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ORIGINAL PAPERS

Concordance of Genetic and Breath Tests for Lactose Intolerance in a Tertiary Referral Centre

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Abstract

Background & Aims. Lactase non-persistence causes gastrointestinal symptoms after milk ingestion. Hydrogen breath test (BTH) and genotyping of a single nucleotide polymorphism (SNP) C>T 13,910 base pairs upstream of the lactase gene represent potential methods for diagnosis of this autosomal-recessive trait. The aim of the study was to compare the results of both tests in detecting lactose non-persistence in a tertiary referral centre. **Patients.** A group of 58 patients admitted to a German university hospital for symptoms suggesting lactose intolerance**. Methods**. BTH after lactose ingestion (50 g) and SNP - 13,910C>T genotyping using single nucleotide primer extension (SNaPshot) technology (CC genotype - lactase non-persistence; TC/TT genotypes - lactase persistence). **Results**. Overall, 17 (29%) patients had a positive and 41 (71%) had a negative BTH result; 15 (26%) patients were CC-positive and 43 (74%) were CC-negative [28 (48%) TC; 15 (26%) TT]. The genotype frequencies did not deviate from the Hardy-Weinberg equilibrium. In the CC-positive group, concordance between both tests was 100%. In contrast, in the CC-negative group concordance was 95%, and positive BTH results could be attributed to other gastrointestinal pathologies in two patients. BTH had 100% negative predictive value, 88% positive predictive value, 100% sensitivity and 95% specificity, as compared to genetic testing. **Conclusions**. In carriers of the CC-genotype, BTH and genotyping correlate perfectly, and the genetic test provides an unambiguous result. In BTH-positive individuals with a negative genetic test there is good reason to suspect secondary causes of lactase deficiency.

Key words

Breath test - lactase - lactose intolerance – single nucleotide polymorphism.

Diagnostic Accuracy of IgA anti-Tissue Transglutaminase in Patients Suspected of Having Coeliac Disease in Iran

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Abstract

Background and aim. As there are little data about the sensitivity of the IgA anti-tissue transglutaminase (IgA anti-tTG) antibody test in the clinical practice setting, we evaluated the sensitivity of this serologic test in a group of patients who were suspected of having coeliac disease and had serologic testing performed at commercial laboratories. **Patients and methods.** The study was performed at Poursina Hakim Research Institute in Isfahan-Iran. A total number of 350 consecutive patients were enrolled in our study. They were divided into 3 groups: classical mode of presentation, atypical mode of presentation and patients with non specific prolonged gastrointestinal symptoms. Upper gastrointestinal endoscopy, histopathologic examination of biopsies from the second part of duodenum and serologic evaluation were performed for every patient. Biopsy specimens were evaluated according to Marsh (1992, revised in 1997). **Results.** The overall sensitivity and specificity of IgA anti-tTG antibody were 38% and 98%. The positive and negative predictive values for the anti-tTG antibodies were 57% and 96%, respectively. The sensitivity was 80% in patients with Marsh IIIC. **Conclusion.** In contrast to other reports suggesting a diagnostic accuracy of more than 90% for anti-tTG antibody in coeliac disease patients, our data showed that we are still far from an ideal screening serologic tool which can rely on the antibody test as the sole way of identifying patients with coeliac disease. This could result in many missed diagnoses, in particular in patients with lesser degrees of Marsh classification.

Key words

Anti-tissue transglutaminase antibody - coeliac disease - duodenal biopsy - sensitivity.

Metabolic Syndrome, Insulin Resistance and Adiponectin Level in Patients with Chronic Hepatitis C

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Abstract

Aims. To assess insulin resistance and adiponectin profile in patients with chronic hepatitis C (CHC), according to the presence or absence of metabolic syndrome (MS). **Patients and methods**. One hundred and fifty-two patients with histologically proven CHC, genotype I were prospectively studied. Parameters of MS according to the IDF criteria were evaluated. Insulin resistance was established by homeostasis model assessment (HOMA-IR]. An index ≥ 2.0 was designated as IR and ≥ 4 as prediabetic state. Serum adiponectin levels were measured by ELISA. **Results**. MS was found in 61.48% of cases. HOMA-IR was significantly higher in patients with CHC and MS vs those without MS (7.88±1.11 vs 4.29 ± 0.5, p=0.023]. Adiponectin levels had an inverse behaviour (9,946.1 ± 5,811 ng/ml vs 13,215.5 ± 815.5 ng/ml, p< 0.001]. By multiple linear regression analysis the independent predictors associated with HOMA-IR ≥ 4 in patients with CHC and MS were visceral obesity, adiponectin levels, activity and degree of steatosis. Only visceral obesity and HOMA-IR were independently associated with adiponectin. A significant negative correlation was established between adiponectin and insulin (r = - 0.169, p=0.003] and between adiponectin and HOMA-IR (r = - 0.188, p=0.02]. **Conclusions.** CHC with MS was associated with a higher insulin resistance and lower adiponectin level. Adiponectin level and insulin resistance were significantly correlated.

Key words

Chronic hepatitis C - metabolic syndrome - insulin resistance - serum adiponectin

Analysis of Histopathological Changes that Influence Liver Stiffness in Chronic Hepatitis C. Results from a Cohort of 324 Patients

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Abstract

Aim. The current study aims to assess the role of the histological parameters in liver biopsy for explaining the variance of liver stiffness, as well as the performance of transient elastography in quantifying liver fibrosis in patients with chronic hepatitis C. **Methods**. 324 consecutive CHC patients were prospectively included in this study. All of them had positive HCV-RNA in serum and had underwent percutaneous liver biopsy for grading and staging the diseases (METAVIR scoring system). All were referred to liver stiffness measurement 1 day prior to biopsy. **Results**. Liver stiffness values were strongly correlated with fibrosis ($r=0.759$, $p<0.0005$). They also correlated with steatosis ($r=0.255$, $p<0.0005$), necroinflammatory activity ($r=0.378$, $p<0.0005$) and hepatic iron deposition ($r=0.143$, $p=0.03$). The univariate regression analysis demonstrated that fibrosis ($R^2=0.610$, $p<0.0005$), activity ($R^2=0.145$, $p<0.0005$) and steatosis ($R^2=0.037$, $p=0.002$) were correlated with liver stiffness. In multiple regression analysis, all three variables independently influenced liver stiffness: fibrosis ($p<0.0005$), activity ($p=0.039$) and steatosis ($p=0.025$). Together they explained 62.4% of the variance of the liver stiffness. The areas under ROC curve for the diagnosis of fibrosis $F\geq1$, $F\geq2$, $F\geq3$, and $F=4$ were 0.936, 0.862, 0.910 and 0.938, for the cut-off values of 4.9 kPa, 7.4 kPa, 9.1 kPa and 11.85 kPa respectively. **Conclusions**. Transient elastography is a useful method for chronic hepatitis C assessment. Fibrosis is the main predictor of liver stiffness, but activity and steatosis also influence liver stiffness.

Key-words

Chronic hepatitis C - noninvasive - fibrosis - transient elastography - liver stiffness.

Pegylated Interferon α-2a and Ribavirin Combination Therapy in HCV Liver Transplant Recipients. Experience of 7 Cases

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Abstract

Background: Hepatitis C virus (HCV) related cirrhosis represents the leading indication for liver transplantation (LT) worldwide and HCV reinfection is the rule among transplant recipients. Combination therapy with interferon and ribavirin is the treatment of choice for established recurrent hepatitis C. **Aim:** To evaluate the efficacy and safety of the combination of pegylated interferon α-2a and ribavirin in LT recipients with histological recurrence of hepatitis C. **Methods**: Seven LT recipients with chronic hepatitis C recurrence were treated with peginterferon α-2a with an initial intended dose of 180 μg/week and an intended dose of ribavirin 800-1000 mg/day for at least 12 months and followed-up for at least 24 weeks. **Results:** Early virological response rate was 57.1%. Three patients (42.8%) had end of treatment virological response and all had also sustained viral response (SVR). Five patients had end of treatment biological response, out of which 4 had also sustained biochemical response. Three patients had both SVR and sustained biochemical response. Four patients had end of treatment histological response, out of which 3 patients had also SVR. Cytopenia was the most common adverse event: anemia (57.1%), leucopenia/neutropenia (71.4%), thrombocytopenia (42.8%). **Conclusion:** Combination of pegylated interferon and ribavirin can be safely and successfully used in liver transplant recipients.

Key words

Liver transplantation - recurrent hepatitis C - antiviral therapy

18F-FDG Positron Emission Tomography CT (FDG PET-CT) in the Management of Pancreatic Cancer: Initial Experience in 12 Patients

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Abstract

Introduction. Staging and restaging of pancreatic malignancy can be demanding. Often, there are liver lesions seen on diagnostic CT suspicious for secondary deposits. Positron emission tomography (PET)-CT may have a great potential in confirming or ruling out actual malignancy in those areas. **Methods** We prospectively studied 12 pancreatic adenocarcinoma patients, who had undergone PET-CT imaging as part of their staging or restaging process. Imaging was performed after intravenous administration of 10 mCi F-18 FDG. Results were compared with CT, histopathological findings and/or clinical follow up. **Results**. PET-CT correctly identified 11 lesions and ruled the absence of disease in 4 out of 4 patients (PPV 92%, NPV of 100%, and accuracy 94%), compared to CT which had (PPV 79%, NPV 50% and accuracy 75%). CT identified 4 metastatic liver lesions in 12 patients of which 3 were actually benign processes. **Conclusion**. FDG-PET detects pancreatic malignancy and metastatic disease with higher accuracy than conventional CT. The ability of PET-CT to rule out or correctly identify metastases greatly enhances the physician's decision-making process to choose the right therapeutic intervention.

Key words

PET scan - pancreatic cancer - CT scan - PET-CT scan - liver metastases

The Culture Site of the Gallbladder Affects Recovery of Bacteria in Symptomatic Cholelithiasis

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Abstract

Aim. Traditional methods for bile culturing may miss a large number of underlying bacterial infections that could lead to acute or chronic cholecystitis. **Aim**: to evaluate possible differences regarding the site of material collection and thus to detect the most suitable sample site for gallbladder culture. **Methods.** A cohort of 137 patients with symptomatic cholelithiasis was enrolled. After surgical excision of the gallbladder, bile cultures were separately performed from fundus, body and neck. Identification of bacteria as well as computation of mean bacterial concentrations were performed with standard microbiological techniques. Wilcoxon's paired and Chi-square tests were used for comparison between continuous and discrete parameters, respectively. **Results.** Thirty-one patients (22.6%) demonstrated at least one positive culture sample. Positivity was 31/31 (100.0%) in neck samples, 20/31 (64.5%) in body and 13/31 (41.9%) in fundus samples ($P<0.001$). The microorganisms identified were *Escherichia coli* (14 cases) and *Enterococcus faecalis* (10 cases), followed by *Staphylococcus aureus* (3 cases), *Pseudomonas aeruginosa*, *Enterococcus faecium*, *Enterobacter aerogenes* and *Enterobacter cloacae* (1 case each). Mean bacterial concentrations in positive samples derived from the neck (272.2 ± 187.5) were higher ($P<0.01$) when compared to those derived from both the body (38.2 ± 28.7) and the fundus (12.5 ± 11.3). Mean bacterial concentrations in positive samples derived from the body were higher ($P<0.01$) than those derived from the fundus. **Conclusion**. The neck of the gallbladder hosts the biggest bacterial load in comparison with the body and the fundus. This difference might be attributed to the presence of Rokitansky-Aschoff sinuses, which is the main histological characteristic of the region.

Key words

Cholelithiasis - bacterial infection - bile.

Two Stage Endoscopic Approach for Management of Choledocholithiasis during Pregnancy

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Abstract

Background and aim. Management of choledocholithiasis during pregnancy is difficult. The aim of this study was to evaluate the safety and efficacy of managing common bile duct (CBD) stones during pregnancy using a two-stage procedure without any fetal radiation exposure. **Patients and methods**. Eleven consecutive pregnant women treated endoscopically for choledocholithiasis between 1996-2005, at a tertiary referral center, were included in this study. All the patients were treated by biliary sphincterotomy and stenting without any fluoroscopy or ultrasound assistance during pregnancy and definitive ERCP and stone clearance after delivery. Patients were followed at one week and were asked to come for definitive treatment after delivery. **Results**. All 11 patients were experiencing pain and jaundice while two patients had cholangitis. Abdominal ultrasound revealed dilated CBD in all patients and stones in 8 patients. Every patient demonstrated marked relief after the first stage procedure without any complication. ERCP after delivery revealed no CBD stones in one patient, 5-8 mm size stones in 8 patients and large stones (>15mm) in two patients. One patient with large CBD stones required mechanical lithotripsy while another required surgery. CBD was cleared in 8 patients with small stones. Long-term fetal and maternal outcome was good in all the patients. **Conclusion**. A two stage approach consisting of initial sphincterotomy with stenting without fluoroscopy during pregnancy followed by definitive ERCP after delivery seems to be a justified approach. This is the best most definitive way of avoiding radiation exposure to the fetus.

Key words

Choledocholithiasis - pregnancy - endoscopic management.

REVIEWS

Noninvasive Biomarkers for the Screening of Fibrosis, Steatosis and Steatohepatitis in Patients with Metabolic Risk Factors: FibroTest-FibroMax™ Experience

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Introduction

Nonalcoholic fatty liver disease (NAFLD) is characterized by hepatic steatosis occurring in those who do not consume high amounts of alcohol. The prevalence of NAFLD is high in the general population with metabolic risk factors and insulin resistance being mainly associated with overweight, diabetes, hyperlipidemia and hypertension [1, 2]. Two histological patterns of NAFLD have been described: fatty liver alone and, in a minority of patients, necroinflammatory form of NAFLD known as non-alcoholic steatohepatitis (NASH) that may progress to cirrhosis and hepatocellular carcinoma [1]. Although confirmation of the diagnosis of NAFLD can be achieved by imaging methods, they do not provide data on staging the disease (steatohepatitis and fibrosis), which until recently required a liver biopsy for confirmation. Due to the high prevalence of NAFLD in at risk populations [1], the limitations of biopsy [3, 4] and the developing of reliable noninvasive blood tests [5-8], liver biopsy should no longer be considered mandatory as first-intention screening of liver lesions [9, 10].

Neuroendocrine Deregulation of Food Intake, Adipose Tissue and the Gastrointestinal System in Obesity and Metabolic Syndrome

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Abstract

Obesity is an excess of fat mass. Fat mass is an energy depot but also an endocrine organ. A deregulation of the sympathetic nervous system (SNS) might produce obesity. Stress exaggerates diet-induced obesity. After stress, SNS fibers release neuropeptide Y (NPY) which directly increases visceral fat mass producing a metabolic syndrome (MbS)-like phenotype. Adrenergic receptors are the main regulators of lipolysis. In severe obesity, we demonstrated that the adrenergic receptor subtypes are differentially expressed in different fat depots. Liver and visceral fat share a common sympathetic pathway, which might explain the low-grade inflammation which simultaneously occurs in liver and fat of the obese with MbS. The neuroendocrine melanocortinergic system and gastric ghrelin are also greatly deregulated in obesity. A specific mutation in the type 4 melanocortin receptor induces early obesity onset, hyperphagia and insulin-resistance. Nonetheless, it was recently discovered that a mutation in the prohormone convertase 1/3 simultaneously produces severe gastrointestinal dysfunctions and obesity.

Key words

Obesity - sympathetic nervous system - metabolic syndrome - adrenergic receptors - prohormone convertase 1/3 - type 4 melanocortin receptor

CASE REPORTS

Hepatobiliary Cystadenoma: a Report of Two Cases

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Abstract

We report two cases of hepatobiliary cystadenoma. *Case 1*. A 58-year-old male presented with dull abdominal pain and recurrent jaundice. Abdominal echo revealed biliary tracts dilatation; ERCP revealed amorphous filling defect inside the dilated CBD, a cystic tumor in the left lobe communicated with bile duct was disclosed by MRI/MRCP. He received left lobectomy and microscopic findings proved hepatobiliary cystadenoma. *Case 2.* Abdominal ultrasound detected a huge cystic tumor over the left hepatic lobe in a 69-year-old male. Abdominal CT revealed a large cystic mass lesion over the left hepatic lobe with septations and multiple papillary projections. A liver biopsy was performed and microscopic findings proved biliary cystadenoma. An abdominal ultrasound 6 months later revealed intrahepatic spread of cystadenocarcinoma over both lobes.

Hepatobiliary cystadenoma is a rare benign cystic tumor of the liver. It usually occurs in middle-aged women and can undergo malignant change and become lethal. It is frequently misdiagnosed and should be suspected when a uni- or multilocular cystic lesion with papillary infoldings is detected in the liver by CT or ultrasound. ERCP/MRCP have a role in pre-operative evaluation. Elevated serum and cystic fluid tumor markers CA19-9 are only seen in some patients; cystic fluid cytology does not provide adequate diagnostic aid. Its morphologic features maybe confused with biliary papillomatosis or IPMN of bile duct. Its prognosis is excellent after complete resection.

Key words

Hepatobiliarycysta denoma - hepatobiliary cystadenocarcinoma - hepatic cystic tumor - IPMN - biliary papillomatosis - obstructive jaundice.

Primary MALT Lymphoma of the Gallbladder. Case Report

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Abstract
Primary lymphomas of mucosa associated lymphoid tissue (MALT) are exceedingly rare. We report the case of a 51 year old female diagnosed with primary MALT lymphoma of the gallbladder after cholecystectomy. Further staging workup was negative for metastatic disease. When the disease is localized to the gallbladder, primary MALT lymphomas of the gallbladder carry an excellent prognosis, and surgical resection is curative in the majority of cases.

Key words
Gallbladder - MALT lymphoma - NH lymphoma - prognosis

Prolonged Treatment with Interferon Alpha and Peginterferon Induces Rheumatoid Artrhitis Syndrome and Erythema Nodosum

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Abstract

The antiviral treatment of chronic C hepatitis has improved significantly over the past decade with the introduction of interferons (IFNs), and more recently, pegylated IFNs. Up to two-thirds of all patients treated with pegylated IFN combined with ribavirin can now achieve viral eradication if treated according to current guidelines. Despite this success rate, hematological, immunological, rheumatological and dermatological side effects have been reported in chronic hepatitis C patients treated with IFN-alpha. The subjects of this report are two young females with chronic hepatitis C, who developed rheumatoid syndrome and/or erithema nodosum during antiviral treatment with IFN-alpha or pegylated IFN combined with ribavirine.

Key words

Interferon alpha - peginterferon - chronic hepatitis C - rheumatoid arthritis syndrome - erythema nodosum.

Synchronous Occurrence of Advanced Adenocarcinoma with a Stromal Tumor in the Stomach: A Case Report

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Abstract

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal neoplasms of the digestive tract. Synchronous occurrence of a gastrointestinal stromal tumor with a tumor of different histogenesis is very rare and has been documented in the literature mainly in case reports. We present the case of a 78-year old female patient who underwent surgery for an advanced gastric carcinoma during which a gastric stromal tumor was incidentally discovered. A review of the literature is also conducted on the extremely rare synchronous occurrence of malignant tumors of different histogenesis in the stomach.

Key Words

Gastric adenocarcinoma - gastrointestinal stromal tumor - synchronous occurrence

CLINICAL IMAGING

Intraductal Ultrasonography for the Assessment of Preoperative Biliary and Pancreatic Strictures

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Abstract

Diseases of the biliary and pancreatic ducts are often difficult to diagnose. Although transcutaneous ultrasonograpy, computer tomography and magnetic resonance greatly improved in performance, two major problems have not been completely solved yet: first, the differentiation of malignant and benign bile duct strictures, and, second, the assessment of the resectability of carcinomas underlying biliary strictures. Ultrasound probes can be inserted through the working channel of the duodenoscope and passed selectively both into the biliary and pancreatic ducts. Ultrasound frequencies of 20 or 30 MHz enable a penetration of up to 2 cm and a resolution of 0.07 to 0.18 mm. The main clinical indication for intraductal ultrasonography of the biliary tract is obstructive jaundice, which requires assessment of bile duct strictures and local tumor staging. Miniprobes can contribute to the differential diagnosis of strictures localized in the main pancreatic duct, and also to localizing small endocrine tumors. Small tumors of the papilla of Vater can be staged before a possible endoscopic resection. Feasibility of the method is excellent in expert hands with almost no added morbidity.

Key words

Intraductal ultrasonography - biliary stricture - pancreatic duct stricture.

Spiral Computed Tomography and Magnetic Resonance Angiography Evaluation in Budd Chiari Syndrome

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Abstract

Budd-Chiari syndrome is caused by the obstruction of the hepatic venous outflow at the level of the hepatic venules, large hepatic veins, and inferior vena cava up to the confluence with the right atrium. When it is untreated, the mortality rate for patients is high. Because the clinical presentation of this syndrome is nonspecific, imaging investigation - computed tomography and magnetic resonance - are important diagnostic steps. Contrast-enhanced multiphase spiral computed tomography (CT) and magnetic resonance (MR) angiography permits morphologic and functional assessment of parenchymatous liver changes in this particular entity.

In this review, we present the spectrum of vascular and hepatic parenchymal abnormalities in Budd-Chiari syndrome observed on multiphase contrast enhanced spiral CT and MR angiography.

Keywords

Budd Chiari syndrome - spiral computed tomography - magnetic resonance angiography