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Predictors of Variceal or Nonvariceal Source of Upper Gastrointestinal Bleeding. An Etiology Predictive Score Established and Validated in a Tertiary Referral Center

Daniela Matei1,2, Ioana Groza1, Bogdan Furnea1, Lidia Puie1, Cristina Levi1, Andrei Chiru1, Carmen Cruciat1, Gabriela Mester1, Stefan Cristian Vesa3, Marcel Tantau1,2

ABSTRACT

Background & Aims. For upper gastrointestinal bleeding (UGIB), guidelines recommend pharmacological treatment before endoscopy. Therefore, it is important to establish an early diagnosis of the variceal or non-variceal source of bleeding. This study aims to analyze the clinical and laboratory parameters which are predictors of the UGIB etiology, and to develop a score for predicting variceal or non-variceal bleeding.

Methods. This study comprised patients presenting to the emergency department of a tertiary care center with UGIB, throughout a 1-year period. Clinical, ultrasound data and laboratory parameters were noted.

Results. Of the 517 patients with UGIB, 29.8% had variceal and 70.2% non-variceal bleeding. Six factors were associated with variceal hemorrhage: cirrhosis (OR=10.74, 95%CI: 3.50-32.94, p<0.001), history of variceal hemorrhage (OR=13.11, 95%CI: 3.09-55.57, p<0.001), ascites (OR=4.41, 95%CI: 1.74-11.16, p=0.002), thrombocytopenia (OR=2.77, 95%CI: 1.18-6.50, p=0.03), elevated INR (OR=4.77, 95%CI:1.47-15.42, p=0.009) and elevated bilirubin levels (OR=2.43, 95%CI:1.01-5.84, p=0.04). Two factors were associated with non-variceal bleeding: the use of NSAIDs (OR=0.32, 95%CI: 0.13-0.83, p=0.01) and of anticoagulants (OR=0.04, 95%CI: 0.00-0.89, p=0.04). A prediction score for UGIB etiology was designed based on this model. We calculated a cutoff value of 0.968, higher values being predictive of variceal bleeding. Positive predictive value (PPV) and negative predictive value (NPV) were: 82.7% and 97%, respectively. The score was validated prospectively in another group of 162 patients: PPV and NPV were 72.7% and 95.3%, respectively.

Conclusions. Several factors were identified as predictors for the etiology of UGIB. Due to its high PPV and NPV, our UGIB etiology score might be useful in predicting variceal bleeding and could assist in the selection of pharmacological therapy before endoscopy.

Key words: upper gastrointestinal bleeding (UGIB) – variceal bleeding – non-variceal bleeding – predictive factors – etiology – predictive score
Perforation during Esophageal Dilatation: A 10-Year Experience

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ABSTRACT

Background & Aim: Esophageal stenosis can be caused by malignant, postsurgical, benign diseases etc. Endoscopic treatment options consist primarily of balloon dilatation and bougination. Both interventions carry a certain risk of further complications such as perforations. We aimed to evaluate this risk in our patients.

Methods: Frequency, perforation rates, further diagnostics, therapy, outcome and underlying diseases in 368 patients who underwent endoscopic dilatation or bougination in a 10 year period were evaluated.

Results: Overall, 1497 endoscopic interventions were performed for treatment of esophageal stricture, causing 8 perforations (0.53% per intervention, 2.17% per patient) and one lethal outcome (0.05% per intervention, 0.27% per patient). In 1286 bouginations, 8 perforations (0.62%) and one death occurred (0.08%), whilst no perforation was noted during 211 balloon dilatations. Outcome of the 8 perforations was greatly influenced by co-morbidities, causing a prolonged hospitalization and the death of one patient.

Conclusion: Although complication rates are fairly small, patients should be under supervision or in contact for 24-72 hours after each intervention. In cases where perforation is suspected, radiological examinations should be conducted early. The perforation rate and mortality per patient may be used for patient information. Therapy and prognosis depend on the cause of perforation, localization and size of the perforation site as well as concomitant diseases.

Key words: esophageal stenoses - balloon dilatation - bougination - perforation.
Factors Influencing the Type, Timing and Severity of Symptomatic Responses to Dietary Gluten in Patients with Biopsy-proven Coeliac Disease

Stephen M. Barratt¹, John S. Leeds², David S. Sanders³

ABSTRACT

Background & Aim: There is a paucity of data reflecting the symptomatic responses to dietary gluten (SRDG) in patients with Coeliac Disease (CD). We aimed to determine the type, timing and severity of SRDG with reference to a range of disease-related factors.

Methods: Postal survey of 224 biopsy-proven patients including gluten-free diet (GFD) adherence, symptom checklist, ROME II criteria and The Hospital Anxiety & Depression Scale. Case-note review was also conducted.

Results: 26% of respondents were male. Full GFD adherence: n=159 (70%). Irritable bowel syndrome (IBS): n=50 (22%). Anxiety: n=30 (13%); Depression: n=33 (14%); Anxiety & Depression: n=72 (32%). Pruritus, fatigue and bloating were a more common SRDG in the partial/none GFD adherent group (p<0.05). Co-existing IBS was associated with a greater prevalence of nausea and fatigue in response to gluten (p<0.05). Fully GFD adherent patients are more likely to have SRDG <1hr than partial/none adherent (OR 4.8; p=0.004), as are a third of patients with co-existing IBS (OR 1.5; p=0.027) and those patients at risk of both anxiety and depression (OR 1.9; p<0.04). Inadvertent exposure to dietary gluten in the fully GFD adherent group is more likely to result in a severe SRDG in comparison to symptoms arising prior to consistent GFD adherence (OR 2.3; p=0.01). IBS sufferers are also more likely to rate their SRDG as severe in nature (OR 1.4; p=0.038).

Conclusion: Patients with consistent GFD adherence experience a SRDG faster and more severe in comparison to prior gluten exposure possibly demonstrating an adept immunological response. Anxiety and depression also enhance the speed of symptom onset and co-existing visceral hypersensitivity is a risk factor for severe reactions to dietary gluten.

Predictors of First Recurrence in *Clostridium difficile*-Associated Disease. A Study of 306 Patients Hospitalized in a Romanian Tertiary Referral Center

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ABSTRACT

Background & Aims: *Clostridium difficile* is recognized as the major cause of nosocomial gastroenteritis usually related to antibiotic treatment. Although treatable, *C. difficile* – associated disease (CDAD) tends to recur in many patients. The purpose of the study was to analyze the risk factors for recurrence in patients with CDAD after the first treatment with vancomycin, metronidazole or both.

Method: We conducted a retrospective study of all patients admitted to the Teaching Hospital of Infectious Diseases Cluj-Napoca, Romania, between January 2011 and October 2012 with the diagnosis of CDAD or who developed diarrhea after admission. A clinical diagnosis was made and culture and toxin A and B detection were carried out. We performed a statistical analysis taking into consideration: age, gender, previous hospital exposure, previous antibiotic treatment, and treatment duration. The patients were followed-up for at least 60 days.

Results: We included 306 patients (177 women and 129 men) with a median age of 71 years; 208 patients (68%) had prior hospitalization and 195 (64%) had received prior antibiotic treatment. Actual treatment consisted of vancomycin in 76 (25%) patients, metronidazole in 132 (43%) and both combined in 98 (32%) patients. The average duration of treatment was 10 days. Sixty patients (20%) experienced 95 recurrences and 9 patients died (3%). Treatment with metronidazole, vancomycin or both for 10 or more days did not prevent recurrences. Age over 70 (RR 1.5, CI 95%: 1.055-2.71) and use of PPI (RR 1.3, CI 95%: 1.16-3.1) significantly increased the risk of first recurrence of CDAD.

Conclusions: CDAD recurrence rates were similar to those reported in the literature. The risk of first recurrence was significantly higher in patients older than 70 who also received PPI treatment.

Key words: *Clostridium difficile*-associated disease – nosocomial gastroenteritis – risk factors – recurrence.
Small Bowel Inflammatory Involvement in Behçet’s Disease Associated Spondyloarthritis Is Different from Other Spondyloarthritides. A Prospective Cohort Study

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ABSTRACT

Background & Aims: Behçet’s disease presents some similar clinical features with seronegative spondyloarthritides (SpA), raising the question whether a subgroup of patients with Behçet’s disease belong in fact to the latter. As the already known inflammatory involvement at the level of the small bowel in SpA patients could not be extrapolated for patients with Behçet’s disease associated SpA (BehSpA), the present study aims to investigate and compare it in these diseases.

Methods: 54 consecutive patients with a form of SpA, and 7 patients with BehSpA were enrolled and submitted to videocapsule endoscopy (VCE) examination. After reviewing the VCE findings, calculation of the score of small bowel mucosal inflammatory change (Lewis) was performed for each patient. The comparison was made with a control group, sex and age-matched to the patients in the study groups.

Results: The Lewis score differed in the groups considered for analysis (mean of 439, 179 and 81 in the SpA, BehSpA and the control group, respectively, with p = 0.04 for the comparison SpA vs. BehSpA and 0.05 for the comparison BehSpA vs. controls). C reactive protein (CRP) level was markedly reduced in the BehSpA group vs. the other SpA group (2.08 and 14.02 mg/L, respectively; p = 0.053).

Conclusion: The significant difference in intestinal inflammatory involvement in BehSpA versus the other SpAs, as well as the significantly lower serum levels of CRP, as revealed by the present study, clearly draw a line between the two disease entities.

Key words: Behçet’s disease – spondyloarthritis – small bowel inflammatory involvement – Lewis score – videocapsule endoscopy.
Correlation of Imatinib Resistance with the Mutational Status of KIT and PDGFRA Genes in Gastrointestinal Stromal Tumors: a Meta-analysis

Ju–Han Lee,* Younghye Kim,* Jung–Woo Choi, Young–Sik Kim

ABSTRACT

Background & Aims: Imatinib resistance is the most important clinical issue in patients with gastrointestinal stromal tumor (GIST). However, the association of imatinib resistance with the genetic characteristics of GIST has not been clearly defined. Our meta-analysis aimed to investigate the association between imatinib resistance and KIT and PDGFRA mutations in GIST.

Methods: We identified all relevant studies in PubMed and Embase. The effect sizes were calculated as prevalence or odds ratio (OR) with a random–effects model.

Results. We identified 10 eligible studies that included 1083 GIST cases. Total imatinib resistance was found in 35.5 % of PDGFRA-mutant tumors (OR = 2.9, P = 0.038), 33.7% of wild-type tumors (KIT and PDGFRA non-mutant tumors; OR = 2.8, P = 0.002), and 27.4% of KIT-mutant tumors (OR = 0.3, P = 0.001). Primary imatinib resistance was found in 50.0% of PDGFRA-mutant tumors (OR = 10.9, P = 0.031), 33.4% of wild-type tumors (OR = 5.9, P = 0.060), and 8.9% of KIT-mutant tumors (OR = 0.2, P = 0.025). KIT exon 9-mutant tumors showed primary resistance more frequently than exon 11-mutant and other tumors (OR = 7.6, P < 0.001). Regarding secondary resistance associated with KIT second-site mutations, the exon 17 mutation (54.5%) was most frequent, followed by exon 13 (38.3%) and 14 (13.4%) mutations.

Conclusion. Our meta-analysis indicates that imatinib resistance is closely associated with KIT and PDGFRA genotypes in GIST. Thus, the mutational status of KIT and PDGFRA might predict response to imatinib in GIST patients.

Key words: gastrointestinal stromal tumor – imatinib – resistance.
New Genetic Markers for Diagnosis of Hepatitis C Related Hepatocellular Carcinoma in Egyptian Patients

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ABSTRACT

Background and aim: Early detection of hepatocellular carcinoma (HCC) enhances effective and curative management. New genetic markers with distinct diagnostic ability are required. Aim: determine the expression of GPC3, PEG10, SERPINI1, MK and QP-C in the peripheral blood of HCC patients.

Methods: 74 HCV patients were recruited and divided into three groups; chronic hepatitis (I), liver cirrhosis (II) and HCC (III). Demographics, laboratory and imaging data were collected. Child score and metastatic work up were completed. The expression of the five candidate genes in the peripheral blood was performed by qRT-PCR assay.

Results: Groups were gender matched, age in group I was significantly lower than in groups II and III (37.7 vs 50.4 and 55.6, p value <0.005). CHILD score; group II and III A/B/C = (7/5/6) and (20/6/3). AFP was significantly higher in group III than I and II (204 vs 3.9 and 6.9, p < 0.01). In HCC group 69% of the lesions were < 5 cm, and had 1-2 nodules; 14% had metastases. GPC3, PEG10, SERPINI1 and MK mRNA were significantly higher in the HCC group compared to the other groups while QP-C mRNA was higher in chronic hepatitis C group compared to other groups. The gene expression values in HCC patients were independent of the tumor size, AFP levels or extrahepatic metastasis. Combined measurement of the five gene markers showed 100% sensitivity and 33% specificity, 48% PPV and 100% NPV.

Conclusion: GPC3, PEG10, SERPINI1 and MK are genetic markers that can represent a useful tool for detection of HCC.

Biliary Papillomatosis: Correlation of Radiologic Findings with Percutaneous Transhepatic Cholangioscopy

Jung-Hee Yoon

ABSTRACT

Aim: To correlate the radiologic findings with percutaneous transhepatic cholangioscopy (PTCS) in patients with pathologically confirmed biliary papillomatosis.

Methods: Thirteen patients diagnosed with pathologic papillomatosis or intraductal papillary neoplasms of the bile ducts were retrospectively reviewed. The imaging results from ultrasonography, multi-detector computed tomography (CT), endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP) and percutaneous cholangiography (PTC) were correlated with the findings of PTCS.

Results: Papillary neoplasms of the bile ducts usually appeared on ultrasound as a non-shadowing echogenic mass (60%) within dilated bile ducts. Localised dilatation of the bile duct with mild enhancing nodularities was the most common multi-detector CT finding (61.5%), followed by localised biliary dilatation with mild wall thickening (15.4%). MRCP showed that the bile duct was locally dilated and filled with material of intermediate signal intensity (60%). An abnormal filling defect (71.4%) was the most common finding when PTC was used. In six patients who underwent PTCS, underlying fish egg-like intraluminal nodularities were noted with or without multifocal cauliflower-like papillary masses. In nine cases, the pathologic finding was intraductal papillary cholangiocarcinoma in the underlying biliary papillomatosis. Three patients were diagnosed as papillomatosis with high grade dysplasia and one as villous adenoma with underlying papillomatosis.

Conclusions: Imaging is useful for detecting bile duct tumours that cause obstruction, but its ability to detect fine features of intraductal papillary tumours is limited. Percutaneous transhepatic cholangioscopy is an effective approach that allows the direct visualisation and tissue confirmation of growing papillary tumours.

Key words: intraductal biliary neoplasm – intraductal papillary neoplasm of the bile duct – intraductal tubular neoplasm of the bile duct – intraductal tubulopapillary neoplasm of the bile duct – biliary tract neoplasms/diagnosis – papilloma/diagnosis.
Non-celiac Gluten Sensitivity. Is it in the Gluten or the Grain?

Petula Nijeboer¹, Hetty J. Bontkes², Chris J.J. Mulder¹, Gerd Bouma¹

ABSTRACT

Celiac disease is an immune-mediated inflammatory disorder of the small intestine caused by sensitivity to dietary gluten and related proteins in genetically predisposed individuals. Over the past several years, the concept of non-celiac gluten sensitivity (NCGS) has gained significant interest from the scientific community and mass media and the number of individuals embracing a gluten-free diet is rapidly growing. This condition is characterized by gastrointestinal or extraintestinal symptoms that respond to gluten withdrawal without evidence for underlying celiac disease or wheat allergy. Symptoms display significant overlap with the irritable bowel syndrome. Many important factors regarding this relatively novel condition remain to be elucidated; no discriminative markers to support a diagnosis of gluten sensitivity have been identified yet and its pathogenesis remains obscure. Here we review the current knowledge on NCGS, and outline potential pathogenic pathways of different gluten related disorders in order to gain clues about the pathophysiology of this novel condition.

Key words: gluten sensitivity – non-celiac gluten sensitivity - NCGS - celiac disease – wheat allergy – irritable bowel syndrome – IBS - gluten free diet – grain – wheat
Acute Upper Gastrointestinal Bleeding Secondary to Kaposi Sarcoma as Initial Presentation of HIV Infection

Sara A. Mansfield, Stanislaw P.A. Stawicki, Rachel C. Forbes, Thomas J. Papadimos, David E. Lindsey

ABSTRACT

Despite our decades of experience with Kaposi Sarcoma its true nature remains elusive. This angioproliferative disease of the vascular endothelium has a propensity to involve visceral organs in the immunocompromised population. There are four variants of the disease and each has its own pathogenesis and evolution. While the common sources of upper gastrointestinal bleeding are familiar to surgeons and critical care physicians, here we present the exceedingly rare report of upper gastrointestinal bleeding attributable to this malady, explore its successful management, and review the various forms of Kaposi Sarcoma including the strategies in regard to their management.

Key words: Kaposi sarcoma – upper gastrointestinal bleeding – endoscopy – highly active anti-retroviral therapy (HAART) – clinical management
Double-duct Sign: Do Not Forget the Gallstones

Leendert H. Oterdoom, Stijn J.B. van Weyenberg, Nanne K.H. de Boer

ABSTRACT
A double-duct sign is the combined dilatation of the common bile duct and pancreatic duct, often caused by cancer of the pancreas. We present a patient with colicky pain in the right upper quadrant of her abdomen. On radiological imaging and endosonography, she had a double-duct sign due to choledocholithiasis and no mass in the pancreatic head. A literature search was performed, which indicated that in selected patients with a higher likelihood of pancreas cancer (for example jaundice or pancreatic mass on radiological imaging) up to 85% of patients do indeed have a pancreatic cancer. In an unselected population, regardless of presenting symptoms, a double-duct sign on endoscopic retrograde cholangiopancreatography (ERCP) was caused by a pancreas malignancy in 58% of patients. In selected patients without jaundice but with a double duct sign, pancreas cancer was only seen in 6% of patients. The sensitivity and specificity of the double-duct sign observed by ERCP for pancreatic cancer varies between 50-76% and 63-80%, respectively. Our patient with symptomatic choledocholithiasis underwent an uncomplicated ERCP with stone extraction and papillotomy and was referred for a cholecystectomy.

Key words: choledocholithiasis – pancreas – pancreas cancer – diagnosis.
Development of Multiple Focal Nodular Hyperplasia Lesions after Portocaval Shunting. A Case Report

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ABSTRACT

It has been postulated that altered hepatic blood flow, particularly reduced portal flow, is responsible for the induction of hyperplasia of liver cells and nodule formation. This report describes the case of a 31-year old female patient developing multiple focal nodular hyperplasia (FNH) lesions two years after portocaval shunting and extended right hemihepatectomy due to the suspicion of a malignant liver tumor. Portocaval shunting became necessary due to iatrogenic thrombosis of the entire portal vein after preoperative embolization of the right portal vein. This observation provides for the first time direct evidence for the pathogenesis of FNH in humans.

Key words: focal nodular hyperplasia – liver – etiology – portocaval shunt
ABSTRACT

Minimal Hepatic Encephalopathy (MHE) is a potentially reversible spectrum of neuro-psychiatric alterations in patients with acute or chronic liver disease, in the presence of a normal neurological examination. Studies demonstrated that early diagnosis and treatment of this complication increases the quality of life of the patients and leads to an overall better liver disease management. Currently, a practical method of diagnosing MHE is through psychological tests, with modest accuracy. A highly sensible and specific non-invasive method of diagnosis is Magnetic Resonance Spectroscopy (MRS) which identifies the key neuro-biochemical profile of hepatic encephalopathy. In selected cases of equivocal psychological test results, MRS is justified and adequate according to the authors’ opinion.

Key words: Minimal Hepatic Encephalopathy – Magnetic Resonance Spectroscopy – Neuropsychological test
CASE REPORT / TECHNIQUE

Esophageal Per Oral Endoscopic Miotomy (POEM) for Achalasia: First Case Reported in Eastern Europe

Marcel Tantau1,2, Alina Tantau1,3

ABSTRACT

Traditional endoscopic treatment of achalasia consists of endoscopic balloon dilatation with the inconvenience of the recurrence of symptoms and the necessity of repeated sessions. Surgical laparoscopic procedure has been advocated to be more efficient especially in young patients because it sections the lower oesophageal sphincter via a transabdominal approach. The long term most severe complication has been refractory reflux oesophagitis due mainly to the alteration of the oesogastric antireflux anatomy (Hiss angle). Surgical myotomy was classically associated with an antireflux procedure. Peroral endoscopic myotomy (POEM) via a mucosal orifice is as efficient as surgical miotomy but the antireflux anatomy of gastroesophageal junction is not altered, so the reflux symptoms are reduced. Second, POEM is mini invasive in comparison with laparoscopic surgery.

The paper presents our first and successful case of this endoscopic surgical procedure in a 41 year old patient.

Key words: achalasia – dysphagia – peroral endoscopic myotomy.
Endoscopic Ultrasound in the Diagnosis and Treatment of Upper Digestive Bleeding: a Useful Tool

Andrada Seicean

ABSTRACT

The use of endoscopic ultrasound (EUS) in identifying the causes of upper digestive bleeding is less individualised. EUS can find the small vessel responsible for intermittent active bleeding in case of Dieulafoy ulcer or for discriminating it from vascular abnormalities. The EUS diagnosis of portal hypertension has to describe esophageal and gastric varices, perforant and paraesophageal veins, dilatations of the azygos, portal, superior mesenteric vein and splenic vein. Few studies have involved EUS in the prediction of variceal bleeding and variceal bleeding recurrence, and in the guided therapy of gastric varices or submucosal gastric neoplasms. The EUS aspect of hemobilia is that of an enlarged inhomogeneous common bile duct, without a Doppler signal, and the origin of the bleeding can be identified as a biliary tumor, bile duct stone or vascular abnormality. The EUS image of the pseudoaneurysm responsible for hemosuccus pancreaticus is that of a cystic lesion with Doppler signal; sometimes, a pseudoaneurysm can be found to communicate with a blood vessel and EUS-guided therapies have been reported. Despite the limitations of the current devices and accessories, EUS has established its place among the endoscopic and radiologic tools. However, rational patient selection is mandatory.