96 centers were screened for eligibility. A total of 156 patients with histologic evidence of adenocarcinoma were identified. This cohort included 64 cases undergoing EFTR after incomplete resection of a malignant polyp (group 1) and 92 non-lifting lesions (group 2). Endpoints of the study were: technical success, R0-resection, adverse events, and successful discrimination of high-risk versus low-risk tumors.
Results: Technical success was achieved in 144 out of 156 (92.3%). Mean procedural time was 42 minutes. R0 resection was achieved in 112 of 156 (71.8%). Subgroup analysis showed a R0 resection rate of 87.5% in Group 1 and 60.9% in Group 2 ($p < .001$). Severe procedure-related adverse events were recorded in 3.9% of patients. Discrimination between high-risk versus low-risk tumor was successful in 155 of 156 cases (99.3%). In Group 1, 84.1% were identified as low-risk lesions, whereas 16.3% in group 2 had low-risk features. In total, 53 patients (34%) underwent oncologic resection due to high-risk features whereas 98 patients (62%) were followed endoscopically.
Conclusion: In early CRC, EFTR is technically feasible and safe. It allows exact histological risk stratification and can avoid surgery for low-risk lesions. Prospective studies are required to further define indications for EFTR in malignant colorectal lesions and to evaluate long-term outcome.

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O11

Pain after FTRD in the upper and lower GI tract – a single center experience

Background: The full-thickness resection device (FTRD) has shown favorable results concerning efficacy and safety in the resection of oesophgeal, gastric, duodenal as well as colorectal lesions. However data on occurrence of postinterventional pain are limited.

Methods: Data of 40 consecutive patients (14 female 26 male, mean age 61.3 years) who underwent endoscopic full-thickness resection (EFTR) by FTRD in our institution between 2017 and April 2019 were collected and analyzed retrospectively. Pain was assessed from endoscopy reports, medication charts and hospital admisson records.

Results: 14 patients underwent EFTR in the upper GI tract (n=1 esophageal leiomyoma; n=2 inflammatory fibrinoid polyps; n=undetermined cystic submucosal lesion; n=4 ectopic pancreas; n=1 malignant gastric polyp; n=1 gastric NET; n=1 duodenal GIST; n=2 duodenal adenoma; n=1 duodenal NET). 4/14 patients reported pain and 2/14 patients were hospitalized for pain management. Complete resection was achieved in 12/14 patients. 26 patients underwent EFTR in the lower GI Tract (n=1 diagnostic; n= 1 schwannoma transverse; n=5 rectal/colonic NET; n=1 granularcell tumor; n=5 serrated adenoma appendix/coecum/ascending; n=8 tubular adenomas with/ without HGD; n=4 adenocarcinoma in situ; n=1 hyperplastic polyp transverse. 7/26 patients reported pain after the procedure with 2 patients requiring hospitalisation (appendicitis). 3/26 patients presented with minor bleeding requiring endoscopy. Complete resection was achieved in 23/26 patients.

Conclusion: This study confirms the feasibility of duodenal EFTR in the upper and lower GI tract and indicates good efficacy and safety. 11/26 (42%) of patients reported postinterventional pain but only 4 required hospitalization.

Beta6-Integrin – A novel Serum Marker predicting overall Survival in Pancreatic Adenocarcinoma

O12

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Background: Pancreatic adenocarcinoma (PAC) remains a major clinical challenge leading to approximately 30'000 deaths per year in the US. Conventional cancer therapies are mainly palliative in nature and 5-year survival is way below 10%. Thus, the need for novel biomarkers to improve diagnosis, surveillance and predicting tumor biology is paramount.
Methods: ITGB6 serum levels were measured in a pro- and retrospective PAC patient cohorts using ELISA. Next, we examined whether the combination of ITGB6 and CA 19-9 would be more accurate than CA 19-9 alone in diagnosing PAC using patients with chronic pancreatitis (cP) as control group.
Results: Using an initial cohort of 24 PAC patients, we found that detection of ITGB6 in serum is associated with a significantly shortened survival (difference median survival 294 days, $p = 0.0205$, fig. a). Next, ITGB6 levels were measured in a prospective cohort 20 PAC and 6 cP patients. All patients with ≥ 1 ng/mL ITGB6 in serum displayed pancreatic cancer indicating that ITGB6 serum concentrations together with CA 19-9 may refine the diagnosis for PAC (fig. b). However, too few patients were included in order to demonstrate significance.
Conclusion: Our findings show that detectable ITGB6 serum levels may be associated with shortened overall survival. Furthermore, the addition of ITBG6 to CA 19-9 may aid the diagnosis of PAC in patients with cP. However, our results need to be validated in a larger, prospective cohort.

EOSINOPHILIC ESOPHAGITIS-LIKE DISEASE WITH LACK OF SIGNIFICANT ESOPHAGEAL EOSINOPHILIA: DESCRIPTION OF A NEW DISEASE ENTITY

O13

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BACKGROUND: Observation of an eosinophilic esophagitis-like (EoE) disease with typical symptoms, but eosinophil-free biopsies has questioned the role of eosinophils (eos) in EoE. Here, we determined clinical, endoscopic and (immuno)-histological features of patients with chronic EoE symptoms, but less than 15 eos/hpf. METHODS: Patients with typical symptoms of esophageal dysfunction, but a peak eos count of <60/mm^2 (<15/hpf), from 6 EoE-centers were included. Biopsies were re-examined by 2 reference pathologists. Patients with EoE-like disease were evaluated with immunohistological (IHC) examinations and compared to conventional EoE, healthy controls. RESULTS: We analyzed 71 patients (age at diagnosis 43.8y±21.0, 52.1% females). Median follow-up was 10.4 months (IQR 1.0-28.8) with 3 visits per patient (IQR 2-4). Family history for EoE was positive in 22.5%. All patients had clinically active disease: 68 patients (95.8%) reported dysphagia, 49 patients (69.0%) experienced food impactions and 3 children reported vomitus, abdominal pain, and failure to thrive. Endoscopic activity was seen in 52.1% with a median EREFS score of 1 (IQR 0-3). Endoscopic dilation was needed in 25 patients (35.2%). Most patients showed histological disease activity based on the EoE histological scoring system (HSS), particularly basal zone hyperplasia and dilated intercellular spaces. Absence of HSS features was found in 15 patients. However, in 11/15 lymphocytic infiltration was detected. IHC analysis was available for 54 patients. IHC confirmed absence of significant eosinophilic infiltration in all but one patient with a mean number of EPX (eosinophil peroxidase) positive cells of 13.1±24.4 per mm^2, but revealed considerable T cell infiltration (largely CTRH2 negative, in 53/54 patients). T cell infiltration was higher than in conventional EoE (140.1 vs. 47.1 cells/mm^2, p=0.021). Mast cell infiltration was less prominent than in EoE (25.4 vs. 61.3 cells/mm^2, p<0.001) and comparable to controls (19.8 cells/mm^2). Measurement of chemokine expression revealed higher numbers of TSLP positive cells compared to EoE, controls (68% vs. 21%, p<0.001 and 68% vs. 18%, p<0.001). Expression of LEKTI, a protease inhibitor responsible for epithelial homeostasis, was decreased compared to controls (LEKTI positive area 14% vs. 26%, p<0.001), but to a lesser extent than in EoE (14 vs. 9%, p=0.023). In 8 patients EoE developed after 14.0 months (IQR 3.6-37.6). 39/71 patients were treated with topical steroids resulting in symptom relief in 87.2%. CONCLUSION: EoE-like disease is a new entity with distinct (immuno)-histological features, but shares clinical features with EoE. Decreased LEKTI expression implies an epithelial barrier defect. Despite the absence of significant eosinophilia, considerable disease activity can be observed. Follow-up is warranted to assess for progression to EoE.

IL-20 cytokine signaling modulates eosinophilic esophagitis

O14

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Background: Eosinophilic esophagitis (EoE) is a T-helper type 2 (T_H2) mediated chronic inflammatory disease. The interleukin-20 (IL-20) family consisting of IL-19, IL-20 and IL-24 has recently gained attention in T_H2-mediated chronic inflammatory diseases. However, little is known about their role in the esophagus.

Methods: We analyzed IL-20 cytokine expression and eosinophil infiltration in human esophageal biopsies and murine tissues. An EoE disease model in mice was induced by epicutaneous sensitization and subsequent oral challenge with ovalbumin.

Results: The expression of IL-20 cytokines was increased in patients with active EoE and diminished after topical corticosteroid treatment. Immunohistochemistry staining demonstrated the expression of the IL-20 receptor (IL-20R) type 1 in the esophageal epithelium of patients. To further investigate IL-20 cytokines in EoE an EoE disease model in mice was established characterized by increased expression of IL-20 cytokines and infiltration of eosinophils and basophils into the esophagus. In Il20rb$^{-/-}$ mice, the EoE-like disease is characterized by lower disease scores and less infiltration of CD45$^+$ immune cells in the esophagus. More specifically, eosinophil and basophil numbers are reduced. *In vitro* stimulation with IL-20 cytokines of the human esophageal keratinocyte cell line KYSE-180 resulted in phosphorylation of STAT3 and increased expression of eotaxin-3.

Conclusion: Our results with patient biopsies and mouse models indicate an active role for IL-20 cytokines in EoE. Potentially, IL-20 cytokines act on epithelial cells to modulate eotaxin-3 expression required for the chemotaxis of eosinophils and basophils.

Endoscopic Vacuum Therapy by EsoSponge® : treatment of oesogastroduodenal leakage. Who's the best patient ?

O15

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Background : Perforations and anastomotic leakages of the gastrointestinal tract represent an emergency that can be complicated by a significant risk of morbidity or mortality. Endoscopic vacuum therapy (EVT) by EsoSponge® is an established and effective treatment option of these complications. We describe here our experience through a serie-report. **Methods:** Patients treated with EVT for a perforation of upper gastrointestinal system were analysed from prospective register from November 2016 to May 2019, at HUG. After a radiologal diagnosis, a polyurethane sponge was endoscopically positioned in the wound cavity or nearby of the perforated orifice, connected to an external drainage, in agreement with the visceral surgery team. The sponge was changed endoscopically every 3-4 days. **Results:** Ten patients were treated (3 women, 7 men). Mean age was 55.2 years (range 22 to 75). Causes of perforation were reflux surgery (1), duodenal ulcer (1), cervical abscess with chronic fistula (1), status post bariatric surgery (2), oncologic surgery (1), Boerhaave Syndrome (4). The technical success for the procedure was 100%. EVT allowed the closure of the perforation in 6 patients after an average of 12.6 days (range 11 to 44). Average number of sponge insertions was 4.5 (range 2 to 10). A surgical treatment was needed in 4 patients due to an unfavorable evolution. Three of them presented a septic shock before closing the orifice and one showed no treatment efficacy after 3 EVT changes. The 3-month survival rate is 100%. **Conclusions:** EVT appears to be a technically feasible and safe procedure in upper gastrointestinal tract perforation in accordance with previous studies. EVT was effective in 2/3 patients. We believe that EVT should be proposed as a first-line endoscopic treatment in upper GI perforation, only in case of oesophageal perforation or leakage of oesogastric anastomosis.

Endoscopic Ultrasound-guided Radiofrequency Ablation for Pancreatic Neuroendocrine Tumors: a retrospective single center study

O16

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Background. Generally, pancreatic neuroendocrine tumors (NETs) are surgically treated but the operative procedure includes a significant risk. An alternative curative management is necessary. Endoscopic ultrasound-guided radiofrequency ablation (EUS-RFA) is a promising technique that has been recently developed. We evaluated the technical success, the safety and the efficacy of pancreatic EUS-RFA.
Method. This is a retrospective single center study. 7 patients were included with a NET < 3 cm between December 2017 and March 2019. EUS-RFA was performed with the EUSRA™ 19-gauge needle from Taewoong® with a power of 50 Watts during maximum 10 seconds in most cases, except for one patient where we used a power of 30 Watts during 45 seconds after recommendation of the manufacturer.
Results. Mean size of NETs was 11.8mm (range 7.4-18). Histologically, one NET was of grade 2 and localized in the isthmus; six NETs were of grade 1 and localized in the uncinated process (2), in the isthmus (2) and in the body (2). Overall, 3 of the NETs were insulinomas. EUS-RFA was feasible in all cases (100%). Clinical success was obtained in 6/7 patients (86%) without remnant in a mean follow-up of 8 months (range 2-15), with a mean number of sessions of 1.14 per patient. The only patient treated with 30 Watts during 45 seconds has developed a pancreatic fistula treated surgically after failure of an endoscopic management. The 3 patients treated for insulinoma did not face any symptoms or hypoglycemia anymore, immediately after the first application. All tumoral factors returned to a normal level in case of initial elevation. 3 patients experienced mild post-procedural abdominal pain treated conservatively.
Conclusion. EUS-RFA of pancreatic NETs is a feasible and effective procedure. In case of proximity between the tumor lesion and the Wirsung, a preventive pancreatic prosthesis must be positioned. More studies are needed to establish the optimal values of power required to treat lesions.

Five-year audit of endoscopic submucosal dissection (ESD) in daily clinical practice

O17

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Background: ESD provides a modern endoscopic resection technique with a high rate of en bloc resections for lesions in the upper and lower gastrointestinal tract (GIT).

Methods: We like to report our results of ESD in daily clinical practice at a swiss private hospital over a five-year period and therefore retrospectively analysed 320 ESD cases (cs) of 286 patients (pts) with at least one ESD resection. All ESD were performed by one experienced endoscopist (PN).

Results: 320 ESD (286 pts) were performed and now analysed (143 f, mean age 64.4). Surgery after ESD was needed in 29 cs (9.1%). Of these, 20 cs (6.3%) were ESD-related: 14 (4.4%) technical problems, 6 severe adverse event (SAE). 9 (2.8%) were not ESD-related: 6 unfavourable histology (histo), 3 recurrences (rec). Major SAE occurred in 14 cs (4.4%) and consisted of perforation (perf) (9 cs, 2.8%), delayed bleeding (4 cs, 1.3%) or infection (1 cs, 0.3%). From further analysis 13 (4.1%) cs with a not completed ESD were excluded (10 had subsequent surgical resections, 2 second ESD, 1 snare resection). The definitive study population consisted of 307 cs in 277 pts. Median lesion size was 3 cm, median intervention time was 14 min. So far, local rec was found in 8 cs (2.6%). Esophagus (N=26, 8.5%): 2 adenocarcinoma, 2 superficial SCC, 9 Barret's mucosae, 13 others. Stomach (N=80, 26.1%): 4 GIST, 11 hyperplastic polyps, 11 ectopic pancreatic tissue, 7 Vanêk's Tumour, 3 NET, 1 solitary nodal malign lymphoma, 43 others. Duodenum (N=17, 5.5%): 5 adenoma, 1 NET, 11 others. Colon (N=111, 36.2%): 1 adenocarcinoma, 98 adenoma, 12 others. Rectum (N=73, 23.8%): 5 adenocarcinoma, 1 squamous cell dysplasia, 51 adenoma, 16 others.

Conclusion: ESD is a safe technique in daily clinical practice if performed by experienced endoscopists. With a high rate of successfully treated tumours it appears to be a favourable choice of treatment for such lesions.

Feasibility of ileal intubation in colonoscopy with Endocuff: a prospective open label comparison

O18

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Background: Endocuff (EC) is a mucosal exposure device attached to the distal tip of the colonoscope. Adenoma detection rate (ADR) can be improved with EC and the examination time (without reducing the ADR) can be reduced (1,2). The use of EC influencing the ileum intubation rate (IIR) has been investigated in only two studies as secondary endpoint with contradictory results (3,4).

Methods: We prospectively analysed the use of an EC and ileum intubation at the Kantonsspital St. Gallen in Switzerland between January to December 2018 performed by 3 experienced endoscopists and 1 trainee. Scientific data security were approved by the local ethics commission (EKSG14/099). EC was only applicated for screening or follow-up colonoscopy. The withdrawal time had to be at least 6 minutes. Significance was calculated with the Fishers Exact Test. Adenoma detection rate (ADR) was determined.

Results: We included 570 patients, median age 60 years (range 21-94), 51% were male. Of the 570 colonoscopies, 63% were performed with EC (n=359). Colonoscopy with EC and intubation of the terminal ileum was achieved in 85.8% (308 of 359 patients). Without EC, the ileum was intubated in 82% (173 of 211 patients). There was no significant difference (p=0.234). ADR with EC was 45% and without EC 43%, p< 0.00001. IIR for the trainee (n=87) was 71% with EC and 76% without EC (p=0.81).

Conclusions: Colonoscopy with the use of Endocuff achieved the same ileum intubation rate as without Endocuff. The need of ileum intubation therefore is not an argument against the use of Endocuff. In contrast, the ADR significantly improves with the use of an EC.

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Clinical outcome after single EsoFLIP dilation in patients with achalasia

O19

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Background

Achalasia is a chronic esophageal motility disorder characterized by impaired relaxation of the lower esophageal sphincter, determined by an elevated integrated relaxation pressure (IRP>15mmHg) and absent peristalsis. A new advanced hydraulic dilation technology, the esophageal functional luminal imaging probe (EsoFLIP), facilitates a comprehensive 2D color plot illustration of a hollow organ, simultaneously assessing diameter, cross-sectional area and intra-balloon pressure. The aim of our study was to evaluate the treatment response after single EsoFLIP dilation in patients with achalasia and evaluate the safety profil.

Methods

Dilation was performed under endoscopic control with the EsoFLIP device using a self-developed dilation algorithm starting with an initial balloon volume of 30ml, followed by stepwise volume additions of 5 ml until a maximum of 50ml. Further volume increases were individually tailored at 1-2ml intervals until a maximum diameter of 25-27mm across the EGJ was reached and/or intraballoon pressure exceeded 100 kPa. Symptom scores were assessed by the Eckardt score (ES) before and earliest 1 week after intervention. Timed barium esophagogram (TBE), obtaining images at 1,3 and 5 minutes after drinking the contrast agent, was performed before and after dilation to assess esophageal emptying.

Results

Treatment-naive patients with idiopathic achalasia with type I-III (n=26, mean age 54: range 25-86, 7 females) underwent a single hydraulic dilation performed with the EsoFLIP device. Diagnosis was based on high-resolution manometry findings according to Chicago Classification 3.0. The median maximum dilation volume was 62 ml, corresponding to an EGJ median maximum dilation diameter of 25.6 mm with a median maximum cross sectional area of 515 mm^2 at an intraballoon pressure of 42 kPa. Total ES was reduced from 7 at baseline to 1 post-intervention (p<0.001). The median height of the barium column was reduced from 5.6 cm to 2.5 cm at 1 minute in the TBE (p=0.006), 5cm to 0.5cm at 3 minutes (p<0.002) and 3.0 cm to 1.0 cm at 5 minutes (<0.005). No major complications like hospitalization, perforation or severe bleeding occurred. Two of the included patients developed/aggravated reflux symptoms caused by dilation (assessed by need for post interventional acid-suppressive medication).

Conclusion

Our interim results of a single, individualized EsoFLIP dilation in patients with achalasia in a real-world setting demonstrate good efficacy in both subjective and objective short-term treatment outcome with favorable side effect profile. We are currently collecting further data from our cohort including additional tailored dilations.

Functional Luminal Imaging Probe (EndoFLIP®) unveils endoscopically non-visible esophageal strictures in dysphagia patients

O20

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Background: Esophagitis and esophageal strictures are common complications of GERD. Subtle strictures may sometimes escape endoscopic detection. Current guidelines for dysphagia of unclear etiology after extensive workup suggest empiric panesophageal bougie dilation. The Functional Luminal Imaging Probe (EndoFLIP) uses pressure and segmental impedance measurements to determine luminal diameter and distensibility.

Cases: We present 2 cases of patients with dysphagia of unclear etiology, non-responsive to high-dose PPI. Patient 1 presented with symptomatic reflux and dysphagia with overlapping endoscopic signs of GERD and eosinophilic esophagitis, but without histologic features of EoE. Signs and symptoms of GERD responded to PPI. Patient 2 suffered from dysphagia, intermittent cervical, and retrosternal cramps. Endoscopy showed a small hiatal hernia, barium swallow and CT were unremarkable. HR-Manometry studies produced conflicting results: ineffective esophageal motility and distal esophageal spasm.

Results: EndoFLIP measurement uncovered endoscopically non-visible strictures in the distal esophagus and obviated the need for further cumbersome testing or empiric therapies. Targeted endoscopic dilatation using the EsoFLIP balloon led to complete symptom resolution in both patients.

A Specific Subtype of Hepatitis E Virus Circulates Widely in Switzerland

O21

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Background: Infection by hepatitis E virus (HEV) genotypes (gt) 3 and 4 has been recognized as a primarily porcine zoonosis. Here, we analyzed HEV sequences from patients with hepatitis E acquired in Switzerland.

Methods: RT-PCR and Sanger sequencing were carried out on plasma samples from 114 patients with PCR-proven acute or chronic hepatitis E acquired in Switzerland, followed by subtype assignment and phylogenetic analyses.

Results: Genotyping revealed that almost all infections were by HEV gt 3; only three were by gt 4. Importantly, 77% of the gt 3 isolates were by the newly proposed subtype 3s. This subtype has been identified only in Switzerland so far, in swine and in food products, indicating that it circulates widely in the country, including in the food chain. Interestingly, three immunosuppressed solid organ transplant recipients were found to be infected with rabbit HEV.

Conclusions: Our observations lend support to the proposed HEV subtype 3s circulating and representing the major cause of hepatitis E acquired in Switzerland. This specificity is likely explained by the fact that 96% of the pork meat consumed in Switzerland is from local production and that only very limited amounts are imported or exported. Next-generation sequencing of full-length HEV genomes is ongoing and shall allow to further validate the hypothesis of a Swiss HEV subtype.

Real-World Effectiveness and Safety of Glecaprevir plus Pibrentasvir in HCV: Postmarketing Observational Data from Switzerland

O23

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Background: In the era of pangenotypic treatment regimens against hepatitis C virus (HCV) infections, data from postmarketing observational studies (PMOS) are crucial to better understand the treatment patterns used in specific countries and treatment outcomes under real-life conditions. We report data from Switzerland from an ongoing, multinational PMOS on the pangenotypic regimen of glecaprevir (NS3/4A protease inhibitor) and pibrentasvir (NS5A inhibitor), coformulated as G/P. **Methods:** Adult patients infected with chronic HCV genotypes (GT) 1-6 were eligible to participate in the PMOS if they started G/P at the treating physician's discretion according to local clinical practice, international recommendations, and local label. Baseline and safety data were summarized for all patients who received ≥1 dose of G/P. Effectiveness (% patients with sustained virologic response at 12 weeks after end of treatment [SVR12]) was assessed for all treated patients who reached post-treatment Week 12 (per protocol analysis, data cut-off 31 Jan 2019). **Results:** In Switzerland, 107 HCV patients received ≥1 dose of G/P (94.4% non-cirrhotic; 43.9%/14.0%/29.0%/13.1% GT1/GT2/GT3/GT4; 89.7% treatment-naïve; 91.6% assigned to 8-week G/P regimen). Common concomitant drugs included methadone (8.4%), acetylsalicylic acid (7.5%), mefenamic acid (7.5%), and amlodipine (5.6%). At the cut-off date, 71 of 73 patients (97.3%) achieved SVR12 (95% CI 90.5%, 99.2%). The 2 failures were due to relapse; both failures were GT3, without cirrhosis, treatment naïve, current or former illicit drug-users. G/P was well-tolerated with no serious adverse events (SAEs) and no AEs leading to discontinuation or interruption of G/P treatment. The only AEs reported in >1 patient were fatigue (3.7%), dyspepsia (2.8%), nausea (1.9%), and headache (1.9%). Treatment and follow-up are currently ongoing. **Conclusion:** Real-world effectiveness and safety of G/P in patients from Switzerland were consistent with those seen in the multinational registration trials.

Liver function assessment by ^{13}C-methacetin test before and after placement of a transjugular portosystemic shunt: A prospective pilot study

O22

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Background: Transjugular intrahepatic portosystemic shunt (TIPS) placement can lead to severe complications such as hepatic encephalopathy or acute-on-chronic liver failure. Risk factors for the development of such post-TIPS complications are ill-defined. A point-of-care diagnostic ^{13}C-methacetin test for the determination of maximal liver function capacity (LiMAx®) has been developed and validated by predicting adequately post-operative liver failure after liver resection. The aim of this prospective study is to evaluate the performance of LiMAx® before and after TIPS placement and to ideally correlate pre-TIPS measurements to post-TIPS outcomes.

Methods: To date, fifteen patients undergoing TIPS placement were tested before (-1 day) and after (+1, +7, + 28, +72 and +180 days) the intervention for: LiMAx®, hepatic encephalopathy (critical flicker frequency, Stroop & connect the numbers test), laboratory (MELD score) as well as imaging of the TIPS flow by Doppler ultrasound. Patients with TIPS indication for acute bleeding were excluded.

Main result: ^{13}C-methacetin test shows a rapid, persistent and significant decline already one day after TIPS placement.

Conclusions: Our preliminary results indicate that the ^{13}C-methacetin (LiMAx®) test is a sensitive method for capturing decrease in liver function after TIPS placement and could serve as predictor for post-TIPS complications.

Large-scale screening is not useful to identify individuals with hepatitis B or C virus infection: Final results of a Swiss prospective study

O24

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Introduction: Current treatments are able to control HBV replication and to eradicate HCV in almost all cases. Further improvements in the management of HBV and HCV infections will be possible by focusing on treatment impact at a population level for which screening is an essential step. As many patients with HBV or HCV infection are still undiagnosed, large-scale screening could be useful. **Aim:** To investigate whether large-scale screening for HBV or HCV infection (e.g. risk-based vs. age- based) could identify infected individuals. **Methods:** Individuals between 18 and 80 years attending the pre-operative consultation prior to minor surgery in a general surgical outpatient clinic were tested for HBsAg, anti-HBc and anti-HCV from November 2014 to November 2018. The presence of anti-HCV was confirmed by an Immunodot test. HBV DNA and HCV RNA were determined in HBsAg- and anti-HCV-positive individuals. **Results:** Among 3000 individuals tested, 7 were positive for HBsAg (0.26%) and 4 had detectable HBV DNA. Twelve individuals were positive for anti-HCV antibodies (0.44%). Two of them had detectable HCV RNA (0.07%) and 10 had undetectable HCV RNA (5 spontaneously and 5 after a successful antiviral treatment) (Fig 1). When compared to HCV negative people, HCV positive individuals had already been screened more frequently for HCV (83.3% vs. 12.8%, p<0.001) as well as for HBV infections (66.7% vs. 21.5%, p=0.001), had more frequently anti-HBc antibodies (33.3% vs. 4.2%, p=0.001), had more frequently HCV household members (16.7% vs. 1.7%, p=0.02), and had used more frequently intravenous drugs (66.7% vs. 0.1%, p<0.001), nasal drugs (58.3 vs. 6.2%, p<0.001) or cannabis (58.3% vs. 7.9%, p<0.001). None of HCV positive individuals were immigrant from an endemic area. The median age of HCV positive individuals was not different from that of those who were HCV-negative (52 years [range: 39-59] vs. 44 years [95% CI: 43-45], p=0.1). Most of the positive individuals were already aware that they were infected (86% of the HBV positive individuals and 100% of the HCV viremic individuals). **Conclusions:** In this prospective study performed in a general surgical outpatient clinic, a large-scale screening was not useful to identify individuals with undiagnosed HBV or HCV infection. Screening for HBV and HCV infection should focus on individuals with well-known risk factors.

Assessment of radiological rectal cancer restaging after chemoradiotherapy

O25

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Background: Patients with rectal cancer and complete response to chemoradiotherapy (CRT) can be treated with the aim of organ preservation by applying a watch and wait strategy. However, if secondary radical surgery is needed due to cancer recurrence, this may be associated with an increased complication rate or even worse prognosis. This study aims to assess the accuracy of radiological restaging after CRT.

Methods: Patients undergoing surgery for rectal cancer after CRT at our institution prior to the implementation of an organ preservation program were analyzed retrospectively. For all patients radiological T and N restaging by MRI after CRT but prior to surgery was compared to final pathological T and N staging. The rates of over- and understaging and sensitivity for radiological prediction of complete response were calculated.

Results: Radiological T stage after CRT was underestimated in 20% (11/55), correct in 38.2% (21/55) and overestimated in 41.8% (23/55) of patients. Radiological N stage was underestimated in 14.6% (8/55), correct in 63.6% (35/55) and overestimated in 21.8% (12/55) of patients. Five patients out of 55 patients (9%) showed pathological complete response after CRT. Radiologically, complete response was suspected in only one of these five patients (sensitivity for complete response 20%).

Conclusions: Radiological assessment after CRT resulted in the correct tumor and nodal stage in about half of the examined patients. Overestimation of T and N stage was more frequent than underestimation, this is most probably due to remaining scar tissue after CRT. No patient was incorrectly staged as T0 or N0. Pathological complete response could be predicted correctly in only one of five patients. Therefore, clinical examination and endoscopy remain very important in the evaluation of rectal cancer after CRT. Further, histological or molecular markers are needed to better predict response to CRT and to identify patients that qualify for organ preservation.

Meta-analysis of randomized controlled trials of surgery for rectal cancer

O26

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Background

The mainstay of treatment of rectal cancer includes total mesorectal excision (TME) of the rectum. The present analysis compares surgical approaches for rectal cancer.

Methods

A systematic literature review and Bayesian network meta-analysis of randomized controlled trials (RCT) was performed.

Results

29 RCT's with 6'237 participants were included comparing: open vs laparoscopic vs robotic vs transanal TME. No differences were identified in intraoperative and postoperative morbidity expect blood loss, wound Infections, hospital stay and time to bowel movement which were less with minimal invasive techniques. Also no difference for nodes retrieved, involved distal margin, overall survival, and recurrence. Laparoscopic surgery resulted in more incomplete TME's and in more involved circumferential resection margins (CRM). Robotic surgery resulted in longer distal resection margin. Transanal TME had higher probability of being the best treatment for complete TME and regard to involved CRM

Conclusion

The different surgical techniques result in comparable perioperative morbidity and long-term survival. Minimal invasive approaches improve postoperative recovery, and the open and transanal approaches may improve oncological resection.

Survival after hepatectomy for colorectal liver metastases is a function of intrahepatic recurrence but is not dependent of recurrence at the liver resection margin: a bicentric experience

O27

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Background: Resection margin status is associated with oncologic outcomes following liver resection for colorectal liver metastases (CLM). Previous studies however, did not differentiate between true local recurrence at the resection margin (TLR) versus recurrence elsewhere in the liver. This study aims to determine if resection margin represents a surrogate of advanced disease while not determining location of recurrence.

Methods: Clinicopathological data of patients who underwent curative hepatectomy for CLM between 2012 and 2017 at two major hepatobiliary centers in Bern, Switzerland, and Berlin, Germany, were assessed. Follow-up cross-sectional imaging following hepatectomy was reviewed by an independent radiologist to identify the presence and location of recurrent disease. Location of intrahepatic recurrence was distinguished between TLR (only at the resection margin) versus intrahepatic recurrence elsewhere with or without additional TLR.

Results: During the study period, 345 patients underwent liver resection for CLM with curative intent. Surgical margins were positive for tumor cells (R1) in 66 patients (19%). After a median follow-up time of 34 months, tumor recurrence was identified in 154 patients (45%). Location of recurrence disease was independent from the R1 status (p = 0.555). TLR was not associated with worse overall survival among patients with recurrent disease (TLR vs. any recurrence ± TLR: 3-year OS: 78% vs. 64%, p = 0.454). Additionally, 3-year overall survival was equivalent in patients with TLR or recurrence elsewhere intrahepatic ± TLR (78% vs. 55%, p = 0.436). Patients with intrahepatic recurrence benefited from local hepatic therapy in comparison to patients that did not receive local hepatic therapy (3-year OS: 77% vs. 52%, p = 0.001).

Conclusions: TLR after liver resection for CLM is not associated with worse overall survival compared to other intrahepatic or extrahepatic recurrence. If local treatment for intrahepatic recurrence is possible survival can be prolonged.

Single cell RNA-seq Atlas of a Regenerating Liver in Mice

O28

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Background Liver regeneration is initiated by loss of hepatic tissue to restore homeostatic levels of liver mass and function. The main mechanism is proliferation of parenchymal cells, nevertheless this complex and orchestrated process requires the coordination of multiple cell types in a spatially and temporally regulated manner. Using single cell RNA-seq, we reveal the cell specific contribution to early events during liver regeneration.

Methods Liver regeneration was initiated using a standard two-thirds partial hepatectomy (PH) model in C57Bl/6 mice. Hepatic cells were isolated by a two-stage collagenase in situ digestion. scRNA-seq libraries were prepared from 5000 cells from sham control, 3 hours, 6 hours and 24 hours after PH in duplicate using the Chromium Single Cell 3' library & Gel Bead Kit v3 according to the manufacturer's protocol (10xGenomics). Samples were sequenced on a NovaSeq 6000 S2 flow cell. Seurat clustering algorithm and SinglerR were used to identify different cell populations and their markers.

Results We profiled the transcriptome of 12607 single cells of the parenchymal and non-parenchymal fraction over 4 time points from 8 mice. Unsupervised clustering identified 20 subpopulations of cholangiocytes, B cells, stellate cells, dendritic cells, granulocytes, monocytes, T cells, NK cells and distinct types of hepatocytes, macrophages and endothelial cells varying over time.

Conclusion Our results provide a genome wide picture of liver regeneration at a single cell level and reveal the regulated genes in each cell population after partial hepatectomy.

Minimal-Invasive Versus Open Hepatectomy for Colorectal Liver Metastases: Bicentric Analysis of Postoperative Outcomes and Long-Term Survival Using Propensity Score Matching Analysis **O29**

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Background: Minimal-invasive hepatectomy (MIH) has been increasingly performed for benign and malignant liver lesions with promising results. However, oncological results after MIH for the treatment of patients with colorectal liver metastases (CLM) need to be clarified. **Methods:** Clinicopathological data of patients who underwent liver resection for CLM between 2012 and 2017 were assessed within a training cohort at a Swiss major hepatobiliary center and a validation cohort at a major hepatobiliary center in Germany. Postoperative outcomes und long-term survivals of patients following MIH were compared with those of patients undergoing conventional open hepatectomy (OH) after 1:1 propensity score matching. **Results:** During the study period, 91 patients underwent liver resection for CLM with curative intent at the Swiss center. Twenty-five patients underwent MIH and were compared with a matched cohort of 25 patients who underwent OH. MIH was associated with lower major complication rate (4% vs. 28%, p=0.049) and shorter length of hospital stay (5 vs. 9 days, p<0.0001) compared to OH. Postoperative mortality (0% vs. 0%) was comparable between MIH and OH. After a median follow-up time of 47 months, 5-year overall survival (OS) was significantly higher after MIH than after OH (59% vs. 45%, p=0.046).
When evaluating the validation cohort of 270 patients in the German center matching 53 patients undergoing MIH with 53 patients undergoing OH, the benefits of MIH for CLM could

be confirmed. MIH was associated with lower postoperative major complication rate (17% vs. 36%, p=0.028), and shorter length of hospital stay (9 vs.11.5 days, p=0.025) compared to OH. Postoperative mortality was comparable between MIH and OH (0% vs. 6%, p = 0.243). After a median follow-up time of 26 months, 5-year OS was significantly higher after MIH than after OH (61% vs. 42%, p = 0.004). Comparing the results of the two surgical departments, major complication rates (4% vs. 17%, p=0.155), mortality rates (0% vs. 0%), 5-year OS rates (61% vs. 59% p=0.366) and 5-year disease-free survival rates (58% vs. 44%, p=0.330) were not significantly different.
Conclusions: MIH for CLM is associated with lower postoperative morbidity and shorter length of hospital stay, resulting in oncologic outcomes superior to those achieved with the established OH. Our findings suggest that MIH should be considered as the preferred method for the treatment of curatively resectable CLM.

Inherited polymorphic p53 response elements in the human genome interact with somatic p53 mutations to affect patient survival: a pan-cancer analysis. **O30**

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Background: p53 is a transcription factor that acts as a tumour suppressor in a wide range of human cancers. This key role of p53 implies that inherited single nucleotide polymorphisms (SNPs) in functional p53 response elements (p53RE) could affect cancer progression. The identification of such variants and their possible interaction with somatic p53 mutations has the potential to identify tumours with an aggressive biological phenotype and guide personalised treatment strategies.
Methods: In an integrative analysis, we utilize newly abundant genomic functional data, binding pattern algorithms and catalogues of inherited human variation to generate detailed genome-wide maps of polymorphic p53RE. We explore those maps to identify p53RE SNPs in the human genome that may influence patient survival utilizing the Cancer Genome Atlas (TCGA) database. In total, 7021 patients who underwent a surgical intervention across all cancer types with known somatic p53 mutation status and an in-depth characterisation of germline genetic variation were included in the study.
Results: We identify functional p53 RE SNPs that show significant allelic differences in patient survival both across all cancer types as well as in individual p53-dependent common tumours, such as colorectal, breast, lung and brain cancers in a p53 mutation status-dependent manner (up-to p=1.96x10^{-6}, hazard ratio, HR=5.41, Cox multivariate analysis).
Conclusions: The identified polymorphisms in functional p53 REs have the potential to serve as predictive biomarkers of cancer survival and could help guide personalised treatment strategies in a wide range of p53-dependent tumour types.

MINIMAL LENGTH OF PROXIMAL RESECTION MARGIN IN ADENOCARCINOMA OF THE ESOPHAGOGASTRIC JUNCTION: A SYSTEMATIC REVIEW OF THE LITERATURE. **O31**

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The minimal length of proximal margin (PM) in esophagogastric junction cancer has not been established yet and its impact on patient survival remains unclear. Pubmed, Embase and Scopus databases were searched for «adenocarcinoma of the esophagogastric junction», «adenocarcinoma of the gastroesophageal junction» and «cardia cancer», each combined with «proximal margin». English written studies that specified PM length in AEG were included. Survival data in relation to PM were extracted. 13 studies, that were all retrospective case series, with in total 2648 patients met inclusion criteria. While 93% of 230 patients with Siewert type I had esophagectomy, 69% of 1270 patients with Siewert type II and 93% of 872 patients with Siewert type III had transhiatal extended gastrectomy. Minimal PM length was treated by 5 studies and ranged between 2--6cm. While 3 studies defined minimal PM by the necessary length to obtain R0 resection, 2 studies found minimal PM length significantly associated with survival. Multivariate analyses revealed in 2 studies an independent impact of PM on survival, whereas 1 study did not found any significant relation between PM and survival. 1 study showed that PM length was significantly associated with survival in T2--4N0--2 tumors, but not in T1 or N3 tumors.

In conclusion, available retrospective studies did not allow a conclusion for a minimal length of PM and showed no clear evidence for an impact of PM length on survival. Taking into consideration available data and the shrinkage phenomen, a PM > 2cm might be necessary to obtain a sufficient PM.

4 years experience of robotic-assisted (da Vinci Xi) giant hiatal hernia repair: feasibility, quality and comparison to the standard laparoscopic approach **O32**

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Background
After 4 years of experience we evaluate the feasibility and quality of robotic-assisted giant hiatal hernia repair compared to the standard laparoscopic technique during that period.

Methods
This is a retrospective analysis of prospectively collected data between July 2015 and May 2019 of patients with type III or IV hiatal hernia who underwent elective surgical therapy. In 51 patients robotic-assisted surgery was performed, a conventional laparoscopic hiatal hernia repair was done in 38 patients. Mann-Whitney-U Test was used for statistics. Significance level for P-Value < 0.05.

Results
Mean operating time was 221min (Rob) vs. 165min (Lap) (p<0.05). 51 (Rob) compared to 23 (Lap) mesh-augmentations were carried out. Intraoperative complications occurred in 5 (Rob) vs. 7 (Lap) patients (p=n.s.). Postoperative morbidity was 10% (Rob) to 0% (Lap) (p=n.s.). There were 6 (Rob) compared to 1 (Lap) recurrences (p=n.s.) during the study period (1-46m).

Conclusion
The da Vinci Xi System is safe, feasible and equivalent to the laparoscopic technique. Even during the learning curve perioperative results applying robotic technique are comparable to the laparoscopic approach.

Laparoscopic surgery for gastric cancer: the European point of view. O33

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Abstract Objective
Multiple Asian studies have proved the feasibility of laparoscopic approach for surgical
treatment of gastric cancer. The difference between Asian and European patients could limit their application in Europe. We reviewed the literature for European studies comparing open gastrectomy with laparoscopic approach in the treatment of gastric cancer.

Method
We searched the keywords gastric cancer and laparoscopy in MEDLINE and EMBASE. We included all studies published between 1990 and 2016 and conducted in Europe.

Result
We found 1 randomized and 13 cohort studies compared laparoscopic with open gastrectomy. We found no mean difference in the number of lymph nodes harvested between laparoscopic and open group (mean difference: -0.49. 95% CI: -2.42; 1.44, p=0.62) and no difference of short term or long term mortality (Short-term Odds Ratio: 0.74, p=0.47 , Long-term Odds Ratio: 0.65, p=0.11). We found a longer operative time in the laparoscopic group (Mean difference: 35.75 minutes, p<0.01) but lesser re-operation rate than the open group. (Odds ratio:1.55 p=0.01)

Conclusion
European based population studies found results comparable with their Asian counterpart. In the current state of evidence, minimally invasive surgery for gastric cancer is safe and can achieve the same oncological results.

First experience of gastric peroral endoscopic pyloromyotomy (GPOEM) in a Swiss university endoscopic unit. E2

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BACKGROUND
Gastric peroral endoscopic pyloromyotomy (GPOEM) has been regarded as a new and minimally invasive therapy for refractory gastroparesis. This study assessed clinical outcomes and safety after GPOEM performed in a tertiary referral center.
Methods We retrospectively reviewed the first patients who underwent Gastric peroral endoscopic myotomy (G-POEM) from November 2018 to February 2019.
Results This study included 4 patients, 3 males and 1 female. All patients had refractory gastroparesis confirmed on gastric emptying scintigraphy (GES). 1 patient had idiopathic gastroparesis, 1 patient had diabetic type 1 gastroparesis and 2 patients had postsurgical gastroparesis (gastropexie and laparoscopic Nissen fundoplication respectively). GPOEM was technically successful in all cases. The mean procedure time was 52 min. Mean length of hospital stay was 36 hours (24 hours for 3/4 of patients and 72 hours for 1/4 patients). We faced off only with mild adverse events with one case of intra operative submucosal bleeding treated endoscopically. Overall, clinical success was 100 % (4/4) with a significant improvement in quality of life. The mean GCSI score at baseline was 3.05 and 0.17 at 3 months after GPOEM. 2 patients had resolution of diarrhea after endoscopic procedure. Symptoms improvement was almost immediate with a diet consisting of clear drinking 6 hours postoperatively and a normal diet the day after surgery.
Conclusions GPOEM results in improvement for all symptoms of gastroparesis in our few patients. This short series demonstrates that gastric peroral endoscopic myotomy is a safe and effective treatment for gastroparesis.

Endoscopic treatment of large esophageal leaks E1

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Background: Esophageal leak is a life-threatening condition. Self-Expandable Metallic Stents (SEMS) are used to treat a wide variety of esophageal conditions. However, large leaks remain a therapeutic challenge. Use of SEMS might be insufficient and require other endoscopic procedures as the endoscopic Vacuum Therapy (eVAC). The aim of this study is to assess the efficacy of these endoscopic procedures.
Methods: We realized a retrospective, monocentric study in a tertiary university center of patients who underwent endoscopic treatment (SEMS and eVAC) for large esophageal leak, between January 2016 and December 2018. Large esophageal leaks were defined as a defect of more than 1 cm. All patients were included without restriction.
Results: A total of 21 patients (85.7% male, mean age of 69 years) were included. 3 patients (14.3%) had non surgical perforation,18 (85.7%) had an anastomotic leakage post surgery, for an oncological constellation in 16 patients (76.2%). For leakage post surgery, first stent was positioned after a median of 11 days after surgery. We used fully-covered SEMS in 6 patients and double-type SEMS from Taewoong® in 15 patients. In all patients, a median of 3 stenting sessions was necessary to achieve healing of the esophageal leak. We used eVAC for 3 patients requiring a median of 7 endoscopic sessions, with a 3 or 4 day interval between these. Fully esophageal rupture healing was completed for 19/21 (90.4%) patients, including the patients who have benefited from eVAC. Because of a pejorative evolution of their condition, 2 patients died before finishing the endoscopic treatment. Successful treatment was completed after a median of 63 days with no relapse after a median of 127 days of follow-up.
Conclusions: Endoscopic treatment of large esophageal leaks is effective. SEMS is the first-line endoscopic treatment. eVAC appears to be an effective option for leaks refractory to SEMS procedure.

Endosopic removal of multiple ingested batteries using a strong magnet E3

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Background: Endoscopic removal of ingested batteries can be challenging if there is a high number of batteries in the stomach, especially when food residues impair visibility in the stomach.
Methods: We describe a novel method for efficient removal of multiple batteries using a strong magnet.
Results: A young female patient was repeatedly referred to our emergency unit after ingestion of multiple batteries (median 8, range 1-50, battery types AA and AAA). Since the usual removal techniques with polypectomy snares and retrieval nets are time consuming, we put a small strong magnet into a foreign body retrieval net already inserted through the working channel of the endoscope. After insertion of an overtube into the distal esophagus, we could easily pass the endoscope loaded with the magnet into the stomach, attach one battery at the time to the magnet, and retrieve it by pulling back the endoscope. The strong magnet was also very helpful for attaching batteries that were not visible due to food residues. Protection of the airways with an overtube was also effective, since no aspiration and no other complication occurred in more than 70 endoscopic interventions.
Conclusions: The use of a strong magnet greatly facilitates removal of multiple batteries from the stomach, even when food residues impair visibility.

Endoscopic ultra-sonography guided drainage of the main pancreatic duct: a Swiss multi-center experience. E4

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Background: Symptomatic main pancreatic duct (MPD) obstruction or leakage are conventionally treated by a trans-papillary drainage. When this approach fails, endoscopic ultra-sonography pancreatic drainage (EUS-PD) appears actually as an efficient and minimal-invasive alternative technique.
Methods: We retrospectively analyzed data from all patients who underwent EUS-PD in the endoscopy centers of the CHUV in Lausanne and Inselspital in Berne between April 2016 and March 2019.
Results: 46 patients (73.9 % male, mean age, 56 years) were included. Technical success, defined as MPD drainage with plastic stent placement, was obtained in 42/46 patients (91.3 %) and led to clinical success (i.e. significant pain reduction at follow up) in 85.1 % of cases. The median diameter of the pancreatic duct was 6mm (3-18mm) and mean procedure duration of 45 minutes. Adverse events were reported as mild (i.e. managed during endoscopy) or severe in 5 cases (10.8 %) each. Among the patients for whom follow-up was continued, 4 (8.7 %) were finally addressed to surgery for persisting symptoms.
Conclusion: EUS-PD is a very efficient and safe alternative to surgery when trans-papillary approach is impossible.

Feasibility of cecal retroflexion in screening colonoscopy with Endocuff E5

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Background: Endocuff (EC) is a mucosal exposure device attached to the distal tip of the colonoscope. It has been shown that both EC and cecal retroflexion can improve the adenoma detection rate (ADR) [1-3]. Feasibility and safety of retroflexion in the cecum with EC has not been reported.
Methods: We prospectively analysed cecal retroflexion with EC in screening colonoscopy at the Kantonsspital St. Gallen in Switzerland between January to December 2018 performed by one experienced endoscopist. The withdrawal time had to be at least 6 minutes. Adenoma detection rate (ADR) was determined.
Results: We included 88 patients, median age 62 years (range 32-76), 55% were male. Cecal retroflexion with EC was feasible in 80 patients (91%). We had no complications especially no perforation. ADR was 68% (n=54).
Conclusions: Cecal retroflexion with Endocuff is feasible without complications in screening colonoscopies.

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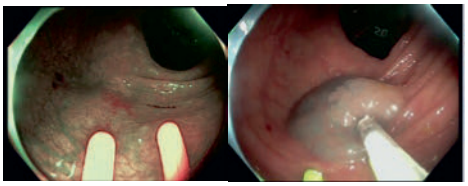
Figure 1a/b: Cecal retroflexion with Endocuff with sessile serrated adenoma



Endobiliary Radiofrequency Ablation (ELRA) for Malignant Billiary Obstruction over 24 months follow-up E6

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Endo Luminal Radiofrequency Ablation (ELRA) for billiary tract neoplasia is a novel treatment modality that is already used in oesophageal, rectal, liver and pancreas tumours.
A 58-year-old woman presented with acute cholestasis 08/15. Due to unclear anatomy after papillotomy and bile stone removal, an MRCP revealed a sclerotizing mass forming stricture at the hilar with dilatation of the left intra-hepatic ducts consistent with Klatskin Tumour (Bismuth IVa). After laparoscopy the situation was judged as inoperable and a ncSEMS was inserted. Tumor progression resulted in restenosis and a second ncSEMS was placed through the first stent in the left main hepatic duct 07/16. After progredient tumor ingrowth despite chemotherapy (Gemcitabine, Cisplatin), we obtained informed consent and performed ELRA 05/17 (Taewoong Medical, Korea). The ELRA-catheter (7Fr, ablation length 18mm) was placed under radiologic control in the tumor stenosis. The bipolar electrode implements a temperature sensor to control ablation (7 Watt, 70°C for 2 minutes). The procedure was repeated to cover the whole length of stricture. Necrotic debris was removed with a balloon while patency was confirmed by contrast. This was repeated every 2-4 months. No immediate or late adverse events were recorded.
On the patients last visit 05/19 she remained asymptomatic at 24 months follow-up after 11 ELRA sessions. She is not jaundiced, gained weight, ECOG=1 and CA 19-9 reduced to 28.9 U/ ml (149 U/ml). Surveillance CT showed presence of the unilateral SEMS in the common and main left biliary duct with slight left intrahepatic duct dilatation and decreased tumor mass, consistent with radiological improvement.
ELRA is a novel modality in the treatment of palliative non-resectable malignant biliary obstruction that proved maintaining SEMS patency.

Endoscopic full-thickness resection (FTRD) of a non-ampullary lesions of the proximal duodenum in a 67 year old patient with attenuated polyposis coli E7

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Background: Pyloric gland adenoma (PGA) is an underdiagnosed, rare entity, mostly be founded in the stomach. Similar to colorectal adenomas PGA`s have a high risk of malignant transformation to adenocarcinoma up to 21-40 %. Endoscopic resections in the duodenum harbor a significant risk of complications. EMR is the current standard technique for treatment of duodenal non-ampullary adenomas. Complete resection rates are considerably high at about 90 %. Adverse events as bleeding was reported up to 25%. ESD is not recommended for resection of duodenal lesions since the perforation rate may be as high as 35%. Use of FTRD in the duodenum are limited to a single case study of 20 patients. Methods: A 67 year old patient with attenuated polyposis coli presented for screening. Gastroscopy showed a 20 mm large, non-ampullary lesions in the proximal duodenum (pars I). The margins of the duodenal lesions was marked with a high-frequency (HF) probe. An integrated balloon dilatation (20mm) of the upper esophageal sphincter and the pylorus was performed to facilitate advancing of the FTRD (Ovesco Endoscopy AG). After pulling the duodenal lesion into the cap with a grasper the FTRD clip was deployed and the lesion immediately resected with the preloaded snare. The resected specimen was retrieved for histopathological analysis. A single-shot antibiotic prophylaxis with 2 g ceftriaxone i.v. was administered during the intervention. Second-look endoscopy was scheduled 24 h after resection. Result: Pyloric gland adenoma of 18 mm in the proximal duodenum (immunohistochemistry positive for Mucin-1, Mucin 5, Mib 1). Conclusions: Herein we present the first case of FTRD duodenal resection in a patient with attenuated FAP and a PGA. There are currently no specific guidelines for the removal and surveillance of PGA. ASGE recommends resection and surveillance endoscopy at 3-5 years interval.

Sloughing oesophagitis: a rare histologic and endoscopic finding

E8

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Background: Sloughing esophagitis or esophagitis dissecans superficialis is a rare benign illness. Endoscopically, it is characterized by sloughing of large fragments of oesophageal mucosa (1). Although the exact pathogenesis remains unexplained and the histopathologic features are inadequately described, an association with caustic or hot beverages ingestion, autoimmune bullous dermatosis (such as pemphigus vulgaris), and drugs such as potassium chloride, nonsteroidal anti-inflammatory drugs and bisphosphonates, has been reported (2). Usually asymptomatic, occasional symptoms may be dysphagia, nausea, bleeding, vomiting, heartburn and odynophagia (3). **Case report:** a 62-year-old woman with a history of WHO obesity class III, status post Roux Y bariatric surgery was seen in the surgical outpatient clinic complaining of upper abdominal pain, pyrosis and light dysphagia. Initial workup included an Esophagogastroduodenoscopy that revealed sloughing of the mucosa in the lower, mid and upper oesophagus, consistent with desquamation and giving the impression of a sheet of mucosal cells. Biopsies were taken from the proximal and distal oesophagus, histopathology of which was reported as squamocolumnar mucosa with acute and chronic inflammation. Microbiology exanimation excluded viral (CMV, HSV) and fungal infection. Patient did not take any medication and responded well to a PPI treatment with alleviation of the symptoms. **Conclusion**: Sloughing oesophagitis is a rare benign entity that endoscopists must be aware of in order not to mistake it with other entities such as reflux, viral oesophagitis or squamous cell carcinoma. The diagnosis is based on biopsies. The natural course appears to be benign with a good prognosis.

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Malignant granular cell tumor (GCT) in the oesophagus - rare and difficult to diagnose

E9

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Background: GCTs are uncommon tumors most probably derived from Schwann cells. Esophageal GCTs are particularly infrequent, and malignant variants have been reported to occur exceedingly rare.
Case presentation: A 41-year-old man was submitted to endoscopy because of unspecific chest pain. During endoscopy, he was found to have a one centimeter subepithelial, polypoid like lesion, Paris 0-Is. Further evaluation using EUS confirmed the presence of a 8 x 6 mm well-demarcated hypoechoic lesion, uT1a, uN2. Repeated biopsies showed highly cellular tissue with atypical cells, not further characterized by immunohistochemistry. The lesion was successfully resected en bloc by a cap-assisted EMR technique. Histology revealed large polygonal cells with abundant granular cytoplasm showing diffuse Periodic Acid Schiff positivity, consistent with a granular cell tumor. Careful histological examination of the GCT, however, detected marked atypia in the tumor cells, infiltrative growth pattern and irregular borders, justifying the final diagnosis of a malignant GCT. The resection margins were tumor free. Follow up after EMR was unremarkable.
Conclusion: Esophageal GCTs should be considered as differential diagnosis of subepithelial lesions in the distal part of the esophagus in asymptomatic patients. Biopsies can show marked reactive changes of the overlying epithelium and ulcerated stroma, which may be a diagnostic pitfall. EUS is the most beneficial diagnostic tool. Complete endoscopic resection of esophageal GCTs either by EMR or ESD is recommended, in particular in the very rare event of a malignant GCT.

EUS-guided hepaticogastrostomy (HGS) with transgastric cholangioscopy (tPOCS) and metal stent insertion for a distal common bile duct (CBD) stenosis in a patient with chronic pancreatitis

E10

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Background: Endoscopic retrograde cholangiography (ERC)-guided drainage is the gold standard to relieve benign or malignant biliary obstruction. If ERC fails, percutaneous transhepatic biliary drainage (PTBD) is usually considered the alternative treatment. However, PTBD is prone for adverse events in up to 77% and can significantly impair quality of life.
Case description: An 80-year old man presented with cholestasis and recurrent cholangitis because of a distal CBD stenosis secondary to chronic pancreatitis. After ERC failure, a PTBD was inserted. Because of recurrent infections, the PTBD had to be removed after several months. Surgical options were declined due to significant comorbidities. Given periodic symptoms, an EUS-guided transgastric HGS stent was placed. Three months later a tPOCS was performed with electrohydraulic lithotripsy (EHL) of several stones in the CBD. After balloon dilation of the distal CBD stenosis, a fully covered metal stent with a long extraction thread was inserted. Six weeks later the stent was extracted and a repeat tPOCS showed an improved stenosis and no residual stones.
Conclusions: EUS-guided HGS with transgastric treatment of biliary obstruction and stones is feasible and safe in patients who failed ERC and PTCD. It allows not only direct visualization of the stenosis but given the large access route and stable scope position, it even offers the possibility of guided biopsies, wire manipulation, dilation of stenoses, EHL, and metal stenting. Metal stent extraction through the HGS is possible, given special stent design with a long extraction thread.

Endoscopic submucosal dissection and unroofing of a symptomatic antral duplication cyst. A case-report.

E11

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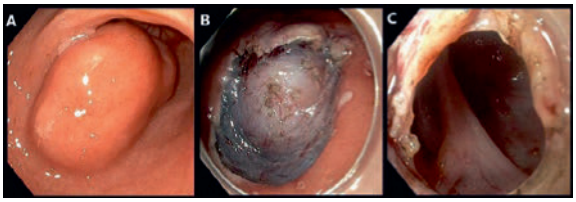
Background: Duplication cysts (DC) are rare congenital malformations that can occur throughout the entire gastrointestinal tract. About 4-9% of these are located in the stomach, where they can cause abdominal pain and symptoms of gastric outlet obstruction. In this case, the preferred method of treatment is surgical excision. Few case reports describe an endoscopic approach by either endoscopic submucosal dissection (ESD) or electrosurgical incision or snare.
Case description: We report a case of a 52-year-old woman with long-standing symptoms of a gastric outlet-obstruction including early satiety, postprandial pain and vomiting due to an antral duplication cyst. She refused surgical excision but agreed to an endoscopic treatment by ESD with unroofing of the cyst, which was performed during a two-day hospitalization. Six months later, she reported complete relief of symptoms.



Conclusion: ESD and unroofing of symptomatic gastric duplication cysts seems to be a feasible option for patients who are no candidates for a surgical intervention.

An Unusual Subepithelial Tumor of Duodenum

E12

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Background: Subepithelial lesions of Duodenum are uncommonly found on upper endoscopy. Differential diagnosis and prognosis are multifaceted.
Methods: We describe an unusual cause of subepithelial lesion in a 64-years-old female patient with a severe anxiety disorder and no further comorbidities.
Results: A 64-years-old female patient was referred for a gastroscopy und colonoscopy because of severe iron deficiency anaemia. The colonoscopy was unremarkable. In the upper endoscopy we found a large, 4 cm pedunculated polyp with a broad base in the second portion of duodenum. We consider GIST as the first differential diagnosis and possible source of intermittent bleeding. Polypectomy was performed after previous application of an endoloop. The histologic and immunhistochemic evaluation found a 15 mm gangliocytic paraganglioma (GPG), extending to the resection margins. In the Re-endoscopy a few weeks later the endoloop was dropped and no tumor was detectable in the biopsy of the resection base. GPG is a benign tumor of the gastrointestinal tract with a low malignant potential. In most cases, it is located in the second portion of the duodenum near the ampulla of Vater. Overall incidence is very low, with only about 200 cases reported since. The treatment of choice is complete endoscopic or surgical resection. Because of the small malignant potential and the R1 resection of the tumor in our case the further approach needs to be discussed interdisciplinary.
Conclusion: GPG is a very rare cause of submucosal Tumor of Duodenum with a good prognosis. Although the malignant potential is low, complete resection, in most cases endoscopically is the treatment of choice.

Endoscopic rescue therapy of a distally perforated, retroperitoneal stent after EUS-guided pancreaticogastrostomy

E13

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Endoscopic therapeutic transgastric pancreatic duct access is gaining increasing popularity for various reasons and report of potential complications is crucial for an improved outcome.
A 42-year old woman was admitted with recurrent acute abdominal pain related to an alcohol induced chronic pancreatitis with a significantly dilated pancreatic duct (PD). ERCP failed twice and surgical interventions were declined, because of severe malnourishment and advanced liver disease. Given increasing symptoms, we opted for an EUS-guided pancreaticogastrostomy (PGS), inserting a straight stent, which allows an unproblematic stent extraction using a stent retriever and consecutive PD access during follow-up procedures.
The patient missed her regular 3-month follow-up appointment and presented with acute abdominal pain five months later. CT scan showed a distally perforated transpancreatic position of the PGS stent. Wire canulation of the dislodged stent failed, therefore it was extracted by a snare. After careful insertion of a thin papillotome into the gastrostomy site, wire access of the PD was gained. Using a combination of cumbersome drilling maneuvers with a 5F stent retriever and the cystotome, the wire was advanced into the duodenum. After balloon dilation of the stenosed tract, a stent was placed though the pancreas into the duodenum, creating a gastropancreaticoduodenostomy. Six weeks later a pancreatoscopy confirmed completely resolved PD stones and a partial regression of the ductal stenosis. Retroperitoneal perforation of a PGS stent is a rare complication, but in view of generally poor surgical candidates, an endoscopic strategy is definitely preferable over a surgical intervention. Interventional endoscopists who are dealing with this kind of EUS procedures should be aware of this complication and have the armamentarium of solving challenging problems.

Endoscopic intra-abdominal rescue therapy of a dislodged EUS-guided hepaticogastrostomy stent

E14

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EUS-guided hepaticogastrostomy (HGS) is a well accepted alternative treatment for patients with biliary obstruction and failed ERCP. Complications include abdominal pain, infection, hemorrhage, pneumoperitoneum, biliary leakage and dislodged stents. In cases of dislodged stents, those patients suffer early on from acute biliary peritonitis and need urgent surgical repair. We report the case of an 86-year old fragile female who was admitted with painless jaundice and massively congested intrahepatic ducts secondary to a locally advanced pancreatic cancer with hilar lymphadenopathy. An ERCP was attempted, but only pancreatic access could be gained and a prophylactic stent was placed. To relief cholestasis, an EUS-guided HGS was performed, but overnight, she became hemodynamically unstable and a papillary bleeding was stopped by applying three clips. Next day the patient vomited heavily, developed an acute abdomen and a CT scan showed a dislodged HGS stent. A large gastric defect could be easily accessed by a nasal gastroscope and the SEMS was accidentally extracted during the attempt of replacement. A Jagwire was advanced through the hepatic access site and an 80mm long Gioborstent could be placed. A second SEMS was inserted to prevent repeat dislocation by extending far into the stomach.
Dislocation of a HGS stent is a rare but important complication. Given often weak patients, a rescue therapy apart from surgery would be beneficial. In our case the stent has been in place correctly for two days and therefore it was possible to access the abdominal cavity through the already large gastric defect. Stents with a longer uncovered part inside the liver should anchor better and normally it should be easier to reposition them without complete dislocation. Using fully or almost fully covered stents, the described technique might be preferable, as it provides a better control of the exact stent replacement.

Oeso-mediastinal fistula complicating tuberculosis and cervical lymp node involvement

E15

S.Guglielmi, G.Guglielmi, S.Mönig, J-P Janssen, L.Spahr. Gastroenterolology, Radiology, Visceral Surgery, Pneumology, HUG

Oesophageal involvement is a are complication of tuberculosis (Tbc), that may occur due to adjacent abscess or contamination by infected saliva in an preexisting injured oesophageal mucosa. We report here a case of a favorable evolution of an oeso-mediastinal fustula following medical treatment of Tbc. Patient/Methods : A 19 year-old indian woman living in Switzerland since 2017 was diagnosed with miliary Tbc in October 2018, with pulmonary and ganglionic (hepatic hilum and cervical adenopathy) involvement. She had no HIV infection. Quadritherapy treatment was initiated followed by resolution of fever and night sweats. However, after 1 month of treatment she developed progressive dysphagy and lost 8 kg of BW consecutively. An upper GI endoscopy showed an 2 cm ulcer located in the mid third of the oesophagus, with biopsies negative for granulomas and cancer, but positive for Mycobacterium Tbc (PCR). CT-SCAN revealed a paradoxical increase in size of cervical adenopathy and pneumomediastinum secondary to oeso-mediastinal fistula. A multidisciplinary team discussion considered surgery or endoscopic covered stent, but decision was made to manage the patient conservatively by optimizing antibiotic treatment (Bactrim for 1 month), PPI (omeprazole) and magaldratum (Riopan 4 times daily). A surgical drainage of cervical adenopathy was also secondarily performed. Results : Dysphagia progressively improved over a 2-month period, and a repeat endoscopy demonstrated a slightly retractile scar with complete mucosal healing of oesophagus and no stenosis. A similar positive evolution was also seen at follow-up imaging. She regain weight and completed the full course for Tbc treatment uneventfully. Conclusion : This is a rare complication of miliary Tbc, the management of which is poorly codified. Early diagnosis and optimized medical treatment led to symptoms resolution and control of this severe infectious disease.

Rescue EUS-guided gastro-pancreaticogastrostomy after failed transgastric ERP in a patient with obstructive chronic pancreatitis in the pancreatic head

E16

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Background: Endoscopic retrograde pancreaticography (ERP) is an effective treatment for pancreaticolithiasis. In cases of failed ERP, endoscopic ultrasound-guided pancreaticogastrostomy (EUS-PGS) has recently gained popularity. This transgastric route offers pancreatic duct access for further advanced interventions.
Case description: A 72-year old male with a past medical history of chronic alcoholic pancreatitis presented with a recurrent episode of acute pancreatitis. An EUS showed a 7mm, impacted intraductal stone in the pancreatic head and a leakage of the distal main duct. An EUS-PGS was performed and confirmed the rupture of the pancreatic duct (PD). Given severe abdominal inflammation, the only possible PD puncture site was from below the gastric incisura. A plastic stent was inserted for three months and the patient rapidly improved. However, given the difficult unstable scope position, a transgastric ERP failed. Due to recurrent symptoms one year later, a repeat EUS-PGS was performed gaining PD access through the gastric body. As the previous PGS-site was still patent, a stent was inserted entering the distal pancreatic duct and exiting through the old puncture site, creating a gastro-pancreaticogastrostomy. Currently the patient is symptom free and a transgastric pancreatoscopy with stone therapy is planned in the near future.
Conclusions: EUS-guided PGS with intraductal treatment of main pancreatic duct obstruction or rupture is feasible and safe in patients after failed ERP. To allow transgastric PD access for further interventions, the selection of the initial puncture site is crucial, while the gastric body is preferred.

Endoscopic ultrasound-directed transgastric ERCP (EDGE) in a patient with choledocholithiasis after Roux-en-Y gastric bypass (RYGB) and inadvertently interposed colon

E17

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Background: Increasing prevalence of obesity led to growing rates of bariatric surgery, including RYGB. Conventional endoscopic retrograde cholangiography (ERC) is rarely successful in these cases given altered anatomy. Current alternatives like balloon enteroscopy-assisted ERC or PTBD are often cumbersome or can cause impaired quality of life and have a significant risk of peri-procedural complications.
Case description*:* We present a 78-year-old woman with acute cholangitis and a past medical history of a RYGB with cholecystectomy. Endoscopic ultrasound (EUS) showed the residual stomach in close proximity to the efferent small bowel loop. An EUS-guided gastro-jejunostomy was performed by placing a lumen apposing metal stent (LAMS). Nine days later she was admitted with rectal bleeding. During gastroscopy the stent was dislodged and a colon loop was found to be interposed between the small bowel loop and the residual stomach. We inserted two LAMS, one connecting the colon with the residual stomach and the other the small bowel loop with the colon.
Results: A regular ERC with complete stone clearance of the common bile duct was then performed and the two metal stents were removed. Finally, the connection between jejunum and colon was closed by an Over-The-Scope-Clip. Six weeks later a colonoscopy revealed no residual fistula between colon and residual stomach.
Conclusions: EDGE in patients with post-RYGB anatomy is normally an effective and safe treatment modality for performing ERC. However, interventional gastroenterologists must be aware of potential complications and its treatment options.

First experiences with ESD + in a 3 cm rectal polyp. A case study at the Stadtspital Waid, Zurich

E18

Breidert M, Tajasev V, Locher R, Zellweger M

Abstract

Background
Endoscopic submucosal dissection (ESD) provides an “en bloc” resection of even large laterally spreading mucosal tumors. It seems also suitable for patients at elevated surgical risk. Due to the retrieval of an “en bloc” specimen and because of the low local recurrence rate, ESD seems to be the preferable procedure over standard “piecemeal” resection, especially because of the high rate of early cancers in large rectal polyps.

Methods:
Case study of resection of a rectal polyp about 3 cm in size (pitt pattern IIIL) with ESD + (Aqanife an Coagrasper with AWC®) in a 48-year-old patient in our clinic. The AWC® (Additional Working Channel) is an endoscopic system for providing an additional working channel for flexible endoscopes.

Results:
The lesion could be removed with good results after an examination duration of 70 min. Histology revealed complete ablation of a tubulo-villous anenoma with mainly low-grade and focal high-grade dysplasia.

Conclusions:
Dissection of polypoid lesions in the rectum by ESD + is safe. The procedure can be considerably accelerated by more exercise.

Endoscopic control interferes with EndoFLIP measurements

E19

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Background: The functional lumen imaging probe (FLIP) system is an FDA approved tool evaluating the esophagogastric junction (EGJ) dynamically. Even though it has been commercially available since 2009, it is still rarely used due to missing consensus in how to perform and interpret test results. Therefore, we aimed to analyze the influence of endoscopic control on the FLIP measurements.

Methods: In this single center, we reviewed data of 93 patients undergoing EndoFLIP between 2016 and 2018 with and without visual endoscopic control. Indications for EndoFLIP diagnostics were symptoms of esophageal dysmotility. EndoFLIP measurements were performed at the EGJ and distal esophagus using 30ml, 40ml and 50ml distension volumes. All recorded values (distensibility, cross-sectional area (CSA), diameter, balloon pressure) were compared in the different distension volumes between the two measurements using a Wilcoxon Rank Sum test.

Results: There was a significant difference in distensibility, CSA and diameter with index distension volume (40ml) at the EGJ comparing the two measurements: Median CSA was 86.0 mm^2 in the group with inserted endoscope, respectively 110.0 mm^2 without endoscope ($p<0.001$), median diameter 10.3 resp. 12.0 mm ($p<0.001$) and median distensibility 2.1 resp. 3.4 $mm^2/mmHg$ ($p<0.001$). There was no significant difference concerning the measurements in the distal esophagus

Conclusions: Our results show a significant difference in EndoFLIP measurements with and without endoscopic control. This underlines the importance of establishing a consensus on how to technically perform EndoFLIP measurements in order to define normal values and by this, guiding future EndoFLIP diagnostic.

Diaphragm Disease im Colon ascendens ohne Einnahme von nichtsteroidalen Antirheumatika – ein Fallbericht

G1

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Background: Diaphragm Disease des Colons ist eine seltene Erkrankung, bei der membranartige Stenosen im Darm zu Blutungen und Abdominalbeschwerden führen. Sie ist in der Regel mit der Einnahme von nichtsteroidalen Antirheumatika (NSAR) assoziiert.
Methods: Klinischer Fallbericht
Results: Eine 67-jährige Patientin mit rezidivierenden Abdominalschmerzen und Gewichtsverlust wurde zur Abklärung einer Eisenmangelanämie zugewiesen. Endoskopisch zeigte sich im Colon ascendens eine nicht passierbare Stenose mit einer 2-3 mm durchmessenden Öffnung in einem membranartigen Segel. Wir führten eine laparoskopisch assistierte Ileozökalresektion mit Ileo-Ascendostomie durch. Intraoperativ sahen wir einen narbigen Schnürring im Bereich des Colon ascendens. Histologisch zeigte sich im Bereich der Stenose die normal strukturierte Mukosa, die Submukosa war hingegen vollständig fibromuskulär obliteriert.
Conclusion: Diaphragm disease im Darm ist in den meisten Fällen NSAR-assoziiert, in unserem Fall bestand jedoch keine vorangehende Einnahme von NSAR. Das typische histologische Zeichen ist eine lokalisierte submukosale Fibrose. Diese unterscheidet ein Diaphragma von einer stark ausgeprägten normalen Plica im Darm und könnte die Folge von durch Fibrose heilenden Verletzungen der Darmmukosa sein. Eine maligne Entartung ist bisher nicht beschrieben. Die Therapie besteht im Stoppen der NSAR Einnahme, der endoskopischen Dilatation der Stenosen sowie der allfälligen Resektion der betroffenen Darmabschnitte.

A rare case of gastric outlet obstruction in a patient with multiple myeloma

G2

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Background and clinical case summary: A 61-year-old man with multiple myeloma and cast-nephropathy with suspected manifestation of amyloidosis was admitted for gastroscopy because of nausea and emesis. Video fluoroscopy (Fig.1) demonstrated a gastric outlet obstruction with subtotal stenosis of the pylorus. Gastric amyloidosis could be confirmed histologically (Fig.2) (AL-amyloid) with deroofing-biopsies consistent with the clonotype of the patients myeloma. Botox injection was ineffective. Endoscopic balloon-dilatation (Fig. 3) from 15 mm to 20mm was succesfully performed with a persistent clinical response.
Conclusions: Gastric amyloidosis is a very rare cause of gastric outlet obstruction. Only 1% of patients have a histologically proven gastric amyloidosis. Among these patients only 0.13% have a gastric outlet obstruction [1-5]. Therefore general treatment recommendations are missing. Proceeding a pubmed research for gastric outlet obstruction and gastric amyloidosis revealed four case reports. The value of endoscopic balloon dilatation has not been described in the literature but seems to be a valid treatment option.
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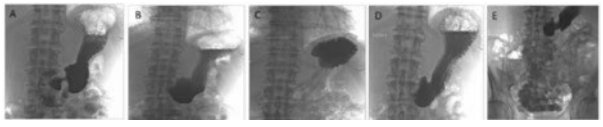
Fig 4 A-E (Video fluoroscopy: Propulsion and retropulsion with subtotal transport of contrast. A after 5 min, B after 40 min, C-E after 90-100min)



"Spontaneous" bowel perforation caused by oral preparation for colonoscopy

G3

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Background and clinical case Summary: We report the case of an 88 year old woman, admitted for colonoscopy because of non-bloody diarrhoea with diffuse mild thickening of the colonic wall in the ultrasound of the referring physician suspecting an inflammatory bowel disease. At admission the patient was afebrile with normal blood pressure and heart rate with mild pain on palpation of the right lower abdomen with normal bowel auscultation. CRP and leucocytes were mildly elevated. Oral bowel preparation with the first litre of Macrogolum was initiated in the evening. Nine hours later the patient was found dead in her bed. Autopsy demonstrated a fecal peritonitis due to a perforated diverticulitis of the sigmoid (Fig.1).
Conclusions: Large bowel perforation caused by oral preparation for colonoscopy is extremely rare (0,002%) and is only reported in malignant stenotic process in the large bowel (1,2). Malignant stenosis located in the recto-sigmoid or left colon were reported to be the cause leading to high intraluminal pressure induced by bowel lavage and consecutive perforation. Diverticulitis has not been reported to perforate induced by the bowel preparation. This catastrophic case underlines, that especially in elderly patients significant intraabdominal inflammation and even bowel perforation can be present without significant abdominal pain. The elevated inflammatory markers should have prompted a higher index of suspicion of (stenosing) diverticulitis. Forced bowel preparation should have been delayed until adequate non-invasive imaging (preferably ultrasonography or CT) was performed.

References:
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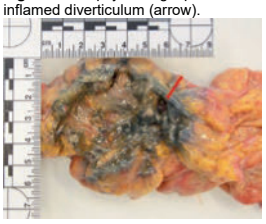
Figure 1 Autopsy findings: part of the sigmoid (serosal side) with perforation of an inflamed diverticulum (arrow).



The intra-individual Variability of Fecal Calprotectin in healthy individuals

G4

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Background: Fecal Calprotectin (FC) is a marker for intestinal inflammation, which allows the clinician to distinguish between functional and organic intestinal disease, and to monitor chronic inflammatory bowel disease (IBD). So far, there are no studies that analyzed the day to day variability of FC in the intestinally healthy. Our aim was to determine that intra-individual variability.
Methods: 163 healthy volunteers without gastrointestinal symptoms, colitis related manifestations or intake of NSAID gave three stool samples of the morning bowel movement on three consecutive days. The FC-analysis was made by enzyme-linked immunosorbent essay (ELISA) with a cut-off of 50µg/g by MCL Laboratorien Niederwangen.
Results: Of the 163 volunteers (aged 17-66y, mean 37y, median 32y, f=100), 114 (69.9%) showed FC- values of 50µg/g and lower in all three samples, thus having inconspicuous results throughout. 49 volunteers (30.1%) showed at least one value deemed pathologic. Of these 49, 40 (24.5%) showed both normal and elevated (>50µg/g) values and 9 (5.5%) showed elevated values throughout. By applying a cut-off of 100µg/g, 26 volunteers (15.9%) showed at least one elevated measurement and only 4 (2.5%) had values consistently over 100µg/g.
Conclusions: The presented data show a high variability of FC in a short amount of time in a third of the healthy volunteers. This opens the discussion if repeat measurements of FC would be helpful for optimal decision making. Further investigations in a non-healthy population are recommended.
The data also support the question, if raising the cut-off to 100µg/g would be appropriate to keep the rate of false positive results low without missing relevant disease, as several investigators have recommended already.

Audit of colon polyps' surveillance programme in daily clinical practice

G5

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Background: It is well established that screening colonoscopy reduces colorectal cancer (CRC) mortality. Therefore many countries have surveillance recommendations, as does Switzerland. According to our knowledge there have been no studies that examine the applicability of these recommendations to clinical everyday practice.
Methods: The medical history database in our office was searched and the first 109 consecutive pts with polypectomy and at least one follow-up colonoscopy were analyzed. We divided the pts in three risk groups according to the SGG-guidelines; high-risk with a recommended surveillance interval of 3 years, low-risk with 5 years and the no-risk group without additional surveillance.
Results: Of 109 pts (f=55, age 18-88y) at index colonoscopy, 24 (22%) had a no-risk finding (small hyperplastic polys in the rectosigmoid), 20 (18.4%) had a low-risk, and 65 (59.6%) had a high-risk finding. In the no-risk group the mean interval was 5 years (2-7y) for the surveillance colonoscopy, 5 (20.8%) now showed higher risk lesion, of which 4 (16.7%) showed high-risk. In the low-risk group at initial exam, 3 (15%) repeated a low-risk finding and 7 (35%) changed to a higher risk category. In the group of high-risk at initial exam, 26 (40%) had high-risk findings.
Conclusions: In this small pilot study we found the suggested control intervals for the low- and high-risk groups to be adequate, since 50% in the low-risk group showed equal or higher risk findings, and 40% in the high-risk group repeated lesions with high risk of developing CRC. Our no-risk group showed a higher risk finding after an average of 5 years in 20.8% of the pts. Therefore the 10 year control strategy for this group should be discussed and explored further in a larger study.

Prospective Study of Risk Score Strategies in the Prediction of Advanced Colorectal Neoplasia at Colonoscopy

G6

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Introduction: Current referral pathways in Australia for colorectal cancer (CRC) screening do not differentiate well between low and high-risk populations, and therefore may not be efficiently utilising resources. Whilst multiple CRC risk scoring systems currently exist and are utilised to stratify patients into low and high risk groups for priority of colorectal screening, there remains a need to identify which system has the greatest diagnostic accuracy. Therefore, we prospectively compared three existing CRC risk score systems in their ability to predict advanced colorectal neoplasia in Australian population; the Asia-Pacific Colorectal Screening (APCS) score; Hong Kong Score (2014); and Imperiale Score (2015).

Methods: Patients scheduled for colonoscopy assessment, both with or without gastrointestinal symptoms, were recruited. FOBT positive patients were included, but those who had an examination of the colon, including colonoscopy, within the last five years were excluded. Univariate and multivariate logistic regression was applied to identify significant risk factors for advanced neoplasia. For each patient, the 3 different risk scores were applied and the performance of each score in the prediction of advanced neoplasia was compared by examining the area under the curve (AUC) value.

Results: A total of 361 patients undergoing colonoscopy (48.2% male, median age 60 years) were prospectively recruited. The prevalence of adenomas was 31.6%, and 10.0% for advanced adenoma including 8 CRC (2.2%). Upon multivariate analysis, age and male sex were found to be significant risk factors (P=0.001, P=0.002). For predicting the prevalence of advanced neoplasia, the APCS score had AUC 0.71 (95%CI 0.63-0.79), Hong Kong Score 0.69 (95%CI 0.61-0.78), and Imperiale Score
0.68 (95%CI 0.59-0.77). Using a non-parametric comparison of the AUCs, there was no statistical significance between each of the scores for both symptomatic and asymptomatic populations (P=0.37 for APCS vs Hong Kong Score; P=0.32 for APCS vs Imperiale Score; P=0.43 for Hong Kong Score vs Imperiale Score).

Conclusion: All three scores are equally effective in stratifying the population into low and high risk colorectal neoplasia groups, and may be used to prioritise patients for colorectal screening.

Phytobezoar causing gastric outlet obstruction as a late complication after biliopancreatic diversion with duodenal switch

G7

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Background: Bezoars are a known cause for mechanical intestinal obstruction and are more common after previous gastric surgery. The most likely cause of bezoar formation after bariatric surgery is impaired gastric motility. Bezoar formation is recognized as a rare, late complication of gastric bypass surgery. There are only few reports of bezoar formation after sleeve gastrectomy and so far none after biliopancreatic diversion.
Methods: We present a case of a phytobezoar causing gastric outlet obstruction as a late complication after biliopancreatic diversion with duodenal switch.
Results: A 50-year old patient presented with acute inability to eat and drink, vomiting and epigastric pain. She had undergone a biliopancreatic diversion with duodenal switch type Marceaux 12 years earlier and no symptoms previously. CT scans showed a massive dilatation of the gastric sleeve with no other abnormalities. Gastroscopy revealed a large phytobezoar (10 x 5 cm), which was divided into smaller parts and subsequently removed endoscopically. Histologically the bezoar consisted of indigestible plant material.
Conclusions: With the increasing number of sleeve gastrectomies, we expect more patients presenting with gastric Bezoars. The preferred treatment is endoscopical removal.

Microbial and Metabolic Profile of Longitudinally Sampled Colorectal Cancer Patients

G8

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Background: Many studies characterizing the gut microbiota in context of many diseases involve the fecal samples due to the convenient accessibility. However, much less is known about microbiota profile over time at the active site of diseases, specifically at the most distal part of the small bowel which is essential in maintaining the microbiota derived immune and metabolic homeostasis. To investigate the dynamic microbial profile at the ileum and colon, we longitudinally profiled the gut microbiota of patients with ileostomies and colostomies with advantage of re-sampling without adding any distress to host.

Method: We deeply characterized ileum and colon microbiota of 72 colorectal cancer (CC), 35 IBD and 42 non-IBD (Control) with ostomies. Additionally, ~20 patients with CC were included into the study to characterize microbial changes before and after stoma surgery until the ostomy was reversed. The microbiota composition of samples was determined by 16S-rRNA sequencing and we analysed the same samples for metabolomic differences via quantification of relative metabolite concentrations, carried out with an untargeted mass spectrometer.

Results: Disease groups are clustered into three distinct groups mostly characterized by altered bacterial composition and lower diversity in IBD patients. Longitudinal microbiome analysis data shows that there is generally personalized microbiota within individual subjects. The microbial profile in longitudinally sampled CC patients before and after surgery is characterized with an increase of Proteobacteria and *Enterobacteriaceae* and relative metabolomic changes.

Conclusion: The microbial composition of the small bowel microbiota with a deeper resolution in characterization is scarce. This study adds valuable detail of the dynamic composition of the small bowel microbiota without adding any distress to the study participants. It also demonstrates the real dynamic microbiota changes at the specific site over time either in short or long period, such as alpha diversity reduction after surgery.

Healing earth is an effective therapeutic option in patients with NERD

G9

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Background: Non erosive esophageal reflux disease (NERD) is a common upper gastrointestinal disease with a significant loss in life quality. Lifestyle modifications, proton pump inhibitors and laparoscopic fundoplication are proven treatment modalities for NERD. Another treatment option is Luvos® Healing Earth, a natural composition of minerals and trace elements with acid-binding capacity and ad- and absorbing properties. The aim of this study was to assess the efficacy and safety of healing earth in NERD.
Methods: A study designed as an observational study included 146 patients with NERD symptoms and previously endoscopically-confirmed NERD. The patients received Luvos® Healing Earth daily for 14 days. Endpoints included the clinically assessment of the QOLRAD score (Quality of Life in Reflux and Dyspepsia) and the Eypasch index (Gastrointestinal quality of life).
Results: Of 137 patients, which completed the study, 79.7% rated the effect of healing earth as very good or good. Reflux symptoms did not occur again in 71% of cases until the end of the observation period. The effect of healing earth occurred very fast (45 min - 90 min). The vast majority of patients (92.3 %) received only a single dose for a significant complaint reduction. A clinically important increase in all 5 dimensions of the QOLRAD was observed. Parallel an increase of the Eypasch index was documented. No adverse events were observed.
Conclusions: Luvos® Healing Earth is an effective and well-tolerated treatment to reduce reflux symptoms and increases life quality in symptomatic NERD patients.

Diagnosis of Gastric Cancer in the Excluded Stomach after Roux-en-Y Gastric Bypass by Jejunogastrostomy

G10

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Background: For patients after bariatric surgery, diagnosis of gastric cancer is a challenge because of the altered gastro-intestinal anatomy. This case report demonstrates a novel method to examine the excluded stomach after Roux-en-Y gastric bypass (RYGB) surgery.

Case: A 56-year-old female patient was admitted with upper abdominal pain, nausea and diarrhea. Her past medical history was significant for ethyl-toxic liver cirrhosis and condition after RYGB surgery 16 years ago. Computed tomography scan revealed a liquid-filled excluded stomach with diffuse wall thickening of the gastric antrum and contrast medium uptake, which was suggestive of gastric tumor. The excluded stomach could not be reached by double-balloon enteroscopy. Under endoscopy ultrasound guidance, we created a jejuno-gastrostomy using a Hot AXIOS stent and electrocautery-enhanced delivery system (Boston Scientific) and installed a 20 mm fully covered and self-expanding lumen-apposing metal stent (LAMS), which allowed biopsies to be taken. Histology confirmed a poorly differentiated ulcerating adenocarcinoma of the stomach with signet cell differentiation.

Discussion: In patients with RYGB, only the pouch of the stomach can be examined endoscopically using conventional oesophago-gastro-duodenoscopy until one reaches the alimentary limb. In addition to the traditional approaches with surgical (laparoscopic) exploration, percutaneous endoscopy by gastrostomy or double-balloon enteroscopy, jejunogastrostomy is an effective and safe alternative.

The Branched-Chain Amino Acid Transporter CD98 Heavy Chain Supports the Development of Colonic Macrophages

G11

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Background: A comprehensive macrophage development is critical for the intestinal immune system, but the underlying mechanisms of the macrophage development remains elusive. **Methods**: To study the significance of the branched-chain amino acid transporter CD98hc for colonic macrophage development we carried out single-cell RNA sequencing (scRNA-seq) in wt and in an inducible CD98hc knock-out mouse model. **Results:** CD98hc is highly expressed by monocytes and macrophages in the colonic lamina propria, and in biopsies of IBD patients. We generated the inducible knock-out mouse system CD98hc$^{\Delta CX3CR1}$, in which tamoxifen-injection lead to the deletion of CD98hc in colonic macrophages and liver Kupffer cells but not in Langerhans cells. After quality filtering for scRNA-seq the observation of cells on a principal component analysis (PCA) or tSNE visualization, patterns of expression of cluster-specific genes, hypervariable genes and arbitrarily chosen monocytes and macrophages marker genes suggested a differentiation trajectory from monocytes to macrophages. The calculation of the relative proportion of control and CD98hc-deficient cells, across clusters and across the PCA space, indicated an enrichment of CD98hc-deficient cells in monocyte clusters, which was also apparent when the relative proportions of control and CD98hc-deficient cells projected on the nodes of FlowSOM trees. These results indicate a block in the 'monocyte waterfall'-development to mature macrophages in the colonic lamina propria in tamoxifen-treated CD98hc$^{\Delta CX3CR1}$ mice associated with an enrichment of apoptosis-associated genes. Consequently, the numbers of macrophages but not monocytes were significantly reduced after CD98hc silencing. **Conclusion:** The deletion of CD98hc results in a developmental arrest of intestinal macrophages. CD98hc plays a pivotal role for the development of intestinal macrophages.

Spontaneus intramural esophageal dissection (IOD): a case report

G12

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A 26-year old man presented to the ER complaining of epigastric cramping pain for a week refractory to regular pain medication and high dose PPI therapy. Upper Endoscopy revealed a narrowed upper esophagus with mucosal laceration on passing the scope and a 3cm intramural rupture in the mid esophagus leading into a submucosal space stretching to the Z-Line. Sequential oesophageal biopsies did not show signs of EoE, Granulomas, CMV, HSC, fungi oder malignancy but changes consistent with a severe acute ulcerative inflammation. No pneumomediastinum was observed on CT scan. Past medical history revealed no dysphagia but multiple food allergies and moderate alcohol intake.

The therapeutic approach consisted of short term drainage by an Esosponge placed in the esophageal lumen, parenteral nutrition and broadspectrum antibiotic and antifungal treatment for 10 days. A gastrografin study after 7 days was unremarkable, so oral nutrition was started with a concomitant topical steroid trial. Gastroscopic controls showed a continuous healing with closing of the submucosal space.

Dicussion: IOD is a rare condition of unknown etiology; typical symptoms include chest pain and dysphagia. Endoscopic examination identifying the orifice of the dissection tract is essential for differentiation from complete oesophageal rupture and determines management. Conservative treatment is usually sufficient for uncomplicated IOD; Various causatives such as eosinophilic esophagitis, mechanical trauma, Mallory-Weiss tear, iatrogenic causes as well as drug induced injuries have been described in the literature.

Chenodeoxycholic-acid induced vascular endothelial cell activation: effects on VE-cadherin and endothelial permeability. [1]S. Vukovic, [1]R. Sfriso, [1]M. Sorribas, [1]R. Rieben, [1,2]R. Wiest. [1]Department for Biomedical Research, University of Bern, [2]Department of Visceral Surgery & Medicine, Bern University Hospital, Bern, Switzerland.

G13

Background: Permeability of the intestinal vascular endothelium (=gut-vascular barrier GVB) controls the exchange of molecules between the blood plasma and the interstitial fluid maintaining blood and tissue homeostasis. We have demon-strated GVB-disruption in liver cirrhosis but mechanisms involved are unknown. The GVB-function largely relate to cell-cell-junctions with the main component being vascular endothelial (VE)-cadherin. However, the effect of bile acids (BA), known to circulate increasingly in liver cirrhosis, on VE-cadherin-expression and the GVB are not known. BA, such as chenodeoxy-cholic acid (CDCA) exert their effects via transcription factors of which Farnesoid X receptor (FxR) is one of the most important. Thus, we aimed to investigate the effect of CDCA and/or pharmacological FxR-stimulation on VE-cadherin-expression and endothelial permeability. *Methods*: Artificial 3D microvessels coated with porcine aortic endothelial cells (PAEC) were exposed to pulsatile flow for 48h and then immune-stained for VE-Cadherin with expression quantified by confocal microscopy. PAEC-monolayers were also put in transwell-assays on ThinCert inserts (Ø3 µm pores) and permeation tested by adding 40 kDa FITC-Dextran (read-out= fluorescence in receiver plate). Stimuli applied were different concentrations of CDCA or fexeramine, a potent FxR-agonist. *Results:* CDCA dose-dependently increased endothelial permeability in transwell-assays and down-regulated VE-cadherin in 3D microvessels. Fexeramine likewise dose-dependently reduced VE-cadherin-expression, however, failed to impact on endothelial permeability. *Conclusion:* CDCA impacts on VE-cadherin-expression and leads to endothelial hyperpermeability which likely contributes to GVB-disruption in cirrhosis. FxR however, does not seem to be essential for the observed CDCA-induced hyperpermeability indicating other signaling pathways playing a role.

CLOSE FOLLOW-UP IS ASSOCIATED WITH FEWER STRICTURE FORMATION AND RESULTS IN EARLIER DETECTION OF HISTOLOGICAL RELAPSE IN THE LONG-TERM MANAGEMENT OF EOSINOPHILIC ESOPHAGITIS G15

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BACKGROUND: No evidence-based recommendations exist regarding optimal follow-up schedule in patients with eosinophilic esophagitis (EoE) under maintenance therapy. Neither reasonable intervals for clinical visits nor follow-up schedules for disease-relevant biomarkers have been determined. METHODS: We evaluated a long-term surveillance concept at two large EoE referral centers (Swiss EoE Clinic, Mount Sinai Center for Eosinophilic Disorders), where clinical, endoscopic and histological disease activity is assessed on annual basis regardless of EoE symptoms. Data on 197 adult patients on a maintenance steroid therapy with available clinical, endoscopic and histological follow-up were analyzed so far at the time of this submission. Patients were classified as having had close follow-up (duration between visits <18 months) or non-close follow-up (≥18 months). RESULTS: We analyzed a total of 336 follow-up visits of 197 patients (148 males, age at diagnosis 38.9±15.3y). 169 (50.3%) visits were within a close follow-up schedule (median duration between visits of 1.0y (IQR 0.9-1.2), while 167 visits (49.7%) were not (median duration between visits 2.9y (IQR 2.0-4.1)). Adherence to prescribed steroid treatment was comparable at visits within close follow-up vs. non-close follow-up (43.1 vs. 41.1%). There was no difference regarding clinical (16.3 vs. 18.8%), endoscopic (30.4 vs. 28.4%), histological (24.2 vs. 25.7%) and complete remission (7.7 vs. 7.8%) between the two groups. However, stricture formation was significantly less frequently observed at visits within a close follow-up schedule (22.6 vs. 32.5%, p=0.043). Subsequently, we analyzed our data by patients and included a total of 74 subjects who achieved histological remission and had at least one additional follow-up visit (with assessment of endoscopic and histological disease activity). 53 patients had a close follow-up schedule (duration between visits 11 months (IQR 6-13.7), number of visits 3 (IQR 1-4)), while 21 patients did not have close follow-up (duration between visits 25 months (IQR 19.3-33.3), number of visits 2 (IQR 2-3)). While adherence rates to steroid maintenance therapy were similar between the two groups (43.4 vs. 42.9%), histological relapse was detected significantly earlier in patients with a close follow-up schedule (1.1y vs. 4.7y, p<0.001). CONCLUSIONS: Remission rates did not differ between patients following a close or a non-close follow-up strategy; however, stricture formation was significantly less frequent with a close follow-up schedule. In addition, close follow-up led to a shorter time to detection of histological relapse and therefore no increase in unnecessary procedures. We advocate for regular assessment of disease activity in order to detect relapsing disease as early as possible, which might minimize the risk for disease complications.

Colon Modeling Open Source Tool (CMOST) for modeling of the natural history of colorectal cancer G14

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Background: Colorectal cancer (CRC) is a leading course of cancer related mortality. CRC incidence and mortality can be reduced by CRC screening. Colonoscopy is potentially the most powerful CRC screening intervention. However, the efficacy of colonoscopy screening has not been tested in randomized controlled trials and remains unknown. Many open questions regarding colonoscopy screening remain including the best approach to the quality of colonoscopy. Microsimulation models have been advanced to simulate the natural history of CRC and CRC screening but none of the models is publicly available.

Methods: We developed Colon Modeling Open Source Tool (CMOST) as a microsimulation model of the natural history of CRC. CMOST is publicly available and supports the simulation of CRC screening interventions.

Results: Colonoscopy screening at the ages 50, 60 and 70 years reduces the incidence and mortality of CRC by 53% and 61%, respectively. In this setting, approximately 3.5 colonoscopies will be performed for each individual of the screening population and it needs 132 colonoscopies to prevent a CRC case and 25 colonoscopies per life year gained.

Colonoscopy screening with a reduced bowel preparation (Aronchick scale ≤3) reduced the effectiveness of the respective screening colonoscopy. However, an immediate repeat colonoscopy had only very limited benefit.

Conclusions: CMOST enables simulation of CRC screening interventions. CMOST can be used to determine the best use of colonoscopy screening. Our calculations suggest a strongly reduced benefit of an immediate repeat of a screening colonoscopy with a poor bowel preparation.

Upper gastrointestinal ulcerations with granulomatous hepatitis and bilateral adrenal masses after Thailand travelling H1

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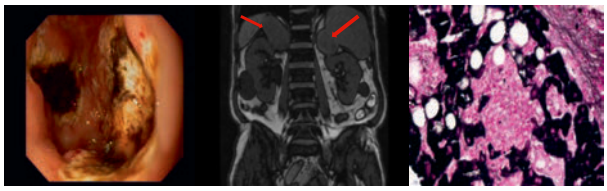
Background and clinical case summary: A 67-year-old Swiss man presented with dysphagia and weight loss of 15kg after he had returned from his annual beach holidays in Thailand. On physical examination buccal aphthous lesions were observed. Laboratory findings showed anemia (hemoglobin 113g/l), leucocytosis (12.6G/l) and an elevated C-reactive protein (156mg/l). Alkaline phosphatase (318U/l) and gamma-glutamyl transferase (336U/l) were also elevated while transaminases and bilirubin were normal. No evidence of viral or autoimmune hepatitis neither PBC was found, also no bile duct obstruction on ultrasound. Gastroscopy revealed oesophageal and gastric ulcers (Figure 1) with inflammation, necrosis and yeast cells in histopathology. Treatment with pantoprazole and fluconazole was initiated and dysphagia disappeared. Because of bilateral adrenal masses with low lipid content on MRI (Figure 2) an endocrinologic pathology was excluded. Thoracoabdominal CT showed no evidence of neoplasia and *Histoplasma* antibodies were negative. Biopsy of the adrenal glands showed necrotic tissue and massive infiltration by yeast cells. Fungal cultures and panfungal PCR were both positive for *Histoplasma capsulatum*. Liver biopsy showed liver cirrhosis with granulomatous hepatitis and isolated fungal elements (Figure 3). Disseminated histoplasmosis was diagnosed, involving the adrenal glands, liver and the upper GI-tract. HIV-PCR were negative. Antifungal therapy with liposomal Amphotericin B (3mg/kg) for 5 days followed by long-term itraconazole 200mg tid improved the patient's condition with normal liver values and the adrenal masses decreased.
Conclusions: In immunocompetent travelers disseminated histoplasmosis is uncommon, especially in patients without known immunosuppression (1). Disseminated histoplasmosis in combination with oropharyngeal and gastric ulcerations (2), granulomatous hepatitis (3) and enlarged adrenal glands (4) especially in immunocompetent patient has so far not been reported.

Figure 1 Figure 2 Figure 3



Usefulness of contrast-enhanced ultrasound evaluating focal steatosis in the liver of cystic fibrosis – A case report in a cirrhotic and non-cirrhotic liver – Video Session

H2

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Introduction: Cystic fibrosis (CF) is the most frequent autosomal recessive disorder in European countries. The flip side of improved survival due to increased life expectancy is the higher risk of gastrointestinal and hepatobiliary complications and malignancies related to CF (1,2,3). Up to 40% of patients develop chronic liver disease (focal biliary fibrosis/liver cirrhosis) (2,3). Therefore, liver ultrasound is regularly performed in CF-patients. Here, we describe two CF-patients who presented focal hyperechogenic liver lesions on ultrasound with the use of contrast-enhanced ultrasound (CEUS) to rule out hepatic malignancy in 5 minutes.
Methods: Detected focal liver lesions (FLL) in the screening liver ultrasound were assessed by CEUS using 1.5 ml intravenously injected Sonovue®. Arterial enhancement followed by hypoechoic appearance ("wash out") in the portal venous or delayed phase was considered as malignant FLL according to the current guidelines (4). Missing "wash out" of the FLL up to 5 min. was considered as benign. Representative still images and video clips were recorded.
Results: In a 32 year-old male and asymptomatic 26 year-old female CF-patient with cirrhosis we documented an incidental hyperechogenic FLL. CEUS demonstrated no arterial hypervascularisation and no wash out corresponding to a benign focal steatosis. Because of missing widespread experience in young CF-patients with cirrhosis we performed a biopsy of this FLL to rule out a malignant FLL. Histology confirmed a regenerative nodule with steatosis.
Conclusion: The accuracy of CEUS as first non-invasive diagnostic in the differentiation of benign and malignant FLL is excellent and comparable to CT and MRI (4,5). Experience of CEUS in CF-patients with FLL is missing. With the aid of CEUS in our two patients we could easily demonstrate typical focal steatosis in 5 minutes with the same criteria (no contrast enhancement and no wash-out) as in non CF-patients. CEUS offers immediate results without diagnostic delay and uncertainty for the patients. The lack of radiation exposure in these young patients with chronic disease, no nephrotoxic contrast agent, a low rate of adverse effects and economic aspects are further advantages comparing CEUS with CT or MRI.

Illustrations to support patient counseling before and after liver transplantation

H3

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Background: Patient's adherence to health relevant medical and behavioral recommendations before and after liver transplantation improves clinical outcomes. Therefore, healthcare professionals should provide self-management support and education. In our hospitals, oral counseling sessions are complemented by handing-out written brochures with information and advice. However, in patients with a foreign-language as well as for the education of complex content, it remains a challenge. Our aim was to develop language-independent illustrations to support counseling of patients before and after liver transplantation.

Methods: We used a participatory action research approach. In two meetings, physicians and nurses from the Cantonal Hospital St. Gallen, the University Hospital Zurich and a professional illustrator (only participating in the second meeting) (n=8) engaged in one complete action cycle: 1) constructing, 2) planning, 3) acting, and 4) evaluating.

Results: In constructing, every participant presented three real clinical practice situations in which illustrations would have facilitated patient counseling. In planning, all situations were discussed and three overriding themes for illustrations were identified: Understanding the disease (e.g., portal hypertension), organizational aspects (e.g. need for medical check-up before listing) and life after transplant (e.g., medication taking). Finally, the group decided to start with four draft illustrations. In acting, the illustrator created drafts and presented them to the healthcare professionals in the second meeting. The group evaluated the drafts using the "Thinking aloud" technique. Based on these results, the group discussed specific adaptations and agreed to create additional drafts. Finally, twelve illustrations and two illustrated self-observation plans before and after transplantation were drafted. In a second action research cycle, drafts will be evaluated by patients and other health care providers and revised before implementation in practice.

Conclusions: Early involvement of relevant stakeholders is key in practice development projects and the application of new tools. We expect a high acceptance and use of the illustrations for counseling before and after transplantation. This in turn, might improve safety in deprived patient groups.

This abstract is the result of two Astellas Pharma AG-initiated, organized and financially supported meetings.

Regulation of lymphangiogenesis by Paneth cells in normal physiology and experimental portal hypertension

H4

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Background and Aims: The mesenteric lymphatic network contributes to the transport of fluid and intestinal mucosal associated immune cells along the gut-liver axis. We have previously reported a decrease in intestinal vascularization and number of Paneth cells along with diminished lymphangiogenesis in absence of intestinal microflora[1]. However, the association of Paneth cells with the regulation of lymphatic vascular development is unknown. We hypothesized that Paneth cells, as part of the innate intestinal immune system, regulate the development of lymphatic vessels and affect portal pressure under the control of intestinal bacteria.
Method: We induced Paneth cell depletion in Math-1 Lox/LoxVillcre^{ERT2} mice by injecting three consecutive doses of tamoxifen and performed partial portal vein ligation (PPVL) to induce portal hypertension. After 14 days, intestinal and mesenteric lymphatic vessels were assessed by immunohistochemistry (IHC) using lymphatic vessel endothelial hyaluronic acid receptor 1(Lyve-1) antibody. The lymphatic vessels were quantified using Metamorph to calculate pixel ratio. Expression of genes involved in the regulation of lymphatic vessels was evaluated by RT^2 profiler PCR array in intestinal tissue. These results were further confirmed by performing quantitative PCR of more specific lymphangiogenic genes. Intestinal organoids from control and Paneth cell depleted mice were exposed to different bacterial derived products. Proteomic analysis of conditioned media was performed using MaxQuant to analyse differentially regulated proteins in lymphangiogenesis in the absence of Paneth cells and/or in portal hypertension.
Results: Portal pressure was significantly attenuated in Paneth cell depleted mice compared to control mice after PPVL (n=11/group, 9.78±1.23 cmH_2O vs 11.45±1.41 cmH_2O, respectively, p<0.002). Depletion of Paneth cells resulted in a significantly decreased density of lymphatic vessels compared to control as assessed by IHC (n=5, pixel ratio), in the intestine (0.176% ±0.12 vs 0.367%±0.15, p=0.01) and in the mesentery (0.160%±0.06 vs 0.404%±0.20 p=0.001). Quantitative PCR showed a decreased expression of genes involved in the regulation of lymphangiogenesis, including VEGF-C, VEGF-D, VEGF-A, Nrp2, Angpt-2, Tie-1, Tie-2, TGF-α, HGF and CXCL-1 in Paneth cell depleted mice. Moreover, the expression of specific markers of lymphangiogenesis such as transcription factor Prox-1 or growth factor VEGFR3 and protein FOX-C2 were significantly decreased in Paneth cell depleted mice after PPVL. In the absence of Paneth cells, proteomic analyses showed a significant downregulation of several proteins involved in lymphatic vessel development and morphogenesis, as well as in processes of lipid metabolism and transport.
Conclusion: In the absence of Paneth cells, the intestinal and mesenteric lymphatic vessel networks were significantly underdeveloped. This was associated with an attenuated portal hypertension. These findings suggest that Paneth cells not only play an antimicrobial role in the intestine, but also contribute to the regulation of lymphatic vessels and portal pressure.

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Quality of life measurement using wrist actigraphy in HCV genotype 1 infected, treatment naïve patients suffering from fatigue and receiving ombitasvir, paritaprevir, and ritonavir tablets and dasabuvir tablets (Viekirax®/Exviera®; 3D regimen): The HEMATITE Study

H5

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BACKGROUND & AIMS: Physical and mental fatigue is the most common symptom reported by patients with Hepatitis C Virus (HCV), which highly impacts their overall quality of life. This cardinal symptom presents regardless of the stage of liver fibrosis and is difficult to quantify objectively. Similar to other potential reasons for physical fatigue, increasing evidence suggests a direct viral impact on the central nervous system. Data demonstrating a longitudinal change of debilitating physical fatigue and increased daytime physical activity upon treatment (Tx) with 3D regimen are missing to date. The rationale for this observational study is to observe the impact of 3D regimen on physical activity of HCV+ patients suffering from debilitating fatigue by using wrist actigraphy. **METHODS:** HEMATITE is an observational, prospective, open label, single-arm, Swiss multi-centric, real-life study in HCV+ patients (GT1). The study consists of a Tx preparation phase of 4 weeks (wks), a Tx phase with 3D regimen according to routine clinical practice (12 wks) and a post Tx phase (12 wks) to evaluate Tx response. Fatigue was assessed at every visit using the Fatigue Severity Score (FSS) questionnaire, according to routine clinical care. In addition, physical activity data was collected by providing patients with a wrist-worn activity tracker to be worn for 4 wks before Tx (baseline (BL)) and for 4 wks before each visit. **RESULTS:** 40/41 patients reached SVR12. The FSS decreased significantly from BL to post Tx visit week 12 (5.92 ± 0.61 vs. 3.34± 1.42 (mean ± SD); p<0.001). The physical workday daytime activity data could be analyzed from 37 out of 45 (scale down (sd)ITT). Neither the mean activity nor the change of the mean activity between BL and Tx week 12 showed any significance. **CONCLUSIONS:** As expected >97 % of the patients achieved SVR12 upon 3D regimen therapy. Moreover, the 3D therapy also reduces fatigue in HCV+ patients, as shown by the FSS, suggesting a causative role of HCV in this extrahepatic manifestation. HCV treatment is therefore effective in reducing/eliminating fatigue.

Early outcome in patients with non-alcoholic fatty liver in comparison with non-alcoholic steatohepatitis undergoing gastric bypass: a propensity score matched analysis

H6

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Abstract

Background
Incidence of non-alcoholic steatohepatitis (NASH) in the obese population is reported up to 10-20% and postoperative weight loss as well as metabolic outcome after Roux-en-Y gastric bypass (RYGB) may be impaired in these patients.

Objectives
In the present study we compare postoperative glycemic control, liver function and weight loss in two groups of patients with non-alcoholic fatty liver (NAFL) and NASH who underwent RYGB.

Methods
We retrospectively evaluated 515 patients undergoing RYGB with concomitant liver biopsy between 1997 and 2013. Clinical follow up was performed at 12 months after surgery. Furthermore, we performed a propensity score matching without missing values (PSM) 1:1 on age, sex, BMI, incidence of diabetes and American Society of Anaesthesiologists (ASA) score.

Results
Within the entire cohort, at baseline before matching, the NAFL (n=421) and NASH (n=94) groups were comparable in age, body mass index (BMI), ASA score and sex ratio whereas the incidence of diabetes differed significantly (23% vs 47%; p<0,001).

At baseline the NAFL group had significantly lower glycemia (6,3 ± 2 vs 7,9 ± 3,2; p<0,001), insulinemia (24,1 ± 15,2 vs 42,3 ± 45,2; p=0,001), aspartate aminotransferase (ASAT) (21,9 ± 11,8 vs 39,1 ± 28,8; p<0,001) and alanine aminotransferase (ALAT) (32 ± 25,1 vs 62,7 ± 46,6; p<0,001). In the same way, the homeostasis model assessment insulin resistance (HOMA-IR) was significantly lower (7,1 ± 5,5 vs 14,3 ± 14,2; p<0,001).

At the one year follow up of the entire cohort, the two groups were only comparable in ASAT (22,6 ± 9,1 vs 31,3 ± 39,9;p=0.140). The BMI (29,8 ± 5,1 vs 31,8 ± 6 kg/m2;p=0.01), , ALAT (23,9 ± 14,2 vs 32,2 ± 27,4;p=0.046). Glycemia (4,8 ± 0,74 vs 5,27 ± 1,2; p=0.03), insulinemia (7,1 ± 4,13 vs 10,3 ± 4,3; p<0,001) and HOMA-IR (1,6 ± 1 vs 2,3 ± 1; p=0,001) were significantly higher in the NASH group. In contrast to this the percentage excess weight loss (EWL) (78,2 ± 20,5% vs 70,8 ± 21,3%; p=0,007) was significantly lower.

At Baseline, the PSM analysis of 31 patients in each group and showed us a significantly lower ASAT (23.5 ± 14,7 vs 39,3 ± 26; p=0.006), ALAT (33,4 ± 27,1 vs 61 ± 30,3; p=0.001) in the NAFL group. But after 1 year, the PSM demonstrated similar EWL (72,3 ± 17,2% vs 74,4 ± 17,2%, p=0.6), ASAT (23,3 ± 8,2 vs 34,3 ± 49;p=0.22), ALAT (21,1 ± 9 vs 31,7 ± 31,1;p=0,08) and glycemia (5,1 ± 0,9 vs 5,1 ± 0,9;p=1), whereas HOMA-IR (1,6 ± 1 vs 2,3 ± 1;p=0.014) and the insulinemia (7,1 ± 3,9 vs 10.2 ± 4,3; p=0.005) differed significantly between the groups.

Conclusion
Patients with NASH seem to improve their liver function after gastric bypass and show a lower weight loss in comparison with patients with NAFL. Meanwhile, glycemic control seems to be compromised in patients with NASH after gastric bypass in comparison with NAFL even in well-matched obese patients.

Evaluation of the prognostic value of histologic parameters in severe alcoholic hepatitis

H8

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Background and Aims: Alcoholic Hepatitis (AH) Histologic Score (AHHS) has been proposed as a new prognostic tool to assess the risk of death at 3 months in severe AH. **Aim**: To study the prognostic value of AHHS and of Laennec system for survival at 3, 6 and 12 months.
Method: Liver biopsies of patients with severe AH (Maddrey DF >32) were analyzed independently by 2 pathologists. Fibrosis, neutrophils, bilirubinostasis and megamitochondria were assessed to classify patients into mild, moderate or severe AHHS. Patients with cirrhosis were also classified according to the Laennec system (4A, 4B and 4C) based on fibrous septa thickness and nodules size.
Results: 55 consecutive patients were included (median age: 54 years [95% IC: 50-56], median Maddrey DF: 71 [95% IC: 64-78]). 43 (78%) were treated with corticosteroids. Four patients (8%) were lost to follow-up at 12 months, 24 (44%) died and 1 (2%) underwent liver transplantation. Histologic scoring, available in 53 patients, showed mild AHHS in 3, moderate AHHS in 11 and severe AHHS in 39. 4 patients had no cirrhosis, 7 patients were classified as Laennec 4A, 15 as 4B and 27 as 4C. Survival rates in mild, moderate and severe AHHS were 100%, 64% and 74% at 3 months (p=0.5), 100%, 55% and 69% at 6 months (p=0.4), and 100%, 55% and 49% at 12 months (p=0.4), respectively. In AHHS, fibrosis showed the best interobserver reproducibility (agreement=100%, K=1.00) and a trend for predicting 1-year survival (100% vs. 49% for patients without and with cirrhosis, p=0.14). AHHS AUROC curve for 12-month survival was 63.4% (95% CI: 46.4-75.9, p=0.03), not different from that of other prognostic scores (Child-Pugh score 58.9%, MELD score 65.5%, Lille score 65.5%, p value for all comparisons ≥0.5). When compared to patients with Laennec 4B or 4C, survival rates of patients without cirrhosis or with Laennec 4A were 91% vs. 68% at 3 months (p=0.14), 82% vs. 64% at 6 months (p=0.2) and 73% vs. 48% at 12 months (p=0.14), respectively. In multivariate analysis adjusted for age and for MELD score, AHHS was not associated with 1-year mortality (risk ratio: 1.27, 95% CI: 0.95-1.70, p=0.1). When considering Laennec system instead of AHHS, Laennec 4B or 4C was not associated with increased mortality at 1 year (risk ratio: 3.52, 95% CI: 0.82-15.17, p=0.09).
Conclusion: AHHS has little added value to predict survival in patients with severe AH. The severity of fibrosis seems the histologic parameter with the strongest prognostic value.

A buyers' club to improve access to hepatitis C and HIV treatment for vulnerable populations

H7

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Background – The estimated prevalence of active hepatitis C virus (HCV) infection in the general Swiss population is 0.4%-0.5%. The prevalence is higher among vulnerable populations such as migrants, intravenous drug users and people living in prison (PLP). Health care systems are struggling to finance costly therapies (such as direct antiviral agent) through public funding for uninsured patients, despite their unprecedented high cure rates.
Methods - A personal importation scheme is based on the legal right of patients to import any drug into Switzerland for personal use. A "Buyers' club", which is a structure that aims to help patients to import generic medicines safely, was established in October 2018 at University Hospitals of Geneva. To assess the impact of this initiative, we compared the real cost of imported generics with their corresponding Swiss prices. Quality and efficacy were also primary outcomes**.**
Results - From October 2018 until April 2019, 7 PLP and 7 migrant patients were treated for HCV, 7 for HIV and 1 HCV/HIV co-infected patient for both viruses. HPLC-UV analysis demonstrate that all generics meet good standards of quality. The total costs for the HCV imported generic medicines were CHF 15,525, compared to CHF 477,225 for the corresponding Swiss brand medicines. The HIV imported generic costs were CHF 4,163, compared to CHF 41,624 for the corresponding brand medicines. Two patients with HCV have already terminated their 12-week follow-up and have cleared their infection.
Conclusions - Our personal importation scheme allows to import generics at 4% of the Swiss corresponding costs. This strategy seems highly promising to improve universal access to hepatitis C and HIV medicines to vulnerable populations, such as uninsured patients, with minimal disruption of the conventional, patent-based model of care, and should be expanded to other diseases and settings.

Robust MAIT cell activation in response to interactions with primary human liver cell subsets

H9

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Background: Mucosal-associated invariant T (MAIT) cells, representing the most abundant T cell type in human liver, respond to bacterial metabolites, presented by MHC-like molecule MR1 on antigen (Ag)-presenting cells (APCs). A study in mice suggested that the MAIT cell Ag precursor is able to cross the intestinal barrier to reach both the circulation and liver. Activated murine and human liver MAIT cells from cirrhotic patients were described as pro-fibrogenic. It remains poorly understood which cells in the liver are involved in MAIT cell activation, and, consequently, how their pro-fibrogenic function could be prevented.
Methods: We assessed Ag-presentation capacities of primary human liver cell subsets to human blood- and liver-derived MAIT cells. Responses were evaluated by defining activation markers and cytokine expression profiles of MAIT cells upon stimulation with synthetic Ag or bacterial lysate from *E. coli*. To assess reversibility of the activation process, APCs were pre-treated with non-stimulatory MR1 ligands. To define tissue localization of MAIT cells, immunofluorescence staining was performed on cryopreserved human liver biopsies.
Results: Human hepatocytes, hepatic myofibroblasts, endothelial cells and billary epithelial cells had the capacity to present Ag to MAIT cells. Human liver-derived MAIT cells produced large amounts of IL-17, a cytokine with prominent pro-fibrotic properties. MAIT cell activation was prevented by the presence of non-activating MR1 ligands 6-Formylpterin and 5-formylsalicylic acid. Presentation capacities differed markedly among the investigated liver cell types, with hepatocytes being the most efficient liver-derived APCs. Liver cells exposed to Ag precursor had the capacity to generate active Ag endogenously. MAIT cells localized dispersedly to the parenchyma in healthy liver when analysed *in situ*.
Conclusions: Our results provide new insights to the understanding of intrahepatic MAIT cell activation. By using both primary liver-derived APCs and liver-derived MAIT cells, and applying naturally occurring Ags, we show the large *in vivo* interaction potential of this abundant intrahepatic cell type. Occupancy of MR1 with non-stimulatory ligands creates a therapeutic opportunity to prevent pro-fibrogenic properties of MAIT cells.

Hepatic gene expression analysis identifies marked differences in acute alcoholic microvesicular steatosis compared to alcoholic steatohepatitis (ASH) H10

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Acute alcoholic microvesicular steatosis (MIC), « alcoholic foamy degeneration », is a potentially severe form of alcoholic liver disease (*SwissMedWeekly 2018 ; 148(suppl 232) : A16*). Pathogenesis of MIC is unclear, and clinical presentation could mimic ASH. Patients/Methods: We studied hepatic gene expression in a subgroup of heavily drinking patients presenting with MIC (n=7, M/F 3/4; 46 yrs, AlkPhosph (AP) 195 IU/L, triglycerides (TG) 4.23 mmol/L, focal or no liver fibrosis : 5/7) or ASH (n=17; M/F: 8/9; 49 yrs; AP 138 IU/L, TG 1.3 mmol/L; all with cirrhosis). At histology, MIC was defined as > 50% microvesicular steatosis and no inflammation, while ASH included polynuclear infiltration + macrosteatosis+ ballooned hepatocytes. Liver mRNA was extracted (snap-frozen tissue), followed by microarray hybridization /gene expression analysis. Significant differential expression was defined as > 2-fold difference in mRNA. Results : At transcriptome analysis, the main pathways differentially expressed in MIC compared with ASH are related to cell cycle (upregulated), stellate cell activation, fibrosis and inflammation (downregulated). Other important genes related to lipid metabolism were identified. *Table: MIC vs ASH*

Function	Gene symbol	Fold-change	p value
cell cycle	CCNA2, MKi67	+5.87, +3.8	0.006, 0.002
	CD34, HGF	-3.01, -2.19	0.002, 0.003
inflammation	ALOX5AP, CCR2	-8.57 , -2.87	0.0002, 0.0014
	TNFSF14, CCL21	-2.62, -6.51	0.01, 0.0016
lipid metabolism	THRSP	+12.55	0.02
	CD36, PLIN2	+2.66, +4.55	0.0005, 0.013
fibrosis	FGF	-6.51	0.0019
	COL5A1, LOXL1	-4.54, -5.67	0.002, 0.0055
detoxification	CYP4F22	+3.36	0.0004

Conclusions : Multiple genes show significant differential expression in MIC when compared to ASH, involving liver cell repair, lipid metabolism and detoxification process. These observations may help clarify the pathogenesis of MIC (*supported by FLAGS*)

Loss of Claudin-3 Results in Metabolic Reprogramming and Impaired Regeneration in the Murine Liver H11

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Background: Tight junctions (TJs) are essential components to maintain the blood biliary barrier in the liver. The proteins that comprise hepatic TJs and their contribution to homeostasis and regeneration remained largely unexplored. Here, we elucidate the cell type specific expression of TJ genes in murine livers, and explore the regulation and functional importance of the transmembrane protein Claudin-3 (CLDN3) in liver regeneration.
Methods: Native livers were used for single cell RNA-seq / tissue RNA-seq. CLDN3 localization was determined by immunofluorescence. $CLDN3^{+/+}$ or $CLDN3^{-/-}$ mice were subjected to 2/3 partial hepatectomy (PH). Proliferative indices were quantified with Ki67 and pHH3. Cell cycle driver gene expression was determined by RT-qPCR. Barrier function was assessed with bile acid measurements, cytokine expression and immune cell quantifications by FACS. Differential gene expression was analyzed with DESeq2. Lipid and triglyceride levels were quantified with Oil-Red-O.
Results: We quantified the expression TJ genes in native liver tissue. Single cell RNA sequencing revealed that TJ transcripts can be found in hepatocytes and cholangiocytes but also on non-parenchymal cell populations. The TJ gene Cldn3 was regulated following PH. $CLDN3^{-/-}$ mice had impaired liver regeneration following PH, which was possibly caused by inefficient baseline energy metabolism.
Conclusions: CLDN3 is among the highest expressed and regulated hepatic tight junction genes in native and proliferating livers. CLDN3 had a zonated expression pattern and a functional role in the maintenance of energy homeostasis and liver regeneration. This suggests that tight junctions of the liver are involved in biological processes that go beyond cell-cell adhesion and barrier formation.

Thrombin generation in patients with liver cirrhosis: modern global hemostasis assays provide new insights into a procoagulant state H12

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Background: Cirrhotic patients are at increased thrombotic risk despite prolonged routine coagulation assays. This has been proven in clinical studies. However, *in vitro* studies using thrombin generation (TG) showed some discrepancies. These can be explained by high inter-laboratory methodological variability and differences in severity and aetiology of liver cirrhosis. To reach reproducible results and to assess the clinical value of TG assays, larger studies with standardized methods and a prospective follow-up are necessary.

Methods: We report the results for the first 85 patients included in a single-centre prospective study recruiting patients with liver cirrhosis (n=400). We analysed TG using an automated and standardised assay (ST Genesia, Stago, Asnière, France), including tests with and without thrombomodulin (TM) as activator of the protein C/S (PC/S) system, as well as Thrombodynamics analyser (TD) (Hemacore, Moscow, Russia). A clinical follow-up of 12 months is planned.

Results: We confirm an increased TG with TM in cirrhotic patients compared to healthy subjects. This highlights the reduction of the natural anticoagulants PC/S in these patients. TD shows already without TM an increased and faster propagation of TG at distance of tissue factor compared to healthy subjects. This reflects an increased amplification phase of the coagulation in cirrhotic patients.

Conclusions: We confirm a prothrombotic state in cirrhotic patients due to PC/S deficiency. New insights are: TD shows an increased amplification phase of coagulation in cirrhotic patients, already in the absence of TM; this could be explained by reduced natural anticoagulants, mainly antithrombin. The one-year clinical follow-up should allow to assess the ability of these tests to predict thrombo-haemorrhagic complications.

What if increased INR and aPTT would represent a thrombotic instead of a bleeding risk in cirrhotic patients? H13

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Background: Prothrombin time (PT), its international normalised ratio (INR), and activated partial thromboplastin time (aPTT) are widely used to assess individual bleeding risk. They are also employed as markers of cirrhosis severity. However, it is known that thrombin generation (TG) and, by consequence, thrombotic risk increase with cirrhosis severity. Therefore, the question arises whether increasing INR and aPTT values indicate an increased thrombotic risk in cirrhotic patients.

Methods: We report the results for the first 85 patients recruited in a single-centre prospective study including patients with liver cirrhosis (n=400). We analysed TG with and without thrombomodulin (TM) as activator of protein C/S (PC/S) system using an automated and standardised TG assay. TM-mediated inhibition (TMmI) represents the degree of diminution of TG after addition of TM and reflects the activity of PC/S, approximating *in vivo* TG. Using linear regression, we compared TMmI with Child-Pugh and MELD scores, total bilirubin, albumin, factor V activity (FV), PT, INR and aPTT.

Results: TMmI was positively correlated with albumin, FV and PT (r^2 values of 0.37, 0.47 and 0.48, respectively) and inversely correlated with Child-Pugh and MELD scores, total bilirubin, INR and aPTT (r^2 values of 0.26, 0.25, 0.29, 0.42 and 0.32, respectively). All slopes were very significantly different from zero (p-values < 0.0001).

Conclusions: We show an association of cirrhosis severity, albumin and FV with TMmI, which is known to be due to PC/S deficiency. This highlights an increasing thrombotic risk with increasing severity of cirrhosis. Remarkably, decreasing PT and increasing INR and aPTT values are associated with a decreasing TMmI, thus reflecting enhanced *in vivo* TG. Therefore, increasing INR and aPTT in cirrhotic patients represent a marker of thrombotic risk. Do not trust INR and aPTT in cirrhotic patients, they lie!

Out of Africa: Hepatitis C Virus Subtype 4r as Troublemaker

H14

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Background and aim: Direct acting antivirals (DAAs) have revolutionized the management of chronic hepatitis C, with sustained virologic response (SVR) rates > 90%. Here, we characterized patients who did not achieve SVR on DAA-based therapy.

Patients and methods: We conducted an observational retrospective study to characterize the patients treated jointly with a specialized nurse in the Service of Gastroenterology and Hepatology of the CHUV between January 2015 and February 2018.

Results: In the slightly more than three years, 306 patients with chronic hepatitis C were treated with first- or second-generation DAAs. Of these, 284 (92.8%) achieved SVR and 22 (7.2%) experienced a relapse. SVR rates increased progressively over the years as a result of a declining proportion of patients with advanced liver disease and the introduction of pangenotypic treatment regimens. Significant resistance-associated substitutions were identified in all tested patients who experienced a relapse, indicating a very low rate of non-virological treatment failure. Remarkably, only 27 of the 35 patients infected with HCV genotype 4 achieved SVR (77.1%; p = 0.001 for the comparison with other genotypes). Of the eight genotype 4-infected patients who failed DAA treatment, five were infected with subtype 4r (62.5%); all of them originated from Africa and their HCV harbored NS5A sequence polymorphisms associated with drug resistance already at baseline.

Conclusions: The rate of non-virological treatment failure was very low, likely as a result of close follow-up by a specialized nurse, favoring excellent treatment adherence. Patients infected with HCV subtype 4r were overrepresented among relapsers, as reported recently from other centers. Hence, patients with chronic hepatitis C of genotype 4 originating from Africa may have HCV subtyped and a triple DAA regimen may be considered as first-line treatment in the presence subtype 4r.

AXL-expressing immune-homeostatic liver macrophages disappear in progressive cirrhosis

H15

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Background: AXL and MERTK belong to the family of TAM receptor-tyrosine kinases and are phagocytic receptors with distinct patterns of expression. On circulating monocytes in cirrhosis AXL and MERTK dampen innate immune responses, promote phagocytosis and have been associated with infection susceptibility. We sought to assess AXL and MERTK expression in cirrhotic livers related to disease severity.

Methods: Liver biopsies from cirrhotic patients (Child A/n=8;B/n=7;C/n=7) were compared to healthy controls (HC/n=4), chronic liver disease without cirrhosis (n=8), and nodular regenerative hyperplasia (NRH/n=3). AXL and MERTK expression on parenchymal and non-parenchymal cells was assessed in hepatic plates using confocal microscopy on multiplexed immunofluorescence.

Results: AXL^+ cells were identified in sinusoids but not in the parenchyma and were predominantly resident macrophages (Kupffer cells, KCs, $CD68^+$). $CD68^+AXL^+$ KCs represented the majority (88%) of the entire KC population in HC, but decreased significantly with cirrhosis progression. By contrast, $CD68^+MERTK^+$ KCs were sparse in HC, but increased with progressive cirrhosis. The number of AXL^+ KCs negatively correlated with Child-Pugh and MELD scores. Numbers of AXL^+ KCs were similar in patients with advanced cirrhosis and NRH with portal hypertension.

Conclusions: We newly described AXL expression on the majority of Kupffer cells in healthy liver, which is subsequently lost during progression of cirrhosis and portal hypertension. The data may suggest a role for AXL in hepatic immune homeostasis and firewall function of the liver facilitating clearance of commensal organisms derived from the intestine. In this context, loss of AXL may relate to pathological bacterial translocation in cirrhosis.

Autoimmune Idiopathic Disorders in HCV patients: Effect of Direct Antiviral Agents - the AIDAA study (SASL 42)

H16

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Background: Chronic Hepatitis C (HCV) may negatively influence evolution and prognosis of some autoimmune idiopathic disorders (AID). The aim of this study was to investigate the influence of direct antiviral agents (DAA) treatment on AID.

Methods: Patients with HCV and AID treated with DAA in three Swiss medical centers were assessed using self-administered Visual Grading Scale (VGS) and questionnaires assessing the perception of AID activity before, during and after DAA treatment.

Results: We enrolled 23 patients (14 male; mean age 57 years, range 42-80) between 2015 and 2018. 11 (48%) had psoriasis, 8 (35%) rheumatoid arthritis, 3 (13%) Sjögren's syndrome and 1 (4%) ankylosing spondylitis. Sustained viral response (SVR) was achieved in all cases. Improvement of AID was reported in 8 patients, while 2 reported a worsening. Overall, we observed a trend to improvement in the perception of the severity of AID (mean VGS 4.74 at baseline vs. 3.57 at SVR, p=0.134). In patients with rheumatoid arthritis, mean Patient Activity Scale II (PAS II) decreased from 4.31 to 3.90 (p=0.068). Women were more likely to have an improved perception of their AID on SVR.

Conclusions: Successful treatment of HCV using DAA does not worsen the severity of AID according to patients' perception. On the opposite, about one third (35%) of patients report a significant improvement of AID symptoms on SVR. Worsening of perceived AID severity occurred only in 2 cases (9%).

ABCB4 deficiency associated Copper Overload mimicking Wilson's disease: a Case report

H17

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Case presentation:
A 21-year-old male patient presented with pruritus, fatigue and elevated liver enzymes (Bilirubin 2.3mg/dl, ALT 181 U/L; AST 106 U/L; γ-GT 212 U/L; AP 220 U/L). Comprehensive work-up provided no evidence of viral or autoimmune liver disease, primary biliary cholangitis (PBC) or -sclerosing cholangitis (PSC). 24-hour urinary copper excretion was increased (101 µg/day), though serum copper and coeruloplasmin levels were normal and Kayser-Fleischer rings not detectable. Liver histology showed features of cholangiopathy, bridging fibrosis and an increased hepatic copper content (102 µg/g dry weight). Thus, a diagnosis of probable Wilson's disease (WD) with a Leipzig score of 3 points was entertained and chelation therapy initiated. However, there was no biochemical response, and sequencing of the Wilson gene *(ATP7B)* yielded no mutations. Indeed, sequencing of the hepatocanalicular phospholipid transporter *ABCB4* revealed two heterozygous nonsense respectively missense mutations: c.139C>T [p.Arg47X] and c.959C>T [p.Ser320Phe]. The patient was diagnosed with progressive familial cholestasis type 3 (PFIC3) and associated copper overload. Ursodeoxycholic acid was started with significant biochemical improvement and stable condition in follow-up.
Discussion:
Variable degrees of secondary copper overload have been recognized in common cholestatic diseases e.g. PBC and PSC. However, ABCB4 deficiency with a PFIC3-like phenotype underlying significant hepatic copper deposition with challenging differentiation from WD has only rarely been reported. Sequencing of both *ATPB7* and *ABCB4* can aid in separating these two entities, as the required therapies are vastly different.

Targeting the mitotic spindle assembly in patient-derived liver cancer organoids

H18

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Background: Liver cancer is the second most lethal malignancy worldwide, with most of the patients being diagnosed only at an advanced disease stage with limited treatment options. Hence, new treatment approaches are required. Interfering with mitotic spindle assembly has been shown to be a promising novel cancer therapy approach. In this study, we want to investigate the anti-tumoral activity of an Aurora A kinase (AURKA) (TC-S 7010) and Polo-like kinase 4 (Plk4) (CFI-400945) inhibitor against biopsy-derived liver cancer organoids reflecting the heterogeneity of the patient population.
Methods: Drug screenings were performed in a 384-well (1000 single cells/well) format using a broad drug dilution series. Drug efficacy was determined after 6 days by measuring cell viability with an ATP-based assay. Results were correlated with the mutational profile of the organoid lines.
Results: The IC50 of AURKA-inhibition in liver cancer organoids harboring TP53 mutations was lower than in TP53 wildtype organoids. Irrespective of the TP53 status, cholangiocellular carcinoma-derived organoids seem to be more resistant to AURKA-inhibition. Interestingly, our preliminary data indicates that high response to Plk4-inhibition is associated with the presence of a TP53-APC double-mutation.
Conclusions: Using liver cancer organoids, we confirm an association between the TP53 mutational status and responsiveness to AURKA-inhibition. Furthermore, Plk4-activity could be associated with TP53-APC-mutation. The mechanism remains to be elucidated.

Liver disease following bone marrow transplantation : clinical and biological characteristics of sinusoidal obstruction syndrome (SOS) and graft-versus-host disease (GVH)

H19

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Gastroenterology/Hepatology, Oncohematology, Clinical Pathology, HUG

Patients undergoing bone marrow transplantation (BMT) may suffer from severe liver disease which may impact on survival. The most frequent causes include SOS and GVH, the diagnosis of which remains a challenge due to similarities in liver function tests (LFT) alterations. In this retrospective study, we determined the pattern of LFT changes and time to appearance after BMT, clinical symptoms, and hepatic hemodynamics in patients developing SOS or GVH in a single institution. Patients/Methods : We included all patients who underwent BMT at the HUG (2009-2019) with a histological diagnosis of GVH or SOS. Clinical, biochemical and transjugular liver biopsy data obtained at time of diagnosis were reviewed, as well as patients' outcome. Results : 16 patients (mean age 38 yrs, 93% male) presented with GVH (n=9), SOS (n=5) or combined lesions (n=1) after a median time of 105 and 165 days after BMT, respectively. Table :mean ± SD. HVPG :hepatic venous pressure gradient

Parameter	SOS	GVH	p value
ALT (IU/L)	104 ± 99	143 ±126	NS
AlkPh (IU/L)	117 ± 83	139 ±103	NS
GGT (IU/L)	229 ± 210	260 ± 161	NS
Bilirubin (umol/L)	19.5 ± 13.5	31.6 ± 35	NS
HVPG (mmHg)	13.6 ± 4	5 ± 2	<0.016
Abdo pain + ascite	n=3	n=1	NS
Jaundice	n=2	n=1	NS

An elevated GGT (> 2 ULN) was the most common alteration of LFT. One month after diagnosis and treatment, a marked reduction in LFTs was observed in 2 patients with GVH, with further degradation in all SOS patients leading to death (n=1). Conclusion: Both GVH and SOS may affect the clinical course after BMT. As clinical symptoms and biochemical alterations poorly discriminate between these 2 entities, liver biopsy and hepatic hemodynamics are essential for a precise diagnosis and to guide therapy.

Preliminary report on the Swiss Autoimmune Hepatitis Cohort Study

H20

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Preliminary report on the Swiss Primary Biliary Cholangitis Cohort Study

H21

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Joachim Mertens, Universitätsspital, Zurich; David Semela, Kantosspital St. Gallen, St. Gallen; Adriana Baserga, Fondazione Epatocentro Ticino, Lugano; Stefano Bellentani, Clinica Santa Chiara, Locarno; Benedetta Terziroli Beretta-Piccoli, Epatocentro Ticino, Lugano, Switzerland and Institute of Liver Studies, MowatLabs, King's College Hospital, London, UK. **Background and aims:** The Swiss Primary Biliary Cholangitis (PBC) cohort study was established in 2017 with the aim of collecting high quality, standardized data and biosamples on PBC in Switzerland. **Methods:** Inclusion criteria: diagnosis of PBC, or isolated positivity for anti-mitochondrial antibody (AMA) and/or for PBC-specific anti-nuclear antibody (ANA); residency in Switzerland. **Results:** 172 patients enrolled by March 2019 within 8 centres. 145 female; median diagnosis age 52 years; 166 white, 4 Asian, 2 black; 25 with PBC/autoimmune hepatitis (AIH) overlap. Three patients required liver transplantation before enrollment, one died 1.5 years after enrollment of liver-unrelated causes. Median retrospective observation was 49 months, median prospective follow-up 12 months; AMA was available in 128, being positive in 91%; 12/16 AMA-negative were positive for PBC-specific ANA; 61 had normal alkaline phosphatase at diagnosis, of whom 26 had a liver biopsy: 22 had histological findings compatible with PBC, 18 at stage Ludwig I-II (5 with overlapping AIH), 4 at stage Ludwig III-IV (1 with concomitant NASH and 1 with previous HCV); 2 had mild unspecific cholestasis, 1 had NASH, 1 had unknown findings. Treatment (available in 114 patients): 110 received ursodeoxycholic acid (UDCA), 1 azathioprine alone, 1 with AIH overlap steroids alone, 2 were not treated; second-line treatments included fibrates in 13 patients, and obeticholic acid in 5 patients. **Conclusion:** This study provides novel information on PBC in Switzerland, supporting that PBC histological changes are often seen in patients with isolated AMA-positivity, at times with concomitant liver diseases.

Epidemiology of hepatocellular carcinoma linked to non-alcoholic fatty liver disease in the canton of Geneva between 1990-2014: a populational and prospective study

H22

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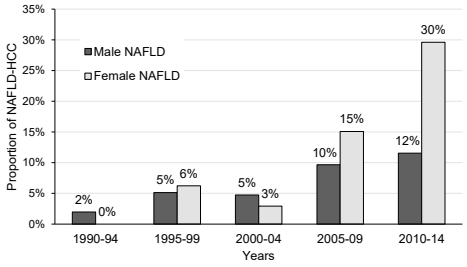
Background and Aims Non-alcoholic fatty liver disease (NAFLD) is a growing cause of hepatocellular carcinoma (HCC), one of the leading causes of cancer-related deaths worldwide. We aimed to assess the natural history and epidemiology of all patients with NAFLD-HCC in the canton of Geneva diagnosed between 1990 and 2014. **Methods** All HCC cases resident in the canton of Geneva diagnosed between 1990-2014 were extracted from the prospective Geneva cancer registry. Clinical information was prospectively collected and completed retrospectively with the Geneva University Hospital electronic health record. NAFLD-HCC was diagnosed when specifically stated or when other causes of liver disease were excluded in the presence of type 2 diabetes, metabolic syndrome or obesity.
Results 920 patients were diagnosed with HCC in the canton of Geneva between 1990-2014. Major aetiologies of underlying liver disease were alcohol (43.2%), hepatitis C and B viruses (20.7% and 9.1% respectively), and NAFLD (8.3%). Compared to non-NAFLD-HCC subjects, the 76 NAFLD-HCC subjects were significantly older, had higher rates of obesity, arterial hypertension and diabetes. NAFLD-HCC patients were more commonly female when compared to non-NAFLD-HCC, (31.6% vs 18.6% respectively, p=0.006). Over the 24 years, the proportion of NAFLD-HCC increased significantly in both sexes, but in particular in women from 0% in 1990-94 to 30% in 2000-14 (**Figure 1**).
Conclusions In a prospective cohort of HCC subjects spanning 24 years, NAFLD-HCC accounted for 8% of all HCCs. Compared to non-NAFLD-HCC, NAFLD-HCC patients were older, more comorbid and more frequently female and NAFLD seemed to drive an increase in HCC incidence in women in the past decade. This study underlines the specific clinical characteristics of NAFLD-HCC, which will help to guide future recommendations and research.

Figure 1: Proportion of NAFLD-HCC by sex between 1990-2014



The gene signature-MELD score and alcohol consumption determine long-term prognosis of patients with severe alcoholic hepatitis

H23

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Background: Accurate prediction of long-term prognosis of patients with severe alcoholic hepatitis (AH) is mandatory to guide therapeutic strategy. The gene signature-MELD (gs-MELD) score, a combination of a gene signature and the MELD score, has been proposed as a new prognostic tool and showed better diagnostic accuracy than all other prognostic scores for assessing the risk of death at 6 months (Trepo *et al*. Gastroenterology 2018;154:965-75). **Aim**: To assess the long-term prognostic value of the gs-MELD score among patients with severe AH. **Methods**: Patients with severe AH (Maddrey Discriminant Function >32) treated with methylprednisolone orally at a dose of 32 mg/day for a maximum of 28 days were followed for 5 years from the date of corticosteroid therapy initiation. The primary endpoint was survival at 5 years. The gs-MELD score was generated as described previously. Patients with a gs-MELD greater than 2.66 were considered to have a poor prognosis. Patients were considered abstinent if they had no alcohol consumption during follow-up. **Results**: 48 consecutive patients with histologically proven severe AH from 4 European centers were included (median age: 52 years [95% CI: 48-56], median Maddrey Discriminant Function: 50 [95% IC: 45-58]). None had active infection at the start of corticosteroids. Median gs-MELD score was 2.6 (95% CI: 2.2–3.0). 14 (30%) were considered non-responders to corticosteroids at day 7 according to the Lille score. During follow-up, 19 patients (40%) were abstinent, 24 (55%) died and 4 (8%) underwent a liver transplantation. At 5 years, rates of survival without death or liver transplantation were 57% (95% CI: 36-78) and 14% (95 % CI: 0-30) in patients with favorable and with poor gs-MELD score (p<0.001), and 61% (95% CI: 35-86) and 22% (95% CI: 6-39) in abstainers and in consumers (p=0.001), respectively. In time-dependent multivariable proportional hazards models, the gs-MELD score (hazard ratio: 5.78, 95% CI:2.17–15.38, p<0.001) and alcohol consumption (hazard ratio: 12.18, 95% CI:3.16–46.95, p<0.001) were independently associated with 5-year mortality. **Conclusions:** While only the gs-MELD score determines prognosis at short-term, both gs-MELD score and alcohol consumption are independently associated with the risk of death at 5 years. Therapeutic strategies should target alcohol consumption to improve long-term prognosis.

„Unusual presentation of recurrent, large and symptomatic focal nodular hyperplasia of the liver“ - Video Case

H24

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Background: Focal nodular hyperplasia (FNH) is a rare benign hepatic tumour, mostly non-invasively diagnosed by highly sensitive imaging techniques such as magnetic resonance imaging (MRI) or contrast-enhanced ultrasound (CEUS). In most patients, FNH is an incidental finding without significant increase in size over time or malignant transformation not necessitating any intervention. We present a well-documented unusual case of recurrent, large and symptomatic FNH lesions within 8 years.

Methods and results: A first large FNH of 10 cm in liver segment IVa was diagnosed in a symptomatic middle-aged male in 2011 by MRI and CEUS. Biopsy of the liver lesion confirmed FNH by histology and liver segment resection was undertaken. Followed by an unremarkable post-operative period over two years without any signs of recurrence the patient was dismissed. A second large symptomatic lesion (9.5 cm) in liver segments VI/VII was found in 2019. In contrast to the first lesion, evaluation of the second lesion by MRI and CEUS showed venous washout suggesting potential malignancy despite negative tumour markers. Due to these atypical imaging findings, liver biopsy and right-sided hemi-hepatectomy were performed with histological confirmation of recurrent FNH.

Summary: Although usually benign and asymptomatic, FNH can present with rapid growth, recurrence and symptoms warranting interventions such as resection or embolization. Here, we demonstrate state of the art diagnostic workup of focal liver lesions by CEUS, MRI, plugged ultrasound-guided biopsy followed by histological assessment as well as pre-operative assessment of liver function by ^{13}C-methacetin capacity test before liver resection.

Insulin resistance in Hepatitis C virus infection: Relative contribution from liver vs. extrahepatic sites

H25

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Background: Chronic hepatitis C (CHC) is associated with insulin resistance (IR), which may lead to type 2 diabetes. Although hepatitis C virus (HCV) infects only hepatocytes, it may induce IR in extrahepatic tissues. We aim to investigate the role of the liver in the control of glucose homeostasis in HCV infection.
Methods: Seventeen non-diabetic, lean CHC genotype 3 patients were treated with an IFN-free regimen for 12 weeks. Patients underwent a 2-step euglycemic hyperinsulinemic clamp before and after 6 weeks of antivirals. A panel of 27 cytokines was analyzed in patients' plasma. C57BL/6J mice infected with AAV8 expressing the HCV-3a core in hepatocytes were subjected to metabolic tests and biochemical analyses. Hepatokine mRNA levels were measured by RT-PCR in HCV-3a core mice livers and in HCV-3a core-expressing HepG2 cells.
Results: Clamp analysis showed a significant improvement of the peripheral insulin sensitivity upon HCV suppression (+13.1% [4.6-36.7], *p*=0.003). A distinct subset of hepatokines was modified by the antiviral therapy. Mice expressing the HCV-3a core in the liver were insulin resistant as compared to control mice. In mice livers as well as HCV-3a HepG2 cells, mRNA levels of selected hepatokines (vaspin, IGFBP7, ANGPTL4) were modified in agreement with the changes of their circulating levels in treated patients. **Conclusion:** HCV-3a induces peripheral IR that can be reverted by antiviral treatment-induced viral suppression. In addition, HCV infection affects the hepatokine secretion profile to induce peripheral IR, providing a model of hepatogenous diabetes.

Chronic hepatitis D and hepatocellular carcinoma: a systematic review and meta-analysis of observational studies

H26

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Objective: We aimed to determine whether chronic hepatitis D is associated with an increased risk of hepatocellular carcinoma compared to chronic hepatitis B virus monoinfection, by performing a systematic review and meta-analysis of published epidemiologic studies.
Design: We searched Pubmed, Embase and Web of Science, as well as study references and conference proceedings. We considered cohort and case-control studies allowing the calculation of effect estimates for the association between chronic hepatitis D (exposure) and hepatocellular carcinoma (outcome) in comparison to chronic hepatitis B. Data were pooled using random-effects models.
Results: Eighty-eight studies (64 case-control studies including 20782 patients and 24 cohort studies including 74822 patients) were included. Eleven studies accounted for confounders, in either study design or analysis, and 11 cohorts were prospective. The overall analysis showed a significantly increased risk of hepatocellular carcinoma in patients with chronic hepatitis D, despite substantial study heterogeneity (pooled odds ratio 1.29; 95% CI 1.03-1.61; I^2=68.34%). The association was particularly strong in studies with more robust design (pooled odds ratio 3.02; 95% CI 1.94-4.7; I^2=63.94%), and in HIV-infected patients (pooled odds ratio 7.13; 95% CI 2.83-17.92; I^2=0%).
Conclusions: This review found a significantly higher risk of hepatocellular carcinoma in patients with chronic hepatitis D, underlining the burden of hepatitis D virus infection and the need for accrued screening and the development of novel and effective antiviral therapies.

A combination of the ACC inhibitor GS-0976 and the nonsteroidal FXR agonist GS-9674 improves hepatic steatosis, biochemistry, and stiffness in patients with non-alcoholic steatohepatitis

H27

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Background and aims: Preclinical data suggest that the combination of an ACC inhibitor and FXR agonist is more effective than monotherapy in the treatment of NASH. Here, we describe the combination of the ACC inhibitor, GS-0976, with the nonsteroidal FXR agonist, GS-9674, in patients with NASH.
Method: Twenty patients with NASH diagnosed by a magnetic resonance proton density fat fraction (MRI-PDFF) ≥ 10% and liver stiffness ≥ 2.88 kPa by magnetic resonance elastography (MRE), or historical biopsy consistent with NASH and F2-F3 fibrosis were enrolled. Patients received GS-0976 20 mg and GS-9674 30 mg orally once daily for 12 weeks. Data from two cohorts treated with either GS-0976 20 mg or GS-9674 30 mg daily for 12 weeks are provided for comparison. MRI-PDFF and MRE and serum fibrosis markers were centrally read at baseline (BL) and week 12 (W12). Deuterated water was administered to measure hepatic de novo lipogenesis (DNL).
Results: In the combination cohort, 55% had diabetes and the median BMI was 38.7 kg/m2. Compared with BL, significant reductions at W12 in combination-treated patients were observed for PDFF (median: 16.4% vs 9.8%; p < 0.001), MRE-stiffness (3.76 vs 3.43 kPa; p = 0.018), serum TIMP-1 (263.4 vs 240.7 ng/ml; p = 0.012), PIII-NP (10.6 vs 8.4 ng/ml; p = 0.003), ALT, and GGT. At W12, a ≥ 30% relative decline in PDFF was observed in 14/19 patients (74%). Compared with monotherapies, combination therapy resulted in greater reductions in hepatic PDFF, ALT, GGT, and hepatic DNL. Combination treatment was safe and well-tolerated with AE rates similar to monotherapies; no patient reported ≥ grade 2 pruritus or discontinued study medications due to AEs.
Conclusion: The combination of GS-0976 and GS-9674 for 12 weeks was safe and led to improvements in hepatic steatosis, liver stiffness, liver biochemistry, and markers of fibrosis in NASH.

A Phase 3 Study Comparing Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide With Continued TDF Treatment in Virologically Suppressed Patients With Chronic Hepatitis B: Week 48 Efficacy and Safety Results

H28

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Background and Aims: TAF, a novel prodrug of tenofovir (TFV), was recently approved for treatment of CHB. We evaluated efficacy and safety in stable, virally-suppressed patients who were switched from TDF to TAF vs. continued TDF for an additional year.
Method: In this Phase 3 study (NCT02979613), CHB patients on TDF for ≥48 weeks with HBV DNA <LLOQ for ≥12 weeks and <20 IU/mL at screening were randomized (1:1) to TAF 25 mg QD or TDF 300 mg QD, each with matching placebo, and treated for 48 weeks. The primary efficacy analysis was the proportion of patients with HBV DNA ≥20 IU/mL at Week 48 based on the modified US FDA-defined Snapshot algorithm; the study was powered to show non-inferiority in efficacy of TAF compared to TDF, with a 4% margin. Key prespecified secondary safety endpoints were assessed sequentially: changes in hip and spine bone mineral density (BMD), and changes in estimated creatinine clearance by Cockcroft-Gault (eGFRCG). Markers of bone turnover and renal tubular function were serially assessed.
Results: 488 patients were randomized and treated at 42 sites in 8 countries. TAF demonstrated non-inferior efficacy to TDF with a similar rate (0.4%) having HBV DNA ≥20 IU/mL at Week 48, (difference in proportions: 0.0%, 95% CI, -1.9% to +2.0%). TAF treatment resulted in increases in hip/spine BMD with less impact on bone turnover makers; switching from TDF to TAF also resulted in increased eGFRCG and decreases in markers of tubular function. Rates of ≥Grade 2 adverse events (AEs) and serious AEs were low and similar between groups. No viral resistance was observed in the 3/243 (1.2%) and 2/245 (0.8%) TAF and TDF patients, respectively, who qualified for testing.
Conclusion: Virologically-suppressed CHB patients who were switched to TAF demonstrated noninferior efficacy to continued TDF with improved bone and renal safety.

Global real world evidence of sofosbuvir/velpatasvir as a simple, effective regimen for the treatment of chronic hepatitis C patients: Integrated Analysis of 12 clinical practice cohorts

H29

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Background & aims: SOF/VEL is a pangenotypic, panfibrotic, protease inhibitor (PI)-free, single duration, single tablet regimen (STR), offering a simplified treatment option to address this goal. This integrated analysis of real-world data from clinical practice cohorts representing a heterogeneous patient population evaluates the efficacy of SOF/VEL for 12 weeks, without ribavirin (RBV), in patients with HCV across all genotypes (GT) and fibrosis stages, including patients with compensated cirrhosis (CC).
Methods: Data from 12 clinical practice cohorts across North America and EU, representing 7 countries, are included. Adults were treated according to local standards of care, with CC determined by the treating physician according to local clinical practice. Data on GT1-6 patients with CC or without CC (NC), treatment naïve (TN) or treatment experienced (TE) [pegIFN+RBV ±PI], who completed SOF/VEL for 12 weeks prior to April 2018 were included. Patients with a history of decompensation, prior NS5A inhibitor exposure, treatment duration >12 weeks or addition of RBV were excluded.
Results: Overall, 5541 patients with HCV GT1-6 were included. The median age was 54 years, 52.8% were male and GT distribution was as follows: 30% GT1, 30% GT2, 33% GT3, 6.0% GT4-6, 1% mixed or unknown GT. CC was present in 1108 (20.7%) patients. 660 (12.4%) TE patients were included. 98.5% of patients (5134/5214) achieved SVR, with 98,7%%; 97,6%; 100% SVR respectively in NC, CC patients and patients with unknown cirrhotic status, and 97.8%, 98,3%, 96,4%% SVR respectively in patients with current/historic IV drug use, TE patients and GT3 patients with CC.
Conclusion: Simplicity is key in reaching the WHO goals for HCV elimination. SOF/VEL for 12 weeks is a simple and highly effective regimen that cures HCV patients, irrespective of GT, cirrhosis status or treatment history, with a manageable drug interaction profile, which will contribute to the implementation of test & treat strategies.

LIM Protein Ajuba Promotes Cancer Cell Proliferation and Survival in Hepatocellular Carcinoma

H30

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Background: The LIM-domain protein Ajuba is a structural protein involved in the maintenance of cell junctions, migration, differentiation, and proliferation. There are discrepancies as to whether Ajuba is a driver or suppressor of proliferation in cancer, therefore, the aim of this study is to characterize expression and function in hepatocellular carcinoma (HCC).
Methods: Ten human liver cancer cell lines and primary tumors were screened for Ajuba protein and mRNA expression. Its function was investigated by modulating protein levels with lentiviruses expressing shRNA targeted sequences or an overexpressing (OE) construct. The biological impact of Ajuba knockdown and OE transduced cells was tested in-vitro with various biological assays including a PCR Array, mass spectrometry and a 42-parameter panel for mass cytometry, and an in-vivo syngeneic mouse tumor model.
Results: Steady state levels of Ajuba mRNA in human liver cancer cell lines and primary tumors were significantly higher than in control liver tissue. Ajuba expression correlated with reduced life expectancy. Lentiviral transduction of HCC cells effectively knocked-down Ajuba protein levels resulting in a decrease of cell proliferation, migration, and colony formation, which coincided with a G2-phase cell cycle arrest. Using mass spectrometry and mass cytometry new protein interaction partners as well as pathways in which Ajuba is involved were identified. Using a syngeneic tumor model in C57BL/6 mice, HCC with knocked-down Ajuba expression had a significantly reduced tumor volume compared to controls.
Conclusion: Ajuba appears to be central to HCC cell proliferation and knock down reduces tumor growth and cell survival.

Look-back procedure to reach non-compliant and lost to follow-up HBV patients

H31

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Background: Hepatitis B Virus (HBV) infection is a contagious disease whose chronic form may be complicated by cirrhosis and
hepatocellular carcinoma (HCC). Regular surveillance of patients is therefore essential to prevent complications and avoid transmission.
Methods: We identified individuals who had not been seen for more than 15 months. Data was collected through paper and electronic medical records of all patients with an history of HBV infection seen at our hepatology center in the last ten years. Of them we enrolled only that ones with positive HBs antigen. We then contacted lost HBV patients by mail, letter and phone.
Results: The total number of patients with HBV infection was 433, of them 314 (72%) were HBsAg positive, among them 90 (29%) were lost to follow up (FU). Of those, 70 patients (78%) could not be reached or refused further FU, while 20 (22%) were reached and visited again. Median time without any specialist visit had been 3.75 years. At the following visit 2 of them (10%) needed a change in therapy because of fibrosis worsening or development of resistance under their ongoing treatment. Two more patients presented worsening liver fibrosis not requiring a new therapy. An average time of 1 medical working hour per patient was necessary to identify each patient lost to FU.
Conclusions: Based on the available literature, lost HBV patients have the same, if not worse clinical outcomes compared to those under regular FU. In our study we did not detect any new cases of cirrosis or HCC, but we were able to identify some patients in need of therapeutic changes. We conclude that a lookback procedure with the aim to find lost to FU patients, although time consuming, should be considered in each hepatology center.
* SC and CT contributed similarly to this study

Lysosomal compartment dysregulation as a treatment strategy for hepatocellular carcinoma

H32

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Background: Lysosomal sequestration of anti-cancer compounds reduces drug availability at intracellular target sites, thereby limiting drug-sensitivity and inducing chemoresistance. For hepatocellular carcinoma (HCC), sorafenib (SF) is the first line systemic treatment as well as a simultaneous activator of autophagy-induced drug resistance. The purpose of this study is to elucidate how combination therapy with the FDA-approved photosensitizer verteporfin (VP) can potentiate the antitumor effect of SF, overcoming its acquired resistance mechanisms.

Methods: HCC cell lines and patient-derived in vitro and in vivo preclinical models were used to identify the molecular mechanism of action of VP alone and in combination with SF.

Results: We demonstrate that SF is lysosomotropic and increases the total number of lysosomes in HCC cells and patient-derived xenograft model. Contrary to the effect on lysosomal stability by SF, VP is not only sequestered in lysosomes, but induces lysosomal pH alkalinization, lysosomal membrane permeabilization (LMP) and tumor-selective proteotoxicity. In combination, VP-induced LMP potentiates the antitumor effect of SF, further decreasing tumor proliferation and progression in HCC cell lines and patient-derived samples in vitro and in vivo. We further describe the impact of RAS oncoprotein status on lysosomal compartment stability after LMP.

Conclusions: Our data suggest that combination of lysosome-targeting compounds, such as VP, in combination with already approved chemotherapeutic agents could open a new avenue to overcome chemo-insensitivity caused by passive lysosomal sequestration of anti-cancer drugs in the context of HCC.

Concurrent biliary toxoplasmosis and portal-hypertensive cholangiopathy: a rare cause of haemobilia

H33

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Introduction: T. gondii infection is the most common protozoan infection in immunocompromised patients. An association with cirrhosis has been described and may be linked to impairments in cellular immunity (1). Infection is capable of changing the course of the disease (2). Also, the development of portal hypertension in cirrhosis very rarely manifests itself with haemobilia (3). **Case description:** A 44-year-old, HIV and HBV treated patient with Child B liver cirrhosis was referred to our emergency department with a 2-week history of melena and transfusion-dependent anemia. Initial endoscopic assessment revealed haemobilia. MRI of the abdomen showed signs of portal hypertension and slightly dilated intrahepatic bile ducts. Endosonography, ERCP and cholangioscopy revealed small pericholedochal vessels and intrahepatic, intraluminal biliary bleeding. Microscopic and immunohistochemical biliary biopsies analysis revealed the presence of T. gondii. After extensive workup failed to reveal other sources of bleeding, it was decided to put the patient on a course of pyrimethamin and sulfadiazine. The patient remains well since with no signs of recurrent gastrointestinal bleeding. **Discussion:** ERCP did not show classical signs of portal biliopathy (strictures, dilations, displacement of bile ducts). While T. gondii infection is not known to cause angio-invasive disease in other organs, the association of this clinical course, stability under antiparasitic treatment as well as lack of other plausible explanations suggests co-occurrence of both mechanisms caused this patients' symptoms. To our knowledge, no cases of T. gondii associated haemobilia in this setting have been reported.
Selected references: 1. Montoya et al, Lancet 2004 **2.** Alvarado-Esquivel et al, Parasites Vectors 2011 **3.** Chattopadhyay et al, World Journal of Gastroenterology 2012

REGENERATE: A Phase 3 International, Placebo-Controlled Study Evaluating Obeticholic Acid Treatment for NASH

H34

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Background: This M18 pre-specified interim analysis of the ongoing Ph3 REGENERATE study evaluated the effect of OCA on liver histology in patients (pts) with biopsy-confirmed NASH.

Methods: Pts with NASH and fibrosis stages F2-3 (ITT) were randomized to placebo (PBO), OCA 10mg or OCA 25mg QD. Primary endpoints were fibrosis improvement (≥1 stage) with no worsening of NASH, or NASH resolution with no worsening of liver fibrosis. The safety population included F1-3 pts (N=1968). Clinical outcomes will be evaluated at the end-of-study.

Results: The ITT population included 931 pts (PBO [n=311], OCA 10mg [n=312] or OCA 25mg [n=308]). The primary fibrosis endpoint was met by 11.9% PBO, 17.6% OCA 10mg (p=0.0446 vs PBO), and 23.1% OCA 25mg (p=0.0002 vs PBO) pts (ITT). The primary NASH endpoint was not statistically significant (ITT) (OCA 25mg p=0.1268 vs PBO). Pruritus was the most common AE (19% PBO, 28% OCA 10mg, 51% OCA 25mg) and was predominantly mild to moderate in severity. SAEs occurred in 11% PBO, 11% OCA 10mg and 14% OCA 25mg pts.

Conclusion: OCA improved liver fibrosis, key histologic features of steatohepatitis and liver biochemistry, demonstrating consistent efficacy with an overall AE profile similar to previous studies.

Ustekinumab (UST) Induced Clinically Meaningful Improvement and Remission as Measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) in Patients with Moderate to Severe Ulcerative Colitis

IBD2

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Background: The UNIFI studies evaluated the safety and efficacy of UST IV induction and SC maintenance in patients with moderately to severely active UC.

Methods: In the induction study, patients were randomized to a single IV dose of placebo (PBO, n=319), UST 130 mg (n=320), or UST ~6 mg/kg (n=322). Patients who were in clinical response 8 weeks after receiving UST IV induction were eligible for the maintenance study and randomized to SC PBO (n=175), UST 90 mg q12w (n=172), or UST 90 mg q8w (n=176). An IBDQ score ≥170 indicated remission, and clinically meaningful changes were evaluated by two definitions (≥16 or >20 points).

Results: Eight weeks after IV induction, patients receiving UST reported significantly greater mean improvement in IBDQ scores, and greater proportions of patients achieved clinically meaningful improvements from baseline and IBDQ remission compared with PBO (p<0.001 for comparisons of each UST group vs PBO). Through 44 weeks of the maintenance study, mean IBDQ scores worsened in the PBO group, were maintained in the UST q12w group, and improved in the UST q8w group (p<0.001).

Conclusions: UST IV induction induced significantly greater improvements in IBDQ scores compared with PBO. In induction responders, significantly more patients who received UST SC maintenance sustained the improvements through Week 44.

Effects of Ustekinumab (UST) Induction Therapy on Endoscopic and Histologic Healing in Ulcerative Colitis

IBD1

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Background: UST is an effective therapy for moderate-to-severe UC, however data regarding histologic improvement and the combination of histologic and endoscopic improvement (i.e. histo-endoscopic mucosal healing) are unknown.

Methods: We evaluated the effects of UST on histologic and endoscopic activity in the UNIFI Phase 3 induction study of UST in moderate-to-severe UC (n=961). Colonic biopsies were collected from the distal colon at screening and Week 8. Endoscopic improvement (EI) was defined as a Mayo endoscopy score $\leq$1; histologic improvement (HI) comprised the absence of erosion or ulceration, absence of crypt destruction, and <5% of crypts with epithelial neutrophil infiltration. Histo-endoscopic mucosal healing was defined as both EI and HI.

Results: At Week 8, EI was achieved in 26.6% and 13.8% of subjects treated with UST and PBO, respectively (adjusted treatment difference, 12.8%; 95% confidence interval [CI], 7.9 to 17.8; p<0.001). HI was achieved in 36.8% and 21.9% of UST and PBO-treated subjects, respectively (adjusted treatment difference, 15.0%; 95% CI, 9.0 to 21.0; p<0.001). Histo-endoscopic mucosal healing (HEMH) was achieved in 19.3% and 8.9% of UST and PBO-treated subjects, respectively (adjusted treatment difference, 12.5%; 95% CI, 6.2 to 14.8; p<0.001). Similar rates of EI, HI, and HEMH were achieved following induction treatment with UST 130 mg or 6 mg/kg IV.

Conclusions: Among subjects with moderately-to-severely active UC, those receiving IV UST induction had higher rates of EI, HI, and HEMH than those receiving PBO.

Efficacy and Safety of Ustekinumab (UST) as Maintenance Therapy in Ulcerative Colitis: Week 44 Results from UNIFI

IBD3

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Background: The study objective was to evaluate the safety and efficacy of SC UST maintenance therapy in UC patients (pts) in clinical response to a single IV induction dose of UST.

Methods: Phase 3, double-blind, randomized withdrawal study in pts with moderate-severe active UC who failed conventional or biologic therapy (including anti-TNF and/or vedolizumab) and were in clinical response 8 wks after receiving a single UST IV induction dose. Primary population (523 pts) randomized 1:1:1 to placebo (PBO) SC, UST 90 mg SC q8w or q12w.

Results: Baseline demographics and UC disease characteristics were generally similar among treatment groups. Significantly more pts receiving UST q8w and q12w were in clinical remission at Wk 44 (43.8% and 38.4%) vs PBO pts (24.0%; p<0.001 and p=0.002). Similarly, significantly more UST pts achieved steroid-free remission and endoscopic improvement at Wk 44 as well as maintained clinical response through Wk 44, compared with placebo. The safety was consistent with the known safety profile of UST in CD.

Conclusions: Both UST maintenance regimens achieved clinical remission as well as secondary endpoints among pts with moderate to severe UC induced into clinical response with a single IV dose of UST. No new safety signals were observed.

Efficacy and Safety of Ustekinumab Through Week 16 in Patients with Moderate to Severe Ulcerative Colitis

IBD4

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Background: Efficacy and safety of ustekinumab (UST) induction therapy through Wk16 in patients (pts) with moderate-severe ulcerative colitis (UC) were evaluated.

Methods: Pts were randomized to an intravenous (IV) induction UST dose (130mg or ~6mg/kg) or PBO. Rates include pts who achieved the endpoint at Wk8 after initial IV UST induction and pts who achieved the endpoint at Wk16 following a blinded dose of UST 90mg SC at Wk8 after non-response at Wk8.

Results: 77.6% of pts (130mg: 75.6%, ~6mg/kg: 79.5%) randomized to UST achieved clinical response within 16 wks. At Wk8, 56.5% (130mg: 51.3%, ~6mg/kg: 61.8%) responded. Among Wk8 non-responders who received a SC dose, 59.7% (130mg: 60.6%, ~6mg/kg: 58.4%) were in clinical response at Wk16. Clinical remission was achieved by 18.8% (130mg: 19.7%, ~6mg/kg: 18.0%) within 16 wks. At Wk8, 15.6% (130mg: 15.6%, ~6mg/kg: 15.5%) were in clinical remission. Among Wk8 non-responders who received a SC dose, 9.4% (130mg: 9.8%, ~6mg/kg: 8.9%) achieved clinical remission at Wk16. Fewer pts with a history of biologic failure achieved clinical response and remission within 16 wks compared with non-biologic failure pts. The adverse event (AE) profile for patients who received a single UST IV dose and those with an additional UST SC dose at Wk8 were similar and consistent with the AE profile for PBO.

Conclusions: The data support continuing treatment with UST through at least one SC dose 8 wks after IV induction in pts with moderate-severe UC.

Efficacy of Ustekinumab (UST) in Moderate-Severe Ulcerative Colitis (UC) in Biologic Failure (BF) and Nonbiologic-Failure (NBF) Populations

IBD5

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Background: UST was effective in therapy of moderate-severe UC. Here, efficacy in BF and NBF populations was evaluated.

Methods: Pts were randomized to an intravenous (IV) induction UST dose (130mg or ~6mg/kg), or PBO. Responders to UST IV induction entered maintenance and were randomized to SC 90mg UST (q12w or q8w), or PBO.

Results: Among BF pts, 98.8 % had failed ≥1 anti-TNF and 32.6% both anti-TNF and vedolizumab. In induction, for both BF and NBF pts, significantly more pts achieved clinical remission for UST vs PBO (BF: P<0.001 for both doses; NBF: P<0.05). Though treatment differences were generally similar between BF and NBF pts, proportions were consistently lower for BF pts. In maintenance, for BF and NBF pts, significantly more pts achieved clinical remission for UST q8w and q12w vs PBO (BF pts: P<0.001 and P=0.044; NBF pts: P=0.024 and P=0.020). More BF and NBF pts achieved each major secondary endpoint with UST vs PBO in both induction and maintenance. In BF pts, the efficacy of UST q8w was generally greater than UST q12w.

Conclusions: UST was effective for treatment of moderate-severe UC pts with and without a history of biologic failure.

Association between histological indices and ulcerative colitis (UC) activity measures among patients in the HICKORY (etrolizumab) open-label induction cohort

IBD6

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Background: Cross-sectional studies in UC have shown an association between histologic and clinical measures of disease activity. Using open-label induction cohort data of HICKORY, we evaluated this correlation at end of induction.

Methods: Baseline and week 14 biopsies were scored using RHI and NHI, histologic outcomes assessed by neutrophil presence/absence. Pairwise associations were quantified by Spearman correlation and Cohen's kappa coefficients. ΔRHI and ΔNHI comparison determined presence of a minimal clinically important difference (MCID) in Mayo Clinic score (MCS; ΔMCS≥3).

Results: At week 14, 22%, 23% and 8% of 97 patients achieved neutrophilic inflammation resolution, endoscopic improvement (ES≤1) and remission (ES=0), respectively. ΔNHI and ΔRHI were highly correlated (ρ=0.91). There was little to no association between laboratory results and ΔNHI/ΔRHI/ ΔES and a weak correlation between ΔNHI/ΔRHI and ΔES/rectal bleeding change and stool frequency. NHI, RHI and ES agreement with symptomatic outcomes was weak to moderate. Difference in the mean (ΔMCS≥3) suggests MCIDs of 1 (ΔNHI) and 9 (ΔRHI).

Conclusions: Analyses showed no association between changes in histologic scores and laboratory results. The correlation was weak between histologic and endoscopic score change, and weak to modest between histologic scores and symptoms at the end of induction.

Previously presented: Peyrin-Biroulet L et al. ECCO 2019

Disease activity in patients with inflammatory bowel disease correlates with the serum copper/zinc ratio

IBD7

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Background
Zinc and copper are trace elements that play important roles during immune response and wound healing. Decreased levels of serum zinc and copper have been observed in patients with inflammatory bowel disease (IBD). Here we investigate the correlation of zinc, copper and the copper/zinc ratio (Cu/Zn ratio) with disease activity parameters in patients with IBD.

Methods
In this cross-sectional study 98 patients with Crohn's disease (CD) and 56 with ulcerative colitis (UC) were prospectively enrolled. Disease activity parameters were compared to serum zinc, copper and Cu/Zn ratio.

Results
We have observed zinc insufficiency in 11.2% and 14.3%, copper insufficiency in 20.4% and 7.1% of patients with CD and UC respectively. Anemia, hypoalbuminemia and increased fecal calprotectin (FC) as well as C-reactive protein (CRP) was found to be significantly frequent in zinc deficient patients with IBD. In contrast, copper deficient patients with IBD had significantly lower serum CRP values and a trend to lower FC. In multiple linear regression models, adjusted for age, gender and albumin serum CRP, significantly correlated with serum copper (p<0.001) and the Cu/Zn ratio in both CD and UC (p<0.001), but not with serum zinc levels. FC levels correlated only with the Cu/Zn ratio in patients with UC (p< 0.038).

Conclusion
In patients with IBD, systemic inflammation influences inversely the serum zinc and copper levels. Consequently, the copper/zinc ratio will increase in patients with active disease.

HyperCkemia in IBD patients is TNF class-independent

IBD8

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Background: Infliximab can cause HyperCKemia in up to 30% of the cases, but class-specific occurrence of HyperCKemia has not been studied in detail. Creatine kinase (CK) levels were therefore compared between infliximab and vedolizumab-treated patients with inflammatory bowel disease (IBD). **Methods:** In this retrospective, monocentric study, 131 IBD (82 CD, 49 UC) patients of the Basel IBD cohort treated either with Infliximab or Vedolizumab were included. CK, LDH, CRP and Calprotectin levels were analyzed. **Results:** Significant differences in CK levels between infliximab and vedolizumab-treated patients were not observed. Adjustment of the treatment groups into males and smokers indicated significantly higher CK levels in infliximab-treated males and significantly lower CK levels in former smokers compared to vedolizumab-treated males and former smokers. No significant differences were found between infliximab- and vedolizumab-patients, while adjusted groups showed significantly higher LDH levels with increasing age and significantly lower levels in patients with a longer disease duration. Significant difference in CRP levels between infliximab- and vedolizumab-treated patients was not observed. When adjusted to diagnosis, infliximab-patients with Crohn's disease had a significantly lower CRP. However, significantly higher fecal calprotectin concentrations were noted in infliximab-patients compared to vedolizumab-treated patients, which was independent of diagnosis, gender, disease duration, smoking behavior and age. **Conclusions:** In our cohort, HyperCKemia is not a class-specific effect of anti-TNF antibodies. Interestingly, significantly reduced fecal calprotectin concentrations were observed in vedolizumab-treated IBD patients in a real-world setting, but head-to-head studies have to further evaluate our observation.

Amebic liver abscess after first infusion of ustekinumab in a patient with colonic Crohn`s disease manifestation

IBD9

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Background
Severe infections and serious complications under therapy with ustekinumab are rare observations. To our knowledge, no case of amoebiasis has been reported in the literature to this date.
Methods
Here we report a 50 year old man with a liver abscess due to entamoeba histolytica while on immunosuppressive therapy with ustekinumab.
Results
One year ago, the patient presented during a temporary working residency in Asia to the clinics with spondylarthritis and abdominal pain. A treatment with prednisone and subsequently with etanercept was initiated, but gastrointestinal symptoms remained refractory to both treatments. While on treatment with steroids and etanercept a ruptured appendicitis was surgically removed four months later. After a subsequent colonoscopy the patient was diagnosed with Crohn's colitis affecting the coecum and the ascending colon and started on adalimumab. Due to persistence of abdominal symptoms with a flare requiring hospitalization colonoscopy was repeated and showed persistence of inflammatory changes in the ascending colon with discrete involvement of the rectum. Treatment was switched to ustekinumab. Eight weeks later the patient was admitted to the hospital for fever and severe abdominal pain. Imaging studies revealed an abscess formation in the liver. PCR of the aspirate was positive for amoebiasis. Rapid response to treatment with metronidazole was observed. Retrospective analysis of the appendectomy specimen with H&E and PAS stain demonstrated amoebiasis, while PCR of histological specimens from colonoscopic examinations was negative. Follow up endoscopy 4 weeks after termination of the anti-infective therapy showed endoscopic and histological remission of Crohn`s disease.
Conclusion
This case report emphasizes careful evaluation of patients for latent infections before starting biological treatment and suggests being watchful for serious infectious complications while on therapy.

Efficiency of an integrated workflow with augmented reality in 3D laparoscopic liver resection: clinical evaluation of a new image guided surgery system

S1

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Background: To investigate technical feasibility and clinical benefit of a new augmented reality system in 3D laparoscopic liver surgery.

Methods: All patients (n=10) who received laparoscopic liver resection by a new image guided surgery system with augmented 3D imaging in a university hospital were included for retrospective analysis. Digitally processed preoperative imaging (magnetic resonance imaging or computed tomography) was merged to the 3D laparoscopic image using a landmark-based registration technique. Intraoperative efficiency of the procedure was measured as time needed to achieve sufficient registration accuracy. Technical accuracy was reported as fiducial registration error (FRE). Clinical benefit was assessed trough a questionnaire which was completed by the primary surgeon after each operation. Resection quality and 30 day postoperative morbidity are reported as outcome parameters.

Results: From January to March 2018, ten 3D laparoscopic liver resections of a total of 18 lesions were performed using the novel augmented reality system.
The mean FRE of the last registration attempt was 9.2 mm (SD 2,8). Median time for registration was 8:50 min (range 1:31 – 23:56). Average operation time was 136 minutes (SD 43). The questionnaire revealed the ease of use of the system and the benefit for resection of vanishing lesions as convincing positive aspects, whereas image registration accuracy for resection guidance was consistently judged as too inaccurate. Histology reported complete resection in all retrieved lesions. No major complications (Clavien-Dindo ≥ IIIb) occurred during the 30 days follow-up, although 3 patients required interventional bilioma drainage post-operatively.

Conclusions: Augmented reality in 3D laparoscopic liver surgery with landmark-based registration technique is feasible with only little impact on the intraoperative workflow. The benefit for detecting particularly vanishing lesions is high. For an additional benefit during the resection process, registration accuracy has to be improved and non-rigid registration algorithms will be required to address intraoperative anatomical deformation.

VIDEO OF A LAPAROSCOPIC REPAIR OF A STRANGULATED OBTURATOR HERNIA

S2

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Objective:

Obturator hernia is amongst the rarest hernias of the abdominal wall, probably a "once in a lifetime" encounter for an ordinary surgeon. The presentation is usually acute, as a small bowel obstruction.

Method:

We present the case of a 76 years old lady, admitted to our ED with signs and symptoms of a small bowel obstruction, in evolution for about 5 days. A CT scan confirm a small bowel obstruction due to a strangulated right obturator hernia, concomitant with uncomplicated left obturator and right inguinal hernias. We performed an emergency TAPP repair of all these three hernias.

Results:

The postoperative evolution was uneventful. The patient was discharged on the 6th postoperative day. At a 6 weeks follow up appointment, the patient is symptom free and with no signs of a recurrence.

Conclusion:

The laparoscopic approach is a viable option for complicated obturator hernias. The choice of a mesh repair for complicated hernias is still debated, but probably safe unless there is gross contamination of the operative site.

Intraductal papillary neoplasia of the bile ducts - a rare diagnosis

S3

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Background**:** Considered the hepatic equivalent of intraductal papillary mucinous neoplasm of the pancreas, intraductal papillary neoplasms of the bile duct (IPMN) are however frequently associated with cholangiocarcinoma. We present the short-term outcome of a small retrospective patient series.
Methods**:** Analysis of all patients treated for IPNB or cholangiocarcinoma originating from IPNB (CIPNB) in our institution from 2005 to 2018. Treatment: surgical or endoscopic resection. Follow-up: according to multidisciplinary tumorboard recommendation, MRI/CT after 6 to 12 months or endoscopies.
Results: 5 cases of IPNB and 5 cases of CIPNB are included in this report. 9/10 patients were female, median age was 64.5 years (range 53-82). For patients with IPNB, 2 left hemi-hepatectomies, 2 cholecystectomies and one endoscopic resection were performed. This patient had local recurrence, treated by a second endoscopic resection. One patient had progression to cholangiocarcinoma and underwent bisegmental liver resection followed by palliative gemcitabin. All patients with CIPNB underwent extended hepatic resection. One patient died postoperatively due to acute liver failure. One patient presented with recurrence in segment VIII/V after 84 month. Duration of follow-up ranged from 1 to 144 months.
Conclusion: IPNB diagnosis is rare, which could be attributed to delayed detection in oligosymptomatic patients. Early diagnosis and radical resection are warranted to prevent progression to malignant disease, which significantly reduces survival.

Publication of surgery specific outcomes as quality indicator - time to get involved?

S4

R. Galli, R. Rosenberg. Kantonsspital Baselland

Background
Public reporting of surgery specific outcomes is controversial. Although risk adjustment is necessary for making meaningful comparisons between providers, published data rarely account for patient severity. Mortality after resection for diverticular disease with abscess or perforation is one of the available data on the register published by the *Bundesamt für Gesundheit (BAG)*. The purpose of this work was to analyse patient characteristics and outcome for this category in our institution.

Methods
Patients were identified on the basis of the coding system used by the BAG from our hospital records.

Results
A total of 126 consecutive patients were analysed. Type of diverticular disease according to CDD was the following: 16 CDD 2a, 39 CDD 2b, 39 CDD 2c1, 6 CDD 2c2, 21 CDD 3b, 5 CDD 3c. 32 patients underwent elective procedures, 47 had emergency colectomy, while the remaining 47 had surgery during the same admission either due to failure of conservative treatment or as a scheduled procedure. 48.4% of patients presented ASA Classification ≥ 3. Predicted morbidity was 46.02% and predicted mortality was 6.16%. Overall mortality was 3.97% and rate of severe complications was 10.3%.

Conclusions:
Codes used in the register “Quality indicators for Swiss acute hospitals” refer to a heterogenous group of patients with a wide variability in terms of risk factors. Adjustment considering mode of surgery as well as comorbidities should be considered. Furthermore, hospitals should be aware that data provided to the BAG may not reflect the correct diagnosis leading to a misinterpretation of the results.

Compliance to the Surgical Safety Checklist over time in late and early adopters

S5

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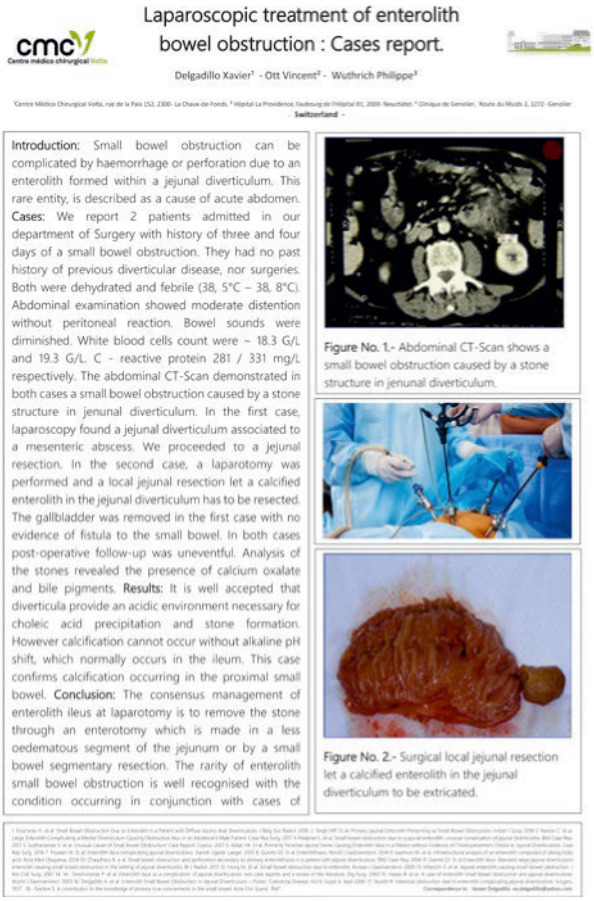
Aims: To compare the compliance of the Surgical Safety Checklist (SSC) in two groups of users: early (Group A) and late (Group B) adopters, and to detect change over time.

Method: Observational study. We collected all SSC protocols in one calendar month period and repeated collection for another month, 8 months later. Analysis was then performed to compare the compliance in different groups and over time.

Results: In total, 824 SSC protocols were collected (348 in Group A and 476 in Group B). There was no statistical difference in the overall compliance between the two groups (96.3% and 94.3%, respectively; p=0.201) and between elective and emergency cases (94.4% and 96.6%, respectively; p=0.148). Equally, there was no significant change in compliance over time in Group A (95.7% vs. 96.9%, p=0.551). In Group B, however, there was a trend to an improved compliance over time (92.5% vs. 96.7%, p=0.052). Compliance to the SSC was 97.6% for internally employed surgeons and 85.5% for consulting surgeons, respectively (p=<0.001).

Conclusion: The Surgical Safety Checklist can successfully be implemented for elective cases as well as for emergency operations using a step-wise approach. While early adopters maintain a high level of compliance to the SSC, late adopters still improve their compliance over time. However, consulting surgeons show a significantly lower compliance than internally employed surgeons. This fact has to be specifically taken into account for any implementation of the SSC in this setting.

S6


Laparoscopic treatment of enterolith bowel obstruction : Cases report.

Delgadillo Xavier[1] - Ott Vincent[2] - Wuthrich Philippe[3]

Introduction: Small bowel obstruction can be complicated by haemorrhage or perforation due to an enterolith formed within a jejunal diverticulum. This rare entity, is described as a cause of acute abdomen. Cases: We report 2 patients admitted in our department of Surgery with history of three and four days of a small bowel obstruction. They had no past history of previous diverticular disease, nor surgeries. Both were dehydrated and febrile (38, 5°C – 38, 8°C). Abdominal examination showed moderate distention without peritoneal reaction. Bowel sounds were diminished. White blood cells count were ~ 18.3 G/L and 19.3 G/L. C - reactive protein 281 / 331 mg/L respectively. The abdominal CT-Scan demonstrated in both cases a small bowel obstruction caused by a stone structure in jenunal diverticulum. In the first case, laparoscopy found a jejunal diverticulum associated to a mesenteric abscess. We proceeded to a jejunal resection. In the second case, a laparotomy was performed and a local jejunal resection let a calcified enterolith in the jejunal diverticulum has to be resected. The gallbladder was removed in the first case with no evidence of fistula to the small bowel. In both cases post-operative follow-up was uneventful. Analysis of the stones revealed the presence of calcium oxalate and bile pigments. Results: It is well accepted that diverticula provide an acidic environment necessary for choleic acid precipitation and stone formation. However calcification cannot occur without alkaline pH shift, which normally occurs in the ileum. This case confirms calcification occurring in the proximal small bowel. Conclusion: The consensus management of enterolith ileus at laparotomy is to remove the stone through an enterotomy which is made in a less oedematous segment of the jejunum or by a small bowel segmentary resection. The rarity of enterolith small bowel obstruction is well recognised with the condition occurring in conjunction with cases of

Figure No. 1.- Abdominal CT-Scan shows a small bowel obstruction caused by a stone structure in jenunal diverticulum.

Figure No. 2.- Surgical local jejunal resection let a calcified enterolith in the jejunal diverticulum to be extricated.

Laparoscopic Extended Left Hepatectomy for Giant Haemangioma. Technical Strategies for Complex Liver Resection. S7

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Background: Left hepatectomy can be performed safely laparoscopically in experienced hands for tumours that do not invade hilar structures or the middle hepatic vein. Proximity of a liver lesion to such structures represents an additional challenge for its laparoscopic removal. This video shows a laparoscopic extended left hepatectomy with the resection of a giant haemangioma in the left liver that displaces the left portal vein (LPV) and invades the middle hepatic vein (MHV).
Methods: A 59 year old woman with a giant haemangioma and abdominal pain was referred for surgical treatment. The laparoscopic liver resection was performed using a 3D optical system. It began with hilar dissection, division of the left hepatic artery and identification of the LPV. Dissection of the left-sided hilar structures allowed a clear visualisation and control of the compressed LPV. After division of the vessel, the left liver was completely mobilised and parenchymal transsection was performed to the right of the MHV under ultrasound guidance using and ultrasonic cavitation device, clips and bipolar forceps as well as an intermittent occlusion of ligamentary vessels. A vascular stapler was used to transsect the left and middle hepatic veins close to the confluence with the vena cava. The surgical specimen was retrieved through an umbilical incision.
Results: Operative time was 359 minutes with a total blood loss of 300ml. The recovery was uneventful and the patient was discharged on the fifth postoperative day. Final pathology showed a haemangioma with tumour free margins.
Conclusions: Laparoscopic resection of tumours in the left liver that invade hilar structures or the middle hepatic vein is feasible and can be performed safely. Standardized advanced laparoscopic techniques are essential for the success of this complex procedure in order to control bleeding and preserve an optimal view during vascular dissection and parenchymal transection.

The other liver metastasis with a crucial impact on the prognosis S8

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Background
Liver metastasis are a dismal sign for patients with colorectal cancer (CRC). However, not every hepatic lesion in a patient with CRC represent metastatic disease.

Methods
We report two patients, who have been operated for CRC and pre- and intraoperatively liver metastasis were radiologically suspected.

Results
An 83-year-old male and 76-year-old female patient underwent surgery for CRC in the colon ascendens and sigmoid, respectively. In the female patient, preoperative CT scan showed a hepatic lesion of 10mm in segment VI. In the male patient, preoperative CT scan revealed no metastatic lesion but intraoperative ultrasound showed a 10mm lesion in segment V. Both lesions were surgically removed and subsequent histology revealed the characteristic parasitic membrane of *Echinococcus species*. The diagnosis was further confirmed by molecular PCR analysis. Based on tumor stage II of the CRC, none of the patients received chemotherapy. The female patient, however, received an antihelmintic therapy for 2 years and both patients are free of disease at a 2 and 3 years of follow up, respectively.

Conclusion
Hepatic metastasis significantly worsens the prognosis of patient with CRC, decreasing the 5-year survival probability from 85% in stage II to less than 10% in stage IV. However, not all hepatic lesions represent metastatic disease and other uncommon etiologies, including parasitic lesion as Echinococcus cysts, should be excluded and intraoperative ultrasound is an important method to detect minor lesions.

Colorectal cancer associated with schistosomiasis - a case report S9

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Background
It is well known that there is a higher risk for urothelial carcinoma in people with a schistosomiasis infection. A causal relationship between schistosomiasis and colorectal cancer has long been suggested in the literature, but it is not uniformly accepted. We report on a female patient with colorectal cancer coexisting with a schistosomiasis infection.

Methods
Case report including Images from the histopathological analysis with vital schistosomas and some calcified schistosoma ova. A review of the literature was made.

Results
Considerable evidence supports an etiological link between Schistosoma japonicum and colorectal cancer in the Far East. Chronic inflammation and epithelial proliferation due to intestinal schistosomiasis may be a promoting factor for carcinogenesis. Our patient originally came from Eritrea where Schistosoma mansoni is endemic. The available data regarding the role of Schistosoma mansoni in colorectal carcinogenesis are conflicting and most often do not show causality.

Conclusions
There is a possible role for chronic schistosomiasis in promoting colorectal carcinogenesis. Further epidemiological studies are needed to investigate the cause and effect relationship between S. mansoni and colorectal malignancy.

Role of PKM2 in macrophage polarization during liver regeneration. S10

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Introduction: The pyruvate kinases (PKs) are ~~a group of four enzymes~~ responsible for the last and limiting step of the glycolytic pathway. The PKM2 isoform is found mostly in proliferating cells such as cancer and stem cells, as well as immune cells. In macrophages, the polymerization of PKM2 has been shown to change depending on their polarization state. The tetrameric protein complex is enzymatically active in the cytoplasm and the nuclear dimeric complex acts as a transcriptional activator via binding with HIF-1alpha. ADD a sentence to state purpose of the study.
Methods: Liver regeneration was studied using a 60% partial hepatectomy (PH) model in C57Bl/6 mice. Regeneration was assessed by evaluating liver to body weight ratio, immunohistochemistry doe Ki67 staining and mRNA expression of pro-proliferative genes (birc5, cyclin b) 48h post-PH. PKs mRNA levels were evaluated in liver tissue by qPCR at various time points post-PH. PKM2 inhibition was realized by treating the mice with shikonin or adenovirus delivering shPKM2. Identification of PKM2 positive cells was compassed by immunohistochemistry and mass cytometry. The polymerization state of macrophages was evaluated using mass cytometry and native western blotting.
Results: PKM2 mRNA level were elevated as early as 3h PH and remained elevated during the regenerative process. Inhibition of PKM2 by chemical and shRNA lead to decrease in liver regeneration capacity post PH. Analysis of PKM2 expression by immunohistochemistry revealed its co-localization with the macrophage marker F4/80. Analysis of macrophage polarization at different time point across liver regeneration process reveled a shift in macrophage function from M1 to M2 between 6 and 12h PH that correlates with PKM2 dimeric to tetrameric polymerization change.
Conclusion: We showed that PKM2 is increased in macrophages shortly after PH and is necessary for liver regeneration. In conclusion, our data demonstrates that changes in macrophage polarization together with PKM2 polymerization support hepatic regeneration following PH.

Robot-assisted gastric GIST resection: a single center experience **S11**

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Abstract

Introduction

Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors, representing 1-3% of all gastrointestinal cancer. Surgical resection is the only curative treatment. Minimally invasive approaches such as laparoscopic and robotic- assisted resections for gastric GIST have proved to be oncologically and surgically safe. We report here a case series of robot-assisted gastric GIST resections in our center.

Study design

We performed a retrospective analysis of all gastric GIST resected between 2007 and 2018 at the Geneva University Hospital, Switzerland.

Results

19 patients underwent robot-assisted gastric resection for GIST, 12 females and 7 males. Median age was 59 years (range 38-79) and median BMI was 27.5kg/m^2 (range, 18.6-41.3). Median tumor size was of 5 cm (range, 1.8-9). 13 were on the posterior wall and 7 were proximal (fundus or cardia). All tumors were completely resected (R0). We noted one conversion to open resection because of a positive margin requiring a radical resection. Median operative time was 157 minutes (range, 90-436). We reported no postoperative complications within 90 days after surgery. The median follow-up was 8 months (range, 1-115) and we reported no oncological recurrence.

Conclusions

Our case series confirm that robotic-assisted resection is safe and offers the same oncological results as the others approaches (open and laparoscopically) for gastric GIST.

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