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MAY 26, 2023
PROGRAM AND ABSTRACTS

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8th GERMAN - ROMANIAN SYMPOSIUM OF GASTROENTEROLOGY

Würzburg, Germany

May 26th, 2023

Scientific Committee

Prof. Dr. Alexander Hann
Prof. Dr. Monica Acalovschi

Program and Abstracts

Scientific Program

Friday, May 26, 2023

Universitätsklinikum Würzburg,

Medizinische Klinik und Poliklinik II

ZOM Hörsaal Chirurgie

08.30 On-site Registration

09.00 Opening Remarks: Prof. Monica Acalovschi, Prof. Alexander Hann

09.10 – 09:50 Session I. Inflammatory Bowel Diseases

Chair: Prof. Mircea Diculescu, Prof. Tilo Andus

Prof. Tilo Andus, Stuttgart: New therapeutic options for IBD

Prof. Mircea Diculescu, Dr. Corina Meianu, Bucharest: IBD and pregnancy - challenges and opportunities

Prof. Adrian Goldis, Timisoara: Possible pitfalls in diagnosing and treating IBD patients

09.50 – 10.10 Coffee Break

10.10 – 11.30 Session II. Inflammatory Bowel Diseases/Gastrointestinal Tumors

Chair: Dr. Sophie Schlosser, Prof. Adrian Goldis

Dr. Katharina Feilhauer, Stuttgart: Pouchitis and fistulae - an interdisciplinary challenge

Dr. Sophie Schlosser, Regensburg: New treatment approaches in gastrointestinal oncology

Prof. Simona Bataga, Targu-Mures: Advances in gastric cancer early diagnosis

Prof. Michael Scheurlen, Würzburg: Challenges in neuroendocrine tumors

Prof. Paul Jürgen Porr, Sibiu: The microbiome and the digestive cancers

11.30 – 11.40 Recreational break

11.40 – 13.00 Session III. Endoscopy and Ultrasound

Chair: Prof. Simona Bataga, Prof. Jörg Albert

Prof. Alexander Meining, Würzburg: What do we expect from artificial intelligence in endoscopy

Dr. Bogdan Procopet, Cluj: New concepts in the interventional treatment of portal hypertension

Dr. Hauke Tews, Regensburg: Multimodal sonography including CEUS: from dignity assession to microcirculation

Dr. Vlad Pavel, Regensburg: Intensive use of ultrasound in a medical intensive care unit

Prof. Michael Jung, Frankfurt: Endoscopy and the risk of infectious droplets

13.00 – 13.40 Lunch break

13.40 – 15.00 Session IV. Scientific Talks

Chair: Prof. Alexander Hann, Prof. Jörg Albert

15.00 – 15.20 Coffee break

15.20 - 16.40 Session V. Liver Diseases

Chair: Prof. Monica Acalovschi, Prof. Andreas Geier

Prof. Martina Müller-Schilling, Reegensburg: Acute-on-chronic liver failure

Prof. Peter Galle, Mainz: Treatment challenge of hepatocellular carcinoma

Prof. Laurentiu Nedelcu, Brasov: Alcohol-associated hepatitis - diagnosis and medical management

Prof. Andreas Geier, Würzburg: Update Viral hepatitis

Dr. Horia Stefanescu, Cluj: Transdisciplinary approach of alcoholic liver disease

16.40 – 16.50 Recreational break

16.50 - 18.10 Session VI. Benign Diseases of the Gut

Chair: Prof. Dan L. Dumitrascu, Prof. Wolfram Zoller

Prof. Dan L. Dumitrascu, Cluj: Epidemiological data from Romania on DGBI (Disorders of brain-gut interaction): lessons from the Rome Epi Global Study

Dr. Lidia Munteanu, Cluj: NSAIDs enteropathy

Prof. Michael Sackmann, Bamberg: Challenges in the treatment of gallstone disease

Dr. Stephan Schmid, Regensburg: Gastrointestinal related challenges on an ICU

Prof. Marcel Tantau, Cluj: Endoscopic diagnosis and treatment of dysplasia in patients with IBD

18.10 Closing remarks and Poster awards: Prof. Monica Acalovschi, Prof. Alexander Hann

SESSION I. INFLAMMATORY BOWEL DISEASES

New therapeutic options for IBD

Tilo Andus

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During the last few years several new therapeutic options have become available to treat patients with inflammatory bowel disease. This allows more effective, and more individualized treatment than before.

However, in many patients with uncomplicated disease, the older and well-known drugs such as 5-aminosalicylic acid, corticosteroids and thiopurines are still the fundament of treatment since they are effective, well known, and inexpensive.

JAK-Inhibitors. Janus-Kinases (JAK-1-3 and TYK-2) are important signal transducers in inflammation.

Therefore, inhibition of the JAKs is a powerful tool against inflammation.

Tofacitinib was the first JAK-Inhibitor approved for the treatment of ulcerative colitis. Induction with 2 x 10 mg orally resulted in clinical remission in 16.6-18.5% in the OCTAVE-1 and OCTAVE-2 studies. Maintenance with 2 x 5-10 mg/d was successful for remission in OCTAVE-sustain in 24.4 – 40.6% of the patients.

Since a significant higher rate side-effects (MACE and VTE) have been reported in a post-marketing study with tofacitinib in patients with rheumatoid arthritis compared to TNF-inhibitors, the PRAC of the EMA sent a warning letter recommending using all JAK-inhibitors only in patients without cardiovascular risk factors or if no other treatment option is available.

However, in the studies of tofacitinib in ulcerative colitis these side-effects have not been observed.

Also, they have not been found in several register studies.

Filgotinib, an orally used JAK-1 selective JAK-inhibitor also was significantly superior to placebo in Ulcerative Colitis patients in the SELCTION-trial leading to clinical remission in 23.1% in the 200 mg/d dose. Long-term data for 4 years showed a very good, sustained response and no new safety-signals.

Upadacitinib, also an orally used JAK-1 selective JAK-inhibitor, led to an impressive remission rate of 26% - 33.5% in the induction trials U-ACHIEVE and U-ACCOMPLISH at a dose of 45 mg/d in patients with ulcerative colitis. Maintenance at 1 year showed 52% sustained remission rates. Side-effects (MACE and VTE) were on placebo-niveau.

Recently, Upadacitinib as the first JAK-inhibitor showed significant activity in patients with Crohn's disease with clinical remission rates of38.9% and 49.5% in the U-EXCEL and U-EXCEED-trials after 12 weeks. In the maintenance trial U-ENDURE 47.6% remained in remission after 1 year. No new safety signals were observed. In February 2023 a positive CHMP-opinion regarding approval by the EMA was published.

Risankizumab was the first **IL-23 antibody** approved for the treatment of Crohn's disease in November 2022. Risankizumab 600-1.200 mg at week 0, 4 am 8 intravenously led to clinical remission in 42-45% in the ADVACE trial and in 40-42% in the MOTIVATE trial. In the FORTIFY maintenance trial remission was seen in 42-51% in the 180 mg and 360 mg s.c. groups. Interestingly there was a strong carry over effect leading to relatively high maintenance rates in the placebo group with 41%. No concerning side-effects were observed.

Another **IL-23 antibody**, **Mirikizumab** has been studied in ulcerative colitis. In the induction study LUCENT-1 a significant superior remission rate of 24.2% was found with 300 mg i.v. Q4W versus placebo. Maintenance of remission with 200 mg i.v. Q4W was 49.9% after 52 weeks. No concerning side-effects were observed. A positive CHMP-opinion regarding approval by the EMA was published.

Sphingosin-1-phosphate receptor modulators trap lymphocytes in the lymph nodes reducing chronic inflammation in multiple sclerosis, an inflammatory bowel disease. **Ozanimod** is the first S1PR-modulator approved for the treatment of ulcerative colitis after inducing remission in 18.4% a a dose of 2 mg/d orally in the TRUE-NORTH trial and leading to a corticoid-free remission at week 52 in 31.7% of the patients. The True North open-label extension safety analysis showed a very low rate of side-effects after 3 years treatment.

Finally, even in old drugs improvement can be achieved. A new 4 mg budesonide suppository showed equal efficacy compared to 2 mg foam in patients with ulcerative proctitis regarding clinical remission and mucosal healing and was preferred by most of the patients compared to the enema.

There are more new developments coming such as the IL-23-antibody guselkumab and the S1P-R-modulatore etrasimod, which hopefully will become available soon.

In conclusion, treatment gets better but more complex. The best sequence of treatment has to be found.

IBD and pregnancy – challenges and opportunities

Mircea Diculescu[1,2], Corina Meianu[1,2]

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

The incidence and prevalence of Inflammatory Bowel Disease (IBD) in Romania has increased more than tenfold in the past 10 years. Unfortunately, the complexity and the severity of these diseases have also increased. If in 2003 we estimated less than 1000 overall patients registered with the diagnosis of IBD in our country, in 2023 there are more than 1000 patients with biological treatments in the National Insurance House registry. Currently in Romania there is just one age prevalence peak for IBD between 20-40 years. This means that most patients are of childbearing age, wish to conceive or are already pregnant and both the patients and their partners raise concern about the risk of ongoing immunosuppressive or biological treatments for them and their future child during pregnancy, the risk of transmitting their disease to the child and the effect of these treatments on fertility. IBD is a disease associated with a lack of knowledge in the field of pregnancy and reproduction and unfortunately there is an increased "voluntary childlessness" in patients with IBD.

We shall attempt to make a systematic review of the available data concerning the outcome of pregnancy on IBD evolution, the effects of ongoing biological treatments on fertility and pregnancy and to discuss the risk of a new flare when stopping biologics during pregnancy.

Unfortunately, the available data is obviously not from clinical trials but from clinical reports, but fortunately the real-life experience in Western countries with such situations has increased a lot.

We may conclude that the priority of a pregnant patient with ongoing biological or immunosuppressive treatment is to remain out of a disease flare and the treatment should only be stopped in highly selected cases and during a certain period of the pregnancy.

Possible pitfalls in diagnosing and treating IBD patients

Adrian Goldis

Department of Gastroenterology and Hepatology, Victor Babes University of Medicine and Pharmacy, Timisoara, Romania

Endoscopic pitfalls in diagnosing IBD. Endoscopy plays an important role in the diagnosis and management of inflammatory bowel disease (IBD). It is important to exclude other etiologies, to differentiate between ulcerative colitis (UC) and Crohn's disease (CD) and to estimate the extent and activity of inflammation. One of the pitfalls in diagnosing IBD is the failure to consider other diseases that result in terminal ileal and colonic inflammation. By far the commonest cause of inflammation is infection: *Clostridium Difficile*, *Shigella* or *Salmonella*. Other conditions that may mimic IBD by evolving with colonic and terminal ileum inflammation are intestinal tuberculosis, Behcet's disease, ischemic colitis or NSAID associated colitis.

When can we stop the biological treatment? General considerations for stopping the biologic therapy are the achievement of deep remission (objective confirmation is needed), the disease history, and the severity and extent should be taken into consideration. The patient must be involved into the decision and always monitoring of the disease should continue after ceasing the treatment. In some studies, after 7 years since treatment stopping, 21% of the patients did not need to restart Infliximab (Reenaers et al, 2018). When stopping anti-TNF therapy, most patients relapse in a 5–7-year period. Although if you restart IFX within the first 2 years the success rate is higher, the longer you wait, the higher the chance of not restarting therapy and experiencing complications of the disease.

Malpractice risk in IBD.The highest risk areas in IBD care are the errors in diagnosis, the complications related to medications, the complications related to the management of patients with severe disease, the hypercoagulability status and the issues related to dysplasia and cancer detection.

Conclusion: Standards of care are what a similarly experienced physician would do in similar circumstances. The available practice guidelines are for guidance and are meant to be flexible, not rigid, as in every IBD patient the disease course will be different from that in other patients, so that it will require a similar, but yet different approach. Acute severe ulcerative colitis is always an unpredictable disease that can have a sudden downfall.

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SESSION II. INFLAMMATORY BOWEL DISEASES / GASTROINTESTINAL TUMORS

Pouchitis and fistulae – an interdisciplinary challenge

Katharina Feilhauer

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In the era of advanced medical therapies, around 30 % of the patients with UC will still undergo colectomy with an IPAA (ileal pouch anal anastomoses) for advanced disease or colitis-associated neoplasia. IPAA with a J-Pouch-reconstruction has become the procedure of choice in the therapy of ulcerative colitis. Although patients experience a dramatic improvement of their quality of life, surgery is not successful in about 5–10% of all treated patients.

Chronic pouchitis, incontinence, secondary diagnosis of Crohn's disease, fistulas, severe surgical complications, rectal stump left for too long, chronic abscess and surgical technical errors can be reasons for pouch failure.

One of the most common reasons for pouch failure is pouchitis with different degrees of severity and different possibilities of therapy.

This talk tries to show the surgical techniques, their possibilities of failure and how to get successful in an interdisciplinary team to avoid complications like fistulas that are difficult to be treated and in the end to avoid pouch loss.

Advances in gastric cancer early diagnosis

Simona Bataga

University of Medicine, Pharmacy, Science and Technology, GE Palade Targu-Mures, Romania

Gastric cancer (GC) is the fifth most common malignancy in the world, after cancers of the lung, breast, colorectum and prostate, representing 5,6% of all cancers

This is a substantive change since the very first estimates in 1975 when stomach cancer was the most common neoplasm, and this is due mainly to the *Helicobacter pylori* discovery, detection and treatment.

Although the incidence and mortality of the disease are declining, the absolute number of GC cases remains stable and it may even increase due to the predicted growth of the world population and increasing longevity.

Patients diagnosed with early stage gastric carcinoma have a significantly better prognosis with 5 year survival rates approaching 90%, so early diagnosis of GC is mandatory. There are several new possibilities to diagnose early gastric cancer

Traditional markers

There are mentioned traditional markers such as: Carcinoembryonic antigen (CEA), carbohydrate antigen 72-4 (CA 72-4), carbohydrate antigen 19-9 (CA 19-9), carbohydrate antigen 15-3 (CA 15-3) and carbohydrate antigen 125 (CA 125) may have a role mainly in therapy monitoring and prognosis rather than early detection or screening of GC. Although they can be found at elevated levels in GC, they are neither sensitive, nor specific, furthermore they are commonly elevated at late stages of the disease.

Markers for atrophy of the stomach mucosa: Pepsinogen detection in combination with G-17 and Helicobacter pylori serology, as "serological biopsy for gastric mucosa", also the ghrelin hormone, the trefoil factor (TFF) and others.

New Blood Based markers called the "Liquid Biopsy", such as: Circulating tumor cells (CTCs), Circulating cell-free ARN, methylation markers, cell-free mRNA, miRNA, lncRNA and other RNA species. miRNAfingerprints circulating tumor DNA, the fraction that derives from primary tumors or metastases and from CTCs called ctDNA and extracellular vesicles (EVs) exosomes, microvesicles and apoptotic bodies.

Endoscopy has increased continuously in the last decades in the direction of a better visualization of mucosa of the digestive tract, such as: Chromoendoscopy, Virtual Chromoendoscopy, magnification and even artificial intelligence.

Conclusion: There are several new directions for the identification of gastric cancer in the early stages which could improve the prognosis of gastric cancer.

The microbiome and the digestive tract cancers

Paul Jürgen Porr

Polisano MedLife Clinic, Sibiu, Romania

The microbiome is involved in the pathogenesis of many digestive and extradigestive diseases.

It also plays a role in the development and progression of colorectal cancer (CRC). The high meat, high fat and low fiber diets represent a certain risk factor for CRC, directly affecting microbiota and bile acids metabolism. This bi-directional relationship between microbiota and bile acids metabolism influences the CRC evolution. Another pathogenetic factor is dysbiosis due to environmental or genetic variations, which can disrupt the immune system and may promote CRC.

Recent studies also revealed a role of the microbiome in esophageal and gastric cancer, as the major risk factor of gastric cancer, *Helicobacter pylori* infection is well known.

Few studies are focused on the role of microbiota in pancreatic and liver cancer.

The microbiome also plays a role in the oncologic treatment (chemo-, radio- and immunotherapy). It can modulate their benefic, but also their adverse effects, altering the efficiency and toxicity of the therapy. Recent studies revealed that modulation of the microbiome by pro-, prebiotics, diets and fecal microbiota transplantation protects the cancer patients from treatment-associated adverse effects.

Modulation of the microbiome can also play a role in cancer prevention.

SESSION III. ENDOSCOPY AND ULTRASOUND

New concepts in the interventional treatment of portal hypertension

Bogdan Procopet

Iuliu Hatieganu University of Medicine and Pharmacy, 3rd Medical Clinic, Hepatology Department, Cluj-Napoca, and Prof. Dr. Octavian Fodor Regional Institute of Gastroenterology and Hepatology, Hepatology Department, Cluj-Napoca, Romania

Many complications of portal hypertension have benefited from interventional treatment by improving their control.In patients with acute variceal bleeding at a high risk of recurrence, pre-emptive TIPS has been associated with better survival, less bleeding recurrence and ascites without increasing the risk of hepatic encephalopathy. It is essential to apply this strategy because waiting until failure to control bleeding and applying a salvage TIPS is still associated with high mortality. Recently efforts were made to identify futility criteria for TIPS insertion in patients with uncontrolled bleeding and high mortality despise TIPS.

In the clinical scenario of secondary prophylaxis of variceal bleeding, despise a better control of bleeding, the TIPS insertion still did not prove a better survival in recent clinical trials using dedicated covered stents. However, it is a matter of study design since both studies aimed to confirm the benefit of rebleeding and were probably underpowered for survival differences.

Regarding the refractory ascites, the other classic indication of TIPS, only recently a benefit in survival was proved. In patients with recurrent ascites, proposing TIPS earlier, when liver function is still preserved, is associated with better survival.

The key point for better survival is probably identifying the subgroup of patients that benefit most (e.g., bilirubin less than 3 mg/dl).

Different approaches to achieve recanalization and improve the chances for liver transplantation were recently developed in patients presenting complications secondary to portal vein thrombosis, either acute or chronic. However, the practice is still heterogeneous, and data about the changes in prognosis are still scarce.

Intensive use of ultrasound in a medical intensive care unit

Vlad Pavel

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Ultrasonography is used for diagnostic, management, and procedural guidance purposes in the intensive care unit (ICU). Rapid and accurate diagnosis and treatment are crucial for critically ill patients. Being widely available, portable, repeatable, relatively inexpensive, pain-free, and safe ultrasonography has become an efficient diagnostic method used by frontline clinicians taking care of critically ill patients [1-3]. Furthermore, ultrasonography not only offers an early diagnosis but also improves patient safety by decreasing the need for transport out of the intensive care unit [4].

Critical care ultrasonography has a wide range of applications in this field and can help in acute situations by providing rapid interventions [5, 6]. By using bedside ultrasonography intensivists can nowadays accurately and rapidly recognize many pathologies such as pneumothorax, aortic dissection, pleural or pericardial effusion, pulmonary edema, hydronephrosis, hemoperitoneum or deep vein thrombosis [1]. Furthermore, ultrasonography plays an important role in the correct determination of the volume status of the critically ill patient [7]. Another essential application of ultrasonography in the ICU is in the airway management. Intubation and tracheostomy are common procedures performed in intensive care [8, 9]. Ultrasound allows physicians to identify anatomical structures of the upper airway and knowing the sonoanatomy aids in performing endotracheal intubation or tracheostomy [10].

Ultrasound use is increasing exponentially in the management of critically ill patients. Imaging investigations such as computed tomography, magnetic resonance imaging, ultrasonography or standard radiography have a share role in the ICU, as they help intensivists in reaching a diagnosis [11]. However, ultrasonography has the unique advantage that it can be easily anytime repeated and can be performed quickly at the bedside by the frontline intensivist in acute life-threatening situations [11].

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Endoscopy and the risk of infectious droplets

Michael Jung

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During gastroscopy and colonoscopy, the endoscopist's face is exposed to body fluids and aerosols. Aerosols and droplets of small size (1 nm -75 µm) may contain viral or bacterial particles, emanating from the patient's mouth and anus.

In a prospective 6-month study the face shield of the endoscopist was investigated for bacterial load (cut-off >15 CFU). The rate of unrecognized exposure for potentially infectious samples was 5.6/100 days in endoscopy suite and may result in a transmission also of viral diseases (e.g. SARS-CoV -2) [1].

Using a laser light scattering instrument droplets generating during speech and aerosols expelled during endoscopy can be visualized and measured in size and quantity. They can be distinguished as liquid droplets from solid particles [2, 3].

In an experiment to investigate the COVID-19 transmission, droplets were measured by laser light scattering during gastroscopy and colonoscopy.

Most droplets were 40-50 µm in size but varied widely in diameter. Approximately 500 liquid droplets were registered during gastroscopy. The number of droplets and particles was higher before and after the endoscopic act, while more droplets were produced per unit time during colonoscopy and gastroscopy.

In particular the biopsy channel may be regarded as a source of infectious droplets, when biopsies and snare polypectomies were performed and the instruments were introduced and removed from the biopsy channel [4]. In contrast no droplets were expelled during air insufflation and water suctioning.

Thus, the Endoscopy team is generally exposed to a considerable risk of infection by droplets and aerosols.

While surgical masks are less efficacious in aerosols < 5µm, the routine use of a N95 (FFP 2) mask will reduce the risk of transmission and is recommended to protect the endoscopist and staff.

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SESSION IV. LIVER DISEASES

Treatment of hepatocellular carcinoma. Current systemic therapy and treatment strategy for advanced HCC

Peter R. Galle

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Over the last 15 years we have seen relevant advances in the systemic therapy of hepatocellular carcinoma (HCC). Drugs licensed in some countries now include four oral multi-tyrosine kinase inhibitors (sorafenib, lenvatinib, regorafenib and cabozantinib), one antiangiogenic antibody (ramucirumab) and six immune checkpoint inhibitors, alone or in combination (atezolizumab in combination with bevacizumab, durvalumab in combination with tremelimumab, ipilimumab in combination with nivolumab, nivolumab and pembrolizumab in monotherapy). Prolonged survival more than two years can be expected in most patients with sensitive tumours and a well-preserved liver function that render them fit for sequential therapies. With different choices available, the robustness of the evidence of efficacy and a correct matching of the safety profile of a given agent with patient characteristics and preferences are key in making sound therapeutic decisions. In Europe, EASL Clinical Practice Guidelines have been published in 2018 and will be updated in due course. A position paper on systemic therapy in HCC from EASL has been published in 2022. European Society for Medical Oncology guidelines have been updated in an online version (2021 eUpdate). Both updates aim to help providing the best possible care for patients today and use a pragmatic approach. Basically, they recommend Atezolizumab plus Bevacizumab or Durvalumab plus Tremelimumab as new first line standard and the "old" first line standard sorafenib or lenvatinib as an alternative option, in particular if there are contraindications against the use of the combination. In second line, the EASL position paper recommends after atezo/bev to use the available multi-TKI as per off-label availability, ESMO recommends available multi-TKI and adds ramucirumab as option. Following sorafenib or lenvatinib, the "old" second line, regorafenib, cabozantinib or ramucirumab are available.

In view of the increasingly high numbers of systemic agents or combinations for the treatment of HCC, a head-to-head comparison and a defined analysis on sequential treatments is unlikely. Biomarker definition of subgroups with the potential of high response rates and/or improved survival is urgently needed. Furthermore, there will be an assessment of the role of systemic therapies in earlier stages.

In addition, in the field of systemic therapy for HCC several new combinations are currently assessed in phase 3 trials and will mature over the next two years, requiring further adjustment of guidelines.

Furthermore, several trials investigate the potential of systemic therapy in intermediate stage HCC and in April data on the potential of Atezolizumab/Bevacizumab in early stage as adjuvant treatment (IMbrave 050) were presented and showed improved recurrence free survival.

Alcohol-associated hepatitis - diagnosis and medical management

Laurentiu Nedelcu

Transilvania University, Brasov, Romania

Alcohol use disorder is a major cause of advanced liver disease. In recent years, the diagnostic criteria of alcohol-associated hepatitis have been revised.

In the evolution of alcohol-related liver disease, in patients with active alcohol consumption, alcohol – associated hepatitis can occur, characterized by an abrupt onset of jaundice, malaise, liver decompensation and coagulopathy.

The pathogenesis of alcohol-induced hepatitis is incompletely elucidated. Different factors are discussed: the role of the gut-liver axis, the mechanisms involved in hepatocyte dysfunction, the occurrence of liver decompensation and multiple organ failure. The diagnosis is built on clinical data, with the application of criteria related to consumption history, physical examination and the elements provided by the laboratory analyses. The set of diagnostic criteria is slightly different from the previous ones, with the intention of identifying less severe or moderate forms of alcoholic liver disease. Imaging is useful to exclude other pathologies. Transjugular liver biopsy is recommended in patients with difficulties in establishing the diagnosis. Alcohol-Associated hepatitis is characterized by four histologic features: the presence of bridging necrosis or cirrhosis, bilirubinostasis, neutrophil infiltration and mega mitochondria. In addition, the biopsy also provides prognosis information. There has been an increased interest in the description of some non-invasive

biomarkers with diagnostic and prognostic significance: keratin-18 fragments, extracellular circulatory vesicles, and microRNA.

Disease management is initiated with treatment of the liver-related complications.

Nutritional support will be provided, and possible sources of infection will be sought. Management of the alcohol use disorder might involve the advice of a specialist in addiction. At a MELD score > 20, prednisolone is administered, and after 7 days the patient is reevaluated according to the Lille model. At a Lille score <0.45, treatment with prednisolone is continued for 4 weeks, and at a Lille score >0.45, corticosteroid therapy is stopped and the possibility of an early orthotopic liver transplantation is taken into consideration.

Future research is aimed at studying liver regeneration, interruption of the inflammatory pathways, restoring of the normal microbiome, discovering new prognostic biomarkers, and identifying the molecular subtypes useful for future personalized therapies.

Update Viral hepatitis

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Chronic viral hepatitis still confers a major burden of hepatocellular carcinoma (HCC), end stage liver disease and mortality on a global scale. Major breakthroughs in antiviral therapy have been made over the past decades which allow viral control or cure in the majority of patients under treatment, at least in Western countries.

Drug therapy of viral hepatitis C (HCV) has been revolutionized by the approval of direct antiviral acting drugs (DAAs) and led to the assignment of the Nobel prize in 2020 for a group of HCV researchers contributing most to this development. These pangenotypic treatment regimes, most widely used Glecaprevir/Pibrentasvir or Sofosbuvir/Velpatasvir, allow an almost universal sustained viral respone (cure) within a definite treatment time of 8 to 12 weeks. Only advanced and pretreated genotype 3 patients have still relevant rates of relapse. For the overall small subset of relapse patients, a triple combination regimen Sofosbuvir/Velpatasvir/Voxilaprevir has been established. The treatment algorithm has been simplified and only requires knowledge about genotype, treatment history and cirrhosis state.

For viral hepatitis B (HBV) definite cure (e.g. HBsAg clearance) is still rarely achievable for the majority of patients. Using nucleotide/nucleoside analogue drugs (NUCs) for an extended duration, almost all patients experience HBV DNA suppression with a very low rate of viral resistance when using the high barrier drugs Tenofovir or Entecavir. Both drugs are equivalent with regard to treatment success and have been shown to reduce mortality in these patients. New recommendations apply when to stop NUC therapy: patients with a drop of HBsAg levels <1000 IU/ml (Asians <100 IU/ml) have the best chance to clear HBsAg after cessation and eventual flares are mostly minor. Stoping rules for NUCs are particularly relevant in resource limited settings.

The most serious course of all chronic viral hepatitis infections is observed with hepatitis delta (HDV) co-/super-infection of HBV patients: more than half of these patients develop cirrhosis within a decade. In contrast to HBV-mono-infection, Peg-Interferon (+/- NUC) treatment is still a valid option for these patients although long-term viral response rates are limited (<30%). Particularly for advanced patients, the approval of the entry-inhibitor Bulevirtide represents an import breakthrough confering long-term viral suppression without the serious side effects of interferon.

As general measures reducing the cancer risk in patients with HBV and HCV, use of statins and aspirine has recently been associated with a significantly lower rate of HCC development.

On a global scale, detection of viral hepatitis, effective treatment allocation and cure rates are still low. Viral hepatitis prevalence is still high in large parts of Asia and Africa where diagnosis and treatment are not widely affordable. The WHO has defined a road to elimination of HBV and HCV by 2030 but major efforts are needed to achieve the ambitious goals.

Transdisciplinary approach of alcohol related liver disease: the Romanian status-quo

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Alcohol related liver disease (ALD) is a multi-faceted condition with multiple determinants and implies various competences for its successful management. Transdisciplinarity has been described as a practice that transgresses and transcends disciplinary boundaries, and therefore represents an integrative approach focused on problem solving.

The prevalence of chronic liver disease (CLD) is the highest in Romania from the entire European region, as well as the mortality from liver related causes. Among these, ALD represents almost half of the cases. These facts could be explained by a limited resource health and social care system, which are under the influence of (a) demographic and socio-economic factors: migration, unemployment, and relative poverty rate; (b) healthcare system factors: shortage of medical staff, low expenditures and outdated infrastructure and protocols, and (c) cultural factors, that combine alcohol abuse heroism with a stigma towards alcoholics.

All these factors made the healthcare professionals working in liver clinics among the first who get in touch with patients with AUD, when they seek medical assistance because of gastrointestinal bleeding, decompensated liver cirrhosis, episodes of alcoholic hepatitis or acute on chronic liver failure. Therefore, the skills and knowledge the hepatologist uses in everyday practice has shifted from clinical - specific to each spectrum of ALD, to more complex ones, needed to diagnose

and quantify alcohol misuse and addiction and to stratify risk of chronic liver disease.

The management of alcohol misuse and ALD is precarious, mainly because there is a lack of understanding towards addiction issues and an increased level of stigma. The hepatologist is often in the middle of this landscape, as many of the alcoholics seek medical care when their liver disease is overt, or advanced, or evidencing complications. Consequently, the liver specialist is subjected to a considerable burden, which he/she copes with by creating a multidisciplinary team, by getting involved in research and development projects, or by education and training.

Any of these solutions are viable, as they are aimed to improve the care (medical and psychological) addressed to patients with alcohol addiction. Apart from individual or local initiatives, comprehensive Governmental measures are required, especially targeted towards community care, education, and prevention.

SESSION V. BENIGN DISEASES OF THE GUT

Epidemiological data from Romania on the Disorders of Gut-Brain Interaction (DGBI: lessons from the Rome Epi Global Study

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Background & Aim: The prevalence of the disorders of gut-brain interaction (DGBI), formerly known as functional gastrointestinal disorders (FGID) is important for clinical practitioners and health economists and managers. The Rome Foundation launched an Epidemiological Global Study involving 30+ countries (50,000+ participants) including Romania (2000+ participants) (Sperber et al 2021). We aim to summarize the main data from the Romanian participation in this study.

Methods: Biographical data and symptoms were collected by a unique operator worldwide online, evaluating the prevalence of more than 20 different DGBI. The Rome IV diagnostic questionnaire was completed through the Internet with numerous built-in quality-assurance measures. We assessed associations between the overlap of DGBI in four gastrointestinal anatomical regions (esophageal, gastroduodenal, bowel, and anorectal) and validated questionnaires including IBS symptom severity scale (IBS-SSS), Physical and Mental QoL scores (Patient-Reported Outcomes Measurement Information System-10 (PROMIS-10)) anxiety and depression (Patient Health Questionnaires-4 (PHQ-4)), and somatization (PHQ-12). Due to the small number of participants with four overlapping GI regions, we combined the data for participants with three or four overlapping regions.

Results: 2000 participants from all over the country, mean age of 42 years completed the survey. There was an equal sex distribution. Groupage after 60 was underrepresented. Diagnostic criteria for any DGBI were met in 40% of the subjects, as worldwide. From these, 29% met criteria for only one DGBI, and 11.5% met criteria for DGBIs in two, three, or four overlapping GI anatomical regions. Females had a substantially higher predominance of DGBI than males. Psychosocial characteristics (such as quality of life, somatization, and concern about digestive problems) and healthcare utilization (such as physician visits and medication use) were associated with having any DGBI. We found a significant association between the number of involved regions and higher scores for PHQ-4 ($p<0.0001$), PHQ-12 ($p<0.0001$), and the mean number of medications ($p<0.0001$). The PROMIS-10 physical and mental scores were inversely associated with the number of overlapping GI regions ($p<0.0001$). No significant association was found between the degree of overlap with IBS-SSS (p-value=0.095), or the mean number of abdominal surgeries (p-value=0.164).

Conclusion: In this study, we provide the first comprehensive evaluation of the prevalence and burden of DGBI in Romania using the Rome IV criteria. The burden of DGBI in Romania is substantial, with 40% of the 2000 participants meeting diagnostic criteria for any DGBI. More DGBI means more distress and a lower quality of life.

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NSAIDs enteropathy

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Non-steroidal anti-inflammatory drugs (NSAIDs) enteropathy is now more frequently recognised since the discovery of the possibility of small bowel mucosa visualisation by video capsule endoscopy. Around 70% of patients taking long term NSAIDs have macroscopic mucosal lesions detected by capsule endoscopy [1, 2]. One third of the patients using NSAIDs have clinically significant lesions on small bowel (mucosal breaks, erosions, ulcers), responsible for gastrointestinal bleeding, pain and/or hypoalbuminemia; this aspect is even more relevant in an era when combining proton pump inhibitors (PPIs) and NSAIDs reduce gastric ulcerative lesions and demasks NSAIDs enteropathy.

Microbiota, neutrophils, and inducible nitric oxide synthase (iNOS) are involved in the pathogenesis of NSAIDs small bowel injuries. Germ-free animals treated with indomethacin showed significantly fewer intestinal lesions compared with normal animals, suggesting that enterobacterial translocation is essential for the development of intestinal lesions [3]. Nonselective NSAIDs inhibit both COX-1 and

COX-2 expression, decrease prostaglandin synthesis that unbalances the gut tolerant immune profile and upregulate iNOS expression. Also, bacterial lipopolysaccharides realized from gut microbiota combine to Toll-like receptor 4 and upregulate iNOS expression. NO combines with superoxides and form damaging species such as peroxynitrite, which is cytotoxic, thus causing intestinal degenerative lesions in 18-48 hours after NSAIDs administration [4].

Chronic NSAID administration could change the composition of the intestinal bacteria and aggravate bile acids cytotoxicity. Gram-negative bacteria thrive and accumulate in the small intestine, producing endotoxins and acids after NSAIDs supplement, which result in increased intestinal permeability and bacterial translocation, and further aggravate the intestinal injury [5].

In the clinical context, the changes of microbiota could be even more complex by the concomitant use of PPIs. It was documented that PPIs increased the severity of NSAIDs enteropathy [6]. A possible pathogenic explanation is based on the evidence of microbiota changes; after the administration of PPIs, the numbers of *Enterococcus, Streptococcus, Staphylococcus*, and potentially pathogenic species *Escherichia coli* was increased significantly [7]

Based on these observations, further animal and human studies focused on the potential role of antibiotics or probiotics/prebiotics to manipulate the microbiota and to decrease the NSAIDs enteropathy. Antibiotics, such as kanamycin, rifaximin, metronidazole could reduce the Gram-negative species which might improve NSAID enteropathy [5, 8]. Species of *Lactobacilli* and/or *Bifidobacteria* showed beneficial effects on NSAIDs enteropathy. Fecal microbiota transplantation and mucoprotective agents might represent alternative treatments [5].

This presentation provides basic and clinical considerations on NSAID enteropathy, highlighting the role of microbiota.

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Challenges in the treatment of gallstone disease

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Background & aim: Gallstone disease is one of the most frequent diseases in gastroenterology, with a steady increase in its prevalence. Cholecystectomy is the standard therapy of symptomatic gallbladder stones, while endoscopic extraction is the standard therapy of bile duct calculi.

Challenges in gallstone disease are manifold and include the prevention of stone formation, the handling of asymptomatic stones, the treatment of difficult bile duct stones, the timing of cholecystectomy after removal of bile duct stones, the prevention of stone formation during rapid weight loss and after bariatric surgery, and the treatment of difficult gallstones such as in Bouveret's syndrome.

Treatment options for preventing gallstones after bariatric surgery and for Bouveret's syndrome, two interdisciplinary challenges, are presented in detail.

Stone formation after bariatric surgery: Bariatric surgery is performed with rapidly increasing frequency. The risk for the formation of new stones after bariatric surgery is up to 40% within two years, thus like the risk for patients during rapid weight loss. Concomitant prophylactic cholecystectomy at the time of bariatric surgery bears a considerable morbidity and is rarely performed. Therefore, new measures to prevent gallstone disease after bariatric surgery are needed.

Ursodeoxycholic acid has been shown to significantly reduce gallstone formation during rapid weight loss; 600 mg per day for six months will reduce gallstone risk to <5%. Similar effects have been shown after bariatric surgery. Additionally, recent data revealed differences in gene profiles as well as in intestinal microbiota in patients developing gallstones after bariatric surgery. This might provide new options for preventive treatment approaches.

Bouveret's syndrome: Gastric outlet obstruction due to gallstones (Bouveret's syndrome) is a rare disease, accounting for <3% of gallstone ileus. It has a high morbidity and mortality (up to 30%). Endoscopic treatment includes gastric decompression, lithotripsy, and extraction of fragments. Laser lithotripsy under endoscopic visualization has evolved as the most effective method. The success rate of endoscopic treatment is 40% to 60% with a low complication rate. Surgical

enteric lithotomy bears a higher risk of morbidity (38%) and mortality (11%), but offers a success rate of up to 95%. Currently, endoscopy is used first line, while enteric lithotomy is applied if endoscopy fails.

Conclusion: Gallstone disease still poses several challenges. A better understanding of the formation of stones could lead to new preventive approaches. Further refinement of techniques might improve endoscopic treatment of difficult gallstones as in Bouveret's syndrome.

Gastrointestinal related challenges on an ICU

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In treating patients with severe gastroenterological diseases such as acute liver failure, acute-on-chronic liver failure, variceal and non-variceal gastrointestinal bleeding, pancreatitis, severe cholangitis, and many more, intensive care medicine plays a crucial role.

In caring for these complex gastroenterologically ill patients, there are several challenges. Hereby, the link with endoscopy is paramount. Endoscopies are essential to treat critically ill patients in the ICU; on the other hand, high-performance intensive care medicine is vital in complex endoscopic procedures. Infectious disease expertise in treating gastroenterological ICU patients is just as crucial as endoscopic skills since many diseases are triggered or aggravated by infections during their course. Furthermore, sonography plays an outstanding role as an always-available bedside diagnostic.

Interprofessional and interdisciplinary collaboration is essential in an ICU focusing on gastroenterology. As the patients are often very seriously ill, close partnership especially with staff nurses and the hospital pharmacy is vital. Intensifying this interprofessional collaboration, e.g., within antibiotic stewardship, can improve medical and economic outcomes. In addition to the interprofessional partnership, interdisciplinary collaboration is also crucial. Here, interventional radiology, transfusion medicine, and the liver transplant team are particularly important.

Interventional radiological methods are used for gastroenterological patients, e.g., in the case of endoscopic failure in gastrointestinal bleeding or cholestasis. Here, the implantation of a transjugular intrahepatic portosystemic shunt (TIPS), as well as partial splenic artery embolization are particularly noteworthy. CT-guided drainage may be necessary if this is not possible by (endo-) sonography.

Interdisciplinary cooperation with the department of transfusion medicine is again essential when performing therapeutic plasma exchange, e.g., in acute or acute-on-chronic liver failure as a bridge to recovery or a bridge to transplant. In patients with liver failure, the possibility of liver transplantation must always be evaluated together with the liver transplantation team.

To sum up, interprofessional and interdisciplinary collaboration is very important in the intensive care treatment of critically ill gastroenterological patients and in meeting the associated challenges.

Endoscopic diagnosis and treatment of dysplasia in patients with IBD

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Patients with long standing inflammatory bowel disease (IBD) which involves 1/3 part of the colon are at a high risk of developing colorectal cancer (CRC). Current noninvasive methods for CRC screening are not optimized for persons with IBD, requiring patients to undergo frequent interval screening by a colonoscopy. Even though the screening based on colonoscopy reduces the CRC incidence, this pathology remains with relatively high risk in patients with IBD.

The primary approach to screening and surveillance has been colonoscopy at 1-5 years intervals with random four quadrant biopsies every 10 cm distance. In the meantime, the guidelines have changed and are emphasized on high-definition scopes, chromoendoscopy and virtual chromoendoscopy, but also random versus targeted biopsies. Nowadays, also a method for non-invasive screening is being researched – microbiome - as a screening tool.

Colorectal cancer in IBD patients is known to be preceded by dysplasia which is a neoplastic epithelial change. So the primary goal of the endoscopic surveillance is to detect early dysplasia. The pathologists classified the grades of dysplasia from no dysplasia, indefinite dysplasia, low-grade dysplasia (LGD) and high-grade dysplasia (HGD). In the case of indefinite dysplasia, the tissue sample has to be reviewed by a second pathologist. If the sample is obtained by random biopsies and is confirmed to be dysplasia, it should be defined as invisible, and if it is obtained by targeted biopsies it should be defined as visible dysplasia. Furthermore, all endoscopists should describe the lesions using the Paris classification [1-4].

Visible precancerous lesions should be described based on size, morphology, clarity of borders, ulcerations, location, presence within an area of past or current colitis, complete resections and any other special techniques used for visualization [3].

After 30 years of being diagnosed with IBD, the incidence of developing colorectal cancer is 18%. Because of the endoscopic surveillance and improved medical treatments this risk seems to be decreasing. The actual risk of developing CRC starts at approximately 7 years after the diagnosis and increases afterwards. There are some risk factors of developing cancer such as a younger age, the severity of the inflammation and the length of the bowel affected, but also the longer duration of the disease. Other factors involved

seem to be colonic strictures, pseudopolyps, family history of CRC, primary sclerosing cholangitis and the presence of dysplasia [1-3].

Endoscopic surveillance. All guidelines recommend endoscopic surveillance for early detection and resection of dysplasia which could lead to colon cancer. The screening has shown an improvement in survival for patients who are at a high risk of developing colorectal cancer. Also, it is necessary to adjust the period between the procedures considering the related pathology. For example, patients known with primary sclerosing cholangitis (who frequently develop IBD) should undergo an annual colonoscopy. On the other hand, considering the risk factors which include the active inflammation, family history, personal history of dysplasia, presence of pseudopolyps, strictures and surgical interventions, the screening procedures should be done between 1-5 years [3-5].

Nowadays, there are a lot of techniques available, thanks to the different types of scopes available. HD colonoscopy is superior to standard colonoscopy and results offer greater image detail and higher rate in adenoma detection. Suspected lesions can be described using the dye-spray chromoendoscopy, which applies a blue contrast of methylene blue to the epithelium of the colon and thus enhances the irregularity of the mucosa, metaplasia and dysplasia [3].

Visible dysplasia. All clearly delineated dysplastic appearing lesions without invasive cancer (mucosal depressions, irregular surface, radiating folds or failing to symmetrically lift after saline injection in the submucosa) or significant submucosal fibrosis should be considered for endoscopic resections especially if the diameter of the lesion is < 2 cm. For lesions < 2 cm, standard polypectomy techniques can be used. For lesions which are larger and highly irregular, advanced polypectomy techniques are required such as endoscopic mucosal resection or endoscopic submucosal dissection. After this kind of procedures, a follow-up colonoscopy should be repeated 3-6 months later. Deep biopsies without resections should be avoided because the lesion will develop a scar and fibrosis which will make it difficult to lift after submucosal injection [1-2].

Invisible dysplasia. If an area of invisible dysplasia is found, then an experienced endoscopist should repeat the procedure using a high-definition dye-spray chromoendoscopy with extensive non-targeted biopsies. Also, during the first examination multiple biopsies should be taken to make a difference between active colonic inflammation and reactive atypia as dysplasia. If the inflammation is present, it must be controlled before the chromoendoscopy. In some centers, because of good preparation and the overall endoscopic quality, the risk of CRC in IBD patients has declined, approaching that in the non-IBD population [1-3].

Virtual chromoendoscopy (VCE). The modalities of virtual chromoendoscopy include narrow band imaging, i-scan and Fuji intelligent color enhancement. These methods apply narrow wavelength spectrums of light in order to illuminate the mucosal tissue using selective light filters or post-image processing techniques which enhance the vascular and surface architecture of the mucosal lesion without the need for dye. There are some studies published in 2017 – 2019, which revealed that VCE was similar to other endoscopy methods such as dye-spray chromoendoscopy, which also had a shorter withdrawal-time [1].

Chromoendoscopy (CE). Chromoendoscopy is recommended to be used only when we have a high-definition scope (HD), and not a standard definition one (SD). Some studies have shown that CE using a SD scope is not superior to using a white light endoscope (WLE) in order to diagnose early dysplasia. A prospective cohort study published in 2018 [1]evaluated each colonic segment first with WLE and afterwards with CE. In this study, 57.4% of the dysplastic lesions were diagnosed only using CE.

Random biopsies. Extensive non-targeted biopsies should be taken from flat colorectal mucosa when using a white light endoscope (with no VCE or CE) and from areas previously affected by colitis. Non targeted biopsies are not routinely required if dye-spray CE or VCE using a HD scope is performed, but it should be considered if there is a history of dysplasia or primary sclerosing cholangitis. In a prospective, randomized, multicenter study there was no difference found in dysplasia detection between white light endoscope with 40 random biopsies and NBI with 10 random biopsies: colonoscopies performed with NBI resulted in fewer biopsy specimens and a shorted withdrawal time [2].

Surveillance of patients with ileoanal pouch and pseudopolyps. Surveillance intervals should be individualized considering the risk of patients to develop colorectal cancer. Patients at a high risk to develop CCR (prior CRC or dysplasia) or those with moderate to severe pouchitis or pre-pouch ileitis should perform annually a colonoscopy.

Targeted biopsies from suspected pseudopolyps is appropriate during colonoscopy. Removing and sampling all pseudopolyps is not required and not practical. Dye spray chromoendoscopy should not be used to detect flat or subtle lesions within pseudopolyps [2].

Conclusion. Patients with IBD which involves more than one-third of the colon are at an increased risk of developing CRC and should perform a regular colonoscopy surveillance to detect early dysplasia. With the use of HD scopes there will be a debate over the role of CE with targeted biopsies versus HD WLE with random biopsies. The surgical intervention should be the last option for these patients; only when endoscopic resection of the lesion is not feasible [1, 3, 5].

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LIST OF POSTERS WITH ORAL PRESENTATION

Automatic cropping of gastrointestinal endoscopic images for the training of artificial intelligence systems – a multicenter study
Ioannis Kafetzis[1], Philipp Sodmann[1], Boban Sudarevic[1,7], Robert Hüneburg[2,3], Jacob Nattermann[2,3], Nora Martens[4,5], Daniel R. Englmann[6], Wolfram G. Zoller[7], Alexander Meining[1], Alexander Hann[1]
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Bile duct tissue acquisition by cholangioscopic guided cryobiopsy technique: First in a human case report
Jan Peveling-Oberhag (Stuttgart), Corinna Zimmermann (Tübingen), Walter Linzenbold (Tübingen), German Peveling-Oberhag (Stuttgart), Markus Enderle (Tübingen), Jörg Albert (Stuttgart), Germany
Klinik für Gastroenterologie, gastrointestinale Onkologie, Hepatologie, Infektiologie und Pneumologie, Klinikum der Landeshauptstadt Stuttgart, Germany

Metabolomics as a predictive tool in patients with advanced chronic liver disease
Oana Nicoară-Farcău[1,2], Petra Fischer[1], Horia Ştefănescu[1], Bogdan Procopeț[1,2]
1) Prof. Dr. O. Fodor Regional Institute of Gastroenterology and Hepatology, Hepatology Unit (IRGH), Cluj-Napoca; 2) Iuliu Haţieganu University of Medicine and Pharmacy, Department of Internal Medicine, Cluj-Napoca, Romania

Quality of life in patients with inflammatory bowel disease in remission: The influence of fatigue, anxiety and depression
Tudor Stroie[1,2], Carmen Preda[1,2], Corina Meianu[1,2], Doina Istratescu[1,2], Roxana Lucuta[2], Mircea Diculescu[1,2]
1) Carol Davila University of Medicine and Pharmacy, Bucharest; 2) Gastroenterology Department, Fundeni Clinical Institute, Bucharest

The influence of playing video games on endoscopic skills performance
Cristian Tefas
Iuliu Haţieganu University of Medicine and Pharmacy, Department of Internal Medicine, Cluj-Napoca, Romania

Polyp identification for generating a colonoscopy report
Yun Chiang[1], Philipp Sodmann[1], Ioannis Kafetzis[1], Thomas J. Lux[1], Zita Saßmannshausen[1], Joel Troya[1], Markus Brand[1], Wolfram G. Zoller[2], Alexander Meining[1], Alexander Hann[1]
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Iatrogenic botulism after a gastric botox injection. A case report
Julian Müller-Kühnle, Sophia Didra, Hermann Eckhardt, Wolfram Bohle, Albert Jörg
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Noninvasive tools for evaluating MAFLD patients: biological scores and ultrasound based steatosis assessment
Radu Cotrau[1,2], Alina Popescu[1,2], Ioan Sporea[1,2], Raluca Lupusoru[1,2], Alexandru Popa[1,2,] Victor Baldea[1,2], Felix Bende[1,2], Roxana Sirli[1,2]
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A comparative analysis of clinical and endoscopic remission after anti-TNF and immunosuppressive combination therapy versus anti-integrin antibodies therapy in patients with moderate to severely active ulcerative colitis. Real word data from a Romanian Tertiary Gastroenterology Center
Roxana Lucuța[1], Tudor Stroie[1,2], Corina Meianu[1,2], Alexandra Scutaru[1], Doina Istratescu[1], Nicoleta Coca[1], Mircea Diculescu[1,2]
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Multi-drug resistant bacterial infections in cirrhotic patients with ACLF
Petra Fischer[1], Horia Ștefănescu[1], Bogdan Procopeț[1,2]
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Automatic cropping of gastrointestinal endoscopic images for the training of artificial intelligence systems – a multicenter study

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Background & Aims: Endoscopy includes a variety of interventions that visualize the gastrointestinal and biliary tract. Images stored during endoscopic examinations show inhomogeneity, due to hardware and software differences, which hinders the development of artificial intelligence (AI). Our goals are to create an endoscopic image dataset that underlines the said diversity and introduce an automated method to segment endoscopic images from the background.

Methods: An AI model that segments the endoscopic image in a source-agnostic manner was trained with 1765 endoscopic images, prospectively collected from four endoscopy clinics with three different processors. Next, a test dataset, called EPIC, was created with images obtained from four different endoscopy centers, with a total of nine processors from four manufacturers with multiple endoscopes. The AI model was additionally tested with images from two publicly available datasets. Our method was compared with a threshold-based baseline method separating dark background pixels from the endoscopic image.

Results: When considering images from the EPIC dataset, computing a minimum bounding rectangle resulted in mean Dice Coefficient (DC) of 0.988 (95% CI: 0.982-0.993) and 0.892 (95% CI: 0.882-0.903) for our method and the baseline respectively ($p<0.001$). Similarly, for images from open datasets, our method achieved mean DC 0.997 (95% CI: 0.996-0.997) against the 0.942 (95% CI: 0.933, 0.95) for the baseline ($p<0.001$).

Conclusions: We introduce an image-processing method that effectively differentiates the endoscopic image from the background, independent of the image source. Furthermore, we provide a test dataset which highlights the vast variability of endoscopic images. Our method could automate pre-processing data from up to 20 year-old endoscopic images to be used in AI training and increase the generalizability of AI systems by reducing the input variability.

Bile duct tissue acquisition by cholangioscopic guided cryobiopsy technique: First in a human case report

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Case Report: Indeterminate biliary strictures still pose a major challenge in endoscopic diagnostics. Brush cytology as well as fluoroscopic or cholangioscopic guided forceps biopsy show inadequate sensitivity. Cryobiopsy is a method for tissue acquisition, which allows for the extraction of high tissue amounts with a minimal diameter endoscopic instrument. For the first time in humans, we demonstrate a cryobiopsy technique in the bile duct during direct cholangioscopy in a 41 -year-old patient with primary sclerosing cholangitis and dominant stricture. Cryobiopsy led to a successful clinical outcome with excellent tissue samples that enabled a histology-based diagnosis of a critical bile duct stricture.

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Metabolomics as a predictive tool in patients with advanced chronic liver disease

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Background & Aim: Precise biomarkers for specific clinical scenarios and disease pathways in liver cirrhosis are lacking and early diagnosis with the available tools is challenging. Metabolomics is a novel technique with a widespread application in hepatology. Therefore, we performed during time an exhaustive metabolomic characterization of various clinical scenarios in patients with advanced liver disease.

Methods & Results: In patients with *compensated advanced chronic liver disease*, one such scenario is identification of patients at higher risk of decompensation. In this respect, a nested study of 167 patients from the PREDESCI cohort was performed by targeted metabolomic serum analysis, using UHPLC-MS (*Oana Farcău-Nicoară et al.*) [1]. Addition of Ceramide and Methionine to the model including HVPG, Child-Pugh and treatment significantly improved performance (C-index of 0.808 [CI95% 0.735-0.882] vs. 0.748 [CI95% 0.664-0.827; p=0.032)] to identify the 33 patients who decompensated during the follow-up. The two metabolites alone, or their combination with Child-Pugh and type of treatment received *(Clinical/Metabolite model)* had a C-Index of of 0.737 [CI95% 0.640-0.833], and, respectively 0.785 [CI95% 0.710-0.860], not significantly different from the HVPG based models.

Another clinical scenario in *development of hepatocellular carcinoma* was evaluated in the IRGH Cluj-Napoca [2]. In a cohort of 69 cACLD patients, of whom 37 had early HCC, using UHPLC-QTOF- (ESI+)-MS we identified 1,25-dihydroxy cholesterol, myristyl palmitate, 25-hydroxy vitamin D2, 12-ketodeoxycholic acid, lysoPC, and lysoPE as notable biomarkers that differentiate compensated cirrhosis from early HCC, and also that ceramide species are depleted in the serum of HCC patients.

In patients with *decompensated cirrhosis*, early diagnosis and characterization of infection is still challenging. Metabolomic analysis of serum and ascites from 54 patients with decompensated cirrhosis from IRGH Cluj-Napoca identified acylcarnitines, stearic acid derivatives, and 12/15 HETE-GABA as the most affected pathways. N-oleoyl ethanolamine was the most promising biomarker to identify bacterial infection, while prostaglandin E2/D2/H2 and N-oleoyl alanine levels were higher in Gram- infections, and ceramides in non Gram- ones. L-phenylalanine and lysophosphatidylethanolamine were the two most relevant identified ascitic biomarkers for spontaneous bacterial peritonitis diagnosis [3].

In patients with *alcohol related liver disease* differentiation of acute decompensation (DC) from alcoholic hepatitis (AH) is virtually impossible. Using untargeted metabolomics (UHPLC-MS) in a cohort of 34 patients with AH and 37 with DC from IRGH Cluj-Napoca we found that in AH patients, Sphinganine-1P (S1P) was the most increased, while Prostaglandin E2 (PGE2) was the most decreased metabolite. The PGE2/S1P ratio <1.03 excellently discriminates between AH and DC: AUC 0.965 (p<0.001). Additionally, decreased ursodeoxycholic acid levels predict mortality with 77.27% accuracy (NPV=100%) in AH patients [4].

Conclusion: Metabolomics, by identifying various dysregulated lipid pathways, can play an important role in biomarkers identification for either a precise diagnosis, or accurate prediction of decompensation or mortality in patients with advanced liver disease. However, further prospective studies that use targeted metabolomics are needed to validate candidate biomarkers.

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Quality of life in patients with inflammatory bowel disease in remission: The influence of fatigue, anxiety and depression

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Background & Aim. Inflammatory bowel diseases (IBD) are chronic conditions with a remitting-relapsing evolution and

an unpredictable course. Patients with IBD have an impaired health-related quality of life (HRQoL) and are affected more often by anxiety, depression and fatigue. The aim of this study was to evaluate the impact of anxiety, depression and fatigue on the HRQoL in patients with IBD in remission.

Methods: One hundred and thirty-two patients diagnosed with IBD that were in clinical and biochemical remission for more than three months were included in this study. They answered a series of self-completed questionnaires: IBDQ 32, FACIT-Fatigue and HADS. Fatigue was considered for FACIT-Fatigue score ≤40 points. Anxiety and depression were considered for HADS-A >7 points and HADS-D >7 points, respectively.

Clinical remission was assessed using the Harvey-Bradshaw Index (HBI) for patients with Crohn's disease (CD) and the Simple Colitis Clinical Activity Index (SCCAI) for patients with ulcerative colitis (UC). Clinical remission was considered for HBI score ≤4 points and SCCAI score ≤1. Biochemical remission was defined as C-reactive protein (CRP) ≤ 5mg/dl and fecal calprotectin (FCP) ≤150 ug/g.

Results: Out of the 132 patients, 76 (57.6%) were men. Eighty-three patients (62.9%) were diagnosed with CD and 49 (37.1%) with UC. The mean disease duration was 6 years (IQR 2 – 10). The mean IBDQ score was 188 (+/- 25.1). Fifty-five patients (41.7%) were affected by fatigue, 45 (34.1%) by anxiety and 24 (18.2%) by depression.

Patients with fatigue had significantly lower HRQoL compared to patients without fatigue: mean IBDQ score 167.7 vs. 202.5 ($p<0.001$). Similarly, patients with anxiety and depression had significantly impaired HRQoL: mean IBDQ score 164.6 vs. 200.1 ($p<0.001$) in patients with anxiety and 164.3 vs. 193.2 ($p<0.001$) in patients with depression.

Conclusion: Fatigue, anxiety and depression are highly prevalent even in patients with inactive disease and they significantly impair the patients' HRQoL.

The influence of playing video games on endoscopic skills performance

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Background & Aim: Gaming is a growing industry, incurring an exponential growth amid the pandemic context. Video games improve the allocation and speed of attention and provide better spatial orientation in visual processing. These same qualities are sought after in GI endoscopists. This study aimed to investigate whether individuals with a gaming history have superior fine motor and visual skill on a virtual reality (VR) endoscopy simulator and if gaming consoles could be added as a proficiency tool in acquiring endoscopic skills.

Method: Firstly, the subjects' baseline psychomotor skills and hand-eye coordination were tested using a VR simulator. Secondly, subjects were assigned to either group C and asked to refrain from any gaming for 14 days, or to group T, who were asked to play on a console for 14 days. All subjects were then retested.

Results: 81 medical students were included in the study. Baseline VR simulator testing showed better scores in those with a higher number of previous gaming hours (0h – 1598, 0-30h – 1970, 30-50h – 2150, 50-100h – 2395, >100h – 2519; $p<0.05$), with males outperforming females ($p<0.01$). After spending an average of 19 hours gaming all parameters showed noteworthy improvement for those in group T ($p<0.01$). No improvement was seen in group C.

Conclusion: Subjects who engage in console gaming have superior psychomotor skills and perform better on VR simulators. Approximately 20 hours of console gaming can improve one's simulator skills. With consoles being accessible, entertaining, and cheap, they could be used as an additional training platform for GI endoscopy residents.

Polyp identification for generating a colonoscopy report

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Background & Aims: The re-identification of colorectal polyps using artificial intelligence (AI) methods is a crucial step towards automatic colonoscopy report generation. Still, nowadays, there is no widely adopted solution for this task. In this study we propose a pipeline to identify polyps, compute the total number of polyps, and retrieve corresponding polyp images for integration into such a system.

Methods: A pipeline consisting of an AI model and a clustering method was generated for polyp identification. The AI model was trained and validated using 549 and 61 full length colonoscopies respectively, collected from 7 different endoscopy centers. Testing of the pipeline was performed using 10 full length colonoscopies to compare different combinations of AI models, data loadings, and data augmentations. The performance of the pipeline was evaluated by normalized mutual information (NMI), an adjusted rand index (ARI), the total number of polyps, and the precision of corresponding polyp images.

Results: The best results of the proposed pipeline were achieved with a NMI of 0.862 and an ARI of 0.835. Additionally, the total number of polyps was calculated accurately in 80% of the test examinations. Regarding the retrieval of corresponding polyp images, the average precision for examinations with 2, 3, 4, and 5 polyps are 0.9915, 0.482, 0.279, and 0.202, respectively.

Conclusions: We developed an AI based pipeline for identifying polyps, calculating the total number of polyps and retrieving polyp images for an automatic colonoscopy report generation system. This approach potentially provides a simplified and accelerated process to automatically creating a

colonoscopy report. This is further supported by the ability to accurately select characteristic images for each of the detected polyps.

Iatrogenic botulism after a gastric botox injection. A case report

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Botulism is a rare, life-threatening disease caused by neurotoxins. It is characterized by a flaccid, descending paralysis that can lead to cranial nerve palsy, weakness of the extremities, and respiratory failure. The cause is the botulinum neurotoxin, which inhibits the release of the messenger substance acetylcholine at neuromuscular junctions. The most common forms are food, wound, infant, and inhalation botulism. Iatrogenic botulism, the overdose caused artificially as part of a medical intervention in the context of therapeutic or cosmetic use, is an even rarer event.

Case report. We report the case of a 37-year-old patient of Turkish origin who presented to a private clinic in Istanbul at the end of February 2023 for gastric Botox injections as part of a desired weight loss plan. During the procedure in Turkey, a total of 5 ampoules of Dysport 500 were injected endoscopically into the stomach wall, which corresponds to 2500 units of botulinum toxin. Already on the first day after the intervention, the patient felt nausea, dizziness, and dyspnea. In the course of the disease, joint pain, slurred speech, double vision, difficulty in passing stools and weakness when coughing and walking were added. According to the patient, she received information from the doctors treating her that the symptoms mentioned were normal for up to 15 days and that she should only eat liquids during this time. No further diagnostics or reappointment took place. Instead, the patient flew back to Germany in early March. When the symptoms persisted for another 5 days, she was referred to our hospital's emergency department.

We explain the detailed processing of the case, starting with the initial suspicion about the diagnosis, amazing findings in consultation with the Robert Koch Institute (RKI) and the resulting therapy.

Noninvasive tools for evaluating MAFLD patients: biological scores and ultrasound based steatosis assessment

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Background & Aim: Several noninvasive assessment tests were developed to predict liver fibrosis and steatosis for patients with fatty liver disease. We aimed to assess the correlation between HSI, FLI scores and Controlled attenuation parameter (CAP), also between APRI, FIB-4 Index and BARD score and Transient Elastography (TE), in a group of MAFLD (metabolic dysfunction associated fatty liver disease) patients.

Method: We conducted a prospective study, which included 83 patients with MAFLD, characterized by hepatic steatosis and either diabetes, overweight/obesity, or metabolic dysregulation (mean age 55.9±10.7 years, 49.4% female, 50.6% male). All patients were evaluated clinically (BMI, waist circumference), by serum markers (AST, ALT, platelets, GGT, triglycerides), as well as by TE with CAP (FibroScan- EchoSens). Based on specific formulas, we calculated APRI, FIB-4 index, BARD, HSI and FLI scores. To discriminate significant steatosis, we used the CAP cut-off S≥2: 310 db/m [1], and for advanced fibrosis F≥3: 9.7kPa [2].

Results: Out of 83 patients with MAFLD, 59/83 (71.0%) were with at least moderate liver steatosis by CAP measurements and TE measurements showed 10.8% of patients with severe fibrosis. Of 59 MAFLD patients with at least significant steatosis, 84.7% patients had an HSI score > 36 and 81.5% had FLI > 60. In the rule-in analysis for significant steatosis, a cut-off value of 46.5 was found for HSI (PPV-93.3%) and a cut-off value of 96 for FLI (PPV-100%). We tried to rule out advanced fibrosis using APRI<2 (97.5% patients) and we found a NPV=88.9%. We found a moderate, but significant correlation between liver stiffness assessed by TE and by APRI ($r=0.29$, $p<0.0001$). Regarding FIB-4 score, 82.9% of patients had FIB 4<2.6, ruling out advanced fibrosis with a NPV=88.2%; the correlation in this case was moderate but statistically significant ($r=0.21$, $p=0.04$); 32.5% (27/83) of patients had a BARD score <2, having a strong negative predictive value for advanced fibrosis, NPV=90.0%.

Conclusion: HSI and FLI can rule in at least moderate steatosis, while APRI, BARD and FIB-4 can rule out advanced fibrosis. These simple scores could be used as a first-line test, in any medical office, to assess the need for further investigation.

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A comparative analysis of clinical and endoscopic remission after anti-TNF and immunosuppressive combination therapy versus anti-integrin antibodies therapy in patients with moderate to severely active ulcerative colitis. Real word data from a Romanian Tertiary Gastroenterology Center

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Method: A comparative, retrospective analysis following the clinical and endoscopic features of patients with moderate to severely active ulcerative colitis, treated with anti-TNF and immunosuppressive combination therapy or anti-integrin monoclonal antibodies in the Gastroenterology Department of Fundeni Clinical Institute, Bucharest.

Clinical evolution was assessed using the Truelove and Witts Severity Index for Ulcerative Colitis. The endoscopic features were assessed using the Mayo Score for Ulcerative Colitis and Montreal Classification.

The initiation of anti-TNF and immunosuppressive combination therapy or anti-integrin therapy considered the severity index and the associated comorbidities. Patients were retrospectively assessed for a period of 36 months from initiation. Clinical and biological follow-up was performed at 3 to 6 months, and colonoscopy was repeated between 6 to 12 months.

Results: Forty-eight patients were assessed retrospectively for a period of 36 months from the initiation of anti-TNF and immunosuppressive combination therapy or anti-integrin therapy and prospectively during the last year. Twenty-three patients had associated significant comorbidities.

Twenty-six patients received anti-integrin therapy, of whom 12 evidenced associated significant comorbidities, all having an endoscopic Mayo score at initiation of 3 points. Six patients did not achieve endoscopic remission: 1 patient had an E1 form, 3 patients an E2 form and 2 patients an E3 form; 1 patient was in active treatment for 0-6 months, 1 patient for 6-12 months, 2 patients for 12-18 months and 2 patients for 18-24 months. In 2 of these patients, we decided to switch to another agent. None initiated IFX therapy.

Among the 14 patients who followed the anti-integrin therapy in the absence of comorbidities, 4 patients did not obtain endoscopic remission: 2 patients had an E2 form and 2 patients had an E3 form; 2 patients had active treatment for a period of 6-12 months, 1 patient for a period of 12-18 months, and 1 patient for a period of 18-24 months. In 2 of these patients, we decided to switch to another agent, 1 patient being initiated with IFX in monotherapy.

Twenty-two patients received anti-TNF and immunosuppressive combination therapy, of whom 11 patients had associated significant comorbidities, all of them having an endoscopic Mayo score of 3 points at initiation. Seven patients din not achieve endoscopic remission:1 patient having an E1 form, 2 patients an E2 form and 3 patients E3; 3 of these patients underwent treatment for 0-6 months, 1 patient for 6-12 months, 3 patients for 18-24 months. In 4 of these patients, we decided to switch to another agent, 3 of them being initiated with Vedolizumab.

Among these 11 patients on anti-TNF and immunosuppressive combination therapy who had associated significant comorbidities, 7 patients did not obtain endoscopic remission: 4 patients had an E1 form, 2 patients an E2 form, and 1 patient an E3 form; 3 of these patients were having active treatment for 0-6 months, 2 patient for 18-24 months, and 2 patients for 24-20 months. In 3 patients we decided to switch to another agent, 2 of them being initiated with Vedolizumab.

Conclusions: Clinical and endoscopic remission rates were higher in patients who received anti-integrin therapy, regardless of the presence or absence of significant comorbidities. On the other hand, patients treated with anti-TNF agents had higher clinical and endoscopic remission rates in the absence of significant comorbidities.

Patients in treatment with TNF-agents had a superior and directly proportional correlation regarding clinical and endoscopic remission.

Patients treated with anti-integrin antibodies obtained endoscopic remission after a longer period of treatment.

Most endoscopic relapses that required therapy changes were recorded in patients who received anti-TNF antibodies.

Multi-drug resistant bacterial infections in cirrhotic patients with ACLF

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Background & Aim: Patients with liver cirrhosis have an increased susceptibility to develop bacterial infections. Most of them are severe and associated with intense systemic inflammation, poor clinical outcome, and high mortality rates. Infections with multi-drug resistant organisms (MDROs) are the worldwide leading cause for developing *Acute-on-Chronic-Liver-Failure (ACLF)*. In previously reported studies, about one-third of culture-positive infections in cirrhotic patients proved to be with MDROs, ESBL (*Extended Spectrum Beta Lactamase*) producing *Enterobacteriaceae* being most frequently involved. In addition, there is an increasing concern regarding infections caused by Carbapenem-resistant Enterobacteriaceae (CRE) in patients with liver cirrhosis.

We aimed to evaluate the prevalence of infections with multi-drug resistant organisms in patients with decompensated cirrhosis and ACLF.

Methods: All consecutive patients with acutely decompensated liver cirrhosis admitted to the ICU of a tertiary referral hospital in Cluj-Napoca, Romania between July 2017 and March 2019 were enrolled in the study. A complete

infectious screening was performed in the first 24 hours after admission and whenever a new infection was suspected during hospitalization. The type of infection was defined according to conventional criteria and existing guidelines.

Infections with multi-resistant organisms were considered those with MRSA, VRE, ESBL+ *Enterobacteriaceae*, Carbapenem resistant *Enterobacteriaceae* (CRE), carbapenem-resistant non-fermentative Gram-negative bacteria (CR-NFGNB)-*A.baumannii* and *P.aeruginosa*. Among fungal infections, *Candida* non-albicans strains were included.

The isolated *Enterobacteriaceae* strains were tested for carbapenemase-producing genes using the Roche LightMix® Modular *VIM/IMP/NDM/GES/KPC/OXA48*-carbapenemase detection kit.

Results: 75 patients with acutely decompensated cirrhosis were enrolled in the study, and among them almost eighty percent had ACLF. Moreover, there was a statistically significant correlation between infection and ACLF at ICU admission (p=0.01). ACLF grades 2 and 3 were more frequent in infected patients: 32% vs. 9% and 64% vs. 42%, respectively.

48 culture-positive infections were registered. Thirty patients contracted a second infection. 46% of bacteria isolated at admission and 60% of bacteria responsible for infections identified during ICU-stay were multi-resistant. ESBL+ *Enterobacteriaceae* were predominant at admission, while carbapenem-resistance was dominant in both *Enterobacteriaceae* and *Non-Fermenting-Gram-Negative Bacteria* responsible for infections diagnosed during hospitalisation. *OXA 48* or *KPC* type carbapenemases were present in 30% of the analyzed *Enterobacteriaceae* and in 40% of the phenotypically carbapenem-resistant *Klebsiella pneumoniae* strains. The length of ICU stay was a risk-factor for a second infection (p=0.04). Previous carbapenem usage was associated with an occurrence of infections with carbapenem-resistant Gram-negative bacteria during hospitalization (p=0.03).

Conclusions: The prevalence of infections with MDROs is high in patients with decompensated cirrhosis and ACLF admitted to the ICU. CR-*Klebsiella pneumoniae* and CR-NFGNB are the most frequently involved MDROs. Previous hospitalization, the length of ICU stay, and previous treatment with broad-spectrum antibiotics increase the risk for their occurrence. Carbapenemase-producing genes in *Enterobacteriaceae* strains isolated in our center are $bla_{\text{OXA-48}}$ and bla_{KPC}.

LIST OF e-POSTERS

Ultrasound surveillance in the prediction of hemodynamic TIPS dysfunction
Andreea Fodor[1], Rareș Crăciun[1,2], Oana Nicoară-Farcău[1,2], Petra Fischer[1], Mina Ignat[1] , Corina Radu[1], Zeno Spârchez[1,2], Horia Ștefănescu[1], Bogdan Procopeț[1,2]
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Self-perceived lactose intolerance versus confirmed lactose intolerance in IBS: systematic review and meta-analysis
Andrei Pop, Stefan Lucian Popa, Abdulrahman Ismaiel, Dan L Dumitrascu
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***In vitro* effects of EGF-functionalized gold nanoparticles in pancreatic adenocarcinoma cell lines**
Cristiana Grapa[1,2], Lucian Mocan[2,3], Alexandru-Flaviu Tabaran[4], Cristian T. Matea[2], Zeno Sparchez[5], Cornel Iancu[2,3], Teodora Mocan[1,2]
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Risk factors for acute diverticulitis
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Comparison of multiple computer-aided polyp detection systems in the same colonoscopy video dataset
Joel Troya[1], Boban Sudarevic[1,4], Adrian Krenzer[2], Michael Banck[2], Markus Brand[1], Benjamin Walter[3], Frank Puppe[2], Wolfram G. Zoller[4], Alexander Meining[1], Alexander Hann[1]
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Fullminant ulcerative colitis - a challenging therapeutic decision. A Case report
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Dynamics of Lille score for predicting outcome in severe alcoholic hepatitis
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Endoscopic ultrasound for structured surveillance after curative treatment of esophageal cancer
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Esophageal Crohn's Disease – A Case Report
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Standard coagulation cut-offs for interventional procedures in cirrhosis. Is thromboelastography rendering them obsolete?
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Diagnosing extrahepatic bile duct tumors: standard EUS-FNA versus contrast enhanced EUS-FNA
Rares Ilie Orzan[1,2], Cristina Pojoga[1,3], Claudia Hagiu[1,2], Ofelia Mosteanu[1,2], Ioana Rusu[1,2], Voicu Rednic[1], Nadim Al Hajjar[1,2], Renata Agoston[2], Andrada Seicean[1,2]
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The impact of coffee consumption on inflammatory markers in patients with inflammatory bowel diseases
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Ultrasound surveillance in the prediction of hemodynamic TIPS dysfunction

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Background & Aim: The role of ultrasound (US) parameters in the surveillance of a transjugular intrahepatic portosystemic shunt (TIPS) has been a matter of debate, yet no clear cut-off values have been defined. Our primary aim was to evaluate the performance of US in the detection of hemodynamic TIPS dysfunction (HD), in the absence of symptoms suggestive for dysfunction. Secondly, we evaluated the role of liver and spleen stiffness as assessed by Fibroscan and 2D share wave elastography in predicting HD.

Methods: We included all patients who received TIPS for portal hypertension (PHT)-related complications and had systematic hemodynamic TIPS revision at 6 weeks after the procedure. Clinical TIPS dysfunction was defined as recurrence of variceal bleeding or inadequate control of ascites. HD was defined as a portal pressure gradient (PPG) ≥ 12 mmHg at revision. Subgroup analysis was performed on elastography measurements of the liver (delta LSM) and spleen (delta SSM). We analyzed 86 patients with available paired US parameters at TIPS placement and first revision.

Results: The main indication for TIPS placement was recurrent variceal bleeding (82.5%), while 17.5% of the patients had refractory ascites. Clinical dysfunction rate was 18.6% at 6 weeks. Median initial and post-TIPS PPG were 16 mmHg (14 - 19) and 7 mmHg (5.5 - 8), respectively. In 74.4% of cases, a decrease higher than 50% in PPG was achieved. Median 6 weeks systematic PPG value was 10 mmHg (7 - 14). HD occurred in 43% of the cases. Portal vein velocity had an AUROC of 0.71 for a cut-off of 40.5 cm/s ($p<0.001$) in detecting HD, with a sensitivity of 0.84 and a specificity of 0.50. In the subgroup analysis (n=30), the percentage change in delta 2D SWE SSM predicted HD with a modest AUROC of 0.77 for a cut-off of 40% ($p=0.03$). However, percentage change in delta LSM in both 2D SWE and Fibroscan, exhibited low performance with AUROC of 0.47 and 0.59, respectively, in discriminating HD.

Conclusion: Patients with 6 weeks HD exhibited a significantly lower decrease in 2D SWE SSM. Non-invasive, US or Fibroscan surveillance cannot substitute systematic hemodynamic TIPS revision for diagnosing HD.

Self perceived lactose intolerance versus confirmed lactose intolerance in IBS: systematic review and meta-analysis

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Background & Aim: Functional gastrointestinal disorders are a common group of disorders related to digestion, with a prevalence ranging from 20% to 40% in the general population. Among these disorders, the most frequently occurring and researched one is the irritable bowel syndrome (IBS), which affects a significant portion of the population, decreasing their quality of life.

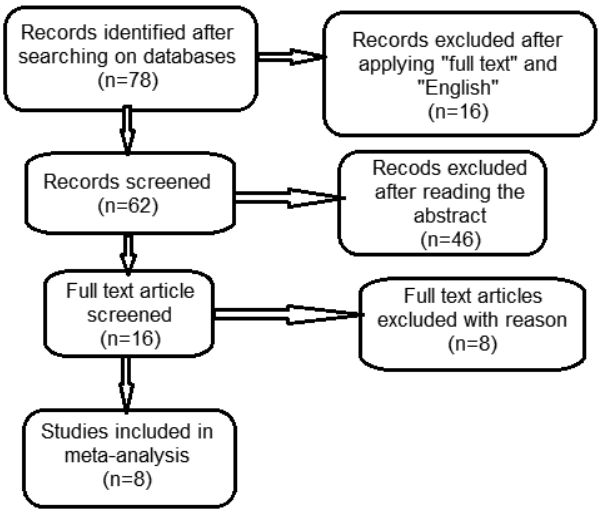
It is challenging to manage these patients because the pathophysiology underlying their condition is not well understood, and non-pharmacological treatments are commonly used. One of the recommendations physicians often make is for patients to follow a lactose-free diet. The relationship between IBS and lactose intolerance is not entirely clear.

We conducted a literature search to investigate a potential link between lactose intolerance and self-reported lactose intolerance, as well as the effectiveness of lactose-free diets in managing IBS patients.

Methods: We found all the articles included in this meta-analysis by searching through multiple databases, including Pubmed, Scopus, and Embase. The studies analyzed were found using the query: [(„irritable bowel syndrome") AND („lactose

intolerance") AND („self reported" OR perceived)]. The search was limited to articles written in English and focused on human adults aged 18 years or older diagnosed with IBS according to the ROME criteria in use at that time.

Results: A total of 78 articles were found from the three databases and subjected to evaluation. The number of articles found in each database were 18 in Pubmed, 49 in Embase, and 21 in Scopus. After applying filters for language (English) and species (only humans) and for „full text" availability, 16 studies out of the 78 were excluded. Then, after removing duplicates and screening the titles and abstracts, 16 articles were subjected to full-text screening. Among these, 16 articles were assessed in detail, and 8 of them were excluded from statistical analysis. Finally, 8 studies met the inclusion criteria and were used for analysis.



Some studies did not find any significant differences in the prevalence of lactose malabsorption between IBS patients and non-IBS controls. However, another study indicated that lactose malabsorption is not necessarily the cause of self-reported milk intolerance.

Many patients with IBS reported lactose intolerance before any objective tests, but the prevalence of lactose malabsorption in this group was similar with that in the general population.

Conclusions: A lactose-free diet for patients diagnosed with IBS is not recommended as routine. Also, the hydrogen breath test is not recommended as a matter of routine in identifying a possible lactose malabsorption in IBS patients. In further investigations, a better comprehension of the factors implicated in lactose perception and tolerance would be clinically relevant due to its implications and merits of consideration.

In vitro effects of EGF-functionalized gold nanoparticles in pancreatic adenocarcinoma cell lines

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Background & Aims: Pancreatic cancer (PC) is one of the leading causes of cancer-related deaths worldwide, with poor prognosis and ineffective therapies. Ongoing research efforts have led to a better understanding of PC pathogenesis, including the role of the epidermal growth factor receptor (EGFR) and its main ligand, EGF. Its overexpression has been linked to PC progression, tumour growth and metastasis. To this end, conjugating nanoparticles with different ligands such as EGF can be used as an improved method of drug delivery, with less systemic toxicity. Our study used gold nanoparticles functionalized with chitosan and EGF on pancreatic adenocarcinoma cell lines (PANC-1), to characterize cellular interactions thus quantifying its therapeutic potential.

Methods: Gold nanoparticles functionalized with chitosan and EGF (GNP-chit-EGF) were prepared in three solutions of different concentrations; PANC-1 cells were exposed to the nanoconjugate for 3 hours, and the cellular transit after exposure was visualized by dark field microscopy with hyperspectral mode. Analysis of mitochondrial membrane potential (MMP), cellular apoptosis, reactive oxygen species (ROS) and superoxide (SOD) production, cell proliferation and viability analysis (MTT) were all made possible using specific detections kits.

Results: Cell transit after exposure to nanomaterial, evaluated through dark field microscopy, confirmed the nanoconjugate intracellular presence. Using light field microscopy, no changes in MMP were detected in all three different concentrations; instead, a resistance to apoptosis was detected proportionate to the increase in nanoconjugate concentration. Regarding ROS and SOD detection, flowcytometry analysis revealed no changes in the emission of mitochondrial reactive oxygen species, irrespective of nanoconjugate concentration while MTT analysis revealed a significant increase of 123% ($p<0.001$) in cell viability.

Conclusion: Cell-nanoconjugate interactions still represent a roadblock for clinical implementation since they are often contradictory and poorly defined. Our study contributes to the global effort of a better understanding of nanoparticle conjugation, its potential use in pancreatic cancer and marks prospective directions for further studies on this subject.

Risk factors for acute diverticulitis

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Background & Aim: Inflammation of one or more diverticula, known as acute diverticulitis (AD), can be followed by a number of complications (perforation, abscess, fistula, peritonitis). It is critical to quickly identify patients who need immediate treatment in order to avoid complications related to acute diverticulitis. Some studies have reported that the neutrophil-to-lymphocyte ratio (NLR) provide predictive data on the severity of acute diverticulitis. Our study aimed to assess the associations between NLR, platelet-to-lymphocyte ratio (PLR), monocyte to lymphocyte ratio (MLR) and systemic immune-inflammation (SII) with the severity of acute diverticulitis and the classifying ability of inflammatory markers concerning Hinchey score.

Methods: We conducted a retrospective single institute study and included patients admitted with acute diverticulitis between January 2012 to February 2023 using computer tomography (CT) or colonoscopy to assess acute diverticulitis (AD). Patient characteristics, clinical signs, laboratory parameters (leukocyte count, neutrophils, lymphocytes, thrombocytes, monocytes), days of hospitalization, surgical outcomes, recurrence rates, the time interval from the first to a recurrent episode and cumulative length of stay due to acute diverticulitis were collected. Complicated diverticulitis (cAD) was defined as > Hinchey 1a. The modified Hinchey score was based on the radiological reports of CT scans. Associations were analyzed for NLR, PLR, MLR, and SII values at admission with patient outcomes. The sensitivity and specificity for the diagnosis of cAD were determined using receiver operating characteristic curve (AUROC) curves.

Results: 147 patients were included in the study, 75 (51.02 %) of these were men. The median age was 60.8 years (range 25–89 years). Based on the radiological criteria including the modified Hinchey score, 65 (44.22%) of the patients were classified with complicated diverticulitis, and 82 (55.78%) with uncomplicated disease. The area under the AUROC classifying a Hinchey score >= 1b, and the corresponding best cutoffs and respective sensitivity and specificity were: for SII: 0.812 (0.73 - 0.888), cutoff =1200, Se=82%, Sp=76%; for NLR: 0.773 (0.676 - 0.857), cutoff =4.06, Se=80%, Sp=69.3%, for PLR: 0.725 (0.63 - 0.813), cutoff =144.38, Se=80%, Sp=56%, for MLR: 0.665 (0.542 - 0.777), cutoff = 0.38, Se=65.7%, Sp=65.2%. When evaluating the recurrences prediction of NLR, no statistically significant association was found (AUROC = 0.476 (0.288 - 0.663)).

Conclusion: Our study indicates that SII, NLR, and PLR have statistically significant and clinically useful classifying abilities to identify higher Hinchey scores, but they cannot predict the recurrences.

Comparison of multiple computer-aided polyp detection systems in the same colonoscopy video dataset

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Background & Aims: Artificial intelligence-based computer-aided polyp detection (CADe) systems are becoming more common in routine endoscopic colorectal cancer screening. These systems are updated on a regular basis and occasionally provide adjustable detection thresholds that impact their performance. However, the impact of these adjustments on the system's performance has not yet been examined. The objective of this study is to assess the effectiveness of several CADe systems on a standardized benchmark dataset, as well as to compare the performance of different versions and configurations of the same system.

Methods: The study included 101 colonoscopy videos. Each video containing visible polyps was manually annotated with a bounding box, leading to a total of 129 705 polyp images. Three CADe systems were evaluated: two versions of GI Genius, two detection types of EndoAID, and the freely available CADe system EndoMind. The evaluation process involved a comprehensive analysis of sensitivity, false positive rate, and time to first polyp detection. Additionally, the quality of the bounding boxes in delimiting the polyp was assessed by calculating the intersection over the union.

Results: EndoAID (type A), the earlier version of GI Genius, and EndoMind detected all 93 polyps in at least one image. Both the later version of GI Genius and EndoAID (type B) missed one polyp. The mean per-frame sensitivity for each system was 50.63 % for the earlier version of GI Genius, 67.85 % for the later version of GI Genius, 65.60 % for EndoAID (type A), 52.95-% for EndoAID (type B), and 60.22 % for EndoMind. Regarding the mean first detection time, the earlier version of GI Genius required 1510 ms, the later version of GI Genius required 607ms, EndoAID (type A) required 659 ms, EndoAID (type B) required 1-316 ms, and EndoMind required 1083ms. The CADe system that presented the fewest number of false positive frames was EndoAID (Type B) with a ratio of only 0.63%. Lastly, EndoMind was the best performing system in terms of bounding box quality with an intersection over union value of 68.32-%.

Conclusion: This study provides a direct comparison of the performance of different CADe systems, as well as different versions and configurations of the same system. The findings demonstrate a substantial variance in the effectiveness of CADe systems based on the specific system, version, and configuration utilized. By providing an objective evaluation of the strengths and weaknesses of CADe systems, this study can help clinicians and researchers select the most appropriate system for their specific needs.

Fullminant ulcerative colitis - a challenging therapeutic decision. Case report

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Case description: A 31 y.o. female, with no significant medical personal history, in the first trimester of pregnancy, experienced an episode of mild rectal bleeding. Fecal Calprotectin was performed which showed elevated values; rectoscopy evidenced an endoscopic aspect suggestive for ulcerative colitis. At 34 weeks pregnant, the patient was admitted to the Obstetrics and Gynecology department, presenting abdominal pain and multiple diarrheic stools with blood (10 stools/day). The patient was transferred to the Gastroenterology department. Abdominal ultrasound showed bowel wall edema, colon-thickened walls of about 7 mm, with loss of the stratification. Laboratory tests showed anemia (Hb 8.2g/dL) and inflammatory syndrome: CRP = 120 mg/L, ESR = 40 mm/1h, ALT = 14 U/L, AST = 20 U/L, albumin= 2 g/dl. Treatment with fluid and electrolyte replacement, Nutrition- tolerated oral intake, albumin infusion, systemic glucocorticoids - hydrocortisone (200 mg IV/24h), oral Mesalazine 2g/day and suppositories 1g/day.

No improvement was observed. Later on, the patient developed painful uterus contractions, so that a transfer to the Gynecology and Obstetrics department was made for a preterm birth (week 35) by Cesarean delivery. The patient was transferred back to the Gastroenterology department, and a CT scan of the abdomen and pelvis was performed, which showed diffuse inflammation of the entire colon wall, up to 7-8 mm thick, loss of haustra, areas with hydroaeric content, mild pelvic ascites. The biological treatment with anti-TNF agent – Infliximab was initiated, first infliximab infusion 300 mg, the next infusion was given in two weeks. After the first infliximab infusion the patient's evolution was slowly favorable with the partial remission of the symptoms and the improvement of the biological constants, but still with 8 stools/day. Abdominal MRI was performed, which showed important wall edema of the entire colon, excluding toxic megacolon. During the hospitalization, the patient presented an acute fulminant ulcerative colitis episode refractory to both glucocorticoids and Infliximab, abdominal pain and distension, hypotension, tachycardia, severe hematochezia with hemodynamic instability -hemorrhagic shock. Surgery was performed with total colectomy with end ileostomy: the rectum was not resected.

Comments: Most drugs used in IBD treatment are considered to be safe both for the mother and the fetus. A conventional steroid-therapy and 5-ASA does not increase the risk of congenital abnormalities. Administration of immunosuppressants, such as AZA or 6-MP should be carefully considered, and the treatment should be monitored both by an experienced gynecologist and a gastroenterologist. Infliximab is recommended by the ECCO for the treatment during pregnancy.

Dynamics of Lille score for predicting outcome in severe alcoholic hepatitis

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Background & Aims: Baseline data and the change in bilirubin level at day 7 is required for calculating the Lille score. However, it is not clear when baseline data should be collected. Our aim was to assess the changes in the Lille score according to two baseline data: admission and day one of corticosteroid treatment.

Methods: All consecutive patients with a history of alcoholism, biopsy proven alcoholic hepatitis (AH), Maddrey score > 32, were included in the study between January 2016 - December 2022. Biological data was recorded at admission (T0) and prospectively at day 1 (T1), day 7 (T7) of corticosteroid therapy.

Results: Two hundred and thirty-nine patients were included; mean age was 51±10; 77.5 % were males; 88.2 % were decompensated. Out of all patients, 82.2 % responded to corticotherapy, as assessed by the Lille score at day 7.

One hundred patients had the blood analysis required to assess both the Lille T0 and Lille T1.

The AUROC curve for survival at 3 months for Lille7 T0 was 0.76 ± 0.05 (95%Cl: 0.65 - 0.86), Lille7 T1 0.78 ± 0.05 (95%Cl: 0.68 - 0.88).

The median follow-up was 13 months (0-78 months), 55% of the patients died by the end of the follow-up. Corticosteroid response as assessed by the Lille7 T1 predicts better one month survival than the Lille7 T0, HR: 5.8 (95 %Cl: 2.4 – 14.2), p=0.0001, respectively HR: 4.05 (95 %Cl: 2.67- 9.84), p=0.002.

Conclusions: The Lille score does not significantly change between admission and corticosteroid initiation.

Endoscopic ultrasound for structured surveillance after curative treatment of esophageal cancer

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Background: Structured surveillance after treatment of esophageal cancer is not established. Due to paucity of data, no agreement exists how surveillance should be performed. The main argument against intensive follow-up in esophageal cancer is that it may not lead to true survival advantage.

Methods: Structured surveillance was performed in 41 patients after surgery (28) or definitive chemoradiotherapy (13) of esophageal cancer. The surveillance protocol included gastroscopy, endoscopic ultrasound, chest x-ray, abdominal ultrasound, and CEA measurement at regular intervals up to five years. We analyzed the relapse rate, time to relapse, localization of recurrence, diagnosis within or without structured surveillance, diagnostic method, treatment of recurrence and outcome.

Results: Median follow-up was 48 months; 17/41 patients suffered from tumor relapse, with 15 asymptomatic patients diagnosed within structured surveillance. Median time to recurrence was 9 months. Isolated local or locoregional recurrence occurred in 6, and isolated distant relapse in 9 patients. All patients with isolated locoregional recurrence were exclusively diagnosed with endoscopic ultrasound. Six patients received curatively intended therapy with surgery or chemoradiotherapy, leading to long-lasting survival.

Conclusion: Structured surveillance offers the chance to identify limited and asymptomatic tumor relapse. Especially in case of locoregional recurrence, long-lasting survival or even cure can be achieved. Endoscopic ultrasound is the best method for the detection of locoregional tumor recurrence and should be an integral part of structured surveillance after curative treatment of esophageal cancer.

Esophageal Crohn's Disease. Case Report

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Background: Esophageal involvement in Crohn's disease is relative rare, with an incidence of 0.3% to 2% reported in literature, but these results may be underestimated, since upper gastrointestinal endoscopy is not performed routinely in the initial evaluation of the disease.

Case description: The case of a 31-year-old female is presented, with a positive family history of Crohn's disease, who was diagnosed two months before with A1L3B1 Crohn's disease. She was treated with Budesonidum, but she declared new onset of chest pain, dysphagia, odynophagia and weight loss.

The upper gastrointestinal endoscopy revealed in the distal third of esophagus a deep, longitudinal, with sharp margins, 20 mm ulcer, and other two 3-4 mm rounded, well circumscribed ulcers in the middle esophagus.

A herpesvirus and cytomegalovirus infection was excluded on histopathology. Double PPI dose associated with Infliximab was started with the disappearance of esophageal lesions at a 3-month endoscopy. But after 5 months, the patient presented a severe flare associated with erythema nodosum lesions. The trough levels showed a low level of IFX (0.6 ug/dl), and the presence of IFX antibodies. Azathioprine was prescribed and the IFX was escalated with clinical remission, disappearance of IFX antibodies, but with a persistence of calprotectine high values (1,300ug/dl) after 3 months.

A second line biological therapy was considered.

Comments: A cross-sectional study has demonstrated that proximal CD (L4) affects younger nonsmoking patients, is less likely to involve the colon (L2), is more frequently present with concomitant ileal involvement and stenosing behavior and has a higher probability of having one or more abdominal surgeries. Esophageal Crohn's disease can be present without any disease.

The use of PPIs resulted in symptomatic improvement, but these drugs did not act in the control of the inflammatory response and should not be used as monotherapy. Treatment should include the association of corticosteroids, immunomodulators and biological therapy.

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Standard coagulation cut-offs for interventional procedures in cirrhosis. Is thromboelastography rendering them obsolete?

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Background & Aim: Patients with cirrhosis have frequent abnormalities in standard coagulation tests (SCTs). Despite not providing an adequate hemostasis assessment, cut-offs based on SCTs still frequently guide interventional procedures and blood product transfusions. Thromboelastography (TEG) provides a global assessment of coagulation, including clotting factors

(R-time), fibrinolysis (Ly30), platelet (maximum amplitude-MA), and fibrinogen (K-time, alpha-angle) function. We aimed to investigate whether conventional cut-offs based on SCTs are associated with TEG abnormalities.

Methods: A consecutive series of patients with cirrhosis and at least one abnormal SCT (using standard cut-offs: INR>2, platelet count<50.000/μL, fibrinogen<200 mg/dL) was analyzed using TEG.

Results: 106 patients were included, of whom 62 (58.5%) were in the Child-Pugh C class. Of the 50 (47.1%) patients with an INR>2, no patient met the criteria for fresh frozen plasma transfusion, while 25 (n=50%) had a hypercoagulable status. Patients with thrombocytopenia <50.000/μL (n=36, 33.9%) had a higher rate of TEG-based platelet dysfunction compared to patients without thrombocytopenia (20% vs. 2.8%, p=0.01), yet overall, only 8 (7.5%) met the TEG-based criteria for platelet transfusion. Regarding fibrinogen, of the 55 patients (51.8%) had values<200 mg/dL, 13 (23.6%) met the criteria for cryoprecipitate transfusion, compared to 3 (5.8%, p=0.01) in patients with fibrinogen>200 mg/dL. Overall, 69 (64.4%) patients had at least one hypercoagulable feature on TEG. The INR-R, platelet count-MA, fibrinogen-K, and fibrinongen-alpha-angle correlation coefficients were all <0.5.

Conclusion: TEG provides a significantly better risk stratification than conventional SCT cut-offs in patients with cirrhosis and might significantly reduce blood product use.

Diagnosing extrahepatic bile duct tumors: standard EUS-FNA versus contrast enhanced EUS-FNA

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Background & Aims: Contrast enhanced endoscopic ultrasound (CH-EUS) is superior to standard endoscopic ultrasound (EUS) for T staging of biliary duct tumors (BDT) but its role in guiding EUS-fine needle aspiration (EUS-FNA) is unknown. We compared the diagnostic performance of CH-EUS-fine needle aspiration (CH-EUS-FNA) and standard EUS-FNA in BTD and aimed to determine the factors influencing the results.

Methods: This randomized controlled study was conducted in a tertiary medical center and included jaundiced patients with BDT on CT scan. Patients were randomly assigned to EUS-FNA or to CH-EUS-FNA group. Final diagnosis was based either on EUS-FNA or surgical specimen results or endoscopic retrograde cholangiopancreatography (ERCP) or 12-month follow-up.

Results: 61 patients were included in the study, 31 in the EUS-FNA and 30 in the CH-EUS-FNA group (mean age 74±11.04 years, mean tumor dimension 20.39±9.17mm). Most BDT were located in the distal bile duct (n= 40). Final diagnosis (based on: surgery in 9 cases, ERCP in 7, EUS-FNA in 41, follow-up in 4) was: cholangiocarcinoma (n=37), pancreatic ductal carcinoma (n=12), other malignancy (n=3), benign lesion (n=9). Diagnostic sensitivity, specificity and accuracy were 84%, 100% and 87%, respectively in EUS-FNA and 82%, 100%, and 83%, respectively in CH-EUS-FNA group (p=0.22). Plastic biliary stent placement or tumor location did not influence the results. CH-EUS hyperenhancement with rapid wash-out was seen in 81.8% of cholangiocarcinoma cases.

Conclusions: Most but not all of cholangiocarcinomas are hyperenhanced, but CH-EUS-FNA had similar value with standard EUS-FNA in diagnosing bile duct tumors.

The impact of coffee consumption on inflammatory markers in patients with inflammatory bowel diseases

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Background & Aims: Inflammatory bowel diseases are chronic diseases that include Crohn's disease and ulcerative colitis. The incidence of these diseases is continuously increasing due to industrialization and lifestyle changes. Recently, coffee has become one of the most frequently consumed drinks, but some studies claim that it should not be recommended to patients with inflammatory bowel disease, especially during the flare periods because of its prokinetic effects on the digestive tract. However, some studies claim that drinking coffee could have anti-inflammatory effects. Our study aimed to evaluate coffee consumption impact on the inflammatory markers in patients with inflammatory bowel disease.

Methods: We analyzed 149 patients with a confirmed diagnosis of inflammatory bowel disease followed up at the Regional Institute of Gastroenterology Cluj-Napoca, Romania. The inflammation evaluation was assessed by the markers commonly used in clinical practice (leukocytes, erythrocyte sedimentation rate, C-reactive protein, and fecal calprotectin).

Results: After excluding smoking patients, 136 patients were included in the statistical analysis. Of these, 56% were known to have ulcerative colitis. 62% of the included patients said that they consumed coffee. Most patients (52%) claimed drinking coffee is not harmful to health and 46% said that coffee does not change their symptoms. However, 21% of the included patients claimed that coffee consumption worsens their digestive problems. Using the Mann-Whitney U test for independent samples, a p<0.05 was obtained for fecal calprotectin level between the patients who consumed and

did not consume coffee. For the other markers, there were no significant differences between the two categories.

Conclusion: Most patients with inflammatory bowel diseases consume coffee. Even though a small percentage of the patients experience worsening symptoms after consuming it, this could be explained by other factors (sweeteners, milk, etc.) and not directly due to caffeine. Through its anti-inflammatory effect, caffeine consumption could have a beneficial effect on inflammation and a decrease in fecal calprotectin levels in patients with inflammatory bowel diseases.

NOTES

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