The 4th German–Romanian Symposium on Gastroenterology

Stuttgart, Germany, March 31 – April 1, 2017

Symposium Chair:
Prof. Dr. med. Dr.h.c. Wolfram G. Zoller
Prof. Dr. med. Monica Acalovschi

Program and Abstracts

Friday, 31 March 2017, 18.00 h

Opening ceremony

Museum of Art (Kunstmuseum), Kleiner Schlossplatz 1, Stuttgart

Guided visit of the Current Exhibition

Wine and dine in the Cube Restaurant of the Museum of Art

Saturday, April 1, 2017

Scientific Program, Klinikum Stuttgart, Katharinenhospital, Olga rooms 1E1/2E1, Stuttgart

08:50 *Opening remarks* – Prof. Dr. med. Dr.h.c. Wolfram G. Zoller

9.00 –11.00 Session I. Chair: Prof. Dr. med. Dr.h.c. Wolfram G. Zoller (Stuttgart), Prof. Dr. med. Robert Thimme (Freiburg)

9.00-09:25 *Prof. Dr. med. Peter R. Galle, Mainz*
Hepatitis B and Hepatitis C – Pathophysiology, therapeutic options and the impact on hepatocellular carcinoma

09:25-09:50 *Prof. Dr. med. Monica Acalovschi, Cluj-Napoca*
Update on the management of alcoholic hepatitis

09:50-10:15 *Prof. Dr. med. Zeno Sparchez, Cluj-Napoca*
Impact of antiviral treatment on the hepatocellular carcinoma incidence and recurrence in patients with liver cirrhosis

10:15-10:35 *Prof. Dr. med. Paul J. Porr, Sibiu*
Non-alcoholic liver disease: multisystemic aspects

10:35-11:00 *Prof. Dr. med. Ioan Sporea, Timisoara*
New elastographic techniques for the liver (including MRI) are ready for clinical practice?

11.00 – 11.30 Coffee Break

11.30-13.30 Session II. Chair: Prof. Dr. med. Karel Caca (Ludwigsburg), Prof. Dr. med. Thomas Seufferlein (Ulm)

11:30-11:55 *Prof. Dr. med. Andrada Seicean, Cluj-Napoca*
The cystic pancreatic neoplasms challenging for endoscopic ultrasonography

11:55-12:15 *Dr. med. Alexander Hann, Ulm*
Palliative chemotherapy in pancreatic cancer

12:15-12:40 *Prof. Dr. med. Michael Jung, Mainz*
Cannulation techniques of the papilla and prevention of pancreatitis in ERCP

12:40-13:05 *Prof. Dr. med. Marcel Tantau, Cluj-Napoca*
Therapeutic endoscopy is still one of the main tools in the therapy of chronic pancreatitis

13:05-13:30 *Prof. Dr. med. Jörg Köninger, Stuttgart*
New aspects in pancreatic surgery

13.30 – 14.30 Lunch Break and Poster Viewing

14.30-17.20 Session III. Chair: Prof. Dr. med. Martina Müller-Schilling (Regensburg), Prof. Dr. med. Wolfgang Stremmel (Heidelberg)

14:30-14:55 *Prof. Dr. med. Jan Wehkamp, Tübingen*
Chronic intestinal inflammation due to complex barrier deficiencies

14:55-15:20 *Prof. Dr. med. Dan L. Dumitrascu, Cluj-Napoca*
How to improve the diagnosis of IBS?

15:20-15:45 *Prof. Dr. med. Adrian Goldis, Timisoara*
Are there any differences between IBD patients from Eastern and Western Europe

15:45-16:10 *Prof. Dr. med. Mircea Diculescu, Bucuresti*
Biological agents in IBD – use and misuse in Central-East Europe

16:10-16:35 *Dr. med. Dr. rer. Nat. Saskia Biskup, Tübingen*
Checkpoint inhibitors – the new therapeutic aspect in GI oncology

16:35-17:00 *Prof. Dr. med. Michael Sackmann, Bamberg*
Aspect of the new German guideline on gallstone disease

17:00-17:20 *Prof. Dr. med. Roxana Sirli, Timisoara*
Cost-efficiency of Contrast Enhanced Ultrasound for the assessment of focal liver lesions

17:20 *Closing remarks* – Prof. Dr. med. Monica Acalovschi, Cluj-Napoca

18:00 Guided Tour of the Mercedes-Benz Museum in Bad Cannstatt and Festive Dinner at the Museum Restaurant
Departure by bus at 18.00 to Bad Cannstatt

Session I

Update on the management of alcoholic hepatitis

Monica Acalovschi

Iuliu Hatieganu University of Medicine and Pharmacy Cluj-Napoca, Romania

Alcoholic liver disease (ALD) is one of the most prevalent causes of advanced liver disease. It represents a spectrum of clinical illness and pathologic changes in individuals with acute and chronic alcohol consumption. Patients may have minimal abnormalities ranging from steatosis to more severe inflammation and fibrosis seen in alcoholic hepatitis (AH) or cirrhosis. The quantity of alcohol consumed is a major risk factor for ALD. However, the risk may also depend on the patterns of alcohol intake: binge drinking (too much too fast) and chronic excessive drinking (too much too often) have been found to influence the risk for ALD. Younger subjects, and those with a high BMI are at risk for more severe AH at presentation. The risk for AH was also shown to be associated with the presence of *PNPLA3* rs738409 (G/G) polymorphism [1], as previously shown for alcoholic cirrhosis [2].

The clinical phenotype of AH is very variable. The mild forms are likely to improve with conservative management. Severe cases have 30-40% mortality at 1 month. This makes an early diagnosis crucial. Diagnosis might be difficult when based only on clinical and biological parameters: a 10-50% risk of misclassification was described. Transabdominal liver biopsy is precluded in severe cases due to the coagulopathy associated with the liver failure. As this information is difficult to obtain, prognostic models have been designed on clinical and biological parameters to identify patients with AH at high risk of early death. The Maddrey Discriminant Function (MDF) was the first score to be developed and still remains the most widely used. Other prognostic scores such the MELD (Model for End-Stage Liver Disease), the GAHS (Glasgow ASH Score) and the ABIC (Age, serum Bilirubin, INR, and serum Creatinine) score have been proposed and are now used in many hospitals to decide treatment. In clinical practice, a MDF of 32 or more, recently a MELD score of 20 have been used to initiate treatment, usually with steroids. Since the description of the bilirubin-based early biological response, the model has been further refined introducing the Lille Score. A Lille score of >0.45 after one week of steroid therapy is used to stop steroid therapy because these patients have a high mortality despite continuing steroids. The MELD score and the MDF are static scores, whereas the Lille is a dynamic score. The EASL Guidelines for management of ALD [3] recognize that many centers rely on clinical criteria, and do not consider biopsy as routine practice. However, the guidance includes biopsy in the therapeutic algorithm and recommends that it should be considered in high-risk patients according to prognostic assessment.

In severe forms of acute AH, glucocorticoids with or without pentoxifylline are, at the moment, recommended by all international guidelines. However, therapy of ALD and especially of severe AH represents a major challenge in the clinical practice. Patients with severe AH, particularly those with a MELD score > 26 with good insight into their alcohol-related disorder and good social support should be referred for evaluation for liver transplantation, as the 90-day mortality rate is very high [4]. Recently, the complex pathogenetic mechanisms driving disease progression to severe AH have been better defined, and novel targets for therapy have been identified.

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Impact of antiviral treatment on the incidence and recurrence of hepatocellular carcinoma in patients with liver cirrhosis

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The incidence of hepatocellular carcinoma (HCC) in patients with liver cirrhosis is about 3.5% per year. Among patients with chronic HCV infection, the early incidence is higher in those with F4 fibrosis in comparison with F3 (2.4% vs. 1.1%) [1].

During the past decades, treatment of chronic hepatitis C with pegylated interferon and ribavirin led to the cure of HCV infection in about 50% of treated patients. A sustained virological response (SVR) has been associated with a reduced risk of developing HCC. The annual incidence of HCC after successful IFN therapy has decreased from 7.88% to 0.49% [2]. The incidence is lower even in those without a SVR in comparison with non-treated cirrhotic patients in one study [2]. It has also been demonstrated that after non-surgical tumor ablation for HCV-related HCC, a successful IFN therapy reduces tumor recurrence rate and prolongs survival [3].

Introduction of the new antiviral drugs (DAAs), directly targeting HCV replication, allowed the achievement of SVR in over 90% of treated patients, irrespective of the liver fibrosis stage.

By improving the liver status, the new treatment was thought to decrease the incidence of HCC. Surprisingly, two recent studies reported a high incidence of HCC recurrence after DAA in patients who received curative treatment for HCC (28.8 and 27.6%, respectively) [4, 5]. Subsequent studies, however, did not demonstrate an increased incidence rate of HCC after curative therapies [6].

The de *novo* incidence of HCC in patients with HCV cirrhosis treated with DAAs is reported to remain unchanged by some authors (around 3% per year), while others reported a higher incidence of HCC (7%) 6-12 months after completion of DAA therapy. If this data will be proven in larger studies, patients with HCV related liver cirrhosis successfully treated by DAAs should be closely monitored to detect the HCC occurrence.

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Nonalcoholic fatty liver disease: multisystemic aspects

Paul Jurgen Porr

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Nonalcoholic fatty liver disease (NAFLD) is becoming in some Western countries the most frequent liver disease, especially in men in the 6th decade. NAFLD is correlated with diabetes mellitus type 2 (DM 2), cardio-vascular diseases, chronic kidney disease (CKD), but also with colorectal cancer, osteoporosis, polycystic ovarian disease, psoriasis and other diseases.

The NAFLD association with DM 2 enhances three-fold the mortality of hepatic cause. The risk of appearance of DM 2 is 5.5-fold higher in patients with NAFLD. If NAFLD is healed, this risk disappears.

The association with cardio-vascular diseases shows a two-fold higher frequency of cardio-vascular events, a five-fold higher frequency of atrial fibrillation, and a 70% higher mortality with hepatic or cardio-vascular cause.

It is known that CKD also occurs more frequently in patients with NAFLD. A proportionality between the stage of CKD and the severity of NAFLD was also demonstrated.

Probably, NAFLD is the pathogenetic factor for cardio-vascular diseases and CKD, and at the same time is a marker of those. NAFLD, visceral obesity and insulin resistance interact with cardio-vascular diseases and CKD, and constitute a complex multisystem with multiple bidirectional cause-effect interactions. For these reasons, NAFLD is aggravating the prognosis of these diseases.

Are new elastographic techniques for the liver (including MRI) ready for clinical practice?

Ioan Sporea

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Chronic liver diseases are frequent in daily hepatological practice. Assessment of chronic liver diseases severity can be performed invasively (by liver biopsy) or non-invasively. The number of liver biopsies is decreasing around the world, especially in Europe, being replaced in many cases by non-invasive methods.

Non-invasive methods for the evaluation of liver fibrosis can be divided into biological tests (such as FibroTest) and elastographic methods, which can be ultrasound based or by magnetic resonance (MRE).

Ultrasound based liver elastography can be divided into strain elastography and Shear Wave Elastography (SWE). SWE is at this moment the main modality for liver stiffness assessment as a marker of fibrosis. SWE includes: Transient Elastography (TE), point SWE (VTQ and ElastPQ) and 2D-SWE (SSI, 2D-SWE.GE, others).

Transient elastography has been used for more than 10 years in clinical practice and many meta-analyses have demonstrated its value for liver fibrosis evaluation, considering liver biopsy as the reference method. The correlation between TE measurements and fibrosis severity on liver biopsy increases with the severity of fibrosis. The results of TE were good in patients with chronic hepatitis C, chronic hepatitis B, non-alcoholic fatty liver disease (NAFLD) and others. Transient elastography is now a validated method for liver fibrosis evaluation and many guidelines (such as the EASL Guidelines) have introduced this method in their algorithm. The combination in the same machine of TE with Controlled Attenuation Parameter (CAP), which can objectively evaluate liver steatosis, eased the evaluation of certain types of hepatological patients.

Point SWE is integrated into standard ultrasound machines and is a simple mean for liver fibrosis evaluation. It can also be performed in patients with ascites, also 2D-SWE and this is an advantage compared with TE. Virtual Touch Quantification (VTQ) was the first point SWE method introduced in clinical practice. Several meta-analyses have shown its good value as compared to liver biopsy or TE. In the last months, several papers have been published demonstrating the good clinical value of ElastPQ.

2D-SWE is an elastographic method integrated into a standard ultrasound machine; it is a numeric and color-coded method and published papers have demonstrated good results for liver fibrosis assessment. Super Sonic Imagine (SSI) was the first used in practice, followed by 2D-SWE.GE.

Many published papers evaluating TE have used liver biopsy as the gold standard, but for the newer elastographic methods, some studies have used TE (considered a validated method) for comparison.

Magnetic resonance elastography has been developed especially in the USA and published papers have proved its good value. Among its advantages are: the evaluation of the whole liver at the same time, the possibility of steatosis quantification and also the fact that it can be used without problem in obese patients.

In conclusion, the body of evidence regarding the value of elastographic methods for liver fibrosis evaluation is large enough to enable their use in daily hepatological activity. The new EFSUMB Guidelines on Liver Elastography 2017, which will be soon published support this reality.

Session II

Cystic pancreatic neoplasms challenging for endoscopic ultrasonography

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Cystic pancreatic neoplasms represent a challenge for the gastroenterologist, surgeon, pathologist, having a heterogeneous natural history and management. They represent up to 30% of pancreatic cystic lesions. Serous cystadenomas and lymphangiomas have a benign behavior, while mucinous cystadenomas, intraductal papillary mucinous neoplasms, cystic neuroendocrine tumours and solid pseudopapillary neoplasm have a malignant potential, and the mucinous cystadenocarcinomas are malignant.

Endosonography (EUS) represents, together with the transsectional imaging methods, an important tool for the diagnosis, follow-up and, sometimes, treatment of these lesions. Its role is especially important in those cysts which merit surgical resection, but the complete differential diagnosis based on EUS techniques remains difficult.

Morphological description by EUS is considered sufficient in typical cases of microcystic serous cystadenoma and hydatid cysts. The items assessed are: location of the cyst, communication with the pancreatic duct, size, wall thickness and mural nodules, homogeneous or inhomogeneous content.

Fine-needle aspiration guided by EUS is indicated in cases with uncertain diagnosis, where it can modify the clinical management, such as discriminating between mucinous from non-mucinous cysts. This is contraindicated when the aspect is typical for serous cystadenoma, secondary-branch intrapapillary mucinous neoplasms without worrisome features, cysts with typical signs of malignancy in patients fitted for surgery, or fluid pancreatic collections containing necrosis.

The fluid sample should be assessed for aspect, viscosity, amylase content, carcinoembriogenic antigen, and cytology. However, cytology is seen in about half of the samples and the cyst puncture should be avoided in lesions smaller than 1.5 cm. By targeting the solid component in the cyst, the diagnostic yield of the cytology increases significantly. Genetic testing such as Kras and GNAS detection may improve the diagnosis, despite the supplementary costs.

Harmonic contrast-enhanced EUS is indicated for the assessment of the microvascularity of the walls, septae and mural nodules, as indicative for malignancy. This new technique, in our experience, helps to guide fine-needle aspiration EUS of the solid components of the cysts, with better results than standard fine needle aspiration EUS.

Cystoscopy via the EUS needle provides important information, but is difficult for cysts located in the head of the pancreas or in small cysts.

Confocal laser endomicroscopy through the needle shows different patterns of the cells and vessels in the wall of the cysts and can act as an optical needle biopsy. The serous cystadenoma appearance is of a superficial vascular network. The endomicroscopy aspect of intrapapillary mucinous neoplasms is that of finger-like papillary projections with an epithelial border and a vascular core, while malignant intrapapillary mucinous neoplasms appear as dark clumps with fluorescent substance leakage due to tumor neovascularization. Combination with cystoscopy increases the diagnostic accuracy, and is superior to carcinoembriogenic antigen detection.

Some therapeutic procedures performed via EUS, such as ethanol or radiofrequency ablation have been assessed, but extensive use is not recommended due to potential severe complications.

EUS follow-up after surgical resection is indicated alternatively with MRI for intrapapillary mucinous neoplasms and solid pseudopapillary neoplasms.

Palliative chemotherapy in pancreatic cancer

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Background: Pancreatic ductal adenocarcinoma (PDAC) has a poor prognosis with less than 7% survivors five years after initial diagnosis. Over 80% of the patients are diagnosed at a stage where surgical resection in curative intend is not possible due to metastasis or locally advanced disease. New chemotherapies that improve median overall survival (OS) in the first and second line during palliative treatment, such as FOLFIRINOX have been introduced in the recent years. These chemotherapies are associated with a higher percentage of adverse events but the toxicities limit their use. Chemotherapies for colon cancer often use a scheme of induction therapy using multiple chemotherapeutic substances followed by a period of fewer active drugs to increase tolerability. In analogy, our study aimed to determine the efficacy of a scheme of alternating induction and maintenance chemotherapy with substances included in FOLFIRINOX to alleviate such toxicities and increase the number of applied cycles.

Methods: We retrospectively identified all patients with PDAC that received chemotherapy using FOLFIRINOX at our institution from 2011 to November 2016. The patients who received induction therapy starting with FOLFIRINOX followed by maintenance therapy with 5FU/LV were referred as the maintenance group and the others as the control group. Applied chemotherapy cycles, adverse events that lead to discontinuation, treatment delay or reduction of the following chemotherapy cycle, response to treatment and OS were assessed.

Results: 56 patients received FOLFIRINOX for PDAC at our institution; 13 patients were treated with induction therapy followed by maintenance therapy (maintenance group). The control group included 43 patients. Most of the patients in both groups suffered from synchronous metastatic PDAC, followed by patients suffering from metachronous metastatic PDAC and patients with locally advanced disease. The overall survival (OS) starting at the beginning of palliative chemotherapy was 18.3 months (95% CI 14.8–21.8 months) in the maintenance group and 8.7 months (95% CI 6.5–11) in the control group. Using the treatment scheme in the maintenance group resulted in 11 patients who received a re-induction chemotherapy with FOLFIRINOX or FOLFOX due to progressive disease during maintenance therapy. Additionally four patients had a treatment pause during maintenance therapy without a negative influence on progression free survival. Leukopenia was the most common adverse event with only three grade 3 events. Oxaliplatin related neuropathy grade 2 was the second most common adverse event.

Conclusion: The use of FOLFIRINOX as an induction chemotherapy followed by 5FU/LV as maintenance therapy is feasible for patients suffering from PDAC. It might help increase the OS with less toxicity.

Cannulation techniques of the papilla and prevention of pancreatitis in ERCP

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Endoscopic retrograde cholangio-pancreatography (ERCP) with intended intervention of the biliary tree aims at: safe cannulation of the bile duct, sufficiently wide access to the biliary tree (endoscopic sphincterotomy) for endoscopic intervention by avoiding post-ERCP pancreatitis (POP). The accepted complication rate in ERCP is 1-8% pancreatitis for the diagnostic procedure and 2-10% pancreatitis in therapeutic ERCP. Risk factors are: young age, female sex, small bile ducts, sphincter Oddi dyskinesia and former events of pancreatitis.

As every manipulation of the inner muscular system of the papilla causes mini trauma of the epithelium, different techniques were recommended to perform the examination as safe as possible. ESGE recommends guide-wire assisted technique for primary biliary cannulation because it reduces the risk of POP, but the quality of evidence is only moderate despite a strong recommendation. The definitions of difficult biliary cannulation are: more than 5 papillary contacts, 5 minutes spent attending to cannulate, and 1 unintended pancreatic duct cannulation. Three meta-analyses and 12 studies (7 cross-over trials) support more or less the guide-wire technique. In 2 further studies (NRT, RCT) there is no difference between the simple contrast medium injection and the guide-wire cannulation. Early pre-cut sphincterotomy is discussed for difficult biliary access also to reduce post ERCP pancreatitis and seems to be advantageous as early procedure in difficult cannulation. Active prevention of ERCP pancreatitis can be performed mechanically by insertion of a small endoprosthesis (5F ≤ 6-7 cm length) in the pancreatic duct, or systematically by application of Indomethacin 100 mg supp. better before than during ERCP, or Diclofenac 50 mg orally before and after ERCP. All these preventive measures aim at maintaining the normal pancreatic liquid flow without any obstructive oedema of the papillary orifice.

Endoscopic treatment in painful chronic pancreatitis

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The goal of endoscopic treatment is to drain the pancreatic duct, reduce the frequency and severity of pain and resolve local complications of the disease. Pain is the main symptom in patients with chronic pancreatitis. The endoscopic treatment is minimally invasive and it can be successfully repeated in cases of pain relapses, which are resistant to common analgesics.

The endoscopic treatment combines several procedures, to restore drainage of the main pancreatic duct: pancreatic sphincterotomy, extraction of pancreatic stones, pancreatic and biliary stenting, the drainage of pseudocysts with conventional endoscopy or with endoscopic ultrasound (EUS).

Ductal stone clearance can be a very challenging procedure, depending on the stones location, size, consistency and presence of the associated ductal strictures. The stricture dilation, intraductal lithotripsy and major/minor papilla sphincterotomy may be helpful in some cases. In non-cephalic large stones (> 5 mm), extracorporeal shock-wave lithotripsy (ESWL) alone or in combination with the endoscopic treatment is recommended. Single or simultaneous, multiple, side-by-side plastic pancreatic duct stents are effective for the management of pancreatic strictures, duct leaks, and disruptions. Several studies have showed the efficiency of pancreatic metallic stents, but unfortunately with a short-time follow-up.

The endotherapy efficacy is comparable with surgery, with a higher success rate in properly selected patients and with a low morbidity. It can be repeated and performed independently regardless of the patient's age. In some cases, it may be considered as a "bridge" to subsequent surgery. Several studies have compared the short-term and long-term outcomes of surgical treatment vs. endoscopic treatment in patients with chronic pancreatitis [1]. Some studies showed the long-term results of surgical treatment are better than endoscopic treatment in patients with dilated pancreatic duct, stones or strictures [2].

The success of endotherapy in biliary drainage in chronic pancreatitis (CP) is poor in most of the published series, with a 10-33% rate of stricture resolution. The choice between endoscopic and surgical drainage should be taken according to medical center expertise, patient co-morbidities and compliance to repeat endoscopic procedures. Multiple simultaneous plastic stents have had better results comparing with single biliary plastic stenting. Recent data shows good results using covered expandable metal stents. In our experience, biliary drainage was successful in 74.29% of patients during a median follow-up period of 15 months.

Surgery remains the option for treatment if endoscopic treatment is not successful, in patients with high surgical risk or a suspect pancreatic inflammatory mass.

The management of pain in patients with chronic pancreatitis is a therapeutical challenge and must be approached via an interdisciplinary collaboration team. The initial approach should be minimal endoscopic treatment. Due to the increased risk of complications and higher costs, additional endoscopic treatment and surgical intervention should be reserved for cases which have no response to the minimal endoscopic treatment.

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Challenges in clinical management of small cystic pancreatic lesions

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The management of cystic lesions of the pancreas remains a major challenge in daily clinic practice. Due to the widespread use of modern abdominal imaging techniques, small cystic pancreatic lesions are found incidently with increasing frequency. The majority of these lesions display intraductal papillary mucinous neoplasm of the pancreas (IPMNs). Apart from main duct lesions where it is common sense that surgical resection is mandatory due to the high incidence of malignancy, the indication for surgical resection in branch duct lesions remains challenging. In these patients, the risk of malignant transformation, especially over a long time period, is hardly calculable but most probably higher than expected [1]. To date, little data is available on the natural history of branch duct IPMNs, and no data exists considering a 20- or even 30-year follow-up.

The therapeutic, and if necessary surgical strategy needs to adequately consider on the one hand the morphological aspect of the lesion, including suspicious radiological features such as main pancreatic duct involvement, nodules, thickness of the cystic wall, and on the other hand the individual patient´s risk if one decides for conservative treatment or surgical resection. Surgical resection of pancreatic tumors is associated with relevant postoperative morbidity and even mortality, which differs widely between high and low volume institutions. In addition, patients´ comorbidity and age may play an important role.

In order to evaluate the surgical risk, we analyzed 320 consecutive patients who underwent pancreatic resection at our institution. Clinical features were assessed and patients with an age over and under 75 years compared with regard to postoperative morbidity and mortality. We showed that regardless of age, individual comorbidity is the main reason for postoperative complications and death. In addition and of utmost importance, none of the patients up to 75 years of age died after pancreatic resection. Thus, the surgical risk is acceptable and not depending on age but rather on individual comorbidity [2].

The indication for surgical resection in small side branch IPMNs is depending on a number of individual clinical characteristics. On the one hand, morphological aspects of the cyst need to be considered with regard to the risk of malignancy. On the other hand, patients´ characteristics such as comorbidity and previous surgery, family history, but not at

least the willingness of the patient to undergo surgery or long term follow-up with the risk of malignant transformation are important features when choosing the adequate therapeutic management.

In conclusion, we are convinced that decision making in the management of cystic and potential malignant lesions needs to include morphological aspects of the cyst, comorbidity of the patient but also age with regard of necessary long term follow-up and risk of malignant transformation over time. In young and healthy patients, surgical resection, if possible using parenchyma-sparing techniques such as pancreatic enucleation or middle resection, should at least be considered.

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Session III

How to improve the diagnosis of IBS?

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Background & Aim: Irritable bowel syndrome (IBS) is the most common functional gastrointestinal disorder. A correct diagnosis is mandatory for a successful management. Improvement of IBS diagnosis is presented.

Methods: A search in the literature on the diagnosis of IBS was initiated and pertinent works were selected and analyzed. The controversial dispute if IBS is an exclusion criterion or that IBS can merely be diagnosed on the presentation of symptoms [1, 2] was also analyzed.

Results: The advent of the Rome IV books has changed the paradigm of functional gastrointestinal disorders, including IBS. Irritable bowel syndrome is now perceived as the expression of the gut-brain axis, given the progress in the pathogenesis of its symptoms, Therefore, IBS should be considered as a positive diagnosis (of course, submitted to differential diagnosis) and not an exclusion criterion. Symptoms reported by patients in order to assess the diagnosis of IBS should occur at least once weekly, in the last three months before presentation and having a history of at least six months. Abdominal pain but no more abdominal discomfort is relevant for diagnosis. Stools should be estimated by using the Bristol Stool Form Scale. The need to phenotype IBS patients is important for a correct diagnosis as a base for appropriate therapy.

Conclusions: Irritable bowel syndrome should be diagnosed with the new Rome IV criteria. It is no longer an exclusion criterion but a self-standing condition caused by the dysfunction of the gut-brain axis.

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Are there differences between IBD patients from Eastern and Western Europe?

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The incidence/prevalence of Crohn's Disease (CD) and ulcerative colitis (UC) is increasing in Europe. It is estimated that 0.3% of the European population suffers from IBD. Hospitalization rates are high, but slowly decreasing in patients with CD, with approximately 50% within 10-years from diagnosis of the European patients requiring hospitalization. In UC, hospitalization rates remained stable and reflect disease severity and risk of colectomy. In European studies, extraintestinal manifestations are present in as many as 20-40% of patients with CD and 15-20% of patients with UC. The health economic burden and permanent work disability in IBD are high in Europe: total yearly direct healthcare cost of 4.6-5.6 billion Euros. The recent statistics show in Europe 3 million individuals with IBD, and globally, over 5 million individuals.

In Europe there are differences in the incidence of IBD between the north and south, with a tendency of increasing rates in the south and a plateauing of the higher northern rates. The highest incidence of IBD in the world is in Faroe Islands, 83 per 100,000 person-years [1].

The ECCO-Epicom (European Crohn`s and Colitis Organization - Epidemiological Committee) study (2010) included 1515 patients aged > 15 years. Of those, 535 (35%) patients were with CD, 813 (54%) with UC and 167 (11%) with unclassified IBD (IBDU). Incidence rate/100,000 inhabitants in 2010 indicated for CD: 6.5 in Western Europe vs. 3.1 Eastern Europe, for UC : 10.8 Western Europe vs. 4.1 Eastern Europe and for IBDU : 1.9 West vs 0 East [2, 3].

One of the characteristics of the adult incident patients in the Eastern and Western European centres in the ECCO-EpiCom 2010 inception cohort were the extraintestinal manifestations (Western Europeans Centers versus Eastern European Centers): none 89.6% vs 87%, skin 1.5% vs 2%, eyes 1% vs 2 %, joints 6.5 % vs 7%, primary sclerosing cholangitis 0.2% vs 0%, pancreatitis 0.2% vs 0% others 1% vs 2% [4].

There are differences between the geographic regions regarding the environmental factors [5]. The Western diet is part of the explanation for the increasing incidence in Eastern Europe. More Eastern European patients with UC have a higher daily consumption of fast food. Daily consumption of fast food is associated with a young age at diagnosis in both CD and UC and a higher risk for surgery and for severe disease extent in UC. High caffeine consumption is associated with the risk of surgery and severe course of disease in CD, and with the presence of extraintestinal manifestations in UC. The use of oral contraceptives was significantly associated with a young age at diagnosis. Significantly more Western vs. Eastern European patients reported an appendectomy before the age of 20. More CD vs. UC Eastern patients had had an appendectomy. More CD patients were current smokers at diagnosis, while more UC patients were previous smokers. For current smoking, a more severe disease behaviour and younger age at diagnosis was found. For previous smoking, a younger age at diagnosis was found in UC patients.

In Romania, the incidence and prevalence of IBD is increasing, but it is still between the lowest in Europe. The EpiCom study is continuing in order to further evaluate the burden of IBD in Europe.

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Biological agents in IBD use and misuse in Central East Europe

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Inflammatory Bowel Diseases (IBD) are very frequent in Western countries (North Europe and North America), but till recently were not very frequent in Eastern European countries. Countries such as Romania have not been confronted with frequent cases and especially not with severe cases.

Our epidemiological study in Romania showed an incidence of about 1/100,000 in ulcerative colitis (UC) and 0.5/100,000 inhabitants in Crohn's Disease (CD). The prevalence was evaluated in 2003 to be 2.4/100,000 for UC and 1.5/100,000 for CD. A prospective nationwide database registered more than 2,400 patients, which indicated a cumulative prevalence of more than 12/100,000 both in UC and CD. It is considered that this figure is only the top of the iceberg, the real prevalence being more than 10 fold, indicating a 10-20 fold increase in prevalence in 10 years! It was suggested that the cause of this tremendous increase is the dramatic change in lifestyle at the turn of the last century, when western lifestyle became widespread in Romania. The consequent change in the microbiota was considered to be the cause of maintaining this trend despite the efforts to reconsider a "healthy lifestyle". But the most dramatic change that happened in Romania, as an example of a transition country, is the huge increase of severe and especially difficult to treat cases for both UC and CD.

Another interesting fact is the important increase in CD patients in most westernized areas such as Bucharest city and Bucharest county and the extreme western parts of the country, where CD has already overtaken UC as prevalence. Possibly this might be due to a previous under-diagnosis of CD. The latest data from another pilot epidemiological study the EPIROM project that included Bucharest and Bucharest county showed that even in this area with easy access to high technology, the delay to diagnosis is 17.3 months for CD and 5.3 months for UC.

According to the Romanian National Insurance House (RNIH), there are more than 800 patients on biological therapy (BT), which equals almost the whole number of cases estimated in 2003 in the whole country! Unfortunately, we have more and more patients who require surgery, even repeated and complex surgical treatment. Access of the patients to BT in Romania is at this moment a problem involving several aspects: correct prescribing, adequate maintenance therapy, patients' access to therapy, patients' adherence to therapy, switch of biologicals, use of biosimilars, Combo therapy, association with corticosteroids, surgical intervention if required, and pregnancy.

Until a few days ago (!!!) we had a Protocol of the Health Ministry and RNIH. A National Commission of the RNIH approved reimbursement for biologicals. The possibility of prescribing biologicals was limited to reference centres, i.e. University Centres in Romania. Any gastroenterologist could indicate therapy with a biological, but a "second opinion" was compulsory from such a Centre. This was an acceptable compromise between limitation of the prescription and the risk of misuse of this medication. Until now, there was no limited access of the patients to the biologicals approved by the Romanian Medicine and Drug Agency (RMDA), because there was not a lack of funding for the total number of patients. The problem occurred for Protocol changes when novel agents (other than anti TNF) were approved in Europe by the EMA. The whole system of changing the protocol required the publication of a new protocol approved by both the Health Ministry and the RNIH.

If we conclude on the problem of use and misuse of biologicals in Romania, there have been many good results:

1. a very active Society of IBD exists, the Romanian Crohn's and Colitis Club (RCCC), anticipating the increase in number and severity of IBD patients;

2. an actual protocol has been conveniently designed and flexible to allow most patients more access to anti TNF therapy;

3. antiTNF agents have been properly used, with very rare cases of misuse detected.

There are however, many more things to be done:

1. increase the number of biological molecules, as more and more patients have an aggressive disease and have already failed all possible combinations, escalation or switch between antiTNF;

2. improve the possibility to change the Protocol as soon as new stable evidence appear;

3. improve the patients' follow-up during therapy, including reimbursement of faecal calprotectin assessment trough levels and antibody levels, and to ensure a larger accessibility of new diagnostic tools, especially for small intestinal CD.

Aspects of the new German Guideline on gallstone disease

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Recently, the working group finished its update of the German guideline on gallstone disease. Yet, the final results remain to be published. However, several important new aspects may already be discussed.

Nearly 1/3 of the patients will develop gallbladder calculi within few months after gastric bypass operation for the reduction of severe overweight. A prophylactic therapy with ursodeoxycholic acid therefore might be appropriate after such interventions. Gallstone prophylaxis might also be indicated in patients with the rare low-phospholipid associated cholelithiasis (LPAC) syndrome. Prophylaxis by ursodeoxycholic acid should be considered in patients treated with somatostatin or its analogues, too.

Cholecystectomy is the standard treatment of patients with symptomatic gallbladder stones. In acute cholecystitis, data from a German multicenter trial reveal the superiority of immediate cholecystectomy performed within 24 hours after admission to the hospital, as compared to a more delayed operation.

The timing of ERCP in patients with symptomatic bile duct stones should be primarily triggered by the presence and severity of concomitant cholangitis. For the primary endoscopic attempt to the bile duct, an approach with a guide wire is preferred, as compared to the traditional injection of contrast medium. Most but not all recent data reveal that rectal indomethacin reduces the rate of ERCP-induced pancreatitis. Since the adverse effects of indomethacin are minor, it might be recommended as a routine measure to reduce post-ERCP pancreatitis.

In mild biliary pancreatitis, cholecystectomy can be safely performed soon after ERCP. Only in patients with severe pancreatitis, cholecystectomy should be postponed until recovery. If bile duct stones can be ruled out by endoscopic ultrasonography or by MRCP, spontaneous passage of bile duct stones can be assumed, and ERCP can be omitted in such cases.

Cost-efficiency of Contrast Enhanced Ultrasound for the assessment of focal liver lesions

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Focal liver lesions (FLLs) assessment is a daily problem in clinical practice since new FLL are quite frequently discovered due to the routine use of imaging methods (ultrasound - US, computer tomography - CT or magnetic resonance imaging - MRI) and due to screening strategies for patients with liver cirrhosis as well as for patients with oncologic diseases.

If some lesions can be easily diagnosed by standard ultrasound alone (i.e. simple cysts) this is not the case for most FLLs; in these cases a contrast imaging method is required for a correct diagnosis. Sometimes even the most modern contrast imaging methods cannot establish a diagnosis and a liver biopsy is required. Until a decade ago routine imaging evaluation of FLL included only contrast CT or MRI, but in the last 15 years Contrast Enhanced US (CEUS) has been proven to be a reliable method for FLL assessment. The European Federation of Societies of Ultrasound in Medicine and Biology (EFSUMB) issued the first Guidelines regarding the use of CEUS in 2004, that were revised in 2008 and in 2012.

Apart from its reliability, its rapidity (CEUS can be performed immediately after the standard abdominal ultrasound, so that in approximately 5 minutes - the total duration of this investigation - a confident diagnosis can be obtained), CEUS is also „non-invasive". There are no side effects of the contrast agent, which can be also used in patients with kidney failure, and no irradiation - as in the case of CT.

Several studies have demonstrated that CEUS is also cost-efficient. Italian and French multicentre studies demonstrated savings of 162 and 128.5 Euros/lesion, respectively, if CEUS was used as a first line contrast-imaging method. In a Romanian study, approximately 4,000 Euros would have been saved using CEUS as a first-line contrast imaging method as compared to contrast-CT and approximately 24,900 Euros as compared to contrast-MRI diagnosis of the 316 FLL included in the study. Data from the multicenter DEGUM German study also demonstrated that CEUS is cost-efficient, with savings ranging from 37 to 101 Euros/lesions. Another German study demonstrated that CEUS was the more cost-effective imaging method in all scenarios in which CEUS examinations were performed at specialized centers, but the costs for CEUS

would be significantly higher if it would be performed in non-specialized centers, considering the high costs of an US machine able to perform CEUS.

Considering its reliability, cost-efficiency, and non-invasiveness, CEUS should be used as a first-line contrast imaging method for newly discovered FLLs.

Serial endoscopic ultrasound predicts survival after neoadjuvant chemotherapy in gastric cancer

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Background: Accuracy of endosonographic tumor staging after neoadjuvant therapy is less reliable than in primary staging. Therefore, the value of serial endosonographic examinations after neaodjuvant chemotherapy is discussed controversely. Previous data suggest that endoscopic ultrasound (EUS) after neoadjuvant treatment using other parameter than classic uTN-criteria may identify patients with a better prognosis. Confirmation of this data is lacking.

Methods: We performed EUS before and after neoadjuvant chemotherapy in 67 patients with locally advanced gastric or gastroesophageal cancer treated with curative intent. The following parameters were assessed for their usefulness to predict recurrence-free follow-up: uT-stage before, and yuT stage after neoadjuvant chemotherapy according to the 7th edition of the UICC staging system; uN-stage before, and yuN-stage, summarized as nodal-positive or nodal-negative disease; absolute maximal tumor thickness in mm, and relative response to neoadjuvant treatment (complete response; regression >50%, regression <50%, or progression after chemotherapy); maximal lymph node size in mm (complete response, regression >50%, regression <50%, or progression after chemotherapy).

Results: After neoadjuvant chemotherapy, 25 patients presented with a decrease in uT stage after chemotherapy. Especially, the number of uT4 tumors decreased from 47 to 28. 14 patients improved by one stage, and 11 patients presented with a decrease of two T-stages (i.e. from initially uT4, to yuT2). The number of patients classified as having nodal-positive disease decreased from 48 to 33. The mean maximal tumor thickness decreased from 15.4 mm to 9 mm. Reduction of tumor thickness measurable by EUS was present in 58/63 patients. In three patients, a complete tumor response could be observed. A thickness reduction of >50% was present in 18, and of <50% in 37 patients. The mean maximal lymph node diameter decreased only minimally, from 12.2 mm to 11.2 mm.

For follow-up analysis, data of 57 patients were analyzed: 2 patients died post-operatively without evidence of tumor relapse, 7 patients were excluded because of a short follow-up of less than 8 months, and 1 patient was lost for follow-up. Median follow-up was 16.3 months (range 2.1 – 80 months); 30/57 patients relapsed after a median time of 8 months (range 2.1 – 43.8 months). Most often, distal metastasis occurred (21), whereas local recurrence occurred in 5 patients, and combined locoregional and distant tumor recurrence was present in 4 patients. Median recurrence-free time was 29.6 months, the 3- and 5-year recurrence-free rate was 47.1%, and 39.3%, respectively.

Endosonographic tumor staging according to yuT-stage after neoadjuvant chemotherapy was predictive for patient´s prognosis, with a significantly lower risk for tumor recurrence in case of yuT0-2 vs. yuT 3-4 tumors (median recurrence-free follow-up not reached vs. 17.7 months; p<0,019). Furthermore, we observed a positive correlation between the amount of uT-stage shift induced by neoadjuvant chemotherapy, and prognosis: recurrence rate was significantly lower in patients presenting with a shift of two or more uT-stages (median relapse-free follow-up not reached vs. 17.9 months, p<0.042). Even more, the absolute tumor thickness after neoadjuvant chemotherapy was of prognostic significance, with a cut-off of 15 mm: in case of a slimmer tumor, median relapse-free follow-up was significantly longer than in patients with a tumor thickness of >15 mm after neoadjuvant therapy (not reached vs. 8 months; p<0.002). Endosonographic T-stage before neoadjuvant therapy, as well as lymph node parameter before or after chemotherapy, had no predictive value.

Conclusion: In spite of the poor concordance between endosonographic and pathohistological TN-stage after neoadjuvant treatment, serial EUS performed before and after neoadjuvant chemotherapy offers the chance to identify

patients at risk for tumor relapse before the time of operation, and may therefore be used for individualized therapy planning.

Accuracy of endoscopic ultrasound in TN-restaging of gastric cancer after neoadjuvant chemotherapy

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Background: Accuracy of endosonographic tumor staging after neoadjuvant therapy in esophageal cancer is less reliable than in primary staging, especially after neoadjuvant chemoradiation. Data about the diagnostic capability of endoscopic ultrasound (EUS) in restaging gastric cancer after neoadjuvant treatment are sparse. We investigated the influence of a modern neoadjuvant chemotherapeutic protocol on the reliability of endosonographic restaging in gastric cancer patients.

Methods: We performed EUS before and after neoadjuvant chemotherapy in 67 patients with locally advanced gastric or gastroesophageal cancer treated in curative intent. Treatment consisted of 4 cycles of FLOT or FLO. All endosonographic examinations were performed with mechanical (UM 160) or electronical (UE 160) radial scanner (Olympus Ltd., Hamburg, Germany). uT-stage before, and yuT stage after neoadjuvant chemotherapy were analyzed according to the 7th edition of the UICC TNM staging system using established endosonographic criteria. uN-stage before, and yuN-stage after neoadjuvant chemotherapy was assessed according to the criteria published by Catalano et al. (minimally two out of four parameter present), and summarized as nodal-positive (N+) or nodal-negative disease (N-). All patients underwent curative resection. In case of gastric cancer, a gastrectomy with D2 lymphadenectomy was performed. In case of a gastroesophageal tumor, a transhiatal approach was choosen. The surgical specimens were histopathologically assessed for ypT and ypN stage according to the 7th edition of the UICC TNM tumor staging system.

Results: The concordance between endosonographic and pathohistological tumor stage after neoadjuvant chemotherapy was poor: according to yT-stage, EUS correctly staged only 15/67 tumors. Overstaging (40 patients) was more common than understaging (12 tumors). Especially in low tumor stages (ypT0-2), no tumor was correctly staged by EUS. But, even in higher T-stages (ypT3-4), the accuracy of EUS was insufficient, mostly due to overstaging. After grouping patients into two collectives (locally limited ypT0-2 vs. locally advanced ypT3-4), accuracy of EUS was still only fair (61%). For lymph node staging, the results of EUS were insufficient, too: in only 36 patients, EUS was in concordance with the histological result. Over- and understaging could be observed in 16, and 15 patients, respectively. All in all, the sensitivity and specifity of EUS for lymph node-positive disease after neoadjuvant chemotherapy was 53%, and 54%.

Conclusion: Concordance between histopathological and endosonographical tumor staging is poor. Classic endosonographic criteria are unsuitable for TN-staging after neoadjuvant chemotherapy in gastric cancer.

Emergency capsule endoscopy for active obscure gastrointestinal bleeding

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Background & Aim: Emergency capsule endoscopy (CE) in patients with active obscure gastrointestinal bleeding (OGIB) is not routinely performed, as it is time consuming. Recently, a few papers have addressed this issue. Our aim was to determine the diagnostic yield of emergency CE in patients investigated for active OGIB.

Methods: We included 23 patients with active overt OGIB (two negative upper digestive endoscopies and one negative colonoscopy) investigated with CE. We considered as a positive result of CE when a lesion with bleeding potential or fresh blood was detected. A negative result was considered if no lesions and no blood were found. We registered the clinical data (hemodynamic status), hemoglobin level, non-steroidal anti-inflammatory drugs (NSAIDs) use. More than one third of the patients (9/23) presented hemodynamic instability during the procedure (six patients with severe cardiovascular pathology, two patients with cirrhosis, one patient with malignant melanoma stage IV).

Results. The results of the investigation are shown in Table I.

The diagnostic yield of emergency CE to identify the bleeding level in active OGIB was 95.65%. The lesions responsible for bleeding were identified in half of the patients (13/23, 56.52%) and confirmed in 43% of patients (10/23). Diagnostic yield of CE for detection of the lesions was 43.47%. A high percentage of the patients were diagnosed with vascular lesions (Dieulafoy's lesions, enteric varices, angiodysplasia). From the subgroup of patients that presented hemodynamic instability, the diagnostic yield of emergency CE was 88.8%. Subsequently, the patients were treated conservatively in 26.08% of cases. In 39.13% an enteroscopy was performed, in 13.04% a standard endoscopy, and in 21.73% surgery. At the six month follow-up, 60.85% of patients had a favorable outcome, 8.69% were in similar clinical conditions, 4.34% repeated bleeding, and 17.39% had passed away.

Conclusion: Emergency CE in patients with active OGIB is an accurate method to identify the level of bleeding and also the potentially bleeding lesions. This made the decision for further management of the patients easier.

Table I. Initial findings by capsule endoscopy (CE) and the final diagnosis of the patients with active OGIB that were investigated with emergency CE.

Active OGIB	No. pts.	The findings of CE (diagnostic yield)	Final diagnosis (accuracy)
Potential bleeding lesions	13	4 enteral tumors 1 gastric tumor 2 enteral varices 1 small bowel angiodysplasia 1 radiotherapy enteritis 1 mesenteric ischemia 1 gastric ulcer 1 NSAIDs enteropathy 1 severe inflammation	2 enteral tumors 1 gastric tumor 2 enteral varices 1 small bowel angiodysplasia 1 radiotherapy enteritis 1 mesenteric ischemia 1 gastric ulcer 1 small bowel amyloidosis **3 false positive results (2 tumors and 1 NSAID enteropathy)**
Visible blood but unidentified source of bleeding	9	Active bleeding, source of bleeding not found	1 Meckel diverticulum 6 Dieulafoy's like lesions (5 in proximal small bowel, 1 in colon) 1 enteric fistula 1 hemosuccus pancreaticus
No blood or incomplete examination	1	Incomplete examination	1 enteric-vascular fistula

NSAID enteropathy is the main cause of obscure gastrointestinal bleeding in patients investigated with capsule endoscopy

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Background & Aim: Literature data regarding capsule endoscopy (CE) argue for small bowel angiodysplasia as the main cause for obscure gastrointestinal bleeding (OGIB). Non-steroidal anti-inflammatory drugs (NSAIDs) are largely used but few data are reported regarding NSAID enteropathy in patients investigated with CE. We aimed to determine the diagnostic yield of CE in patients with OGIB, focusing on NSAID enteropathy.

Methods: We performed a retrospective analysis of 93 patients with OGIB investigated with capsule endoscopy. A more appropriate clinical classification was used for OGIB: overt OGIB active, overt OGIB stopped and iron deficiency anemia. The positive results were quantified separately in these three situations. The clinical predictive factors for a positive result were investigated focusing on NSAID use.

Results: The diagnostic yield of CE in the 23 patients with active OGIB was 96.6%: none of these patients presented NSAID enteropathy. In 39 patients with overt, stopped OGIB the diagnostic yield of CE was 71.8%. NSAID enteropathy was detected in 30.76% of these cases. The CE performed in the first seven days was significantly associated with the detection of a bleeding source (p=0.022). NSAID use was an independent predictive factor for the depiction of a lesion with bleeding potential (p=0.037). In 39 patients with iron deficiency anemia, the diagnostic yield of CE was 45.16% and NSAID enteropathy was diagnosed in 19.35% of patients. Age over 70 years, serum hemoglobin level below 7g/dl, the use of antiaggregants and the presence of cardiovascular disorders were not significantly associated with the depiction of a bleeding source.

Conclusion: In our group of patients, the NSAID enteropathy was the main cause of OGIB in those with stopped bleeding and in those with iron deficiency anemia.

Long-lasting complete remission in a patient with locally advanced adenosquamous carcinoma of the oesophagus

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Introduction: The prognosis in patients with locally advanced oesophageal carcinoma is poor, especially when infiltration of adjacent organs prevents tumour resection. Adenosquamous carcinoma is a rare histological type of oesophageal cancer that has been associated in some studies with an even lower overall survival rate. In this case study we present a 58-year old man with advanced adenosquamous carcinoma of the upper oesophagus, with a large local tumour mass infiltrating trachea and causing considerable tracheal stenosis.

Case report: In December 2011, a 58-year old man presented with a five-month history of painful swallowing and weight loss of 12 kilograms. He also described a stabbing pain in the left ear when swallowing, inability to swallow solid food as well as regurgitation of both solid food and liquids. Apart from considerable tobacco consumption (40 pack years), hypertension and an incidental infrarenal aortic aneurysm (3.2 cm in diameter) there was no previously known illness. Physical examination revealed an inspiratory stridor as well as cachexia with general muscle atrophy. CT-scan, oesophagogastroscopy and bronchoscopy showed a large tumour in the

upper oesophagus with infiltration of the proximal trachea resulting in tracheal stenosis. Furthermore, cervical and abdominal lymphadenopathy was shown, but there was no sign of distant metastases. Histological examination of oesophageal biopsies revealed tumour components with both squamous cell and adenocarcinoma attributes and showed signs of poor differentiation. The tumour was therefore classified as adenosquamous carcinoma (ASC) uT4b uN2 cM0 G3.

According to the national guidelines, the case was discussed in the local tumour board, which advised palliative chemotherapy, excluding both surgery and radiotherapy because of the tumour's advanced local stage. The patient received percutaneous endoscopic gastroscopy (PEG) to ensure sufficient nutrition as well as a tracheostomy to protect the already compromised airway. A permanent central venous catheter (port) was implanted and palliative chemotherapy started with 5-FU and Cisplatin in January 2012 with good response and little side effects after four cycles.

In May 2012 chemotherapy was changed to FLOT due to modest labyrinthine hearing loss. After another three cycles, the tumour and lymph nodes again showed marked regression. In June 2012 chemotherapy was again changed to ILF due to distal polyneuropathy. In September 2012, after six cycles of ILF, staging showed no sign of local or distant tumour manifestation. The patient had gained weight and had only slight problems at swallowing. He was scheduled for a short period of watchful waiting without chemotherapy after which there was still no sign of tumour recurrence.

Subsequently, from November 2012 to June 2016 the patient was seen for a total of 11 interim staging examinations, which showed no recurrence. The port catheter was removed and the tracheostomy closed. The patient continues to do well and had his port removed in 2015. Apart from a slight oesophageal stenosis he shows no sign of illness.

Conclusion: Unexpectedly, this patient developed a lasting full remission after an eight-month course of chemotherapy initially intended to be palliative. Prophylactic tracheostomy, percutaneous endoscopic gastrostomy as well as intermittent parenteral nutrition were supporting factors in providing this remarkable outcome.

Jejunal perforation after ingestion of a blister pill pack

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Background: Perforation of the small bowel due to foreign body ingestion occurs in less than 1% of all ingestions. Although rare, ingestion of a blister pill packaging is becoming more recognized as a causative agent for intestinal perforation.

Case report: A 75 year-old male, with a history of Grand mal seizure due to amyloid angiopathy with multiple cortical bi-hemispheric and cerebellar lacunar strokes, superficial and profound microhemorrhages, bilateral subdural hematomas, admitted to the Neurosurgery Department for the follow up of the subdural hematomas, suddenly developed severe abdominal pain. A gastroenterologist and an abdominal surgeon were requested to examine the patient and at the physical examination the abdomen was painful at gentle palpation, the peritoneal signs and abdominal guarding were present, the bowel sounds abolished. An abdominal CT was performed, which revealed pneumoperitoneum, a fluid collection in the peritoneal cavity, sigmoid diverticulosis and air-fluid levels in the small bowel. An emergency surgery was performed disclosing a generalized peritonitis and a jejunal perforation by a foreign object. Segmental resection of the jejunum was carried out followed by jejunojejunal anastomosis, lavage and drainage. The foreign object was proved to be a blister pill pack. From the moment of the surgical intervention, the patient presented an altered renal function, aggravated after the operation and he gradually got worse, developing Multisystemic Organ Failure. Despite the intensive care treatment, he passed away.

Conclusion: Accidental ingestion of foreign bodies is not an uncommon occurrence. It is frequently seen in children and in older patients, among those patients who are visually or mentally impaired. Most ingested foreign bodies pass through the GI tract without incident. Because blisters have sharp margins, they usually remain in the esophagus or stomach. When the package passes through to the small intestine, the sharp corner of the plastic and aluminum foil of the blister wrapping can cause a perforation of the intestinal wall. Elderly individuals should not be given blister-wrapped tablets for self-administration, but instead should be given their tablets only unwrapped by the nurse or family, particularly those with mental or visual disabilities.

Phenotypic and management tendencies in patients with IBD: a 12 year national multicentric study based on the IBD Prospect

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Background & Aim: The incidence and severity of inflammatory bowel disease (IBD) has increased worldwide. There is a lack of data regarding IBD incidence and phenotype in our country. The aim of our study was to evaluate the

phenotypic changes and management tendencies in our patients with IBD over the last 12 years.

Methods: We analyzed the data of 1,852 patients collected in our national registry (IBD Prospect). For simplicity, the patients were divided into two cohorts. In the first one there were patients included from 2005 to 2010 and in the second those registered from 2011 to 2016. The Montreal classification for Crohn's disease (CD) and ulcerative colitis (UC) was used. Statistical analysis was performed with SPSS version 1.19. We used the Fisher exact test to compare the qualitative data.

Results: We observed an increase in the number of young patients with CD, from 2.47% to 3.94% (not statistically significant, p=0.46) and a significant increase in the ileal involvement (L1), from 14.8% to 27.6% (p =0.0011). In patients with UC, we found a higher percentage of patients with extensive disease (E3), which increased from 26.8% to 32.1% (p=0.10). We also registered significant changes concerning the treatment: an increased use of 5ASA (p=0.0000) and a decreased use of corticosteroids, from 52.9% to 40.6% (p=0.0004).

Conclusion: We found in our country a slight increase in the percentage of young patients with CD and a more frequent ileal involvement. There is a higher number of patients with pancolonic UC, a higher use of 5ASA therapy and a decrease in the use of corticosteroids.

Individual therapy with oral prednisolone in a pregnant patient with ulcerative colitis using a home monitoring system for faecal calprotectin

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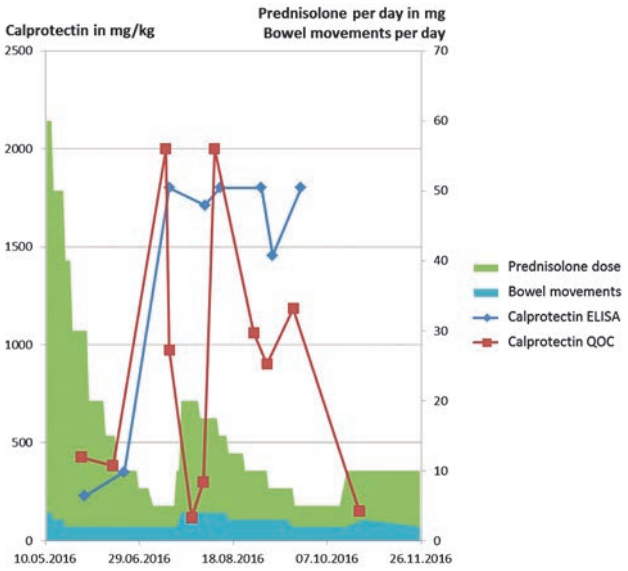
Particularly in pregnancy, chronic diseases are difficult to treat and many patients are very keen to monitor their condition and to adapt the therapy to minimum needs.

A 30-year-old pregnant patient from a peripheral hospital was transferred to our clinic for further treatment of ulcerative colitis. She was at the 15th gestational week and complained about bloody diarrhoea of up to 20 times a day. The colitis had been diagnosed two months earlier. Acute therapy with a body weight-adjusted dose of 70mg prednisolone showed a good response. Despite the pregnancy, glucocorticoids were continued due to the patient's concern about side effects of other immunosuppressants. In order to minimize the prednisolone dose and to detect a treatment failure at an early stage, the patient received test kits for self-measurement of calprotectin in the stool.

We used the QuantOnCal® test kit from Preventis, Bensheim, Germany. The patient determined the calprotectin value at least monthly, as well as at subjective aggravation of her symptoms. Intermittently, samples were also analysed by standard laboratory ELISA test.

The prednisolone dose was adjusted at presentation in our clinic and by telephone interview as well as by the patient herself, depending on the actual calprotectin value (Fig. 1). The patient was in a subjectively good condition during pregnancy and gave birth to a healthy child in week 37.



The calprotectin home measurement kit enabled the patient to adjust the prednisolone dose at a response dependent threshold of 7.5 – 10 mg per day.

In this case we showed the value of a home monitoring system during pregnancy. Due to the easy availability and the rapid result, the therapy could be adapted to the needs much earlier than by the conventional ELISA determination in the laboratory.

Genetic predisposition to primary lactose intolerance and its influence on children's quality of life and dietary habits

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Background: Primary lactose intolerance (PLI) is a frequent condition caused by a genetically programmed and progressive loss of lactase expression. It is considered that PLI is the ancestral variant, while lactase persistence is caused by two polymorphisms: the dominant C/T13910 and G/A22018. Homozygotes (CC or GG) have undetectable lactase levels. In clinical practice only half of the individuals with PLI have symptoms. However, some studies showed that PLI subjects have lower dairy intake.

Aim: To investigate whether genetic predisposition to PLI influences the quality of life and the dairy intake in a group of Romanian children.

Methods: We conducted a prospective study, recruiting consecutive children evaluated in our unit in May-August 2016. Our study population included 87 children aged 6-17 years (mean age 10.64±3.51 years), 45 (51.72%) girls. We used strip genotyping to identify genetic predisposition to IPL. Subjects were asked to complete a validated quality of life questionnaire and a dairy intake questionnaire. We used Spearman's test to evaluate the correlation between PLI and quality of life and the dairy intake.

Results: 45 (51.7%) subjects had a CC genotype; 30 (34.5%) subjects had a GG genotype. Our results were consistent with Hardy-Weinberg equilibrium. We found no correlation between homozygosity for PLI and the dairy intake (CC: r= -0.06, p= 0.54; GG: r= -0.01, p= 0.86). We found no correlation between either CC or GG homozygosity and quality of life (r= -0.11, p= 0.3 and r= -0.1, p= 0.34).

Conclusions: In our group of subjects genetic predisposition to PLI followed the European trends. It did not influence the quality of life and the dairy intake.

The transition of patients with cystic fibrosis at Klinikum Stuttgart – concept and results

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Over 50% of patients with cystic fibrosis in Germany are older than 18 years. This means that the majority of patients have new needs compared to children. The term „transition" and the transfer into adult medicine is therefore a new situation in this field. There is a concept for the transfer of these patients into adult medicine since 2013 at the Klinikum Stuttgart. The pediatrician initiates the preparation for the transition at the patient age of 16 following common consultation-hours with the pediatrician and adult physician in internal medicine.

This paper presents how patients at the Klinikum Stuttgart have developed after their transfer into adult medicine in 2013. The patients were divided into three groups (18-25 years; 26-34 years; 35-50 years), and were compared to each other using certain parameters. One of the parameters was the change of the lung function, which is a measurable parameter, but also there were other parameters such as compliance, family, school/profession. The patients were also pleased to fill out a questionnaire for making their own opinion known. One result was that more support is required with regards to the youngest group where the change to adulthood is immense.

Based upon the results presented in the paper, this is now a focus to further improve the transition at Klinikum Stuttgart.

The efficacy of the simulator in gastrointestinal endoscopy training

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Background: Training in gastrointestinal (GI) endoscopy using computerized medical simulators represents a debated teaching issue. Developing practical skills for "hand-eye" coordination and for handling the endoscopes represents the main learning aims. The strengths are the simulation of the digestive tract peristalsis, the pain indicators (comfort), the ability to perform the procedures without expert supervision, to quantify performance, and generate a final report.

Aim: to determine the results and characteristics of the endoscopic interventions made by the residents in gastroenterology using the Simbionic gastrointestinal endoscopy simulator Mentor II during 2010-2015, in our tertiary centre Cluj-Napoca, Romania.

Methods: A prospective analysis was conducted involving 1770 endoscopic procedures using the Simbionix GI simulator, performed by 60 residents without previous experience in gastroenterology. Indicators of the residents' dexterity and markers of the quality of the procedures were noted. Another important indicator assessed the percentage of visualized mucosa in correlation with the overall time required to complete the procedure. The training period was divided into two modules for the indicators' quantification and comparison.

Results. For upper GI endoscopies, the mean examination number was 21 per resident. Average efficiency was 67%, with a minimum percentage of 38% and a maximum of 87%. A highly statistically significant difference was noted between the first period of training (module I) and the second period (module II) regarding the duration of the procedure (longer for module I) ($p < 0.001$), the percentage of examined mucosa (lower for module I) ($p < 0.001$) and efficiency (lower for Modul I) ($p < 0.001$). A total number of 731 colonoscopies, performed by 42 residents were analysed. There was a statistically significant inverse correlation between the number of the colonoscopies performed and duration of the procedure ($p=0.02$), a direct correlation with the level of efficiency ($p=0.01$) and the number of situations in which the excessive pressure on the lining (potential risk of perforation) ($p=0.005$). No correlation was noted between the number of colonoscopies performed and the percentage of mucosa examined ($p=0.25$), excessive looping ($p=0.3$) and the percentage of time in which the „patient" felt pain ($p=0.66$). Statistically significant differences were noted between the two modules regarding the duration of the procedure ($p < 0.001$), time of arrival at the cecum ($p < 0.001$), time spent in the „loop" ($p < 0.001$) and efficiency ($p < 0.001$).

Conclusions Teaching gastrointestinal endoscopy with Simbionic simulator proved efficient in acquiring practical skills for our residents.

Capnography monitoring of procedural sedation during percutaneous endoscopic gastrostomy (PEG) placement. A prospective, controlled, randomized trial

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Background & Aims: Current guidelines on procedural sedation recommend monitoring of heart rate, blood pressure and oxygen saturation. A number of studies were able to show a reduction of hypoxic episodes through the use of capnography (CA). Our current study investigates the number of mild and severe hypoxic episodes (SPO2 <90% and <85% for >15sec, respectively) during PEG placement comparing pulse oximetric (PO) vs. CA monitoring. Also the time lag for detection of hypoxia was documented for both methods.

Methods: A total of 151 patients were randomized 1:1 in either the PO or CA group after stratification for ASA class, PEG method (push- or pull method), presence of head & neck tumor or tracheostoma. Capnography analyses were performed for all patients but were only accessible for the endoscopic team in the CA group. We used the Capnostream 20p platform (Medtronic, Minneapolis, USA). Statistical analysis was performed using BiAS v8.0 (epsilon, Germany)

Results: 150 patients were evaluable for the primary endpoints (mild/severe hypoxia). There were no significant differences for the two groups regarding sex, age, reason to perform PEG, method of PEG, oxygen therapy prior to intervention, ASA score, history of alcohol or tobacco use or sleep apnea. Overall, episodes of mild and severe hypoxia were observed frequently (42% and 29% of interventions, respectively). In the control group (PO only), 58% and 39% mild and severe hypoxia episodes were observed in comparison to 27% and 19% in the CA group, respectively. Odds ratios for mild and severe hypoxia were 0.26 (CI 0.13-0.55; p=0.0007) and 0.36 (CI 0.16-0.80; p=0.019) in favor of the CA-group. In average CA was able to detect episodes of mild and severe hypoxia 95 seconds (SD=77s) and 92 seconds (SD=53s) before PO, respectively.

Discussion: Respiratory complications of sedation during PEG placement are frequent events. This might be determined by technical aspects of the procedure (e.g. supine patient position, intended depth of sedation) as well as the rather high number of comorbidities in the typical patient collective undergoing PEG insertion. Capnography is able to detect imminent hypoxia at an early time point. This allows an early intervention and consecutively the avoidance of mild and severe hypoxia. Therefore, CA can be recommended particularly for PEG insertion procedures.

Tools for nutritional assessment in patients with liver cirrhosis

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Background & Aim: Malnutrition in patients with liver cirrhosis has become a matter of great interest worldwide, as it was proven to have a negative impact on morbidity, mortality and quality of life. The prevalence reaches up to 60% or more, depending on the severity of liver disease, but also on the method used to evaluate the nutritional status. The aim of this study was to evaluate the nutritional status of hospitalized cirrhotic patients, using different clinical methods.

Method: We evaluated 100 consecutive patients with liver cirrhosis admitted to the Fundeni Clinical Institute in 2015 and 2016. The patients with suspected or confirmed hepatocellular carcinoma were excluded. We evaluated the Child-Pugh, MELD and MELD-Na scores in all patients. Nutritional assessment was performed in all patients, using the Subjective Global Assessment (SGA) score and anthropological measurements: body mass index (BMI), triceps skinfold and mid-arm circumference. We also tested the handgrip strength, using a dynamometer. Based on SGA, the patients were classified as SGA A (no risk of malnutrition), SGA B (at risk of malnutrition or with mild malnutrition) or SGA C (with severe malnutrition).

Results: The majority of the patients were men (72%), with a mean age of 58.19±10.8 years. The etiology of liver disease was: alcohol abuse (49%), followed by chronic viral infections (37%) and mixed etiology (alcohol and viral) (10%). There were only two patients with hemochromatosis, one with autoimmune disease and one with Budd-Chiari syndrome.

According to the Child-Pugh classification, only 23% of the patients had compensated liver cirrhosis (Child-Pugh A). Most patients (46%) were Child-Pugh B, while 31% of patients were Child Pugh C class.

Using the SGA score, we found that almost half of the patients (47%) were moderately malnourished or were at risk of developing malnutrition (SGA B), while 19% had severe malnutrition (SGA C); the remainder (34%) had a good nutritional status (SGA A). When measuring the triceps skinfold, we obtained a 44% prevalence of overall malnutrition; the results were very similar when measuring the mid-arm circumference (45%). The handgrip strength was above the 5th percentile in 69% of patients; thus, 31% suffered from significant malnutrition.

We found no statistical correlation between the BMI and the severity of the disease; the highest mean BMI was found in Child-Pugh C patients. The nutritional status was not influenced by the etiology of the disease.

Conclusion: Malnutrition is common in patients with advanced liver disease. No matter what method is preferred, evaluation of the nutritional status should be performed in all patients, as nutritional intervention might improve patient's outcome.

How to improve the reliability of liver fibrosis evaluation using 2D-SWE.GE

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Aim: To assess the impact of using quality criteria for liver stiffness (LS) evaluation by means of 2D Shear Wave Elastography from General Electrics (2D-SWE.GE), while using Transient Elastography (TE) as reference.

Method: We included 226 subjects in our study, with or without chronic liver disease, in whom LS was assessed by using 2D-SWE.GE (LOGIQ E9, GE Healthcare) and TE (FibroScan, EchoSens). Reliable LS measurements were defined for TE as the median value of 10 measurements with a success rate of ≥60% and an interquartile range (IQR) <30% of the median LS values. For 2D-SWE.GE, 10 LS measurements were acquired in a homogeneous area and the IQR and the IQR/M were calculated in each case. We divided our subjects into three groups according to the 2D-SWE.GE IQR/M: IQR/M<0.10: 41 (18.1%) cases; 0.10<IQR/M≤0.30: 155 (68.6%) cases; IQR/M>0.30: 30 (13.3%) cases. We calculated the correlation coefficient between TE and 2D-SWE.GE in each group.

Results: All 226 (100%) subjects included had 10 valid measurements by means of 2D-SWE.GE and reliable results by TE. A strong positive correlation was found between the LS values obtained by means of 2D-SWE.GE and TE in the IQR/M<0.10 group (r=0.84, p<0.0001). A strong positive correlation was found between the LS values obtained by means of 2D-SWE.GE and TE in the 0.10<IQR/M≤0.30 group (r=0.80, p<0.0001). A weak positive correlation was found between the LS values obtained by means of 2D-SWE.GE and TE in the IQR/M>0.30 group (r=0.41, p=0.02). The correlations were significantly stronger in the IQR/M<0.10 and 0.10<IQR/M≤0.30 groups as compared to the IQR/M >0.30 group (both p=0.0013). No statistical differences were found between the correlations in the IQR/M<0.10 and 0.10<IQR/M≤0.30 groups (p=0.43).

Conclusions: The use of IQR/M<0.30 as quality criteria significantly increases the reliability of LS measurements by means of 2D-SWE.GE. The use of IQR/M<0.10 criteria does not significantly improve the reliability of 2D-SWE.GE LS measurements as compared to the 0.10<IQR/M≤0.30 criteria.

CEUS as the first step in the evaluation of focal liver lesions

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Aim: The aim of this study was to evaluate the performance of CEUS as a first step in the evaluation of focal liver lesions (FLLs) in cirrhotic and non-cirrhotic patients.

Methods: A retrospective study was performed on a cohort of 2904 FLLs evaluated by CEUS according to the EFSUMB guidelines [1] between September 2009 and December 2016. Out of all, 979 (33.7%) FLLs did not completely fulfill the EFSUMB-CEUS criteria and thus had to be confirmed by other imaging technique (contrast-enhanced CT, contrast-enhanced MRI) or histology. Lesions that had been previously diagnosed were excluded. Using CT, MRI and histology for the final diagnosis we calculated the specificity (Sp), sensitivity (Se) and accuracy (Ac) of CEUS for the difficult FLLs that challenged the examiner, in cirrhotic and non-cirrhotic patients.

Results: CEUS established an overall correct diagnosis in 76.8 % (752/979) of the lesions. From the 979 FLLs, 335 (34.3%), (67.7% HCC, 4.7% hemangioma, 3.8% metastasis, 18.2% other benign and 5.3 % malignant lesions) were detected in liver cirrhosis (LC) and 644 (65.7%), (36.1% metastasis, 19.5% hemangioma, 6.8% HCC, 31.3% other benign and 6% malignant lesions) were detected in the non-cirrhotic liver (NC). In LC, CEUS performance for benign lesions was: 87.7% Se, 93.6% Sp and 90.4% Ac. For malignant lesions in LC, CEUS performed: 76.1% Se, 92.4% Sp and 83,8% Ac. In the NC group, CEUS performance for benign lesions was: 82%Se, 95.8% Sp and 88.4% Ac. For malignant lesions in NC: 90.16% Se, 90.13% Sp and 89.4% Ac. CEUS performance on the most frequent lesions: Hepatocellular carcinoma (HCC) in LC: 65.2% Se, 86% Sp, 68.5% Ac. HCC in NC: 65.9% Se, 94.7Sp, 92.1 Ac. Metastasis in LC: 30.7 Se, 97.3Sp, 92.9% Ac. Metastasis in NC: 78.5% Se, 91.2% Sp, 85.5% Ac. Hemangioma in LC: 68.7% Se, 95.6 Sp, 93.4% Ac. Hemangioma in NC: 77.2% Se, 96.1% Sp and 91.3 Ac.

Conclusion: CEUS is an accurate and reliable method as first step in the evaluation of the FLLs. Liver cirrhosis does not significantly influence the CEUS performance.

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Transient Elastography with Controlled Attenuation Parameter (CAP) - a tool for liver disease screening in type 2 diabetes mellitus patients

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The **aim** of the present study was to assess the severity of liver fibrosis and steatosis in a cohort of type 2 diabetic patients, using two non-invasive methods: Transient Elastography (TE) and Controlled Attenuation Parameter (CAP).

Methods: The study included 153 type 2 diabetic patients, who were prospectively randomized (the first 6 patients who were referred to the Metabolic Disease Outpatient Clinic on a consultation day), evaluated in the same session by means of TE and CAP (FibroScan EchoSens) to assess both liver fibrosis and steatosis. Each patient was evaluated for the presence of viral hepatitis (B, C, D) and an AUDIT-C score was performed to exclude alcohol abuse. Reliable liver stiffness measurements (LSM) were defined as the median value of 10 LSM with an IQR/median <30%. For TE and CAP, M and XL probes were used. A cut-off value of 8.2 kPa [1] was used to define clinically relevant fibrosis (F≥3). For differentiation between stages of steatosis, we used the following cut-off values [2]: S2 (moderate) - 255 db/m, S3 (severe) - 290 db/m.

Results: Out of the 153 diabetics screened, we excluded those with associated viral hepatitis, those with an AUDIT-C score >8 and those with unreliable LSM. The final analysis included 101 subjects (65.3% women, mean age 60.7±9.1; BMI 31.6±6.6 kg/m^2) with reliable LSM. Moderate and severe steatosis by means of CAP was found in 15.8% and 74.3% cases, respectively. Clinically relevant fibrosis was detected by means of TE (LSM ≥8.2 kPa) in 26.7% (27/101) of the patients; out of these 74% (20/27) subjects concomitantly had CAP values ≥ 290db/m, which suggest severe steatosis.

Conclusions: In our study, 90.1% of the diabetic patients had moderate and severe steatosis evaluated by CAP, and 26.7% of these had severe fibrosis by TE, suggesting the need for their systematical assessment.

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Development of a semiautomatic segmentation algorithm for the measurement of liver metastases from pancreatic cancer in ultrasound images

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Ultrasound (US) is the most commonly used liver imaging modality worldwide. Due to its low cost, it is increasingly used in the follow-up of cancer patients with metastases localized in the liver. In this contribution, we present the development of an interactive segmentation approach for liver metastases in US acquisitions. A (semi-)automatic segmentation is still very challenging because of the low image quality and the low contrast between the metastasis and the surrounding liver tissue. Thus, the state of the art in clinical practice is still manual measurement and outlining of the metastases in the US images. We tackle the problem by providing an interactive segmentation approach providing real-time feedback of the segmentation results. The approach has been developed with typical US acquisitions from the clinical routine, and the datasets consisted of pancreatic cancer metastases. Even for difficult cases, satisfying segmentations results could be achieved because of the interactive real-time behavior of the approach.

Evaluation of an interactive segmentation algorithm using ultrasound images of liver metastases from pancreatic cancer

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Patients with solely in the liver localised metastatic disease of pancreatic cancer are usually followed up using abdominal ultrasound during palliative treatment. Liver metastases are segmented manually during the regular staging examinations. The results of these measurements often differ from one examiner to another. Additionally, the measurement is time-consuming. In this work, we present the evaluation of a semiautomatic algorithm for segmentation of liver metastases originated from pancreatic cancer. We used a set of 105 different images of metastases. The algorithm and the two examiners had never assessed the images before. First, a manual segmentation was performed and after five weeks a semiautomatic segmentation using the algorithm was done. The order of the images was randomly arranged between the two examinations. The examiners were satisfied in up to 90% of the cases with the semiautomatic segmentation result. Using the algorithm was faster and resulted in a median Dice similarity score of over 80%. In conclusion, this algorithm facilitates fast and accurate segmentation of liver metastases that could simplify this measurement in daily practice.

Radiofrequency vs. microwave ablation in the treatment of naïve and recurrent hepatocellular carcinoma

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Background & Aim. In the treatment of hepatocellular carcinoma (HCC), both microwave ablation (MWA) and radiofrequency ablation (RFA) have proven to be effective. However, there are few studies comparing these two techniques. Moreover, there are few studies which have evaluated the outcomes of percutaneous ablation in recurrent HCC.

Methods. The medical files of 73 patients (2010-2016) with 101 HCC nodules were reviewed. Of the total number of patients, 51 had naïve HCC and 22 had recurrent HCC. Seventy-nine nodules were treated by RFA (umbrella type electrode) and 22 by MWA, using the percutaneous echoguided approach. The treatment efficacy was evaluated at 1-1.5 months after treatment, using contrast enhanced ultrasonography (CEUS), at 4 months by CT (± CEUS) and thereafter at 3-6 month intervals using either CEUS or CT. We compared these two techniques with respect to efficacy, local recurrence rate and risk of complications.

Results. The rate of complete ablation was 90.9% (20/22) in the MWA group vs 92.4% in the RFA group (p=0.81). The rate of local recurrence was significantly lower in HCC nodules treated with MWA compared to RFA (9.09% vs 27.84%; p<0.001). The mean follow-up was significantly lower in the MWA compared to RFA group (12 ± 6.43 months vs 22.77 ± 14.58 months; p<0.001). Local recurrence rate was higher in naïve HCC compared to recurrent HCC (29.47% vs 18.18%, NS). The rate of complications was higher in the RFA group for both major (2.6% vs 0%) and minor complications (15.25% vs 5.55%; p< 0.001).

Conclusions. RFA and MWA are efficient treatment modalities in both naïve and recurrent HCC. The risk of local recurrence was lower in the MWA treated nodules, but in these patients there was a significantly shorter follow-up period. We found a lower risk of complications in the MWA group compared to the RFA group.

Budd-Chiari Syndrome induced by oral contraception in a patient with previously unknown JAK2 mutation, treated with transjugular intrahepatic portocaval shunt: a case report

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Introduction: Budd-Chiari Syndrome (BCS) is an uncommon condition induced by obstruction of the hepatic venous outflow, and still represents a challenge regarding its causes and most effective therapy. This is the case of a patient with BCS occurring after initiating a treatment with an oral contraceptive, and in whom a JAK2 mutation was found. The treatment with transjugular intrahepatic portocaval shunt (TIPS) required adjustment due to the intraprocedural diagnosis of portal vein thrombosis and stenosis of only one perfused hepatic vein.

Case description: A 21-year-old female was admitted following a 4-week course of nausea, abdominal pain and increasing abdominal girth. The patient had no relevant medical history, except for the use of combined oral contraceptives, and had a positive family history for thromboembolic events (her grandmother). The physical examination revealed ascites and hepatomegaly, and the laboratory studies showed an incipient liver failure with disturbed coagulation, reduced Factor V concentration and slightly elevated bilirubin level. Renal function tests, serum ceruloplasmin and hematological parameters were normal. The diagnosis of BCS was established using CT-scanning and ultrasonography, which showed ascites, hepatomegaly and occlusion of two hepatic veins. The etiological investigations showed a mutation in JAK2 kinase (V617F) and an increased megakaryopoiesis and erythropoiesis in the bone marrow biopsy, without signs of a myeloproliferative disorder (MPD) in the complete blood count. The viral and immunological markers and the testing for thrombophilia and paroxysmal nocturnal hemoglobinuria were negative. The patient was treated with anticoagulants and an emergency TIPS was placed via the perfused middle hepatic vein into a right portal vein branch. A portal vein

thrombosis and a secondary stenosis of the middle hepatic vein due to liver swelling were found during the procedure, therefore, the thrombus was rinsed through the TIPS and remained inapparent, and an extension of the TIPS-Tract using an uncovered stent was inserted. The follow-up examination after two weeks showed a complete regression of ascites and improvement of the liver function. The reevaluation after 12 months showed normalized liver function tests.

Conclusion: Conditions accompanied by hypercoagulable states can cause BCS. In our patient, the extensive etiological research revealed a JAK2 V617F mutation, which is frequently associated with MPD, but the complete blood count and the bone marrow biopsy were inconclusive. The JAK2 V617F mutation is a marker for occult MPD, and recent studies found that it can be used for the diagnosis of latent MPD presenting with thrombotic events, or to recognize patients with BCS at risk for subsequent development of MPD. A consequent follow-up is therefore important. The treatment with TIPS in BCS is less invasive and with less morbidity and mortality than surgical shunts, but requires greater skill as hepatic vein thrombosis adds difficulty to the procedure. The difficulty was increased by the fact that the portal vein was thrombosed, and also the hepatic vein was stenosed due to liver swelling. Recent reports showed a favorable long-term prognosis after TIPS, especially in patients without cirrhosis.

Intratumoral heterogeneity of intrahepatic cholangiocarcinoma

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Background: No personalized therapy regimens could demonstrate a benefit in survival of intrahepatic cholangiocarcinoma (iCCA). Since genetic heterogeneity might influence single biopsy based targeted therapy or the outcome of clinical trials, aim of the present study was to investigate intratumoral heterogeneity of iCCA by whole exome sequencing.

Method: Samples from tumor center and tumor periphery of large iCCA lesions as well as a control from healthy liver tissue were obtained from four patients and whole exome sequencing was performed. Mutations that occurred only in the tumor center or periphery were defined as private, whereas mutations present in both samples were regarded as common.

Results: A mean of three non-synonymous private mutations (range 0-14) per sample compared to 33.3 common mutations per sample (range 24-41) was identified. Mean percentage of non-synonymous private mutations per sample was 12% (range 0-58). In all samples of patients 1-3 as well as the central sample of patient 4, ≤10% private mutations were found, whereas 58% of private mutations were identified in the peripheral sample of patient 4. In this sample a private mutation in the DNA mismatch repair protein MSH6 could be identified most likely causing the high amount of private mutations. No substantial intratumoral heterogeneity was found in copy number variation analysis.

Conclusion: Intrahepatic CCA shows a small but distinct intratumoral heterogeneity. Somatic mutations in mismatch repair proteins might contribute significantly to increased spatial tumor burden and thereby may influence clinical management.

Partial splenic embolization used for rescue treatment of esophageal varices

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Background: Partial splenic embolisation (PSE) is a non-surgical procedure, which was first used for treatment of primary and secondary hypersplenism. In 1973, Maddison used an autologous blood clot to perform splenic artery embolization for the treatment of hypersplenism. Nowadays, PSE is used to treat different clinical diseases including esophageal and gastric variceal hemorrhage due to portal hypertension and/or splenic vein thrombosis, as well as for the mitigation of portal hypertension and associated physiological effects of portal hypertension. Moreover, it is a very good alternative to splenectomy. Many studies have shown that partial splenic embolization cannot only decrease the incidence of variceal bleeding, but it can also help to improve the liver function.

Clinical cases: A series of four patients with esophageal varices Grade III-IV is presented. All of the patients were successfully treated with PSE as rescue therapy at the University Hospital Regensburg within one year. All had a significant portal hypertension due to different underlying diseases (factor V Leiden, JAK2 Mutation, Polycythemia vera, primary sclerosing cholangitis). Endoscopic ligature of the varices was not promising for the fundic varices. Placement of a transjugular intrahepatic portosystemic shunt (TIPSS) was not possible because of the local anatomy. In all cases, PSE was successfully performed by our radiologists. Control gastroscopy showed a significant regression of esophageal and gastric varices, now classified as grade II or lower. No patient

showed an episode of bleeding after PSE. The hematologic indices improved. Serious complications of PSE were not observed.

Conclusion: Though limited in its early days by serious complications and high mortality, PSE has since benefited from advances in the available technology and from improvements of the protocol. In patients with portal hypertension it has been shown to induce significant and sustained improvement in both liver function and hematologic indices, as well as a 80% reduction in annual bleeding episodes in patients with recurrent variceal hemorrhage. Our cases show that PSE is a successful rescue therapy option for patients with esophageal varices, when endosopic treatment options or placement of a TIPSS are not promising or possible. All patients had an excellent outcome and a good life quality after PSE. Summarizing, PSE is an excellent rescue treatment option for selected patients with esophageal varices.

Statistical errors in gastroenterology journals

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Human errors are normal in any domain, including medical studies. The articles focused on gastrointestinal and liver research study human or animal subjects. Due to the variability of their biologic characteristics, statistical tools are necessary to make sense of what really happens. A good statistical knowledge and expertise is required to reduce the errors that might occur when choosing these statistical tools and when interpreting and writing their results. Some common errors identified while reviewing such medical articles are presented here, in order to make aware researchers and readers of medical articles, and improve their statistical literacy.

There are many possible types of statistical errors that can be made. Some of them occur in the reporting of the results, sometimes with a less important negative influence. Other errors are those regarding the choice of the statistical tools, and these could have an important negative impact, potentially distancing the results from the truth. There are also errors in the way the results are interpreted. Such errors can be easily spotted by a knowledgeable reader. Sadly, some of the errors cannot be identified when reading the article, i.e. to ascertain whether the authors intentionally or unintentionally hid some information, in order to correctly assess the statistical methods employed in the article. To prevent these errors, a statistician should be involved from the early stages of the study, starting with the research protocol, and then, until the analysis and writing of the final paper. Of course the reviewers and readers should have at least some basic statistical literacy. These actions could diminish the statistical errors in medical papers, but they will never be eradicated.

Direct transpedal lymphangiography including percutaneous sclerotherapy for diagnosis and therapy of refractory lymphatic leakage.

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Aim: To evaluate direct transpedal lymphangiography including percutaneous sclerotherapy for diagnosis and therapy of refractory lymphatic leakage.

Methods: Between 10/2013 and 02/2017, 32 patients underwent direct transpedal lymphangiography. The rationale of the procedure was twofold: a) to diagnose (via pathologic extravasation of iodized oil = lymphatic fistula) and b) to treat (via aseptic inflammation and subsequent scarring) refractory lymphatic leakage in one session. The site of refractory lymphatic leakage was inguinal, iliac, peritoneal, pleural or cervical occurring after lymphadenectomy, arterial reconstruction, esophageal resection or extended neck dissection. In case of persisting lymphatic leakage, direct transpedal lymphangiography was repeated and/or combined with CT-guided percutaneous sclerotherapy. The rationale of CT-guided percutaneous sclerotherapy was to use ethanol for obliteration of the feeding lymphatic vessels and/or the lymphatic fistula itself. Study endpoints included technique, technical success, complications, clinical success (e.g. durable removal of drainage tubes, healing of cutaneous fistula and/or cessation/regression of lymphocele, pleural effusion or ascites) and 30-day morbidity and mortality.

Results: Direct transpedal lymphangiography was performed as a highly standardized procedure. After demarcation of the cutaneous and subcutaneous lymphatic vessels applying a toluidine blue/xylocaine 1% injection into the first, second and third interdigital space of the foot, cut-down at the arch of the foot in local anesthesia, dissection of 1-3 lymphatic vessels, puncture of a lymphatic vessel applying a 26G cannula and slow injection of iodized oil (15-25ml) during 30-60 minutes followed. After documentation of adequate transportation of the iodized oil into the target region applying x-ray images, the cannula was removed and the access closed with vascular and cutaneous sutures. A CT including specific image reconstructions (e.g. coronal MIP, VRT and/or spectral images) 30-60 minutes after and plain x-rays 1 day after the procedure were performed to identify the lymphatic fistula and to rule out accidental iodized oil accumulation within the healthy lung. Primary and secondary technical success rate was > 90% and 100%, respectively. Major complication rate was 0%. CT/plain x-rays identified lymphatic fistulae/

accidental iodized oil accumulation within the healthy lung in > 90%/0% of procedures. Clinical success rate was > 80%. 30-day procedure-related morbidity rate was 0%/. Thirty-day overall and procedure-related mortality rate was < 10% and 0%, respectively. Two patients underwent CT-guided percutaneous sclerotherapy with 2ml 95% ethanol under systemic analgosedation with midazolam and piritramide. In both patients, clinical success occurred within 10 days without major complications and without any 30-day morbidity and mortality.

Conclusion: Direct lymphangiography via pedal lymphatic vessels and including percutaneous sclerotherapy is a highly standardized, safe and effective radiological procedure for diagnosis and therapy of refractory lymphatic leakage. The procedure should be discussed for each patient with refractory lymphatic leakage after inguinal, iliac, abdominal and thoracic lymphadenectomy or arterial reconstruction as well as after esophageal resection and extended neck dissection.

Conflicts of interest: Richter G.M. was speaker for Siemens Healthineers, Erlangen, and received technical and financial support from Siemens Healthineers, Erlangen, Germany. No conflicts of interest for the other authors.

Peritoneal carcinomatosis - the use of endosonography-guided fine needle aspiration biopsy for differential diagnosis

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Background: The most common abdominal cavity masses such as peritoneal carcinomatosis, endometriosis, lymphomas or inflammation often cannot be distinguished by common imaging modalities such as ultrasound or computed tomography (CT). In most cases the only way to clarify the dignity of such abdominal findings is by histologic examination. The following case presents the role of endosonography-guided fine needle aspiration biopsy (EUS-FNA) as a diagnostic tool in the management of such uncertain abdominal findings.

Case report: A 44-year-old patient presented at our hospital with abdominal pain and in severely reduced general condition without any prior history of severe disease. The leading symptom was a massive loss of weight over the course of a few months and sporadic night sweats. Obvious B symptoms.

Orientating abdominal ultrasound showed interenteric fluid as well as a plain thickened peritoneum. A contrast-enhanced sonography (CEUS) for further characterization of the unclear peritoneal findings was performed and showed vascularized peritoneal bulks. A CT scan of the abdomen showed thickened peritoneum, fluid-collections and thickened small bowel loops. The suspicion of a peritoneal carcinomatosis by unknown primary tumour emerged.

In search of a primary tumour with origin in the gastrointestinal tract, a gastroscopy and endosonography were performed. Gastroscopy showed an irregularity of the mucosa in the antrum of the stomach, consistent with the aspect of an early carcinoma. Along with the gastroscopic finding, the endosonography showed a hyperechoic, thickened wall of the antrum; wall layers could not be identified properly. Furthermore, focal nodular appositions on the serosa could be depicted.

Macroscopically, there was no doubt of the presence of a peritoneal carcinomatosis. Several endosonography-guided fine needle aspirations (25 G needle) of the antral wall as well as of some inhomogeneous and enlarged paragastric and mediastinal lymph nodes were performed.

Until that point of time, the diagnosis of a tumour with peritoneal carcinomatosis seemed to be certain. Just a few days after the retention of the results of the cytologic survey, the case took a surprising turn: in the examined specimen there was no evidence of malignant cells. Against all clinical expectations, a granulomatous inflammation with caseating necrosis was found. The assumption of a peritoneal carcinomatosis was finally disproved with the positive PCR result of the FNA specimen for *Mycobacterium tuberculosis*.

After initiation of a specific drug therapy, the patient recovered. After a few months he was reconstituted into an excellent general state of health.

Conclusion: This case shows impressively the potential of EUS-FNA in diagnosing uncertain pathologies and as a method with high sensitivity and specificity for the evaluation of dignity of abdominal cavity masses.

Diagnostic accuracy of EUS-FNA in daily clinical practice

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Background: In controlled studies, EUS-FNA has a high diagnostic accuracy. Diagnostic sensitivity of EUS-FNA is highly dependent on the proficiency and experience of the cytopathologist who evaluates the specimen, and on the expertise of the endosonographer. On the other hand, EUS-FNA is a relatively expensive procedure, requiring a high amount of personal resources and technical equipment. We analyzed if this expense is justified in daily clinical practice in a community-based hospital.

Methods: We retrospectively analyzed 205 EUS-FNA performed during a period of 44 months in our department. Target lesions were: solid pancreatic nodule (64), cystic pancreatic lesions (15), thoracic lymph nodes (28), abdominal lymph nodes (52), retroperitoneal/peritoneal/mesenterial mass (13), tumor of the adrenal gland (9), mediastinal mass (4), hepatobiliary lesions (4), subepithelial tumors (7), and ascites (9). Aspirations were performed using 22G and 25G needles. The specimen was transferred on a slide to create a smear with subsequent Papanicolaou´s staining and microscopic investigations. ROSE (rapid on-site examination) was not performed. Cytological smears were analyzed by a skilled

cytologist (Cytological Laboratory Topalidis, Hannover, Germany). In cystic pancreatic lesion, we used a combination of cytology, and measurement of CEA and Amylase in the cystic fluid for risk estimation of a malignant or premalignant tumor. The final diagnosis was based on surgical findings (43), histology obtained by additional percutaneus punction (5), or clinical follow-up (157 patients). We analyzed sensitivity, specificity, and diagnostic accuracy of the method.

Results: For final diagnosis, our collective included 127 malignant, and 78 benign lesions. Subgroup analysis revealed malignancy in 56/64 solid pancreatic tumors, 40/80 lymph nodes, 2/15 cystic pancreatic lesions, 3/9 adrenal gland tumors, 9/13 retroperitoneal/peritoneal/mesenterial masses, 7/9 ascites, 4/7 subepithelial tumors, 4/4 mediastinal masses, and 2/4 hepatobiliary lesions.

All in all, EUS-FNA correctly identified 119 of the 127 malignant lesions, and 77 of the 78 benign targets. Accuracy for the differentiation between malignant and benign disease was 95%, sensitivity 93%, and specifity 98%. Subgroup analysis showed: solid pancreatic malignancy (64): sensitivity 96%, specifity 100%, and accuracy 96%; malignant lymph nodes (80): sensitivity 95%, specifity 97%, accuracy 96%; cystic pancreatic lesion (15): sensitivity 50%, specificity 100%, and accuracy 93%; retroperitoneal/peritoneal/mesenterial mass (13): sensitivity 88%, specificity 100%, and accuracy 92%; adrenal gland tumor (n=9): sensitivity 88%, specificity 100%, and accuracy 92%; ascites (9): sensitivity 85%, specificity 100%, and accuracy 88%; subepithelial tumor (7): sensitivity 100%, specificity 100%, and accuracy 100%; hepatobiliary mass (4): sensitivity 50%, specificity 100%, and accuracy 75%; mediastinal mass (4): sensitivity 100%, specificity 100%, and accuracy 100%.

Conclusion: EUS-FNA in solid pancreatic lesions and lymph nodes has a high diagnostic accuracy. Due to the relatively small number of lesions, the results are less reliable, but still promising, in additional targets. Therefore, the expense for performing EUS-FNA is justified.

Complications after EUS-FNA in daily clinical practice – who is at risk?

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Introduction: In controlled clinical studies, diagnostic EUS-FNA seems to be a safe procedure. However, in clinical medicine, results often differ between controlled studies and routine use in daily clinical practice. Furthermore, recent reports suggest that certain subgroups such as patients with sarcoidosis might be at an increased risk for complications. Therefore, we analyzed the complications of EUS-FNA and the possibly associated risk factors in our collective.

Methods: We retrospectively analyzed 279 EUS-FNA performed between 9/2012 and 5/2016. Complications were categorized as minor (pain, fever, bleeding with or without need of transfusion) or major (need for operation, interventional treatment, hospital stay, death), as well as immediate (< 24 h) or delayed (> 24 h after punction). Furthermore, the following variables were assessed: age, comorbidity (cardiac, renal, pulmonary, hepatic, immunosuppressive), anticoagulation medication, punctured organ, size of lesion, needle size, and number of needle passages.

Results: In 207 cases, EUS-FNA was performed for the diagnosis or staging of suspected or previously known malignancy, whereas suspected benign disease such as enlargement of lymph nodes of unknown origin was the indication in 72 cases. Mean age of the patients was 66 years (range 18-89). Isolated cardiac comorbidity was present in 94, pulmonary in 9, renal in 6, and combined comorbidity in 34 cases. In all patients, thrombocyte count was > 50.000/µl, and INR <1.5. In 50 cases, aspirations were performed with ongoing ASS, in 3 with clopidogrel.

Approximately 85% of aspirations were performed with needles of 22G (118) and 25G (116) size. In only six aspirations, a 19G needle was used. Data were missing in 39 patients. In 175 punctions, 1-3 needle passages were performed, in 73 > 3 passages (missing data in 31 aspirations). The following organs were punctured: 112 lymph nodes, 82 solid and 25 cystic pancreatic masses, and 61 other organs: adrenal gland (11), ascites or pleural effusion (11), thoracic (4) or peritoneal/retroperitoneal masses (19), subepithelial tumor (11), and bilio-hepatic mass (4). The mean size of the lesion was 24 mm (range 3-120 mm).

All in all, 7 minor and 2 major complications occurred. Major complications included one case of pancreatitis after aspiration of a parapancreatic mass, and one case of mediastinitis in a patient with sarcoidosis after aspiration of a mediastinal lymph node. Minor complications included pain (3), minor bleeding without need for transfusion (3), and one patient with gastrointestinal bleeding with need for transfusion after transgastric aspiration of an abdominal lymph node; 7/9 complications occurred in less than 24 hours after the FNA. Only 2 complications developed after more than 24 hours: mediastinitis after lymph node aspiration, and gastrointestinal bleeding after transgastric aspiration of an abdominal lymphnode.

Conclusion: We observed a complication rate of 3%, with major complications in 0.7%. This is slightly higher than the rates reported in the literature. Most complications were of minor severity without need of intervention. Probably due to the low number of cases, no risk factor could be identified.

Prior dosing of chemotherapy applied to end stage renal disease in patients with pancreatic cancer undergoing hemodialysis

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Background: Although associated with a poor prognosis, recent chemotherapeutic advances lead to an increased survival of patients suffering from pancreatic ductal adenocarcinoma

(PDAC). Due to strict exclusion criteria, these results are not applicable to patients with end stage renal disease. In this study we provide guidance for the clinician to use chemotherapy in a patient with pancreatic cancer on hemodialysis (HD). We advocate the use of a chemotherapeutic application shortly prior to HD to mimic normal renal function when using dialyzable substances.

Methods: We retrospectively identified all PubMed listed studies describing patients with end stage renal disease (ESRD) receiving chemotherapy until October 2016. We selected common and novel chemotherapeutic agents used in the therapy of PDAC. Time of chemotherapy application relative to HD, toxicity and pharmacokinetic measurements were assed.

Results: We identified 59 studies describing 132 patients with ESRD receiving chemotherapy. The application directly before HD was successfully used for the dialyzable substances gemcitabine, 5FU, capecitabine, oxaliplatin, irinotecan and S-1.

Conclusion: Application of chemotherapeutic agents directly before hemodialysis is feasible in patients with end stage renal disease suffering from PDAC.

Non-functional neuroendocrine tumor (NET G1) presenting as a small hypoenhancing pancreatic incidentaloma during endoscopic ultrasound

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Background: With the widespread use of endoscopic ultrasound and cross-sectional imaging, incidentally detected small pancreatic masses of a diameter less than 2cm are an emerging diagnostic dilemma. While larger pancreatic masses without distant metastases are usually treated by pancreaticoduodenectomy because of the high incidence of pancreatic ductal adenocarcinoma (PDAC), the PDAC incidence in small pancreatic masses is only about 4.3-22.5% [1]. Therefore the differential diagnosis has to be carefully evaluated because of the high morbidity and mortality of pancreatic surgery. We present the workup of a pancreatic incidentaloma diagnosed by endoscopic ultrasound, which was previously not seen on initial MRI.

Case Report: A 65-year-old patient presented with recurrent abdominal pain in the right upper quadrant. Serum gamma GT was slightly elevated (292 U/l, normal value <55 U/l), serum alkaline phosphatase, transaminase and bilirubin levels were not elevated. The patient´s general physician ordered an MRCP and MRI of the liver and pancreas; the MRCP suspected a gallstone within the ductus hepatocholedochus.

We performed an endoscopic ultrasound to validate the choledocholithiasis suggested by MRCP. The endoscopic ultrasound examination (Olympus GF-UCT 180, Aloka Prosound) showed several gallstones in the ductus choledochus. During routine scanning through the pancreas, a 4mm echo-poor roundly shaped pancreatic mass was detected. For further evaluation we performed a contrast harmonic endoscopic ultrasound scan of the mass with 4.8ml Sonovue, a second-generation sulfur hexafluoride – filled microbubble contrast agent. The lesion showed an arterial hypoenhancement in comparison to the pancreatic parenchyma. After obtaining informed consent, an endoscopic ultrasound guided fine needle aspiration was performed, using an Olympus EZ Shot2 25 G needle. The lesion appeared soft at puncture. No complications were noted.

The cytologic evaluation showed a well-differentiated pancreatic neuroendocrine tumor (NET G1). The immunhistochemistry showed: synaptophysin and chromogranin positive, and somatostatin receptor negative.

There were no clinical signs of a functional NET. The case was presented at our tumor board, and regular follow up (every 6 months) with endoscopic ultrasound was suggested. Because of the negative somatostatin receptor immuncytochemistry, no 68-Ga DOTATOC PET was performed.

Discussion: Non-functional small pancreatic neuroendocrine tumors (PNETs) are increasingly identified. They carry, in contrast to pancreatic ductal adenocarcinomas, a good prognosis and are usually slow-growing [2]. Hypoenhancement during contrast enhanced EUS is a hallmark of pancreatic adenocarcinoma. In a recent study by Dietrich et al., 92% of small PDAC showed hypoenhancement during contrast enhanced EUS oder contrast enhanced ultrasound (CEUS) [1]. In contrast, 81% of all small PNETs showed hyperenhancement and only 11% hypoenhancement.

With EUS-guided fine needle aspiration of the only 4mm small pancreatic incidentaloma we were able to gain sufficient cytologic material for diagnosing a G1 PNET. The current ENETS guidelines and several studies suggest a non-operative management for small asymptomatic G1 PNETs <2cm [3]. We recommend an EUS-guided follow up every 6 month.

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