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Abstract

Background: Gastroesophageal reflux disease (GERD) is a chronic condition that affects a large proportion of population. The aim of our study was to determine what percentages of patients with persistent heartburn on acid suppressive therapy have evidence of reflux disease while off acid suppressive therapy. Methods: In a prospective study 48 patients with refractory heartburn from Taleghani Hospital were enrolled who had been on a double dose of proton pump inhibitor (PPI) for 8 weeks without improvement. Because of low index of suspicion for GERD as an etiology, all the patients underwent 24h pH-metry while off PPI. The variables of pH-metry such as the fraction time of pH <4 were evaluated by comparing to normal volunteers. Results: The mean “number of acid refluxes” was 49.98 in upright position and 6.29 in supine position. The mean “longest acid reflux” duration was 2.98 minutes in upright and 3.13 minutes in supine position. The total time fraction of pH <4 was 2.97% in upright position, 1.2 % in supine position and 2.74% in postprandial state. The mean DeMeester score was 10.06 (SD=10.48). However, the difference in the total fraction of time with pH <4 was not significant. Conclusion: Our study showed that most of the patients with refractory heartburn did not have acid reflux. Patients with refractory heartburn often do not have evidence of reflux disease on pH monitoring, thus evaluating these patients should be performed while on acid suppressive therapy (using impedance-pH monitoring) in order to clarify the relationship between symptoms and acid and non-acid reflux.

Keywords

Interactions between Symptoms and Motor and Visceral Sensory Responses of Irritable Bowel Syndrome Patients to Spasmolytics (Antispasmodics)

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Abstract

Aim: to evaluate and correlate the symptomatic, motor and sensory responses to two widely used categories of spasmolytic agents in irritable bowel syndrome (IBS). Methods: 118 patients with IBS, diagnosed by Rome II criteria and 45 healthy individuals were studied. In the IBS subjects, pain severity, as well as the sensory response to rectal balloon distention and rectal and sigmoid motility, were studied at baseline and after two weeks therapy with either oral buscopan (20 mg three times a day, n=37), a buscopan suppository (30 mg once daily, n=21), oral drotaverine (80 mg three times a day, n=30), calcium gluconate tablets (one three times a day, n=16) as a control for oral agents, or calendula suppository (once daily, n=14) as a control for those who received a suppository. Results: Buscopan, whether administered as a tablet or a suppository, produced a significant reduction in pain scores among IBS patients with predominant diarrhea. No significant differences were evident among other IBS subgroups or in response to drotaverine. None of the interventions had any effect on any of the parameters of rectal or sigmoid motility studied. However, both buscopan and drotaverine led to a significant augmentation of the rectal threshold for discomfort/pain among IBS patients with predominant diarrhea [21.78±2.8 vs 39.60±2.4 (p<0.05), 20.5±2,8 vs 36.84±3.8 (p<0.05) and 22.18±2.8 vs 36.9±2.42 (p<0.05) for oral buscopan, rectal buscopan and oral drotaverine, respectively]. Conclusion: We conclude that the clinical benefits of supposed spasmolytic (anti-spasmodic) agents may relate more to effects on visceral sensation than motility.

Key words

The Role of Serum Chromogranin A in Diarrhoea Predominant Irritable Bowel Syndrome

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Abstract

Background & Aims: Elevated serum chromogranin A (CgA) levels have been reported co-incidentally in a small group of irritable bowel syndrome (IBS) patients (n=19). Our aim was to ascertain the prevalence of elevated CgA in diarrhoea predominant Rome II IBS (D-IBS) patients and investigate if this could be a marker for octreotide therapy. Methods: Patients with Rome II D-IBS were recruited prospectively and investigated as per British Society Guidelines including serial CgA levels (u/l). Patients with refractory symptoms and elevated CgA were considered for further investigation +/- octreotide therapy. Results: 219 patients were recruited (68% females, mean age 45 years). 81% (n=177) of IBS patients had normal CgA levels (0-20u/l). Whilst 12.3% (n=27) had values between 20-60u/l, 6.8% (n=15) had CgA levels >60u/l; 96% (26/27) with initial CgA level of 20-60u/l had repeated CgA levels which normalised. One patient (3.7%) had a gastric adenocarcinoma. In the 15 patients with elevated CgA levels >60u/l, 8 normalised on repeated testing. In the other 7, there were no cases of carcinoid, n=1 gastric leiomyoma, n=1 rectal tumour and 4 patients had persistently elevated CgA levels but with improvement of symptoms. In one patient, octreotide was commenced which resulted in normalisation of CgA and symptoms. Conclusion: CgA levels appear to be transiently elevated in D-IBS. Future work assessing CgA in patients with refractory D-IBS may potentially identify individuals who will benefit from octreotide therapy.

Keywords
Diarrhoea predominant – irritable bowel syndrome – serum chromogranin A
Assessment of Small Intestinal Permeability using $^1$H-NMR Spectroscopy

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Abstract

**Background:** Evaluation of small intestinal permeability (SIP) is based on the estimation of the urinary excretion ratio of a large and a small molecule (lactulose and mannitol, $L/M$) after oral administration. We evaluated SIP using $^1$H-NMR spectroscopy. **Methods:** In-vitro experiments on known concentration of mannitol and lactulose solutions were performed to measure accuracy and precession of quantification using $^1$H-NMR spectroscopy. Eighteen patients with malabsorption syndrome (MAS) and 28 healthy subjects (HS) underwent SIP evaluation using $L/M$ excretion ratio over 6-h after oral administration of 15 mL (10g) lactulose and 5 g mannitol using $^1$H-NMR spectroscopy and trimethyl silyl propionic acid as external reference and for quantification. **Results:** Median errors of estimation of mannitol and lactulose were 5% (range 1.2 to 5) and 1.3% (range 0.2 to 1.3), respectively in-vitro. Patients with MAS excreted higher quantity of lactulose in urine than HS (median 0.33 mmol vs 0.12, 0 to .676 mmol, p<0.008). There was a trend towards lower urinary excretion of mannitol in patients with MAS than HS (median 3.58, range 0.61 to 15.77 mmol vs. 3.82, 1.34 to 16.42 mmol, p = ns). $L/M$ ratio was higher among patients with MAS as compared to HS (median 0.1172 vs 0.045, p< 0.002). A cut-off value of $L/M$ excretion ratio by receiver-operating characteristic (ROC) curve of 0.049 had a sensitivity and specificity of 72% and 61%, respectively; a cut-off value of 0.078 had a specificity of 90% but low sensitivity (67%). Area under ROC curve was 0.77. **Conclusion:** $^1$H-NMR spectroscopy is an analytical tool for assessment of SIP with reasonable sensitivity and specificity.

**Key words**

Malabsorption syndrome - intestinal function - inflammatory bowel disease - lactulose mannitol ratio.
Introduction of Cytogenetic Tests in Colorectal Cancer Screening

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Abstract

Background and aim. The existing tests practiced on a large scale in colorectal cancer (CRC) screening do not fully accomplish the goal of best specificity and sensitivity or either an optimal cost/efficiency ratio. We aimed to analyze genetic mutations diagnosed in the DNA of exfoliated cells in the stool of the patients diagnosed with CRC through screening. We also aimed to demonstrate the similarity between the detected mutations in tumor samples and in exfoliated cells in the stool in order to prove the reliability of these cytogenetic tests, so that they could be introduced in CRC screening program. Methods. We studied 200 patients diagnosed with CRC from whom we prelevated biopsy and stool samples. Samples were submitted to genetic analysis through denaturing gradient polyacrylamide gel electrophoresis method, and through polyacrylamide gel electrophoresis method for the heteroduplex analysis. Analyzed genes were APC, COL11A1, MLH1, MSH2 and MSH6. The chromosomal study was carried out using the PRINS technique. Results. We discovered mutations in the APC gene (exons 4, 9, 13, and 15c) and COL11A1 gene (exon 54). Our chromosomal study detected instability of chromosomes 1, 7, 9, 20, and in 10 achrocentric chromosomes. Conclusions. Our results plead for the implementation of proposed cytogenetic tests in CRC screening programs.

Key words

Colorectal cancer – tumor biopsy DNA – stool DNA, noninvasive screening tests.
Clinical and Pharmacokinetics Study of Oxaliplatin in Colon Cancer Patients

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Abstract

Aim: to evaluate the therapeutic efficacy of oxaliplatin and to analyze the pharmacokinetics of both ultrafiltrable (free) and protein–bound platinum in patients with metastatic colon cancer.

Method: 60 patients with stage IV colon carcinoma received 4-6 (mean 4.5) cycles of oxaliplatin based combination chemotherapy. Response rate, progression-free survival (PFS) and toxicity were evaluated. The pharmacokinetics of oxaliplatin was evaluated in 8 patients who were given 85 mg/m² or 130 mg/m² using an infusion time of 2-4 h. Pharmacokinetic analysis was performed on blood, plasma and plasma ultrafiltrable by ICP-MS (Inductively Coupled Plasma Mass Spectrometry).

Results: Overall response rate (complete and partial) occurred in 33 (55%) patients. The median time of progression was 9.3 months. Cumulative neurotoxicity, vomiting and diarrhea, myelosuppression appeared in 32.3%, 21.3%, and 39.4% patients, respectively. The mean Cmax and AUC 0-24 of oxaliplatin increased in a dose-related manner. The pharmacokinetics of platinum after oxaliplatin administration was triphasic characterized by a short initial distribution phase and a long terminal elimination phase. The clearance of ultrafiltrable platinum was relatively high and the clearance of platinum from plasma and blood cells was relatively low, which is probably a reflection of the covalent binding of platinum to these matrices.

Conclusion: Oxaliplatin is active and well tolerated in patients with advanced colon cancer. With a relatively low interpatient variability, it is eliminated triphasically and the mean Cmax and AUC 0-24 increases in a dose-related manner. These results provide a scientific basis for the safe and effective use of oxaliplatin in the clinic.

Key words

HCV Genotype 1 is Almost Exclusively Present in Romanian Patients with Chronic Hepatitis C

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Abstract

Aim: To investigate the HCV genotype distribution in Romania in the first national study, to establish the correlations with epidemiological, biochemical, virological and histological features and to compare our results with those from neighboring countries. Patients and methods: Two distinct groups of patients and two methods were used: 153 patients in the frame of ACHIEVE study with genotyping and subtypes determination (Versant HCV genotype 2.0 assay) and 461 patients in the frame of an Epidemiological National Multicenter Study having only genotype determination with a commercial kit (Roche Molecular System). Epidemiological, biochemical, virological and histological features were investigated only in the ENMS group. Results: Genotype 1b was found in 93.46% (ACHIEVE study) and genotype 1 (without subtype identification) in 99.13% of patients (ENMS study). Percutaneous routes of transmission were found in 85.9% of cases. The prevalence of HCV infection increased with age. A high viral load (≥ 600,000 IU/ml) was found in 67.9% of patients, especially those older than 40 years. Significant fibrosis ≥ F2 was present in patients older than 40 years (70.9%). There were no correlations between HCV-RNA levels and histological features or between ALT levels and METAVIR activity or fibrosis scores. A similar homogeneity of HCV genotype distribution has been reported for Moldavia (96%) and Hungary (94.5%). Conclusions: Type 1 HCV genotype was found almost exclusively in Romanian patients with chronic hepatitis C by two different methods of investigation. The pattern showed by this distribution in Romania and some neighboring countries suggests an epidemic profile of HCV infection.

Key words

High Sustained Virological Response Rate to Combination Therapy in Genotype 1 Patients with Histologically Mild Hepatitis C

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Abstract

**Background:** Patients with mild hepatitis C have a significant risk of disease progression at medium- and long-term follow-up and should be considered for antiviral therapy. **Aim:** To evaluate the rate of sustained viral response (SVR) and predictive factors of SVR in HCV genotype 1 patients with mild hepatitis C (fibrosis stage F0/F1) treated with combination antiviral therapy. **Methods:** 260 naïve patients were followed-up during 72 weeks in three referral hepatology centers between 2004 and 2006. Univariate and multivariate logistic regression analysis was conducted. **Results:** Early virological response was 88.1% and SVR was 74.2%. In the univariate analysis, SVR was associated with young age (p=0.001), very low (≤400,000 IU/mL) baseline viremia (p=0.03) and high aminotransferase levels (p=0.04) and was not associated with gender, body mass index, inflammatory activity, steatosis, ribavirin and peginterferon dose changes, premature cessation of therapy. Multivariate analysis identified the following independent predictors of SVR: age <50 years (p=0.0009), viral load ≤400,000 IU/mL (p=0.03) and aminotransferase level >2 times normal value (p=0.02). **Conclusions:** Genotype 1 HCV patients with mild hepatitis have a high rate of SVR, similar to genotype non-1. Young age, very low viremia and significant hepatocytolysis are independent predictors of SVR in patients with mild hepatitis.

**Key words**

Mild hepatitis C – antiviral therapy – sustained viral response.
Transient Elastographic Evaluation of Subjects Without Known Hepatic Pathology: Does Age Change the Liver Stiffness?

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Abstract

Background and aim: Chronic liver diseases are investigated through invasive (liver biopsy) or non-invasive (FibroScan or FibroTest) methods. Recently the non-invasive methods have become more and more popular. The aim of this paper is to evaluate the liver stiffness (LS) measured by transient elastography in individuals without known hepatic pathology (“normal” subjects) and to see if it is influenced by age. Material and method: We examined a group of “normal” subjects by means of a FibroScan device (EchoSens, France). In each patient we performed 10 valid measurements and a median value was calculated by the device. The subjects were individuals without known hepatic pathology: healthy volunteers or patients from departments other than Gastroenterology in our hospital. Results: We evaluated 152 “normal” subjects (87 women and 65 men, mean age 45.3±17.6 years). The mean value of LS in “normal” subjects was 4.8±1.3 kPa, ranging from 2.3 to 8.8 kPa. The mean values of LS in age subgroups were: 18-29 years – 5±1.3 kPa; 30-39 years - 4.5±1.2kPa; 40-49 years – 5±1.1kPa; 50-59 years – 4.7±1.2kPa; 60-69 years – 5±1.3kPa; >70 years – 4.7±1.4kPa. There were no statistically significant differences between the mean values of LS in various age subgroups (p=0.5263). Conclusions: The mean value of LS measured by transient elastography in “normal” subjects was lower than 5 kPa. Age does not modify the LS.

Key words

Liver stiffness – transient elastography – normal subjects.
Perihepatic Adipose Tissue Thickness: a New Non-Invasive Marker of NAFLD?

Flavio Lirussi¹, Nicola Vitturi¹, Lorenzo Azzalini¹, Serena Orando¹, Rocco Orlando¹, Mario Plebani², Giuseppe Realdi¹

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Abstract

**Background and Aims:** Several non-invasive markers have been proposed to assess liver damage in NAFLD. We measured by ultrasound (US) the perihepatic adipose tissue thickness (PATT), i.e. the thickness of the fat between the abdominal muscular layer and the hepatic surface, in addition to waist circumference, BMI, biochemistry and serum adipokines, to predict the severity of liver damage in NAFLD. **Methods:** 63 NAFLD patients and 45 controls were studied. PATT and US steatosis score were assessed in all patients. Histology was obtained in those with an US steatosis score ≥ 2. **Results:** PATT was 13.5±4.1 mm in NAFLD vs 8.0±4.1 in controls (p<0.001). A PATT value of 11.2 mm seems to represent a cut-off below which NAFLD is unlikely. Test sensitivity, specificity and the area under the ROC curve were 100%, 50% and 75%, respectively, suggesting a good discrimination between patients with non-NASH and those with NASH or borderline NASH. In addition, PATT strongly correlated with waist circumference (p<0.001). Both PATT and waist circumference correlated with US steatosis, HOMA-IR, TNF-α, IL-6 and leptin. Based on a multiple logistic regression analysis, waist circumferences ≥ 110, 113 and 122 cm were associated with a probability ≥ 50% of abnormal HOMA-IR, TNF-α and leptin values, respectively. **Conclusion:** PATT and waist circumference could represent non-invasive markers predicting the severity of liver damage in NAFLD.

**Key Words**

Ultrasound – fatty liver – perihepatic adipose tissue thickness – adipokines – metabolic syndrome.
Postcholecystectomy Syndrome - an Algorithmic Approach

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Abstract

Background and Aim: The postcholecystectomy syndrome includes a heterogeneous group of diseases, usually presenting as abdominal symptoms following gallbladder removal. The clinical management of these patients is frequently without an evidence-based approach. Method: We evaluated 80 patients with postcholecystectomy problems consecutively admitted during a period of 36 months. The liver function tests (LFTs) assessment and transabdominal ultrasound (TUS) were followed by endoscopic ultrasound (EUS). Endoscopic retrograde cholangio-pancreatography (ERCP) was then performed depending on the results. With knowledge of the final diagnosis, the probable evaluation and outcomes were reassessed assuming that ERCP would have been performed as the initial procedure. Final diagnosis was confirmed by a combination of imaging findings, as well as clinical follow-up of 6 months. Results: In 53 patients biliary or pancreatic diseases were diagnosed: common bile duct stones, chronic pancreatitis, pancreatic cancer, papillary tumors, cholangiocarcinoma, insufficient cholecystectomy or sphincter of Oddi dysfunction. The other 27 patients had non-biliary symptoms (dyspepsia, IBS, etc.) and were consequently managed according to the symptoms. The sensitivity and specificity of EUS were high in the subgroup of patients with biliary or pancreatic symptoms (96.2% and 88.9%) and helped to indicate subsequent ERCP. Conclusion: An algorithmic approach which used EUS for the initial evaluation of the patients with postcholecystectomy problems decreased the number of ERCPs by 51%, having as a consequence a decreased morbidity and mortality in this group of patients.

Key words
Complications Related To Endoscopic Retrograde Cholangiopancreatography: A Comprehensive Clinical Review

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Abstract

Endoscopic retrograde cholangiopancreatography (ERCP) is one of the most commonly performed endoscopic procedures. It provides the treating physician with both diagnostic and therapeutic options. The recent shift towards interventional uses of ERCP is largely due to the emergence of advanced imaging techniques, including magnetic resonance cholangiopancreatography and ultrasonography. With over 500,000 ERCP procedures performed yearly in the United States alone, it is important that all medical and surgical practitioners be well versed in indications, contraindications, potential complications, benefits, and alternatives to ERCP. The authors present an in-depth review of ERCP-related complications (pancreatitis, bleeding, perforation, etc) as well as special topics related to ERCP (periprocedural antibiotic use, performance of intraoperative ERCP, performance of ERCP during pregnancy, etc).

Keywords

Gastric and Colonic Mantle Cell Lymphoma - Incidental Discovery

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Abstract

A 65-year old patient, with no medical history, was admitted for lower gastrointestinal bleeding. On clinical examination the patient seemed to be in good health. However the examination was completed with a rectosigmoidoscopy revealing the presence of mucosal erosions, ulcerations, multiple papulae. The histopathological examination raised the suspicion of a colonic lymphoma. Gastric biopsies suggested a gastric MALT type lymphoma associated to the colonic lymphoma, but the immunohistochemical profile corresponded to a mantle cell lymphoma. In spite of the general poor prognosis of mantle cell lymphoma, our patient had a good clinical and endoscopic response to the standard cyclophosphamide, vincristine, prednisone (CVP) therapy. The cases of gastric and colonic mantle lymphoma are rare, the response to therapy is poor; fortunately, our patient had a complete resolution after completion of the six cycles of chemotherapy.

Keywords

Gastric – colonic – mantle-cell lymphoma.
Primary Monophasic Synovial Sarcoma of the Duodenum Confirmed by Cytogenetic Analysis with Demonstration of t(X;18): A Case Report

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Abstract

Synovial sarcoma (SS) is an uncommon malignant neoplasm of the soft tissues. It mainly affects the periarticular tissues of the extremities in young adults, but has been described at nearly all sites; nevertheless, the gastrointestinal tract is an exceptional location. We report a case of a primary synovial sarcoma of the duodenum in a 69-year-old woman. Histological study showed a monophasic pattern. The tumor cells demonstrated diffuse vimentin and Bcl-2 expression, partial EMA expression and focal AE1/3 positivity. The differential diagnosis includes gastrointestinal stromal tumors. Cytogenetic analysis confirmed the diagnosis, with detection of the X;18 translocation. The patient presented postoperative complications and died one month following the intervention.

Key words

Duodenum – synovial sarcoma - fluorescence in situ hybridization.
Biliary Rhabdomyosarcoma Mimicking Choledochal Cyst

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Abstract

A 3-year old male presented with complaints of pruritus, abdominal pain for 3 weeks and jaundice. Stools were acholic. There was jaundice, liver palpable 3 cm below right costal margin, no ascites or palpable masses. Serology revealed albumin 2.9 g/dl; ammonia of 31 mmol/l; elevated conjugated bilirubin, GGT, ALT, AST and alkaline phosphatase; alpha fetoprotein 1.3 ng/ml; BhCG 9.1 IU/; PT 12.3 secs, INR 0.9; negative hepatitis A,B,C serology. CT scan showed a non-calcified heterogeneously enhancing mass centered at the liver hilum. MRCP showed a large heterogeneously enhancing, partially solid mass in the region of the porta hepatic. Liver biopsy revealed patternless proliferation of polymorphic oval to spindled shaped neoplastic cells. There was bile ducts distortion. Immunohistochemistry revealed positivity for vimentin, desmin. These findings were diagnostic for biliary rhabdomyosarcoma. There was no evidence of metastasis. Chemotherapy was initiated. Repeat imaging 6 months after initiation of treatment showed improvement in the degree of intrahepatic ductal dilatation and decrease in tumor bulk size. Rhabdomyosarcoma is the most common malignant tumor of the biliary tree in childhood. It is difficult to diagnose and delayed diagnosis influences the prognosis.

Keywords

Primary Gastric Lymphoma with Florid Granulomatous Reaction

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Abstract

Epithelioid cell granulomas are more commonly seen in Hodgkin’s disease and T cell lymphomas. Rarely florid granulomatous reaction with necrosis may be a prominent feature in lymphoma. To the best of our knowledge, a total of 11 cases of Burkitt’s lymphoma with florid necrotizing granulomas have been reported in the English literature. None of these cases have previously had the stomach involved. Here we report a gastric Burkitt’s lymphoma with florid granulomatous reaction diagnosed following a partial gastrectomy. The initial gastric biopsy showed granulomatous gastritis but the radiological and endoscopic appearance was that of a gastric stromal tumour. We conclude that in the presence of a mass lesion, the finding of epithelioid granulomas should warrant re-biopsy to establish an accurate diagnosis and exclude a concurrent malignant process. Hence, major surgery and postoperative complications can be avoided and appropriate treatment regimen can be initiated.

Key words

The Role of Real-time Contrast-Enhanced and Real-time Virtual Sonography in the Assessment of Malignant Liver Lesions

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Abstract

Contrast enhanced ultrasound has recently been introduced and is recommended in daily practice in many circumstances, mainly for the detection and characterization of focal liver lesions. Also, contrast enhanced ultrasound has the potential of becoming the primary liver-imaging modality, preceding CT or MR, for the diagnosis of hepatocellular carcinoma in patients with cirrhosis, detection of liver metastases in oncology patients and guidance and assessment of the outcome of percutaneous tumor ablation procedure. Recently, a new imaging technique that combines in real-time, transabdominal ultrasound with CT or MR, has been introduced in clinical practice. Real-time virtual sonography uses a magnetic positioning system attached to the ultrasound probe in order to calculate the spatial position and to display both imaging methods in real-time. Benefits include an increased diagnostic confidence, direct comparison of the lesions using different imaging modalities, more precise monitoring of interventional procedures and reduced radiation exposure. We describe the role of real-time contrast-enhanced and real-time virtual sonography in the assessment of malignant liver lesions.

Keywords

Magnifying Endoscopy and Chromoendoscopy of the Upper Gastrointestinal Tract

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Abstract

Magnifying endoscopy has been developed to visualize the microstructure of gastrointestinal surface mucosa and mucosal vascularity. Magnifying endoscopy is starting to play an important role in the diagnosis of upper gastrointestinal diseases: Barrett’s esophagus, atrophic gastritis, Helicobacter pylori-induced gastritis, gastric neoplasm. Chromoendoscopy in conjunction with magnifying endoscopy improves diagnostic accuracy and allows the early detection of premalignant and malignant lesions. Standardization of the procedural methodology and consensus terminology of the mucosal patterns are crucial.

Key words

Magnifying endoscopy – chromoendoscopy – malignant and pre-malignant lesions.