Transilvania University
Brașov, Romania

7th ROMANIAN - GERMAN SYMPOSIUM OF GASTROENTEROLOGY

BRAȘOV, June 3-4, 2022

Scientific Committee

Prof. Monica Acalovschi
Assoc. Prof. Paul Jurgen Porr
Prof. Laurentiu Nedelcu
Prof. Ioan Sporea

Program and Abstracts

Scientific Programme

Friday, June 3rd, 2022

Aula Magna, Transilvania University, Brasov

08.30 On-site Registration

09.00 Opening remarks: Monica Acalovschi, Paul J. Porr, Ioan Sporea

09.15 – 11.00 Session I. GI and Liver Diseases – Diagnosis and Therapy

Chair: Wolfram Zoller, Dan L. Dumitrascu

09.15 *Andreas Geier, Würzburg (Online)*
Strategies for NAFLD diagnosis – from high tech to clinical reality

09.30 *Monica Acalovschi, Cluj*
Gallstone disease management: Guidelines versus real life practice

09.45 *Paul J. Porr, Sibiu*
Microbiota and the metabolic diseases

10.00 *Vlad Pavel, Stephan Schmid, Regensburg*
Hemostatic management in acute gastrointestinal bleeding

10.15 *Laurentiu Nedelcu, Brasov*
Proton Pump Inhibitors – between use and overuse

10.30 *Dan L. Dumitrascu, Cluj*
Are H2 breath tests useful?

10.45 Q&A

11.00 Innergy Symposium

11.15 – 11.45 Coffee break

11.45 – 13.15 Session II. GI Diseases – Diagnosis and Therapy

Chair: Tilo Andus, Mircea Diculescu

11.45 *Katharina Feilhauer, Jörg Köninger, Stuttgart*
Rationale of surgical resection in oligometastasing upper GI cancer

12.00 *Simona Bataga, Tg.Mures*
Serrated lesions of the colon-rectum: current management

12.15 *Mircea Diculescu, Bucharest*
IBD prospect RN, a National database for IBD between needs and accomplishments

12.30 *Adrian Goldis, Timisoara*
Fibrosis in Crohn's disease – from evolution to treatment

12.45 *Tilo Andus, Stuttgart*
Inflammatory bowel disease – current treatment

13.00 Q&A

13.15 AlfaSigma Symposium

13.30-15.00 Lunch break and Poster evaluation
Wolfram Zoller, Roxana Sirli, Paul Jurgen Porr, Sebastian Müller

15.00– 16.00 Session III. Chronic Liver Diseases

Chair: Martina Müller-Schilling, Zeno Sparchez

15.00 *Martina Müller-Schilling, Regensburg*
Acute-on-chronic liver failure

15.15 *Roxana Sirli, Timisoara*
Chronic liver disease and diabetes mellitus

15.30 *Sebastian Müller, Heidelberg*
Genetic modulation of fibrosis progression by PNPLA3 and MBOAT7: What can we learn from alcohol detoxification studies?

15.45 *Helmut K. Seitz, Heidelberg (Online)*
The role of cytochrome P4502E1 in acoholic liver diseases: from pathophysiology to treatment

16.15 *Zeno Sparchez, Cluj*
Treatment of HCV infection in patients with hepatocellular carcinoma

16.30 Q&A

16.30 – 16.45 Coffee break

16.45 – 18.00 Session IV. Endoscopy and Ultrasound

Chair: Sebastian Müller, Ioan Sporea

16.45 *Alexander Hann, Würzburg*
Advancing colorectal cancer prevention with artificial intelligence

17.00 *Ioan Sporea, Timisoara*
Ultrasound based elastography for the evaluation of portal hypertension

17.15 *Ernst Michael Jung, Regensburg*
Image fusion and CPUS perfusion imaging for monitoring liver tumor treatments by TACE and ablation therapies

17.30 *Marcel Tantau, Cluj*
Current status in cholangioscopy and pancreatoscopy

17.45 *Michael Jung, Mainz*
How to manage the problem of MRGN contaminated duodenoscopes – Sterilization, disposable endoscopes or what?

18.00 Q&A

18.15 Prof. Elke Roth, Brasov: Cultural interferences in the Transylvanian space

18.30 Closing remarks and Posters awards: Laurentiu Nedelcu, Monica Acalovschi

SESSION I

Strategies for Nonalcoholic Fatty Liver Disease (NAFLD) diagnosis - from high tech to clinical reality

Andreas Geier

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Nonalcoholic fatty liver disease is an increasingly recognized disease entity that may progress to end-stage liver disease. NAFLD defines a spectrum of liver disease characterized by a hepatic steatosis accounting for 5% of the liver in the absence of excessive alcohol consumption (women ≤20g/d and men ≤30g/d). This disease comprises a wide spectrum of liver damage, ranging from nonalcoholic fatty liver (NAFL) without evidence of hepatocellular injury, to nonalcoholic steatohepatitis (NASH) with the presence of inflammation and hepatocyte injury (ballooning) to advanced fibrosis and cirrhosis. NAFLD affects 10–24% of the general population worldwide and has now become the most common cause of chronic liver disease in Western countries.

NAFLD screening is currently not recommended in the general population. Main goal of NAFLD diagnosis is to identify subjects at risk for later development of cirrhosis, decompensation or hepatocellular carcinoma early enough for timely surveillance and intervention. NAFLD is usually suspected in individuals with asymptomatic elevation of aminotransferases and, radiological findings of fatty liver. Imaging studies, elastometry techniques as well as fat quantification tools help in determining the presence and amount of fatty infiltration of the liver, but the diagnosis of NASH as inflammatory disease entity and the exact fibrosis staging can still be confirmed only with a liver biopsy. Non-invasive markers, either blood-based or imaging-based, are therefore urgently required and should be evaluated in large research consortia such as the EU-funded LITMUS network.

Currently recommended algorithms (see current guidelines by all international societies) make use of more-or-less widely available non-invasive tools. A liver biopsy may not be necessary for the simple purpose of making the diagnosis of high-risk patients. In a two-step approach, NAFLD fibrosis risk score (NFS) and the more general fibrosis-4 score (FIB-4) (first step) followed by transient elastography or MR elastography (MRE) (second step) are important non-invasive diagnostic tools to discriminate patients without relevant fibrosis (high negative predictive value) from those with advanced fibrosis (less favorable positive predictive value). Liver biopsy is still the gold standard to diagnose NASH. Biopsy should be considered in patients with suspected progressive NAFLD to stage fibrosis and/or to exclude other competing etiologies.

In contrast to indirect fibrosis markers and scores such as NFS and FIB-4, direct serum fibrosis marker scores including fibrosis markers such as alpha-macroglobulin are commercial tools and not freely available without cost. Even less available and more costly are advanced elastometry techniques. Transient elastography (TE), magnetic resonance elastography (MRE), shear wave elastography (SWE) and acoustic radial force imaging (ARFI) are important non-invasive tools to assess the stiffness of the liver and to identify patients with advanced and non-advanced fibrosis. Hepatic fat measurement can be performed non-invasively in a semiquantitative fashion by controlled attenuation parameter (CAP) based on the Fibroscan device. Magnetic resonance spectroscopy (MRS) or magnetic resonance imaging-estimated proton density fat fraction (MRI-PDFF) are the currently most accurate non-invasive methods to detect and quantify liver fat.

Future efforts must be made to further evaluate the diagnostic potential of these tools in large patient cohorts and the added value of combinatorial approaches. Broad access to this advanced technology needs to be granted outside specialized or tertiary centers and high-income countries. Cross-sectorial integration of NAFLD screening into secondary and tertiary care remains the key task for structural improvement on a population basis. Automated screening tools in primary care as well as platforms for secondary NAFLD diagnosis by elastometry are urgently required. Most of the patients are currently lost in primary or secondary care and never enter diagnostic algorithms or structured surveillance and/or therapy.

Gallstone disease management: Guidelines versus real life practice

Monica Acalovschi, Cluj-Napoca

Gallstone disease has a prevalence of 10-20% in the population in Europe and other developed countries, leading to more hospital admissions than any other gastroenterological condition. Fortunately, less than one fifth of the gallbladder (GB) stone carriers will develop symptoms or complications.

We have guidelines of good-quality and internationally endorsed for gallstone (GS) management. But some of these become obsolete soon after publication, as new data appear from larger series of patients, from randomized control trials or systematic reviews. This makes it necessary to regularly confront the guidelines with real life practice.

Most of the GB stones are asymptomatic. For those symptomatic, laparoscopic cholecystectomy is the best therapy. But in subjects who could remain lifelong asymptomatic, even a low risk of postoperative complications cannot be accepted. There is still controversy regarding what should we do, watch and wait or intervene when asymptomatic GB stones are detected, for example during therapy for common BD stones, or in patients submitted to bariatric surgery, or in those with acute pancreatitis.

Symptomatic GB stones have a higher risk of complications and should be removed. But there is still controversy regarding the timing of laparoscopic cholecystectomy, as recent studies in large series of patients gave contradictory results.

Regarding the common BD (CBD) stones, it was long time believed that whether symptomatic or asymptomatic, they should be removed considering the high risk of severe complications - jaundice, acute cholecystitis or acute pancreatitis. And there is a consensus to always remove CBD symptomatic stones.

In contrast, managing asymptomatic CBD stones is still controversial because of there is a risk for endoscopic extraction. The first step should be to confirm their presence. The ASGE and ESGE guidelines recommend EUS or MRCP as the best investigations to confirm diagnosis in patients with sufficient clinical suspicion but insufficient evidence at abdominal ultrasonography.

Guidelines for GS management should be periodically up-dated with the new data coming from real-life practice. Correct implementation and dissemination of information is very important in order to ensure the best approach to these patients and minimize the difference in medical assistance.

Microbiota and the metabolic diseases

Paul Jürgen Porr

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The intestinal flora (microbiota) is formed beginning with birth and develops in function of different genetic, nutritional and other environmental factors. Therefore, a perfect symbiosis is formed with the human organism, even a vital partnership.

This state of symbiosis is often disturbed by different viral, bacterial or fungal infections, by sudden environmental or dietetic modifications, drugs (especially antibiotics), immunodeficiencies or other diseases, resulting different states of dysbiosis. These determine different digestive diseases, such as pseudomembranous colitis, inflammatory bowel diseases, irritable bowel syndrome, gastric or colorectal cancer a.o.

Other extradigestive manifestations or diseases are also a consequence or are at least influenced by certain dysbioses: autoimmune diseases (autoimmune hepatitis, primary sclerosing cholangitis, primary biliary cirrhosis, rheumatoid arthritis, multiple sclerosis), allergies, psychic disorders, or Alzheimer's disease.

An important category of diseases, influenced by different dysbioses are metabolic diseases: atherosclerosis, obesity, type 2 diabetes, or nonalcoholic fatty liver disease (NAFLD).

Atherosclerosis is correlated with high levels of *Collinsella* and low levels of *Eubacterium* and *Roseburia*. The metabolic transformation of choline from diet into betaine and trimethylamine-N-oxide by microbiota correlates directly with cardiovascular events.

Obesity is correlated with low bacterial richness ("Western style") as a consequence of the Western diet (fast food). But also inversely, obesity can influence the microbiota.

In type 2 diabetes mellitus there are low levels of *Firmicutes* and *Faecalobacterium prausnitzii*. An indirect correlation was also observed between insulin resistance and butyrate-producing microbiota, as well as the beneficial therapeutic and even a prophylactic effect of pre- and probiotics in diabetes.

In NAFLD an alcohol-producing microbiota was observed having a role in the oxidative stress and inflammation, resulting in steatohepatitis. The microbiota is not involved only in the pathogenesis of NAFLD by multiple routes, but also in their progression.

The encouraging evidence that faecal transfer of the microbiota improves the metabolic outcome in patients with metabolic syndrome suggests that it may be possible to use probiotics to improve the metabolic features.

Proton Pump Inhibitors between use and overuse

Laurentiu Nedelcu

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The development of antisecretory medications has revolutionized the management of acid-peptic disorders. Proton pump inhibitors (PPIs) are the most frequently prescribed medications for the treatment of peptic ulcer disease, erosive esophagitis, nonerosive reflux disease with excess acid in the esophagus and for Helicobacter pylori eradication regimens. Proton pump inhibitors are also indicated for prevention of NSAID-induced gastroduodenal ulcer, prevention and treatment of NSAID-induced upper gastrointestinal bleeding, prevention of stress ulcer bleeding in patients in Intensive Care Units, treatment of gastrinoma and of eosinophilic esophagitis.

PPIs have demonstrated their effectiveness and safety over the years. In the last decade the use of PPIs has significantly increased. Many patients are using high doses and long-term treatment. But not all patients require chronic PPI therapy. Articles published in prodigious medical journals (JAMA, Circulation, Journal of Am. Soc. of Nephrology) have drawn attention in recent years to the potential adverse effects of PPIs. Most of the studies were observational and the quality of the evidence was weak. However, the quality of evidence linking PPIs to alterations in the microbiome, to Clostridium Difficile

infection, drug–drug interactions and microscopic colitis is relatively strong.

The term deprescribing is increasingly used in medical practice (more articles in PubMed in the last two years) and defines "the planned process of reducing or stopping medications that may no longer be of benefit or may be causing harm". A group of Canadian authors even published a new guideline "Deprescribing proton pump inhibitors. Evidence-based clinical practice" [1].

The medical community agrees that the benefits of PPIs outweigh their potential adverse effects, and that PPIs should be prescribed for valid indications. When PPIs are prescribed for long-term use, they should be recommended in the lowest effective doses and the treatment should be periodically assessed.

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Hemostatic management in acute gastrointestinal bleeding

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Gastrointestinal (GI) bleeding is a common medical emergency with a wide range of clinical severity [1]. Causes of GI bleeding include: peptic ulcer disease, esophageal or gastric varices, cancer, polyposis syndrome, inflammatory bowel disease, Dieulafoy's lesions, hemangiomas, diverticula, angioectasia and hemorrhoids among others [2].

Many GI bleeding cases stop spontaneously but some patients present with massive hemorrhage requiring close observation with blood pressure monitoring, electrocardiographic monitoring and pulse oximetry in the intensive care unit [1, 3]. Especially in patients with liver cirrhosis, acute gastrointestinal bleeding can be fatal and is associated with a high mortality [4].

Therefore, rapid appropriate hemostasis and the prevention of the relapse of bleeding are very important. The treatment goals of acute massive GI bleeding are airway protection in intensive care environment, correct hypovolemia, stabilize blood pressure, achieve rapid hemostasis, prevent early rebleeding, prevent complications related to bleeding and deterioration of liver function. Treatment with crystalloid or colloid fluids and vasopressors is often necessary to stabilize blood pressure. Antibiotics should be initiated immediately in patients with liver cirrhosis [1, 3]. Transfusion of red blood cell concentrates is often required (if hemoglobin is lower than 7 g/dL). A post-transfusion target hemoglobin concentration of 7–9g/dL is desirable [5]. In patients with upper GI bleeding, high dose intravenous proton pump inhibitor (PPI) therapy should be considered [6].

In patients with coagulopathy, replacement therapy with pharmacological agents, fresh frozen plasma, prothrombin complex or platelets should be administered. If variceal bleeding is suspected, vasoconstrictors such as Terlipressin or Somatostatin should be initiated as soon as possible [3, 5–7]. In patients with suspected lower GI bleeding and hemodynamic instability, a computed tomography angiography is recommended before endoscopic or radiologic treatment [5].

After hemodynamic stabilization and airway protection, endoscopy must be performed. Endoscopy allows identification of the source of bleeding, as well as hemostatic treatment for bleeding lesions. Endoscopic hemostasis is probably the most important technical challenge that must be mastered by gastroenterologists. Several new endoscopic haemostasis technologies have been developed over the years. Physicians must be aware of all available devices to ensure the most effective outcome [8].

If endoscopy fails, interventional radiology procedures must be performed. Transjugular intrahepatic portosystemic shunt or partial splenic embolization are good options in cases of acute variceal bleeding [9]. Surgery should be considered only as the ultima ratio [1].

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Are H2 breath tests useful?

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The principle of breath testing is the assessment of the concentration of some components in the expiratory air, originating from the processing of an ingested substrate in the gastrointestinal lumen. Breath tests are based on the ability of the bacteria to produce H2 after metabolizing substrate such as glucose, lactulose or xylose. Some of the H2 produced by the bacteria, whether in the small intestine or in the colon, is absorbed into the blood flowing through the wall of the small intestine and colon. The blood containing hydrogen travels to the lungs where H2 is released and exhaled in the breath where it can be measured.

Breath testing in gastroenterology represents a group of non-invasive investigations of some pathological or potentially pathological changes of the gastrointestinal tract.

The most frequently used breath tests are the H2-breath test, the C13-breath test and the methane breath test.

The hydrogen breath tests are tests based on the measurement of the H2 concentration in the expired air after the ingestion of a certain substrate.

The most used substrates for the H2-breath tests are displayed in Table I. There are also other hydrogen-based breath tests which have not achieved clinical use. The new European consensus on breath tests is presented.

Table I. Commonly used H2-breath tests

Substrate	Indication	Name
Glucose	Small intestinal bacterial overgrowth (SIBO)	Glucose H2-breath test
Lactulose	SIBO Orocecal transit time	Lactulose H2-breath test
Lactose	Lactase deficiency	Lactose H2-breath test
Fructose	Fructose deficiency	Fructose H2-breath test

In conclusion, H2 breath tests still preserve their diagnostic value, despite recent controversy contesting their importance.

SESSION II

Rationale of surgical resection in oligometastasing upper GI cancer

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Historically, advanced and metastasizing upper gastrointestinal (GI) cancer represented a contraindication for curative surgery. Development of potent chemotherapeutic agents and biologicals, eventually in combination with radiotherapy and interventional techniques allowed for the expectation, that surgery would loose its dominant role in the treatment of solid tumors.

Quite contrary to these expectations, especially in combination with potent drugs and other treatment, resection of the tumor is essential for the patients chance to survive.

This development is reflected in recent guidelines of gastric and esophageal cancer where limited metastasis of local peritoneal carcinomatosis is no longer in principle a contraindication for surgery.

Decision making in treatment of these patients is demanding and requires close communication in highly specialized boards.

Serrated lesions of the colon-rectum: current management

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There are currently two major classes of precancerous polyps of the colon: the conventional adenomas and the serrated lesions. The serrated lesions include the hyperplastic polyps, which are not considered precancerous; sessile serrated lesions (also called sessile serrated adenomas) (SSLs), and traditional serrated adenomas (TSAs).

The sessile serrated lesions can potentially develop more aggressively into colorectal cancer as compared to other colorectal polyps and more rapidly, in approximately 3 years. Serrated polyps of the colon are the precursors of about 15-30% of colorectal cancers: they are usually found in the proximal colon, and account for a proportion of cancers developed after colonoscopy, "the interval cancers".

The serrated lesions are challenging in visualization, being flat and difficult to observe between the pitfalls, so they are more difficult to detect than conventional adenomatous polyps. The gastroenterologist has to be trained for recognising the endoscopic appearance of the serrated lesions.

Regarding the experience of the endoscopist, one principal factor is good endoscopic equipment. ESGE recommends the routine use of high definition systems and pancolonic conventional or virtual (NBI) chromoendoscopy for better detection of serrated polyposis.

In our experience, in the Gastroenterology Clinic, Tg. Mures, the introduction of the NBI equipment significantly increased the detection of the serrated polyps and we also reported an increase in the incidence of the polyps located on the right colon. All the polyps were resected, but the large sessile lesions were more difficult and challenging.

In conclusion, lesions are an important chapter of colon pathology. Improved endoscopic equipment and a trained endoscopist are important to detect and resect the serrated lesions, especially those on the right colon. The detection, diagnosis and resection of the serrated lesions remain a challenge.

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IBDPROSPECT RN, a National Database for IBD: between Needs and Accomplishments

Mircea Diculescu[1,2], Tudor Stroie[1,2]

1) Carol Davila University of Medicine and Pharmacy, Bucharest; 2) Fundeni Clinical Institute, Bucharest, Romania

Over the last 20 years, the incidence and prevalence of inflammatory bowel diseases (IBD) have dramatically increased in Romania. Both Ulcerative Colitis (UC) and Crohn's Disease (CD), but especially CD, have increased in the number of cases, severity and complexity.

Our actual database, the IBDPROSPECT database, was created in 2006 as a prospective study in which only two centers were involved: Cluj and Bucharest Fundeni.

The data collected from this database encouraged us to extend to other 13 centers all over the country. In this context, we included more then 3000 cases from the main university centers in Romania: Bucharest, Cluj, Iasi, Timisoara, Targu Mures, Oradea, Craiova, Constanta.

The data collected showed us that the ratio between UC and CD cases has changed especially in the most "westernized lifestyle" regions of the country together with the global increase in number, severity, and complexity of cases. As comparative figures, in 2003 we had estimated in a multicenter study designed by the Romanian Society of Digestive Endoscopy about 1,000 cases of IBD nationwide, and now we estimate to have more than 20,000 cases and more than 1,500 patients on biologic therapy.

Consequently, we realized that the data collected from the IBDPROSPECT study was outdated and we started to implement another database, updated to the current demands, with the purpose of becoming a real National registry of IBD in Romania, called IBDPROSPECT RN.

Fibrosis in Crohn's disease - from evolution to treatment

Adrian Goldiş

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In Crohn's Disease there is a chronic inflammation which can develop and cause tissue damage, represented by thickening and hardening in the bowel wall, a process called fibrosis. This may cause the intestine to lose mobility, causing a stricture (narrowing) of the bowel, which can then lead to blockage. Different proteins, such as collagens, which are normally involved in the tissue healing process, end up in a state of overproduction, consequently leading to fibrosis. The Lemann index was recently created with the aim of determining the total gut damage score in CD. Medical, surgical, endoscopic, and imaging results from all segments of the digestive tract are combined into a single total score [1, 2]. The Lémann score could be a clearer indicator of the magnitude of structural bowel injury, and it should be used to monitor bowel damage development over time.

Regardless of early anti-TNF exposure, survival curve study of this matched cohort revealed comparable progression of the stricturing behavior in patients. The transition in penetrating behavior was three times lower among those patients who received early anti-TNF, in contrast to patients who did not undergo early anti-TNF, but this decrease did not achieve significance in the unadjusted study. The early anti-TNF response was described as achieving corticosteroid-free remission 6 months after diagnosis, and this outcome was noted in 124 (71%) of the 175 participants with the available data. After 6 months, there was no discrepancy in the prevalence of B2 or B3 complications in anti-TNF responders and non-responders, despite the limited sample size of these subgroups [3, 4].

Internal penetrating disease and intra-abdominal abscesses can be identified with different degrees of accuracy using cross-sectional imaging such as MRI, CT or IUS [EL1]. For deep-seated fistulae, pelvic fistulae, or abscesses, MRI was preferred over ultrasound [EL4] [5].

Small bowel strictures can be detected using cross-sectional imaging [EL2]. As CT exposes patients to radiation, MRI and/or intestinal ultrasound [IUS] are the recommended approaches. In fact, none of the imaging methods will successfully assess the degree of fibrosis [EL3] [5].

Active inflammation and fibrosis usually co-exist, starting from the inflammatory wall thickening and advancing to the fibrotic thick wall which in time leads to fixed strictures. The two processes are commonly overlapping [6].

The use of MRI for the diagnosis of Crohn's Disease is becoming more widespread. The aim of this analysis was to identify and validate MRI predictors for an active CD or extreme CD, as well as a relatable Magnetic Resonance Index of Activity (MaRIA). The MaRIA Score is defined as following:1.5*wall thickness + 0.02*RCE + 5*edema + 10*ulceration. (RCE= relative contrast enhancement). In the study of Rimola J et al. [7], using CDEIS as a reference, it was observed that the following were independent predictors of disease severity: wall thickness, relative contrast enhancement (RCE), presence of edema, and ulcers on MRI.

Regarding the Lémann Index, to create and properly analyse the index, the digestive tract had to be divided in separate organs and segments. The damage evaluation was represented by a scale ranging from 0 - no damage to 10.0, represented by maximal damage or complete resection. Also, in this evaluation, the presence and length of the stricturing lesions and/or the presence of penetrating lesions were considered. Smooth muscle hyperplasia of the SM (submucosa), hypertrophy of the MP (muscularis propria), and chronic inflammation were the most notable histopathological characteristics of the stricturing intestine. Muscle modification was also found to be widespread in all layers. Chronic inflammation was shown to be strongly associated with total muscular hyperplasia or hypertrophy. In comparison, fibrosis was adversely associated with total muscular hyperplasia or hypertrophy. Muscular hyperplasia in the SM was also linked to aggressive inflammation within MU. To summarise, the smooth muscle hyperplasia/hypertrophy contributed the most to the stricturing phenotype. Fibrosis was shown to be less significant in CD-associated 'fibro-stenosis'. Regarding the pathogenesis of Crohn's strictures, we might say that the 'inflammation-smooth muscle hyperplasia axis' could be the most important [8].

In the pathogenesis of stenosis and fistulizing lesions, several different pathways can be involved. Lesions in the transmural space, especially fibrostenosing strictures, are the product of increased tissue remodeling. Uncontrolled extracellular matrix (ECM) formation may result in the obstructive lesions because of tissue remodeling. Around 95% of intra-abdominal fistulas seem to emerge throughout or around the proximal end of a stricture. Mechanical variables such as intraluminal pressure appear to take a role in the formation of fistulae, as shown by the fact that intra-abdominal fistulae appear to pass through the muscular layer along penetrating vessels. The production of chemokines, growth factors, and profibrotic

cytokines by the innate and adaptive immune systems results in the activation of mesenchymal cells. This activation occurs during chronic inflammation in CD, when the epithelial and endothelial defenses are significantly compromised. Elevated ECM deposition and architectural distortion appear in the lack of ongoing inflammation due to an increase of profibrotic factor activity, because of mesenchymal cell activation [9].

Agents that inhibit IL36R signaling can be introduced for the prevention and treatment of intestinal fibrosis in IBD patients [10]. Local ROCK inhibition prevents and reverses intestinal fibrosis by decreasing MRTF and p38 MAPK activation and increasing autophagy in fibroblasts, according to the article Holvoet et al. Overall, the findings suggested that local ROCK inhibition as a CD incorporate therapy may be effective in preventing fibrosis [11].

In conclusion, early diagnosis of fibrosis is of great importance. Fibrosis is certainly reversible in animal models. Instruments that can be used in the clinical trials are in development. The duration of treatment and toxicity are challenging for the time being. The future looks promising, but there is a need for improvement in methodologies for target discovery and pre-clinical drug efficacy testing.

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Inflammatory Bowel Disease – Current Treatment

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Medical treatment of inflammatory bowel disease has become more complicated by the invention of new therapies in the last few years. On the other hand, this allows more effective, and more individualized treatment than before.

However, in many patients with uncomplicated disease, the established and well known drugs steroids and 5-aminosalicylic acid are still the basis of treatment, since they are effective, well known and not expensive.

Standard treatment of ulcerative colitis

The treatment of ulcerative colitis depends on several factors. Most important are disease activity and location of the disease.

Ulcerative colitis always includes the rectum and inflammation can extend continuously up to the sigmoid colon, the descending colon, the transverse colon or up to the cecum. In very severe cases the terminal ileum can be involved as "back-wash"-ileitis. Moderate proctitis ulcerosa usually is first treated topically with 5-aminosalicylic suppositories, enemas or foam preparations (> 1g/d). In more severe cases, budesonide foam or enemas (2 mg/d) or oral 5-aminosalicylic acid (3g/d) may be added. Left-sided ulcerative colitis also is treated topically with 5-aminosalicylic suppositories, enemas or foam preparations (> 1 g/d). In more severe cases budesonide foam or enemas (2 mg/d) or oral 5-aminosalicylic acid (3 g/d) may be added. Subtotal ulcerative colitis and pancolitis are treated primarily with oral 5-aminosalicylic acid (3-4,5g/d). 5-aminosalicylic suppositories, enemas or foam preparations (> 1g/d) or budesonide foam or enemas (2 mg/d) can be added to reduce proctitis which helps to reduce the urging symptoms. Budesonid-MMX (9 mg/d) is another option for this situation, if 5-ASA alone is not helping enough. In more severe cases oral steroids such as Prednisolone (1mg/kg bodyweight) is given. Again, topical treatment may be added.

In refractory cases, patients should be sent to a hospital where intravenous steroid treatment is initiated. If refractory to systemic corticosteroids, cyclosporine A, tacrolimus or infliximab can be used. In cases of still refractory disease, a procto-colectomy must be performed.

In chronic steroid refractory or steroid dependent disease, several other options are available, such as azathioprine, TNF-antibody golimumab, integrin antibody vedolizumab or JAK-inhibitor tofacitinib.

Maintenance treatment is usually performed with 5-aminosalicylic acid in reduced dosing (50% of the dose in active disease). If this is not possible, E. coli Nissle 1917 can be used. In more complicated cases immunosuppressive drugs such as azathioprine or biologics such as TNF-antibodies, vedolizumab or tofacitinib.

Standard treatment of Crohn's disease

Treatment of Crohn's disease also depends on the disease activity and location of inflammation. The most common location is ileocecal. Moderate ileocecal disease can be treated topically with oral budesonide (9 mg/d). If refractory, prednisolone (60 mg/d) must be used.

If small bowel, or the colon is involved, or disease activity is more severe, prednisolone (60 mg/d) is the standard treatment. If refractory to steroids or very severe activity is present, azathioprine, methotrexate, infliximab, adalimumab or ustekinumab can be used. Sometimes combinations of biologics and azathioprine must be used.

In Crohn's disease doctors always must consider and exclude complications such as strictures and fistulae, and abscesses which may have to be treated endoscopically or surgically.

Maintenance treatment can be done with 5-ASA, azathioprine, methotrexate, TNF-Antibodies, vedolizumab or ustekinumab, depending on the individual situation of the patient.

Which drug for which patient?

Several factors are important for the choice of the drug such as efficacy, side-effects, mode of application, and price. Gastroenterologists and visceral surgeons should discuss this with the patients to get an informed consent.

New developments

Several drugs are in the pipeline such as JAK-inhibitors and lymphocyte trafficking inhibitors such as ozanimod and IL-23 antibodies.

SESSION III

Acute-on-chronic liver failure

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The well-known complications of liver cirrhosis include ascites, variceal hemorrhage and hepatic encephalopathy. Bacterial infection is as well a frequent precipitant as a consequence of these complications, and more than one quarter of patients hospitalized with decompensated cirrhosis will have a bacterial infection diagnosed (Olson 2020).

Of clinical importance, bacterial infection remains a leading cause of mortality and morbidity for patients with liver cirrhosis. In addition, epidemiological analyses have shown that infections due to multi-drug resistant bacteria are occurring with increasing frequency in patients with cirrhosis.

Of note, an infection can constitute a cause as well as a complication of the syndrome of acute-on-chronic liver failure (ACLF) (Cannon 2020) which results in poor patient outcomes.

Pathogenesis: Cirrhosis is an immunomodulatory deficiency state and thus predisposes patients with liver cirrhosis to infections through different mechanisms (Liaskou 2019, Irvine 2019). These include:

• *Genetic predisposition*: Genetic variations coding for pattern recognition receptors (PRR), especially NOD2 and TLR2 variants causing impairment of innate host defense mechanisms, have been associated with spontaneous bacterial peritonitis (SBP).

• *Immune dysfunction*: The concept of "cirrhosis-associated immune dysfunction," CAID, includes two underlying mechanisms: 1. Immunodeficiency, which affects both innate and adaptive immune system and 2. a state of persistent but inadequate activation of the immune system leading to the production of proinflammatory cytokines and systemic inflammation. CAID is a condition comprised of both increased systemic inflammation and immunodeficiency and leads to a substantial increase in mortality. Cirrhosis – per se – in the absence of infection is a status of "partial SIRS" characterized by increased pro-inflammatory cytokines (Cannon 2020) .

• *Increased intestinal permeability*: Bacterial overgrowth and intestinal barrier dysfunction can result in bacterial translocation.

• *Alterations in the intestinal microbiome*: Patients with liver cirrhosis are at greater risk of developing small intestinal bacterial overgrowth. The alteration of the intestinal microbiome further facilitates bacterial translocation to the mesenteric lymph nodes.

• *Hepato-adrenal syndrome:* Patients with cirrhosis are at risk of developing relative adrenal insufficiency, increasing the peril of sepsis and mortality risk (Cannon 2020).

Common infections

The most common infections in patients with cirrhosis include urinary tract infections (52%), SBP (23%), and spontaneous bacteremia (21%). Of clinical importance: 24% of patients develop a second infection during their hospitalization; these include: aspiration and ventilation-related respiratory- (28%), urinary including catheter-related- (26%), fungal- (14%), and C. difficile infections (12%).

Spontaneous bacterial peritonitis (SBP) accounts for ›30% of bacterial infections in hospitalized patients with cirrhosis. In patients who survive an episode of SBP, the cumulative recurrence rate at 1 year is approximately 70%. The EASL guideline on "Decompensated Cirrhosis" recommends prophylactic norfloxacin (400 mg/day, orally) in patients who recover from an episode of SBP. Patients who recover from SBP have a poor long-term survival and should be considered for liver transplantation. PPIs may increase the risk for the development of SBP (EASL 2018).

Concurrent infection is diagnosed in up to 22% of patients with cirrhosis with upper gastrointestinal bleeding on hospital admission and in 50% of these patients within the following two weeks. Gram-negative pathogens predominate and the use of prophylactic antibiotics during episodes of variceal bleeding has been established to reduce re-bleeding risk and confer a survival benefit (Cannon 2020).

Clostridioides difficile: Hospitalization increases the likelihood of exposure to *Clostridioides difficile*. In addition, antibiotic prophylaxis for SBP, immunosuppression for treatment of autoimmune hepatitis, and PPI use increase the risk of *C. difficile* in patients with cirrhosis. A *C. difficile* infection associated with greater mortality and longer hospital stay.

Infections in ACLF: The development of infection in a patient with cirrhosis triggers a pro-inflammatory response, cytokine release, and vasodilatation. Circulatory dysfunction leads to organ hypoperfusion, which is frequently followed by multi-organ failure.

MDR organisms: Severe infections including those caused by MDR organisms commonly occur in patients with ACLF and markedly reduce survival. Most importantly, infections in patients with cirrhosis do not always manifest with the typical features of fever and leukocytosis. Often, there is a more "silent" onset, suggested by the onset of encephalopathy, deteriorating renal or hepatic function, or hepatic decompensation.

In summary, SBP and urinary tract infections are the most frequent infections in patients with liver cirrhosis followed

by pneumonia and bacteremia, while pneumonia carries the highest risk of mortality. Bacterial infections must be systematically sought in patients with liver cirrhosis since they may appear as a precipitant or a consequence of ACLF. The severity of liver disease has been described to inversely correlate with the presence of typical clinical symptoms and patients with infection and fever have significantly lower MELD scores compared with those without fever or leucocytosis (Deutsch 2018). Worsening of liver function and consequent increase in MELD score or encephalopathy may be the only signs of an ongoing infection in patients with chronic liver disease.

An early diagnosis followed by an empirical antibiotic therapy adapted to the site of infection is crucial. Moreover, a fungal infection should always be discussed in these high-risk patients. Of clinical relevance, MDR bacterial infections constitute a prevalent, growing healthcare problem in patients with decompensated liver cirrhosis and ACLF across all Europe and negatively affect prognosis. Two multicenter studies have independently documented a high MDRB prevalence among patients with cirrhosis of 31–40% and the prevalence of MDRB in this population has been increasing over the past 5–10 years. The efficacy of empirical antibiotic strategies based on third generation cephalosporins has decreased due to the emergence of MDR bacteria (Fernández et al. 2019; Allaire et al. 2019).

Of clinical relevance, immunization against influenza, pneumococcus, and hepatitis A and B is recommended in patients with chronic liver disease.

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Chronic liver disease and diabetes mellitus

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Chronic liver diseases (CLD) and their final stage, liver cirrhosis (LC), are a major public health problem and a significant cause of morbidity and mortality worldwide, LC being the 13th cause of mortality [1]. Furthermore, diabetes mellitus (DM) is also a common disease, approximately 415 adult patients having DM in 2015, and more than 642 million new cases being expected in the next 20 years [2]. Thus, strictly from an epidemiological point of view, it is expected that a significant number of patients would have both type of diseases. However, the relationship between DM and CLD is much more complex.

Nonalcoholic fatty liver disease (NAFLD) tends to become the most common CLD in the Western world and it is expected that more than 100 million people will have NAFLD by 2030 [3]. DM, hypertriglyceridemia and obesity are the most important etiologic factors of NAFLD, whose spectrum ranges from simple steatosis to steatohepatitis and fibrosis/cirrhosis. Published data state that 60-87% of type 2 DM (T2DM) patients have NAFLD [4, 5], the prevalence of NAFLD being almost 100% in patients with T2DM and obesity. Also, in patients with NAFLD and alcoholic liver disease (ALD) the association with DM worsens the prognosis. In a study published in 2015, diabetic patients with NAFLD had a 3 times higher probability of developing cirrhosis than non-diabetics [6], while in another study DM was an independent predictor of fibrosis progression [7].

Viral hepatitis. Several studies have demonstrated that Chronic Hepatitis C is more frequent in diabetics than in the general population. HCV virus interferences with the insulin signaling cascade leading to insulin resistance (IR) and T2DM [8[. Furthermore, HCV-induced cirrhosis acts as an independent risk for T2DM [9]. Association of T2DM accelerates the progression to liver cirrhosis and hepatocellular carcinoma in HCV infection and attenuates the antiviral effect [10]. On the other hand, sustained virologic response improves insulin resistance [11].

Regarding Chronic Hepatitis B patients, the association with T2DM is a risk factor of advanced hepatopathy, increasing the risk for cirrhosis, especially in males [12]. Furthermore, a poor response to antidiabetic treatment has been associated with an increased risk for cirrhosis and hepatocellular carcinoma [13]. On the other hand, HBV cirrhosis was found to be an independent risk factor for T2DM [14]. Inhibition of virus replication through effective antiviral therapy reduces the onset of T2DM [15].

In conclusion, the interrelation of CLD and T2DM is a complex one since the liver plays a central role in the glucose homeostasis. Chronic liver diseases, especially liver cirrhosis are risk factors for T2DM, while T2DM is a risk factor for CLD, especially NAFLD. Association of DM is a poor prognostic

factor for CLD, accelerating the evolution to cirrhosis and hepatocellular carcinoma.

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Genetic modulation of fibrosis progression by PNPLA3 and MBOAT7: What can we learn from alcohol detoxification studies?

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Background & Aims: In genome wide association studies PNPLA3 and MBOAT7 were identified as important risk genes for the development of alcoholic cirrhosis: however, their functions and molecular mechanisms are still poorly understood. We present first data on the role of PNPLA3 and MBAOT7 genotypes on liver stiffness (LS), steatosis (CAP) and inflammation during alcohol withdrawal.

Method: 763 patients with ALD who were hospitalized for alcohol withdrawal at Salem Medical Center between 2007 and 2018 were genotyped for PNPLA3 s738409 and MBOAT7 rs626283 polymorphisms. All patients had routine laboratory, abdominal ultrasound and a transient elastography measurement (FibroScan) at admission. In 512 patients, data after 6.3 days of alcohol withdrawal was available.

Results: 71% of the patients were male, median age was 52 years, median BMI was 24.7 kg/m^2 and median alcohol consumption was 163 g/day. At admission, no difference between the genotypes of PNPLA3 and MBOAT7 was seen regarding age, BMI, gender, alcohol consumption or transaminase levels. Significant differences were observed for PNPLA3 and MBOAT7 during alcohol detoxification. While MBOAT7 was associated with higher LS, no differences were observed between genotypes upon alcohol detoxification. In contrast, PNPLA3 caused clearly a delayed resolution of LS during the withdrawal of alcohol due to inflammation. This could be recapitulated when looking at the serum markers of liver inflammation. In a sub-analysis of n=108 liver biopsies, inflammation was highly associated with PNPLA3 but not MBOAT7. More interestingly, PNPLA3 was associated with higher steatosis (CAP) although it resolved faster upon detoxification. No effect at all was seen for MBOAT7 on steatosis. A multivariate logistic regression model confirmed that PNPLA3 was associated with steatosis and inflammation but not fibrosis. MBOAT7 was only associated with fibrosis/cirrhosis but not inflammation or steatosis.

Conclusion: This first genotype data on a "human alcohol knock-out" intervention underscore important differences between PNPLA3 and MBOAT7. PNPLA3 seems to primarily drive fibrosis through inflammation and our data on CAP suggest an enhanced fat metabolism. In contrast, MBOAT7 seems to have a direct effect on fibrosis signaling and is neither associated with steatosis nor inflammation. Finally, alcohol detoxification could be a novel interventional approach to further dissect the metabolic mechanisms and their associations with genotypes.

The role of cytochrome p4502e1 in alcoholic liver diseases: from pathophysiology to treatment

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Cytochrome P4502E1 (CYP2E1) is part of the microsomal ethanol oxidizing system, which oxidizes ethanol to acetaldehyde. Chronic alcohol consumption results in a significant induction of CYP2E1, which is dose and time dependent and varies interindividually. CYP2E1 is also involved in the metabolism of drugs, in the activation of procarcinogens and in the degradation of retinol and retinoic acid (RA). As a result serum levels of some drugs are elevated with negative side effects in the presence of ethanol (e.g. central acting drugs) and some drugs such as acetaminophen or isoniazid are enhanced metabolized to toxic hepatic intermediates, when ethanol is absent from the body. The activation of procarcinogens such as nitrosamines and polycyclic hydrocarbons, primarily present in tobacco smoke, is one mechanism in ethanol mediated carcinogenesis. The loss of RA contributes to cellular hyperregeneration and to a loss of cellular differentiation. Furthermore, ethanol metabolism via CYP2E1 generates reactive oxygen species (ROS) which cause lipid peroxidation (LPO). The LPO products 4-hydroxynonenal and malondialdehyde can bind to DNA and may generate highly carcinogenic exocyclic etheno DNA adducts. ROS also stimulates hepatic fibrogenesis resulting in hepatic fibrosis and cirrhosis. It has been clearly shown that hepatic CYP2E1 activity modulates oxidative stress in cell cultures. The severity of alcoholic liver disease (ALD) is reduced in CYP2E1 knock-out mice and when CYP2E1 is inhibited by chlormethiazol (CMZ), but it is enhanced in CYP2E1 overexpressing mice. Most recent data in patients who were admitted to the hospital for alcohol detoxification therapy, demonstrate a significant improvement of serum transaminase activity and of hepatic fat during the treatment with CMZ, and thus CYP2E1 inhibition as compared to chlorazepate. In summary, CYP2E1 is an important player in the pathogenesis of ALD and this proof of principle may open up new strategies in the treatment of ALD and in the prevention of alcohol mediated carcinogenesis through the use of non-toxic inhibitors of CYP2E1.

Treatment of hepatitis C virus infection in patients with hepatocellular carcinoma

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The discovery of direct acting antivirals (DAA) with high rates of sustained virusological response (SVR) was a cornerstone event in the history of HCV treatment. DAAs improve liver function, prevent hepatic decompensation and might even reverse liver fibrosis. Although initial research pointed towards a potential drawback, it is now known beyond doubt that DAA treatment reduces hepatocellular carcinoma (HCC) occurrence or recurrence after curative treatments.

Unfortunately, other controversial issues have emerged:

1) Should the patients with early HCC and HCV be treated before or after surgery/ablation? In patients with HCV-related HCC who are fit for surgery or ablation, the first objective should be to treat HCC. Subsequently, if no recurrence is found on CT or MRI at 3 to 6 months after ablation or resection (based on recurrence risk factors), DAA therapy should be started. However, if follow-up reveals residual/active disease, the decision whether to start or not DAA is debatable.

2) Should patients with HCC on the waiting list receive DAA before or after liver transplantation? In HCV-patients listed for liver transplantation, DAA treatment is highly effective in curing HCV irrespective of the timing. DAAs could be initiated before LT in: a) patients with a MELD score between 23 and 27; b) patients eligible for down-staging therapies before LT, and c) patients from countries with a long waiting time. If the waiting time is short, DAA therapy before or after LT could be equally effective.

3) Should we use DAA in patients with intermediate stage HCC or in patients under systemic treatments? For patients with intermediate stage HCC and HCV co-infection an individualized strategy is warranted, carefully weighing the burden of the oncologic disease on an already vulnerable liver. There is little if any data about HCV treatment in patients with advanced HCC. However, in patients with expected good OS rates a subsequent DAA treatment seems to be a reasonable approach. The introduction of immunotherapy, particularly the combination of atezolizumab + bevacizumab has led to a higher complete or partial response rate and a better overall survival (OS) rate in these patients. This is another category of patients who could benefit from DAAs. However, these speculations should be tested in future clinical trials.

Additional problems come from the small channels of the endoscopes, which are difficult to clean and disinfect.

The specific problem of flexible duodenoscopes is the distal end. The area around the Albarran elevator is difficult to clean and, in addition, when a removable cap has been replaced by a fixed distal end.

Low temperature sterilization (ethylene oxide gas) seems not to be effective enough and comprises increased costs and a more than 16 h procedure. The European Endoscopic Societies (ESGE, ESGENA) (Update 2018 and statement 2017) aim to increase the quality and competency of the reprocessing staff by intensive training of the personnel (ESGENA curriculum 2019).

In particular, regular microbiologically hygienic tests are strongly recommended to check the quality of the reprocessing of the endoscopic unit.

Whether disposable endoscopes could replace conventional instruments is currently unclear because it seems to be difficult to provide adequate priced duodenoscopes of the

same complexity and quality and optical performance. In addition, the problem of trash and rising costs has not been really considered. For the moment, regarding the risk of rest contamination despite meticulous reprocessing, the responsibility lies with the quality of the endoscopy staff to provide a clean instrument for the patient's safety.

SESSION IV

Advancing colorectal cancer prevention with artificial intelligence

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Artificial intelligence (AI) applications such as computer-aided polyp detection (CADe) and classification systems have been introduced into clinical practice. Multicenter randomized studies presented an increase in the adenoma detection rate (ADR) when CADe was used in comparison with examinations performed without its use. Although, on first sight, the assistance of CADe seems promising, its influence on the examiner requires to be further analyzed. Problems such as false positive detections and discontinuous detections of polyps need to be identified and further steps should be undertaken to solve them. In this work, we present an overview of CADe systems for colorectal cancer prevention. We explore the influence of such systems on novice and experienced endoscopy staff using eye-tracking technology. We further present the first clinical study results of a new freely available CADe system able to identify polyps using four different endoscopy processors. This publicly funded AI that we developed is accompanied by additional AIs that help the examiner to track the withdrawal time and to concentrate on endoscopic interventions without disturbing detections.

In conclusion, AI will change the way we are performing endoscopy. Still the disadvantages of AI use such as a prolonged examination time and deskilling need to be identified and addressed from the outset.

Ultrasound based elastography for the evaluation of portal hypertension

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Portal hypertension (PH) is a common complication of liver cirrhosis. Development of esophageal varices and the risk of their rupture is a major risk for patients with advanced chronic liver diseases (cACLD).

Classically, the diagnosis of portal hypertension (PH) is performed using upper digestive endoscopy, which classifies the varices into small, medium or large. More precise, bleeding risk can be assessed invasively by the hepatic venous pressure gradient (HVPG). A value of HVPG>10 mmHg indicates clinically significant PH (CSPH). Because upper endoscopy is not a pleasant investigation for cirrhotic patients and HVPG is invasive, non -invasive modalities for PH evaluation were requested.

Ultrasound-based elastography is a good candidate for this assessment. Studies started more than 10 years ago, using Transient Elastography (TE) (performed with FibroScan) for the liver stiffness (LS) assessment, but lately elastographic evaluation of the spleen using the same method or other elastographic methods, such as point Shear Wave Elastography (pSWE) or 2D-SWE for liver and spleen have been used.

The Baveno VI Consensus stated that:" Patients with liver stiffness < 20 kPa and with platelet count > 150,000 have a very low risk of having varices requiring treatment, and can avoid screening endoscopy (1b;A)" and that: "These patients can be followed up by yearly repetition of TE and platelet count (5;D)" [de Franchis R et al. J. Hepatol. 2015; 63: 743-752]. This Consensus was confirmed by a multicenter prospective study on 310 patients with cACLD , all with LS by TE > 10 kPa and with a recent upper endoscopy, in whom, 33% met the Baveno VI criteria (LS<20 kPa, platelet count >150.000/mm3). In this study, the Baveno VI criteria had a 0.87 sensitivity, and a 0.98 negative predictive value, accurately identifying 98% of patients, who could safely avoid endoscopy [Maurice JB et al. J Hepatol. 2016; 65: 899-905].

Later on, expanding the Baveno VI criteria [performance of different thresholds of platelet counts and LSM for the identification of patients at very low risk (<5%) of having varices needing treatment (VNT)], it was found that the best new expanded classification rule was a platelet count >110 × 109 cells/L and a LSM <25 kPa. In one study, the Expanded-Baveno VI criteria would potentially spare 40% of endoscopies (21% with Baveno VI criteria) in the evaluation of a population of 925 patients [Augustin S. Hepatology 2017 Dec;66(6):1980-1988].

Some studies looked to pSWE and 2D-SWE of the liver using ARFI technology, with contradictory results, giving specific cut-off values for significant portal hypertension [Bota S, et al. Ann Hepatol. 2012; 11: 519-525; Vermehren J, et al. Liver Int. 2012;32: 852-858; Morishita N, et al. J Gastroenterol. 2014; 49:1175-1182; Kim TY, et al. Liver Int. 2015 Apr 15. doi: 10.1111/liv.12846; Procopet B, et al. J Hepatol. 2015; 62: 1068-1075].

More recently, spleen stiffness (SSM) elastography was used for the assessment of portal hypertension. Using first the TE

(and later a modified software for spleen assessment) or pSWE and 2D-SWE, different values were proposed for this. Using the Baveno VI criteria and spleen stiffness by TE, in a cohort of 498 patients with cACLD evaluated retrospectively, a new cut-off of SSM of < 46 kPa was identified, that in combination with the Baveno VI criteria (LSM <20 kPa and platelets>150.00) had 0% high risk varices missed [Colecchia A et al. J Hepatol. 2018; 69: 308-317].

Using 2D-SWE for the liver and spleen stiffness evaluation, in a prospective multicenter study including 158 subjects with pressure gradient measurements, it was found that liver-SWE >29.5 kPa and spleen-SWE >35.6 kPa were able to "rule-in" CSPH (specificity >92%) and that liver-SWE ≤16.0 kPa and spleen-SWE ≤21.7 kPa were able to "rule-out" CSPH [Jansen C et al: Liver Int. 2017; 37: 396-405].

In conclusion, patients with cirrhosis of viral etiology, with LS by TE< 20 kPa and a platelet count > 150,000 have a very low risk of having varices requiring treatment and can avoid screening endoscopy. At the same time, spleen stiffness using TE can be used for PH evaluation. pSWE and 2D-SWE need further assessment for predicting portal hypertension.

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Ultrasound image fusion for monitoring and follow up after ablation therapies and transarterial chemoembolization (TACE) of malignant liver tumors

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Background: The technique of ultrasound image fusion enables the combination of real time ultrasound scanning including contrast enhanced ultrasound (CEUS) with computed tomography (CT), magnetic resonance imaging (MRI) or PET-CT. Critical analysis of our own results and literature will be performed, to evaluate whether fusion is helpful for monitoring and follow up after ablation therapies and TACE of malignant liver tumours.

Method: Experienced examiners can realize fusion by plane and point registration in axial planes of real time ultrasound scanning and stored images of CT, MRI or PET-CT of malignant liver tumors. Fusion with CEUS realizes a dynamic evaluation of the tumors' microvascularization from the early arterial phase (15 sec) up to the late venous phase up to 6 min. Criteria for malignancy are early irregular hyperenhancement and increasing wash out up to the late phase. For image fusion performance up to four different CT or MRI sequences can be used.

Results: Considering our own results and the literature review, technically successful US image fusion can be correctly performed in more than 90% of cases by experienced examiners. Fusion enables to evaluate the success of ablation therapies (MWA, RFA, IRE) in up to 98% cases, compared to reference imaging methods and the follow up. After TACE, fusion by CEUS and CT is superior to the results of CT alone and could realize the follow up with the same diagnostic accuracy such as MRI with correct results in more than 86%. The main advantage of Image Fusion is a live therapy monitoring of liver tumor treatment by fusion with CEUS, if the tumor lesions are not detectable by the B-Mode and CCDS. Fusion of US/CEUS with PET-CT is more difficult to realize, but could be helpful for the follow up after radionuclide application (SIRT). The necessary time to realize fusion with CEUS including examination up to the late wash out is up to 20 min. Until now, only high-end ultrasound systems have offered fusion tools with appositional costs up to 25,000 Euro, but additional 3D techniques are often integrated in matrix high resolution ultrasound probes.

Conclusion: Performed by experienced examiners fusion by CEUS with CT or MRI is very helpful for the localization and successful treatment by ablation therapies or TACE of malignant liver lesions, if surgery is not possible.

How to manage the problem of MDRO (Multi-drug resistant organisms) contaminated duodenoscopes – sterilization, disposable endoscopes, or what?

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Numerous infectious series in the latter years (2014-2016) with MDRO contaminated duodenoscopes have thrown doubts on effective reprocessing of flexible endoscopes. Two nationwide Dutch studies (2018, 2019) revealed contamination of 15% of duodenoscopes and 13% of echoendoscopes with relevant bacteria from the gut despite correct handling. A meta-analysis by Larsen (2020) with 15 studies included, confirmed the same risk findings of 15 % bacterial contamination after reprocessing. The American FDA reported on results from a manufacturer post marketing testing of duodenoscopes of 5% positive tested duodenoscopes with "high concern" bacteria. Despite these alarming results the actual infection rate remains unclear.

Following the Spaulding classification, flexible endoscopes and their components are regarded as semi-critical devices and should undergo high level disinfection after use. Disinfection is defined as an irreversible destruction to a level appropriate to safe use on a patient, which includes all microbiological pathogens, bacteria, but not necessarily all spores.

Reprocessing of endoscopes (duodenoscopes) is a very complex multistep procedure, including three main parts:

Cleaning with bedside cleaning and thorough brushing including leakage test and function test is the first step before high level disinfection is performed in an automatic endoscopic washer-disinfector (EWD) with rinsing, disinfection, and neutralization as final rinsing. While this procedure is completely running electronically, the first and last part of reprocessing (cleaning and drying, transport and storage) are performed manually by the endoscopy personnel.

Regarding the bio-burden of used instruments (5-10 log steps) and the elimination rate of 8-12 log steps, the safety margin with 0-2 log steps seems to be very low. So, the weak points of endoscopic reprocessing are the human influence or the "human factor" in the cleaning process and in drying and storage of the endoscopes. If these reprocessing parts are not performed perfectly, gut bacteria may persist, also Pseudomonas aeruginosa may develop in wet areas with building up biofilms. Biofilms are mucopolysaccharide layers of residual organic material containing protein plugs. These coverings may prevent bacteria from complete elimination by rinsing and flushing because they may resist to current disinfectants.

Additional problems come from the small channels of the endoscopes, which are difficult to clean and disinfect.

The specific problem of flexible duodenoscopes is the distal end. The area around the Albarran elevator is difficult to cleanand, in addition, when a removable cap has been replaced by a fixed distal end.

Low temperature sterilization (ethylene oxide gas) seems not to be effective enough and comprises increased costs and a more than 16 h procedure. The European Endoscopic Societies (ESGE, ESGENA) (Update 2018 and statement 2017) aim to increase the quality and competency of the reprocessing staff by intensive training of the personnel (ESGENA curriculum 2019).

In particular, regular microbiologically hygienic tests are strongly recommended to check the quality of the reprocessing of the endoscopic unit.

Whether disposable endoscopes could replace conventional instruments is currently unclear, because it seems to be difficult to provide adequate priced duodenoscopes of the same complexity and quality and optical performance. In addition, the problem of trash and rising costs has not been really considered. For the moment, regarding the risk of rest contamination despite meticulous reprocessing, the responsibility lies with the quality of the endoscopy staff to provide a clean instrument for the patient's safety.

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16. Multistep diagnosis of a rare hepatic epitheloid angiomyolipoma. A case report
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Cell-block cytology: a promising diagnostic tool in cholangiocarcinoma? A pilot study

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Background & Aim: The high mortality and the increasing incidence of cholangiocarcinoma (CCA) evoke a stringent need for new diagnosis and prognostic methods. Combinations of clinical/biochemical features, imaging techniques and serum tumor biomarkers are commonly used to help in the diagnosis of CCA. However, tumor biopsy is usually required to confirm the diagnosis. The aim of this pilot study was to assess the diagnostic performance of cell-block cytology from the bile in patients with non-resectable CCAs.

Methods: Between October 2019 and January 2020, seven patients diagnosed with non-resectable CCAs and two with pancreatic and gallbladder carcinoma, in whom the endoscopic retrograde cholangiopancreatography drainage failed, were hospitalized for percutaneous biliary drainage. At drainage, 20 ml of bile were collected for cell-block analysis.

The median age of the patients was 62 years, and 5 were women (55.6 %). The median serum bilirubin level was 18.78 mg/dL and CA19-19 level was 260.17 ng/mL. Four out of 9 patients had Bismuth 4 tumor, 1 had a Bismuth 1 tumor, 2 had distal CCA, 1 had pancreatic head carcinoma and 1 gallbladder carcinoma.

Results: In the investigated patients, cell-block analysis from the bile identified 7 out of 9 patients as malignant. The sensitivity of the method was 77.78%, the specificity 100% and the accuracy 80%.

Conclusions: In our series of patients with bile duct cancer, the cell-block method for evaluating bile cytology showed a good diagnostic sensitivity and accuracy. Larger studies are needed to validate the results.

Small bowel video capsule endoscopy: the influence of diabetes mellitus, inflammatory bowel disease and prior abdominal surgery on completeness of examination and transit times

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Background & Aim: Small bowel video capsule endoscopy (VCE) is a well-known non-invasive tool for the examination of the small intestine, as large parts of it are inaccessible to conventional endoscopes. However, life-span of the capsule battery is limited and retention of the capsule can occur in any part of the gastrointestinal tract leading not only to incomplete image acquisition but potentially to bowel obstruction.

Diabetes mellitus is associated with delayed gastric emptying, which could in theory impede capsule propulsion. Furthermore, patients with prior laparotomy or inflammatory bowel disease (IBD) are prone to adhesions, endoluminal strictures or scar tissue. The aim of our study was to investigate the impact of those factors on the retention rate, completion rate, gastric and small bowel transit times and need for endoscopic capsule placement.

Material and Methods: In our hospital, over 50 VCEs are performed annually. We used the data of all 267 capsule endoscopies in the period of January of 2016 until June of 2021 (all Pillcam SB3). All patients were retrospectively evaluated for indication, gender, age, diabetes, IBD, prior abdominal surgery, and gastric and intestinal transit times.

Results: The mean gastric and small bowel transit times were 0.89 (SD 1.04) and 5.02 (SD 1.98) hours, respectively. Quality criteria were well within the recommended range with a completion rate of 89 percent and a retention rate of 1.1 percent (three cases), none of which required surgery.

In contrast to other studies, a preliminary analysis did not reveal obvious differences in transit times for diabetic and IBD patients. The mean gastric passage time was significantly longer in patients with incomplete versus complete endoscopies (1.51 vs. 0.86 hours). Furthermore, two out of the three patients with confirmed capsule retention either had a history of prior abdominal surgery, diabetes or both.

Conclusion: Video capsule endoscopy is generally safe and non-invasive. A prolonged gastric passage time is a risk factor for an incomplete examination. In our patient collective, diabetes and a history of prior abdominal surgery seem to be connected to capsule retention and incomplete endoscopy, although case numbers were too small to show statistical significance.

Prospective comparison US vs. CEUS guided percutaneous biopsy in the diagnosis of large intra-and retroperitoneal tumors

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Background & Aim: Due to the presence of necrosis, the accuracy of echoguided percutaneous biopsy (US-PB) in the diagnosis of large retro (RPT) and intra peritoneal tumors (IPT) is around 70-80%. Contrast enhanced ultrasound (CEUS) is able to delineate necrotic from well-perfused areas inside the tumors. The aim of this prospective study was to compare the sensitivity of US and CEUS guided PB in the diagnosis of these tumors.

Material and Methods: 60 patients (38 males, 22 females, mean age 63 yrs), with 24 IPT and 36 RPT (mean diameter 7.5 cm, range 4-22 cm) detected in oncological patients were referred to the ultrasound department for PB. In 32 patients (11 IPT and 21 RPT) PB was performed using US guidance; 28 patients (13 IPT and 18 RPT) were biopsied using real time CEUS guidance (1.2 -2.4 ml Sono Vue /procedure). The lesions in the CEUS –PB group were larger than those in US-PB group (mean diameter 8.1 cm vs. 6.8 cm) but without statistical significance (P>0.05). PB was performed with an 18G Bard needle coupled on Biopty Gun. CEUS guidance was used in all patients in the arterial phase, the needle being guided in the enhancing areas.

Results: Real time CEUS-PB was technically successful in all procedures (100% technical success rate). The rate of successful single puncture attempt in CEUS-PB (71.4%) was higher than in the US-PB group (56.2%) (p>0.05). The sensitivity of PB was significantly higher in the CEUS –PB group than in conventional US –PB group for all lesions (96.4% vs. 78.1%, p< 0.05) and RPT (100% vs. 78.9%, p<0.05). For IPT the sensitivity was also higher for CEUS-PB (90.9% vs 76.9%) but without statistical significance (p=0.36). The patients with inconclusive pathological results after conventional guided PB were biopsied then with CEUS guidance. In all cases the final diagnosis could be established. No major complication occurred in the two groups.

Conclusions: Percutaneous CEUS-guided PB of intra and retroperitoneal tumors is a feasible and safe technique. It significantly improves the overall sensitivity of the procedure in patients with large lesions.

Multiparametric ultrasound approach using a tree-based decision classifier for the inconclusive focal liver lesions evaluated by contrast enhanced ultrasound

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Background & Aim: Multi-parametric ultrasound (MPUS) is a concept by which the examiner is encouraged to use the latest features of the ultrasound machine. The aim of this study was to reanalyze the inconclusive focal liver lesions (FLL) at CEUS using the MPUS approach with the help of a tree based decision classifier.

Methods: We retrospectively analyzed FLLs that were inconclusive at CEUS examination in our Department over a period of two years (2017-2018). All the reexamined lesions had a second line imaging method performed: (CE-CT), (CE-MRI) or biopsy considered as the reference method. CEUS inconclusive FLLs had been previously evaluated by ultrasound (US) experts with more than 10 years of experience in CEUS, using a single US machine. MPUS reanalysis followed a three steps algorithm: liver stiffness measurement (LSM), time-intensity curve analysis (TIC) and parametric imaging feature (PI). After processing all steps of the algorithm a binary decision tree classifier (BDTC) was used towards a software assisted decision.

Results: From the 91 inconclusive FLLs evaluated, 34 were HCC, 13 metastases, 7 haemangiomas, 7 regenerative nodules, 5 focal fatty alteration, 3 fatty free areas, 4 cholangiocarcinomas, 2 abscesses, 5 adenomas and 11 were benign lesions. AREA was the only TIC-CEUS parameter that showed significant difference between malignant and benign lesion with a cut-off of >-19.3 dB for wash out phenomena, (AUROC = 0.58, Se=74.0%, Sp=45.7%). By adding the value of elastography we increased the performance to an AUROC

of 0.72 and sensitivity of 90.2% for detecting malignant lesions with wash-out. MPUS correctly classified 66/91 lesions with an accuracy of 72.3%. Using the binary decision tree classifier (BDTC) algorithm we correctly classified 71/91 lesions according to their malignant or benignant status, with an accuracy of 78.0%, sensitivity = 62%, specificity = 45% and precision = 80%.

Conclusions: By reevaluating the inconclusive FLLs at CEUS using MPUS, we managed to determine that 78% of the lesions were malignant and in 28% of them we established the lesion type.

Ultrasound guided microwave ablation and transarterial chemoembolization for unresectable solitary-nodule hepatocellular carcinoma – a head-to-head survival comparison

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Aim: To compare the overall survival (OS) of the patients treated with ultrasound guided microwave ablation (MWA) and transarterial chemoembolization (TACE) for a solitary hepatocellular carcinoma (HCC) nodule.

Method: A consecutive series of patients with a solitary, unresectable, HCC nodule under 5 cm in its largest diameter were prospectively enrolled from November 2015 to December 2019. The patients received either MWA or TACE. Treatment selection was decided by the institutional Tumor Board according to the most recent guidelines, considering tumor characteristics, underlying liver function and patient preference. OS was compared using the log-rank test.

Results: A total of 107 patients were enrolled, of whom n=77 (71.9%) were treated with MWA and n=30 (28.1%) were treated with TACE. Patients in the TACE group had larger nodules (34 ± 9 vs. 23 ± 8 mm, p<0.001). There were no other significant differences between groups with regard to patient characteristics. Complete response rate was higher in the MWA group (92.4% vs. 70%, p<0.001). OS was significantly higher in the MWA group: 52 ± 3 months vs. 24 ± 1 months for the TACE group (log-rank 10.25, p<0.001). Subgroup analysis was performed for patients with tumor size exceeding 3 cm. The difference in OS between groups persisted: patients who received MWA (n=11) had an OS of 47 ± 5 months vs. 22 ± 2 months for TACE (log-rank 4.41, p=0.03).

Conclusion: Ultrasound-guided MWA provided a better outcome for patients with solitary unresectable HCC nodules, when compared to TACE. Whenever possible, prioritization of MWA appears to be desirable.

Factors that influence ultrasound-based viscoelasticity measurements in chronic liver disease

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Background & Aim: Liver elastography is a recognized method for liver fibrosis assessment in chronic liver diseases (CLD). Recent developments attempt to assess inflammation by analyzing the viscoelastic properties of the liver tissue. Such a method is Viscosity Plane Ultrasound (ViPLUS) developed by Supersonic Imaging. The aim of this study was to assess the feasibility and factors that influence ViPLUS measurements.

Methods: We prospectively included patients referred to our department for liver fibrosis assessment. All were evaluated in the same session by Viscosity Plane Ultrasound using the SuperSonic Imagine Aixplorer MACH 30 machine and by biological tests. The median value of 5 viscosity measurements (obtained from 5 different frames), expressed in Pascal-second (Pa·s) was considered as indicative of liver viscosity. An IQR to the median ratio (IQR/M) <30% was used as a measurement reliability criterion

Results: Our group included 682 consecutive subjects (mean age 53.6±13.04 years, 53.6% male, mean BMI 29.22±5.87kg/m2, mean abdominal circumference 103± 15.35 cm). ViPLUS assessment was feasible in 94.7% (646/682) subjects: 17% (110) with normal liver, 9.1% (59) with alcoholic liver disease (ALD), 23.7 % (153) with chronic hepatitis B and C (either under treatment or with sustained virologic response), 48% (310) with NAFLD, and the rest 2.2% (14) with other etiologies.

The mean ViPLUS values in normal, HBV/HCV, ALD, and NAFLD patients were: 1.78±0.48 PaS, 2.03±0.55 PaS, 2.89±0.94 PaS, and 1.95±0.42PaS, respectively. The mean ViPLUS values were significantly higher in ALD than in normal (p<0.0001), HBV/HCV (p<0.0001) and NAFLD patients (p<0.0001); significantly higher in NAFLD (p=0.0005) and HBV/HCV subjects (p=0.0002) compared to normal subjects.

In the univariate regression analysis, ViPLUS measurements were independently associated with: BMI (p=0.001), abdominal circumference (p<0.0001), age (p=0.001), AST (p<0.001), ALT (p=0.040), the presence of diabetes mellitus (p<0.001) and the presence of arterial hypertension (p=0.017). In multiple regression analysis, the model including abdominal circumference (p<0.0001), AST (p<0.001) and ALT values (p=0.003) were associated with ViPLUS measurements.

Conclusion: ViPLUS is feasible in more than 94% of patients. The multivariate regression analysis showed that abdominal circumference, AST and ALT have been associated with the ViPLUS measurements.

A comparative study between variceal and nonvariceal gastrointestinal bleeding in patients with liver cirrhosis

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Background & Aim: Acute upper gastrointestinal bleeding (UGIB) is a potentially life-threatening condition associated with high mortality among cirrhotic patients. It has remained the most commonly encountered emergency in gastroenterology practice and represents a considerable health care burden with mortality rates ranging from 15 to 30%. The aim of this study is to evaluate differences in clinical outcomes, such as hospital readmission for recurrent bleeding, mortality and the need for transfusion between acute variceal gastrointestinal bleeding (AVB) and nonvariceal bleeding (NVB) in patients with liver cirrhosis.

Methods: A retrospective study was performed on 230 patients, between January 2017 to May 2019, who presented UGIB and underwent UGI endoscopy in the emergency department of SCJU Targu-Mures. Liver cirrhosis was diagnosed based on medical charts, clinical, biochemical, ultrasound and endoscopic evaluation.

Results: Out of the 230 patients enrolled in the study, the AVB group represented 53% (122 patients) - 93% representing bleeding from esophageal varices and 7% from gastric varices. The NVB group included 47% (108 patients), the main cause being peptic ulcer 39% (gastric ulcer 20%, duodenal ulcer 19%), followed by Mallory Weiss tear 17%, fistula 17%, portal gastropathy 15%, gastric tumor 9% and esophageal ulcer 3%. The ratios of male and female were 3:1 in both groups with no statistically differences between age (59.47±11.5 vs. 62.32±12.65, p=0.075). Alcoholic liver cirrhosis accounted for 189 patients of total cases (82% - AVB: 92 patients vs. NVB: 97 patients) and viral cirrhosis for 41 patients (18% - AVB: 28 patients vs. NVB: 13 patients) (p=0.025 RR: 0.86 CI: 0.77-0.98). The risk of mortality was 19.67% in the AVB and 15.74% in the NVB (p=0.492). There were no significant differences in need for transfusion (53.27% for AVB vs. 54.62% for NVB, p=0.89) or hospital readmission for recurrent bleeding (27.04% vs. 19.4%, p=0.21). Hemostatic treatment was performed for 114 patients with AVB and 45 patients with NVB, with no statistically significant differences between these two groups regarding survival rates after hemostasis (81.57% vs. 82.22%, p=1.00).

Conclusions: Our study showed that rupture of esophageal varices is the main cause of UGIB in cirrhotic patients. Almost one half of cirrhotic patients had bleeding from a non-variceal source, the most frequent being peptic ulcer. Male patients with cirrhosis of alcohol abuse have a higher risk of UGIB. There are no differences regarding mortality, hospital readmission for recurrent bleeding and the need for transfusion between AVB and NVB. Non variceal bleeding in cirrhotic patients is as severe as variceal bleeding, and has a similar mortality rate.

The performance of non-invasive serum tests in predicting clinically significant portal hypertension and posthepatectomy liver failure in patients with cirrhosis complicated with hepatocellular carcinoma

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Background & Aim: Hepatic resection is a curative therapeutic option of hepatocellular carcinoma (HCC) but proper patient selection (based on tumor size and the presence of portal hypertension - PHT) is essential for prognosis.

The aim of the study was to evaluate whether serum liver tests may identify the patients with clinically significant portal hypertension (CSPH), and thus at risk to develop post-hepatectomy liver failure (PHLF). Their performances were compared with liver stiffness measurement (LSM).

Material and Methods: 111 patients with compensated cirrhosis and HCC referred for hepatic resection between 2015 and 2020 in the Regional Institute of Gastroenterology and Hepatology Cluj-Napoca were included. Presence of CSPH was defined as: HVPG ≥ 10 mmHg or presence of esophageal varices, splenomegaly and thrombocytopenia (< 100,000/mm^3). The non-invasive serum tests were performed: APRI, FIB-4, NLR, eLIFT, ALBI. The performance of non-invasive tests in predicting CSPH and prognosis was assessed by AUROC curves.

Results: Among the included patients (65±7 years; 24% alcohol, 45% VHC, 18% VHB and 13% other etiologies), 34% had CSPH, 31% had esophageal varices and 26% had splenomegaly and thrombocytes < 100,000/mm^3. APRI, FIB4 and eLIFT were good predictors of CSPH (AUROC=0.87, 95%CI:0.79-0.95; p<0.05; AUROC=0.88, 95%CI:0.81-0.96; p<0.05 and AUROC=0.83, 95%CI:0.73-0.92; p<0.05, respectively). Still, LSM had the best performance to predict CSPH (AUROC=0.913, 95%CI:0.84-0.98; p<0.05). ALBI and NLR were not able of predicting CSPH.

Regarding the prediction of PHLF, although the statistical significance was not reached, LSM, APRI and FIB-4 had a tendency to predict it.

Conclusions: Although LSM, APRI, FIB-4 and eLIFT may identify patients with CSPH in patients with HCC submitted to hepatic resection, they are not able to predict prognosis in this clinical setting.

From neuroendocrine cells hyperplasia to neuroendocrine neoplasms in inflammatory bowel disease

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Background & Aim: Increased densities of hyperplastic neuroendocrine cells (NEC) in the colonic mucosa of the patients with inflammatory bowel disease (IBD) has been described. There are multiple case reports and case series available of the association neuroendocrine tumor - IBD. The aim of our study was to determine the morphological alterations on NEC in colonic mucosa of the patients with IBD in our Department and the association with neuroendocrine neoplasms.

Methods: A full colonoscopy with multiple biopsies has been performed in 11 patients with colonic IBD and 11 controls. Chromogranin A (CgA) and synaptophysin antibodies (Syn) have been used for the identification of NEC.

Results: In the IBD group NEC had a patchy and superficial distribution, organized in groups or nodules of 3 to 6 hyperplastic cells/crypt with a mean density of 3.16 CgA positive and 2.54 Syn postive NEC/ crypt in IBD group compared to 1.7 CgA positive and 1.28 Syn positive NEC/crypt in non-IBD controls; p=0.0001, p=0.002.

When compared to IBD duration, NEC densities decreased with IBD evolution so that in patients with IBD duration between 1 and 5 years, mean NEC densities were 3.4 NEC/ crypt (CgA) and 2.8 NEC/crypt (Syn) compared to 2.76 NEC/ crypt and 1.72 NEC/crypt, respectively, in patients with disease evolution longer than 5 years; p=0.19, p=0.14.

There were no significant differences between NEC distributions in active versus inactive disease with a mean density of 2.3 NEC/crypt (CgA) and 3 NEC/crypt (Syn) in active IBD colitis and 3 NEC/crypt (CgA) and 3.5 NEC/ crypt (Syn) in inactive colitis; p= 0.1 and 0.2 respectively. No dysplasia of NEC has been described and we found no neuroendocrine tumors in our patients.

Conclusion: Further studies are required to assess the sequence hyperplasyia- dysplasia- neoplasia of NEC in IBD patients.

The burden of non-alcoholic fatty liver disease

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Background: Non-alcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disease worldwide. There has been a general increase in the prevalence of NAFLD, with a rising prevalence from 15% in 2005 to 25% within 5 years. Obesity, type 2 diabetes mellitus, and dyslipidemia are the most common metabolic risk factors associated with this liver condition.

Method: We made a retrospective study on a series of consecutive patients who were hospitalized in the Gastroenterology Department of Tîrgu Mures County Clinical Emergency Hospital between January 1, 2018 and December 31, 2018 and we compared them with the data of a series of consecutive patients who were hospitalized in the Gastroenterology Department between January 1, 2009 and December 31, 2009. Demographical, anthropometrical and clinical data were collected for each patient, and the medical records were studied to check for comorbidities, ultrasonographic aspects and laboratory findings.

Results: In the recent period (2018) 173 patients were diagnosed with NAFLD, mean age 59.91±13.48 years and a male/female ratio of 1.2/1. The cohort of the 110 patients with NAFLD in 2009 had a male/female ratio of 0.7/1 and a prevalence of NAFLD statistically different $p<0.05$, OR = 1.40 (95%CI: 1.09-1.81). Non-alcoholic steatohepatitis (NASH) was found in 63 patients in 2018 and in 30 patients in 2009, with a statistical difference in prevalence $p<0.05$, OR = 1.86 (95% CI: 1.197-2.90). Considering all patients, the most frequent risk factors identified in 2018 were arterial hypertension in 66.47% of cases (115) and obesity or overweight in 44.50% (77). In 2009, hypertension was found in 71.81% of cases (79), hypercholesterolemia in 65.45% (72) and obesity or overweight in 60% (66).

Conclusions: Non-alcoholic steatohepatitis was diagnosed most frequently in male patients in the recent years. Between the two studied periods we found a significant difference in the prevalence of both NASH and NAFLD, but there was no significant difference regarding the metabolic factors, underscoring the importance of identifying new environmental factors involved in NAFLD and NASH development.

Hemoperitoneum with active bleeding after percutaneous radiofrequency ablation for hepatic metastasis. A case presentation

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A 55-year-old male, with a personal medical history of left hemicolectomy for colonic adenocarcinoma on chemotherapy and a hepatic metastasis in liver segment V/VIII was referred to the tertiary medical care for percutaneous radiofrequency

ablation of the liver nodule. Physical examination and blood tests showed no significant pathological changes. Abdominal ultrasound revealed a 2 cm hypoechoic nodule situated in liver segment V/VIII. Percutaneous radiofrequency ablation was performed in 2 sessions, 10 minutes each, using a Radionics 5 cm electrode under deep sedation. After 2 hours of clinical follow-up, an ultrasound check-up was performed that revealed perihepatic hemoperitoneum. Contrast-enhanced ultrasound showed an arterial spurt into the perihepatic hematoma at the puncture site of the liver. Thereupon, the patient was immediately transported to the Operating Room where hemoperitoneum and an active bleeding site were detected. Hemostasis was obtained using electrocautery and powder absorbable hemostat. The patient was stabilized and the follow up showed a complete ablation of the liver nodule and a hyperechoic image at the level of the liver capsule at the former bleeding site, that represented the haemostatic material.

Day-4 Lille score in early prediction of corticosteroid response for patients with severe acute alcoholic hepatitis

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Background & Aims: Corticosteroids are indicated in patients with severe acute alcoholic hepatitis (SAH), defined by a Maddrey`s discriminat function (MDF) score >32 [1]. However, corticosteroid therapy increases the risk of infections and other complications, especially during hospitalization. The introduction of the Lille score helps in differentiating the steroid responders (<0.45) and the non-responders (>0.45) after 7 days of treatment [2]. The aim of this study is to evaluate whether using the Lille score at day 4 (LM4) is as useful as Lille score at day 7 (LM7), in order to earlier assess response to therapy.

Method: A retrospective study was performed including all patients with SAH evaluated between October 2015 and February 2020 in a tertiary Department of Gastroenterology and Hepatology. All consecutive patients with SAH and a MDF >32, without contraindications to corticosteroids were enrolled. All patients received 40 mg of Prednisone per day and response was assessed with LM4 and LM7, according to the cut-off value (CUV<0.45 responder and CUV>0.45 non responder). The 28-day mortality was assessed between LM4 and LM7 responders and non responders.

Results: A total of 52 patients out of 101 (51.5%) had a MDF>32 and received corticosteroids (83.1% male, mean age 54±9.38 years). All included patients had liver cirrhosis. The median value of MDF was 57±30. The mean value of Lille score after 4 days of treatment was 0.64±0.29, vs 0.58±0.32 for Lille score at 7 days, p=0.43. There was no difference between the percentage of patients having a responder Lille score value at 4 days versus at 7 days (29% vs 49%, p=0.28). The area under the ROC curve for predicting mortality for LM4 was similar to LM7 (0.67 vs. 0.68, respectively, p=0.9). By using LM4 and LM7 with CUV>0.45, the 28-day mortality was higher in the non-responder (27% and 31%, respectively) than in the responder cohort (20% and 15%), respectively. If we take LM4 with CUV<0.45 into consideration, 90.3% of patients were correctly identified compared with LM7.

Conclusion: LM4 could be used instead of LM7 in predicting the response to corticosteroid therapy in SAH, as well as the 28-day mortality. Using LM4 we could avoid a prolonged use of this therapy and its complications.

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The significance of endoscopy in diagnosis of acute appendicitis: a case report

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Background & Aim: Acute appendicitis is the most common cause of acute abdomen. A diagnosis of acute appendicitis is generally established clinically. However, additional imaging can be supportive. Endoscopy is not currently part of the standard approach to the evaluation of appendicitis. Here, we describe the case of a patient who underwent colonoscopy to investigate the pathology of the colon due to nausea and diarrhea. This revealed an obstructed, swollen appendix, which is the earliest stage of acute appendicitis.

Case report: A 38-year-old female patient with no medical history presented to the emergency department of Regensburg University Hospital with recurrent abdominal pain. Physical examination revealed a healthy woman with no acute complaints and normal vital signs. Cardiovascular and pulmonary findings were within the normal range. Abdominal examination revealed normal active bowel sounds in all four quadrants. She had mild signs of peritoneal disease. The Murphy sign was positive, so cholecystitis was suspected. Laboratory tests revealed leukocytosis and elevated serum C-reactive protein (CRP), but cholestasis parameters were normal. The patient received intravenous antibiotics. CT scan revealed no evidence of pathology. Gastroscopy and colonoscopy were performed due to

recurrent episodes of nausea and diarrhea. Gastroscopy revealed no pathologic findings. On colonoscopy, the appendix and surrounding mucosa were red and edematous. Biopsies were taken. After the biopsy was taken, there was drainage of pus from the appendix into the coecum. These endoscopic findings were a clear indication of acute appendicitis.

Conclusion: This was an atypical case of acute appendicitis diagnosed by colonoscopy. In cases of delayed or atypical onset, colonoscopy is also suggested as a diagnostic tool detection of an acute appendicitis. Although colonoscopy is not currently the standard approach for evaluating suspected appendicitis, endoscopists should recognize early mucosal changes in appendicitis that may require further investigation and surgical consultation.

Which factors influence the severity of steatosis in patients with metabolic syndrome?

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Background & Aim: Many patients with metabolic syndrome have liver steatosis, which can sometimes lead to severe liver fibrosis. The aim of the present study was to identify the risk factors that could be associated with severity of liver steatosis, in a cohort of patients with metabolic syndrome, using a non-invasive method: Vibration Controlled Transient Elastography (VCTE) with Controlled Attenuation Parameter (CAP).

Methods: 204 patients with metabolic syndrome (MetS) were prospectively enrolled. Evaluation of liver fibrosis and steatosis was made using VCTE with CAP, performed with FibroScan® device (EchoSens, Paris, France) in fasting conditions, using both M and XL probes. Reliable liver stiffness measurements (LSM) were defined as the median value of 10 LSM with an IQR/median <30%. Each patient was evaluated for the presence of viral hepatitis (B, C, D) and an AUDIT-C score was performed to exclude alcohol abuse. For differentiation between grades of steatosis we used the following cut-off values: S1 (mild) – 274 db/m, S2 (moderate) – 290 db/m, S3 (severe) – 302 db/m [1]. Variables tested for the association with steatosis were: body mass index (BMI), waist circumference, HDLc, triglycerides, gender, fasting blood sugar, ALAT. Logistic regression was used for multivariate model to identify predictive factors for moderate and severe liver steatosis. A cut-off value of 9.7 kPa was used to define severe fibrosis (F≥3) [1].

Results: Out of 204 patients with MetS, reliable LSM were obtained in 179 patients (87.7%). The mean age was 62.5 ± 10.8 years, 50.2% were males and the mean BMI was 32.2± 5.64 kg/m2. The distribution of steatosis in our cohort assessed by means of CAP, was as follows: 27.9% (50/179) were S0 (no steatosis), 10.6% were (19/179) S1, 11.2% (20/179) were S2 and 50.3% (90/179) were S3. Severe fibrosis was detected by means of TE (LSM≥9.7 kPa) in 15.6% (28/179) of subjects. In the univariate logistic regression BMI, waist circumference, HDL-c, fasting blood sugar, ALAT were independent factors for moderate and severe liver steatosis diagnosed using CAP. In multivariate regression analysis only waist circumference [OR=1.063, 95% CI (1.029; 1.097), p<0.001] and BMI [OR=1.155, 95% CI (1.054; 1.266) p=0.002] were independent predictive factors for moderate and severe steatosis.

Conclusions: In our group, 61.5% of patients with metabolic syndrome had moderate and severe steatosis evaluated by means of CAP and 15.6% had severe fibrosis. Only body mass index (BMI) and waist circumference were associated with the severity of liver steatosis in the multivariate.

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Hepatic steatosis index (HSI) - a simple predictive score for the presence of steatosis in diabetic patients

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Background and Aim: Fatty liver is a frequent disease that affects one quarter of the world population, being the most common chronic liver disease [1]. Several noninvasive assessment tests have been developed in order to predict liver fibrosis and steatosis for these patients. Our aim was to assess the correlation between the HSI score and Controlled atenuated parameter (CAP), in a group of diabetic patients .

Material and method: We conducted a prospective study, which included 501 patients with diagnosed diabetes mellitus, out of which 377 with steatosis (mean age 60.3 years, 56.8% female, 43.2% male); and 52 healthy subjects used as controls, out of which 8 subjects had steatosis (mean age 37 years, 59.7% female and 40.3% men). All patients were evaluated clinically (BMI), by serum markers (AST, ALT, platelets), as well as by Transient Elastography with CAP (FibroScan- Echosens). Based on a specific formula we calculated the HSI score.

Liver stiffness measurement was considered reliable only if 10 valid values were obtained, with an IQR/median<30%. To discriminate between steatosis stages, we used the following CAP cut-offs: S1 (mild) – 274db/m, S2 (moderate) - 290db/m, S3 (severe) - 302db/m [2].

Results: Out of 501 patients with diabetes, 377 (75.2%) had liver steatosis by CAP measurements. From 377 diabetes patients with steatosis, 3 (0.7%) patients had a HSI score <30, and 366/377 (97.1%) patients had a HSI score >36. From the 124 (24.8%) diabetic patients without steatosis, 1/124 (0.8%) diabetic patients had a HSI score <30 and 104/124 (83.8%) diabetic patients had an HSI score >36. We found differences between the HSI score in patients with steatosis vs without steatosis, p=0.04 and p<0.0001.

In the control group with steatosis, 2/8 (25%) patients evidenced a HSI score <30, 3/8 (37.8%) had a HSI score >36, while 12/44 (27.2%) had a HSI score <30 and 9/44 (20.4%) had a HSI score >36. In this cohort, we did not find any differences between patients with steatosis and without steatosis, p=0.76 and p=0.53, respectively.

The NPV value of the HSI score, for ruling out liver steatosis was 81.1%, at a cut-off point of 35.9.

Conclusion: A HSI score <35.9 can rule out diabetic patients with steatosis, for subsequent liver evaluation done by the hepatologist. This simple score could be used as a first line test, in any medical office, to rule out patients without steatosis.

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Multistep diagnosis of a rare hepatic epitheloid angiomyolipoma. A case report

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Introduction: Hepatic epitheloid angiomyolipomas (HEAMLs) are rare and belong to the group of mesenchymal tumors. They are often misdiagnosed as hepatocellular carcinoma due to their similarities. Because of their malignant potential a thorough diagnostic workup is necessary. In this case report we present a case of HEAML and the steps leading to diagnosis.

Case description: We are reporting the case of a 58-year-old patient who presented to our Outpatient Liver Clinic with an incidentally diagnosed, asymptomatic mass in the right liver lobe during a routine ultrasound checkup. There were no known illnesses and she did not take regular medication. In a first step her general practitioner ordered a Magnetic Resonance Imaging (MRI) where a focal nodular hyperplasia was diagnosed.

We repeated the ultrasound diagnostics, which showed a 4.7 x 4.6 cm inhomogeneous isoechoic mass in segment 6 with well-defined margins. Because of many vascular signals in the Doppler mode, we did an additional Contrast Enhanced Ultrasound (CEUS; GE Logiq E9; 1,2ml Sonovue). There we observed early arterial hyperenhancement at 20 sec post injection with a centripetal filling pattern, complete filling and a large arterial feeding vessel, followed by contrast agent washout beginning at 60 seconds in the portalvenous and late phase. These contrast characteristics are a hallmark of malignant liver lesions, especially hepatocellular carcinoma.

Based on the CEUS results and without signs of liver fibrosis, cirrhosis or elevated aminotransferases, we ordered a liver MRI for further diagnostics. MRI evidenced an arterial hyperenhancement with a quick washout, hypointensity in the late phase and a mixed intensity in dorsal parts of the mass in all sequences was seen. Accordingly, the diagnosis of adenoma, hepatocellular carcinoma or focal nodular hyperplasia was excluded. Everything pointed to a hemangioma partly thrombosed and possibly with a myxoid part.

The case was discussed in our multidisciplinary liver board, and a biopsy of the liver mass was recommended. Percutaneous biopsy was performed and showed a medium to large sized tumor cells with well-defined eosinophilia cytoplasm. The immunohistochemical staining was negative for Hepar1 and CD117 and positive for vimentin, MelanA and HMB45. A HEAML was diagnosed. Because of the tumor size and a potential of malignant transformation, surgery was recommended. A right hemihepatectomy was performed without complications. The postoperative histology confirmed the diagnosis of HEAML, no vascular invasion was found (1 mitoses per 10 HPF, the MIB-1 was less than 1%), so no malignant characteristics were observed. A follow up at six, twelve and 24 months was recommended.

Discussion: HEAML are rare mesenchymal liver tumors which belong to a group of Perivascular Epitheloid Cell tumors. They mainly occur in female patients and can be divided into different subtypes. At the time being, around 80 cases of the hepatic epitheloid subtype have been described, which shows how rare this finding in general is. In contrast to typical angiomyolipomas, which are composed of smooth muscle cells, thick-walled blood vessels and adipose tissue, HEAML mainly consist of epitheloid cells with few or no adipocytes. With a cumulative incidence of malignant behavior at 4.1%, HEAMLs are usually benign, but the epitheloid subtype seems to be a risk factor for malignant transformation and surgery is recommended in those cases. Different ultrasound characteristics were described but the typical HEAML shows homogeneous arterial hyperenhancement on CEUS with washout in the portal or late phase and is mostly found in female patients without signs of cirrhosis. Nevertheless, the final diagnosis should be confirmed by histopathology and immunohistochemistry since HEAMLs are easily overlooked due to their rare occurrence.