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# Prevalence and Associated Risk Factors of Non-Alcoholic Fatty Liver Disease in Hospitalized Patients

*Corina Radu, Mircea Grigorescu, Dana Crisan, Monica Lupsor, Diana Constantin, Liliana Dina*

## **Abstract**

**Background and aim:** Non-alcoholic fatty liver disease (NAFLD) and metabolic syndrome (MS) have become important health issues in many countries. There is increasing interest in ultrasound-diagnosed NAFLD. The aim of the study was to evaluate the prevalence of NAFLD in hospitalized patients and to determine the metabolic features of ultrasound-diagnosed patients. **Methods:** A number of 3,005 hospitalized patients were prospectively assessed. Subjects were submitted to a standard interview and a chart review was made to note anthropometric (BMI and waist circumference), biochemical and abdominal ultrasonography parameters. MS was evaluated according to IDF criteria. Logistic regression analysis was used to identify independent factors associated with ultrasound-diagnosed NAFLD.

**Results:** The prevalence of NAFLD in the enrolled subjects was 20%. Patients with NAFLD had higher values of BMI and waist circumference. MS was present in 61.09 % of cases with NAFLD. At least one risk factor was observed in 88.41%, and in 14.07% of patients all 5 criteria were fulfilled. The odds ratios of the metabolic disorders in subjects with NAFLD compared with those without NAFLD were higher in the overweight and obese group than in the normal-weight group. Central obesity, hypertriglyceridemia, and elevated blood pressure (for total and the overweight group) were independently associated with NAFLD.

**Conclusion:** The prevalence of ultrasound NAFLD in hospitalized patients was similar to the general population. NAFLD was closely associated with metabolic disorders.

## **Key words**

Non-alcoholic liver disease - prevalence - risk factor - metabolic syndrome - central obesity

## Dynamics of Circulating Microparticles in Liver Transplant Patients

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### Abstract

**Background & Aims.** Microparticles are small membrane vesicles released from the cell plasma membrane, particularly in cell stress, apoptosis and altered cellular viability. Hepatocellular carcinoma (HCC) is a hypervascular neoplasm with high levels of apoptosis and necrosis. We investigated the levels of circulating microparticles of both tumor and endothelial origins in liver transplant patients with hepatitis C (HepC) cirrhosis with and without HCC and compared them with healthy people and patients with partial hepatectomy.

**Methods.** Using immunolabeling of microparticles of different origin and flow cytometry-based enumeration of microparticles, the levels of circulating microparticles were studied in 8 patients with HepC and 8 patients with both HepC and HCC before and within two weeks after the transplant.

**Results.** The initial levels of circulating microparticles were increased in patients with HepC and HCC as compared to patients with HepC alone. They were also increased in liver transplant patients as compared to patients with partial hepatectomy or healthy people. Levels of circulating microparticles were dynamically changing after the transplant, showing an initial increase with a subsequent decrease by the end of the second week after surgery. In some patients with a complicated clinical outcome, the levels of microparticles were continuously increasing after the surgery.

**Conclusion.** The levels of circulating microparticles of endothelial and hepatic origin in liver transplant patients dynamically change after surgery and correlate with the clinical outcome. Perspectively, the levels of circulating microparticles may be used in clinical practice as a marker of the functional status of the transplanted liver.

### Keywords

Circulating microparticles - liver transplant - hepatocellular carcinoma - liver cirrhosis - apoptosis.

## Frequency of Hepatitis G Virus Infection among HIV Positive Subjects with Parenteral and Sexual Exposure

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### Abstract

**Background.** Epidemiological data indicate that Hepatitis G virus (HGV) is transmitted predominantly through parenteral routes, with a high seroprevalence among injection drug users (IDUs), although sexual transmission has also been reported. In this study our objective was to compare the frequency of HGV infection in two groups of HIV-positive patients including IDUs and those with sexual risk of exposure.

**Methods.** Presence of HGV-RNA was analyzed in serum samples from 82 HIV-infected patients including 52 IDUs and 30 cases with sexual (heterosexuals) risk of exposure by reverse transcriptase-nested polymerase chain reaction. Hepatitis B surface antigen (HBsAg), Hepatitis B surface antibody (anti-HBs), Hepatitis C antibody (anti-HCV), alanine aminotransferase (ALT) levels, HIV viral load and CD4 cells count were also tested in all subjects.

**Results.** The overall prevalence of HGV infection was 10.97% in HIV infected patients, with no statistically significant difference between the two groups (13.5% among IDUs vs. 6.7% among the sexual cases). We found a higher frequency of HGV co-infection with HCV in IDUs than in the sexual group (11.5% vs. 3.3%). There was no statistically significant difference between IDUs and the sexual group regarding age, viral load, CD4 cells count, ALT levels and the prevalence of HBV infection.

**Conclusion.** The overall prevalence of HGV infection was relatively high in HIV infected patients. HGV-RNA was found more frequently in patients with injection drug use than in those with sexual risk of exposure.

### Key words

Human immunodeficiency virus (HIV) - hepatitis G virus(HGV) - injection drug users (IDUs).

## Radial Endoscopic Ultrasonography in the Preoperative Staging of Pancreatic Cancer

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### Abstract

**Background.** Endoscopic ultrasonography (EUS) is a diagnostic method that aims to detect and stage tumors of the pancreas more accurately. It has a high predictive role regarding tumor resectability.

**Aim.** The present paper aims to assess the diagnostic accuracy of radial EUS in the staging of pancreatic cancer as well as the role of EUS to predict tumor resectability.

**Material and methods.** 30 patients (22 males, 8 females, mean age  $61 \pm 12$  years) with pancreatic masses staged by both radial EUS and surgery (17 patients with intraoperative exploration and 13 with pathological examination of surgical specimens) and with histologically proved adenocarcinoma were included in the study. Surgical examination was indicated in patients with pancreatic masses evidenced by imaging methods other than EUS, without distant metastases proved preoperatively, and without taking into consideration the staging obtained by EUS. Resectability criteria for pancreatic tumors as assessed by EUS were invasion of superior mesenteric artery or invasion of celiac trunk.

**Results.** The accuracy of EUS T staging was 86.6%, that of N staging was 93.3% while that of the vascular invasion was 80%. The accuracy of EUS for predicting tumor stage had a direct impact on the assessment of tumor resectability (83.3%, CI 95%: 81.5- 85.2). It had a sensitivity of 100%, specificity of 75%, PPV of 91.6% and NPV of 100%.

**Conclusion.** The radial EUS of the pancreas is an accurate method for tumor staging. For establishing tumor resectability, association with other imaging methods is advisable for arterial assessment.

### Key words

Pancreatic carcinoma - endoscopic ultrasonography - staging - resectability.

## **Endoscopic Ultrasound Approach of Pancreatic Cancer in Chronic Pancreatitis Patients in a Tertiary Referral Centre**

*Sevastița Iordache, Adrian Săftoiu, Sergiu Cazacu, Dan-Ionuț Gheonea, Daniela Dumitrescu, Carmen Popescu, Tudorel Ciurea*

### **Abstract**

**Background.** A positive correlation between chronic pancreatitis and pancreatic cancer was mentioned, with a risk for cancer development of 2.3 -18.5%.

**Aims.** To assess the frequency of pancreatic cancer in patients with chronic pancreatitis and its correlation with the severity of pancreatitis.

**Methods.** We evaluated 72 consecutive patients with chronic pancreatitis (2003-2005) diagnosed by clinical criteria, endoscopic ultrasound (EUS), computer tomography, and endoscopic retrograde pancreatography. The severity of chronic pancreatitis was assessed by EUS (at least 3 criteria for the positive diagnosis). Diagnosis of cancer was confirmed by cytological (smears provided by EUS-FNA) or pathological examination (specimen after surgery).

**Results.** Pancreatic cancer was found in 17 (23.6%) patients with chronic pancreatitis. In patients with severe and moderate chronic pancreatitis cancer was found in 34% while in patients with mild chronic pancreatitis in 4% ( $p=0.0181$ ). The complications in these patients were: pseudocysts (30.6%), obstructive jaundice (11.1%), diabetes mellitus (2.8%), portal hypertension (2.8%) etc. They were more frequent in the presence of pancreatic cancer. Sensitivity and accuracy of EUS-FNA for the diagnosis of cancer in chronic pancreatitis patients were 50% and 73.7%, respectively.

**Conclusions.** Severity of chronic pancreatitis seems to play an important role in cancer development. Other factors associated with pancreatic cancer were increasing age and complications (such as obstructive jaundice). Due to the low sensitivity of EUS-FNA, patients with a strong suspicion of pancreatic cancer based on imaging tests should be submitted to surgery.

### **Key words**

Pancreatic cancer - chronic pancreatitis – incidence - EUS-FNA.

# Prospective Study on Warfarin and Regional Chemotherapy in Patients with Pancreatic Carcinoma

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## **Abstract**

**Aims:** The aim is to prospectively examine the effect of regional gemcitabine and mitomycin-C with systemic gemcitabine together with warfarin in patients with inoperable pancreatic carcinoma, and compare the effect to systemic gemcitabine alone.

**Methods:** Seventeen patients received 1.25 mg of warfarin daily, gemcitabine 800 mg/m<sup>2</sup> on day 1 and mitomycin-C 8 mg/m<sup>2</sup> on day 2 regionally and gemcitabine 800 mg/m<sup>2</sup> on day 14 peripherally. The cycle was repeated every 4 weeks.

**Results:** Median survival since presentation was 6.8 months, while median total survival was 9.6 months. Excluding the 3 patients who died before receiving any therapy, the median survival since presentation resulted in 10.7 months and the median total survival, 12.7 months. One patient developed bleeding that required transfusion and 2 patients developed anemia (Grades III/IV). Comparing these data to historical controls of large cohorts supports the notion that this regimen offers a viable alternative to systemic gemcitabine alone.

**Conclusion:** A regimen consisting of regional gemcitabine and mitomycin-C with systemic gemcitabine and low-dose warfarin compares favorably to the gold standard of systemic gemcitabine. These data suggest the feasibility of a large prospective study on the use of warfarin and combined regional and systemic chemotherapy in patients with pancreatic carcinoma.

## **Keywords**

Pancreatic carcinoma - warfarin - regional chemotherapy.

## **Propofol Infusion versus Intermittent Meperidine and Midazolam Injection for Conscious Sedation in ERCP**

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### **Abstract**

**Background and aim:** ERCP generally requires longer time than standard endoscopy. Only few studies have shown benefit of intermittent propofol over conventional sedation. This study was conducted to compare satisfaction, recovery score, and recovery/safety profiles for ERCP sedation between continuous infusion of propofol and conventional sedation.

**Patients and methods:** One hundred thirty-four patients with ASA I-III underwent ERCP and were randomly assigned into two groups (n=67 each). Patients underwent propofol sedation or meperidine/midazolam sedation. Supplemental oxygen was offered only when oxygen saturation was lower than 90 %. Oxygen saturation, blood pressure, heart rate, recovery score, times for recovery and satisfaction score after procedure were recorded and analyzed.

**Results:** Average amount of meperidine, midazolam and propofol per each patient were 61.54 ( $\pm$  27.29), 7.80 ( $\pm$  3.73), 299.90 ( $\pm$  146.15) mg, respectively. Time to regain full consciousness in the propofol arm was significantly shorter than in the conventional arm (17.24  $\pm$  5.99 versus 34.25  $\pm$  16.06 min, p<0.001). The rates of desaturation, bradycardia and hypotension in both arms were low and comparable. Propofol provided higher level of recovery scores at 15, 30, 45 and 60 min after the procedure (p < 0.001).

**Conclusion:** Continuous infusion of propofol for ERCP by direction of gastroenterologist yields no difference in the completion rate and adverse profiles when compared with conventional technique but it provides a better recovery profile. The maintainance of appropriate level of sedation by well trained personnel is the key to achieve this success.

### **Key words**

Sedation - ERCP - propofol - midazolam

## Host-Related Predictive Factors for Anastomotic Leakage Following Large Bowel Resections for Colorectal Cancer\*

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### Abstract

**Aim.** To identify the risk, the host-related prognostic factors and their predictive value for anastomotic leakage after colorectal resections following cancer.

**Method.** 993 patients who underwent large bowel resection and primary anastomosis above 12 centimeters from the anal verge, without a temporary or permanent stoma at the Surgical Hospital No.3 (Cluj-Napoca, Romania) were retrospectively reviewed.

**Results.** 32 (3.22 percent) anastomotic leaks were confirmed. Univariate analysis showed that the preoperative variables significantly associated with anastomotic leakage included: weight loss, smoking, cardiovascular disease, lung disease, hypoproteinemia, diabetes, anemia, leukocytosis, presence of two or more underlying diseases. Alcohol use, cerebrovascular disease, bowel preparation, type of anastomosis, tumor location, stage and histology were not significant variables. Hypoproteinemia (total serum protein level  $\leq 6$  g/dl) and anemia (serum hemoglobin level  $\leq 11$  g/dl) remained significant in the logistic regression model. The prognostic role of serum hemoglobin and proteins for the anastomotic leak was assessed using ROC curve analysis. For the cut-off value of serum protein level = 5.5 g/dl, a sensitivity of 61.6 percent and a specificity of 84.2 percent were calculated. The area under the curve was 0.703 (p=0.0024). The area under the curve for serum hemoglobin was 0.616 (p=0.028). A sensitivity of 64.0 percent and a specificity of 64.7 per cent were obtained for a cut-off value of 9.4 g/dl.

**Conclusion.** A serum protein level lower than 5.5 g/dl and serum hemoglobin lower than 9.4 g/dl could be considered as host-related predictive markers for anastomotic leak in large bowel resections for cancer.

### Key words

Anastomotic leak - risk factors - predictive markers.

# The Relationship between Involved Lymph Nodes, Metastatic Nest Diameters and Prognosis in Colorectal Cancer

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## Abstract

**Introduction.** Several studies evaluated the relation between colorectal cancer prognosis and various factors such as: depth of tumor invasion, involved lymph nodes size, counts and locations, metastatic nest expansion. We assessed the prognostic significance of the ratio between metastatic nest and involved lymph node diameter in colorectal cancer cases.

**Methods.** A historical cohort study was conducted on patients with known colorectal cancer and metastatic lymph nodes (Astler Coller's stage C), in whom diagnosis was confirmed at least one year before the study. Less than two months following surgery, patients were treated with the same chemotherapy protocol. Metastatic lymph node sizes were recorded in 63 pathologic samples. Metastatic nest borders were marked using a marker and a 40x magnifying microscope. The greatest metastatic nest to involved lymph node diameter ratio was obtained. The data were analyzed with SPSS analytic software. Actuarial and Kaplan-Meier methods were used to estimate survival. Survival functions were compared by Log rank and Cox regression tests.

**Results.** There was no significant relation between colorectal cancer prognosis and: the greatest involved lymph node diameter, the metastatic nest diameter and the ratio metastatic nest to involved lymph node diameter (p-values in sequence: 0.1, 0.07, 0.2).

**Conclusion.** We found no significant relationship between the colorectal cancer prognosis and the greatest lymph node diameter, the greatest metastatic nest diameter and the greatest metastatic nest to involved lymph node diameter ratio. Further studies are required in order to reach a decisive conclusion.

## Keywords

Colorectal cancer - metastatic nest - lymph node size - prognosis.

## Laparoscopic Cholecystectomy in Elderly Patients

*Alexandros Polychronidis, Sotirios Botaitis, Alexandra Tsaroucha, Grigoris Tripsianis, Anastasios Bounovas, Michail Pitiakoudis, Constantinos Simopoulos*

### Abstract

**Background.** Surgery for cholelithiasis is more common in ageing patients. The use of laparoscopic cholecystectomy (LC) in older patients may pose problems because of the comorbid conditions that are concomitant with advanced age and may increase the postoperative LC complications and the frequency of conversion to open surgery. The purpose of this study was to evaluate the outcome of LC in the treatment of gallstones in the elderly ( $\geq 75$  years old).

**Methods.** A retrospective study was conducted in patients who had undergone LC for symptomatic cholelithiasis: out of these, 153 patients were older than 75 years. Conversion rate to open cholecystectomy, complication rate, operative time, and length of stay were compared with those younger than 75 years. Multivariate analysis was used as a control for baseline differences.

**Results.** Conversion rate to open cholecystectomy in elderly was 13.1% vs 5.8% ( $p < 0.001$ ). Complication rate was 3.9% vs 1.6%. Operative time was 50 min vs 45 min. No significant difference was found in the hospital stay of both younger and elderly patients who had underwent a successful LC ( $p = 0.079$ ). The presence of inflammation was the only independent risk factors for conversion ( $p = 0.014$ ) and had a marginal independent effect on the development of complications ( $p = 0.079$ ) among elderly patients.

**Conclusion.** Even though older patients are more likely to present with diseases in more advanced states, LC is safe and should be regarded as the gold-standard approach for elderly patients with cholelithiasis.

### Keywords

Ageing patients - cholelithiasis - laparoscopic cholecystectomy.

# **Chemotherapies and Targeted Therapies in Advanced Hepatocellular Carcinoma: from Laboratory to Clinic**

*Mihai Voiculescu<sup>1</sup>, Robert E. Winkler<sup>2</sup>, Marius Moscovici<sup>3</sup>, Manuela G. Neuman<sup>4</sup>*

## **Abstract**

Chronic liver diseases alone or in conjunction with other risk factors result in increased liver damage leading to inflammation and fibrosis of the liver and rising rates of liver cirrhosis, hepatic decompensation and hepatocellular carcinoma (HCC). This review will address the determinants of liver injury at the initiation of the tumor and the risk factors for rapid disease progression. Regardless of the etiology, the unifying feature of these tumors are their propensity to arise upon a background of inflammation and fibrosis.

Liver disease is often associated with enhanced hepatocyte apoptosis, which is the case in viral and autoimmune hepatitis, cholestatic diseases, and metabolic disorders. Disruption of apoptosis is responsible for HCC. The mechanisms by which apoptosis occurs in the liver might provide insights into HCC and suggest possible treatments.

We aim to better understand the factors that distinguish a relatively long course of HCC from one with rapid progression. We will accomplish this task with three integrated ideas: 1 - the role of epidemiology in establishing the risk factors of co-morbidity with alcohol and hepatitis viruses; 2 - the role of apoptosis and anti-apoptotic signals in the progression of HCC; and 3 - the role of new advancements that have emerged in the field of molecular-directed chemotherapeutics in HCC in recent years. This review will also aim to describe the molecular targeted therapies of non-resectable HCC and the ways of effective combination in this otherwise chemo-resistant tumor.

## **Key words**

Alcoholic liver disease - viral hepatitis - cytokines - Fas - hepatocellular carcinoma - m-Tor inhibitor - primary biliary cirrhosis - protein kinase C - apoptosis - tumor necrosis factors - vascular endothelial growth factor.

## **Recurrent Intrahepatic Cholestasis of Pregnancy. A Case Report**

*Daniel Muresan, Dan Ona, Gheorghe Cruciat, Ioana Rotar, Florin Stamatian*

### **Abstract**

Intrahepatic cholestasis of pregnancy (ICP) represents a rare but severe pathology with serious consequences on the outcome of pregnancy. We present the cases of two sisters that came to our clinic with ICP in successive pregnancies. The fetus from a pregnancy with cholestasis can be affected by preterm birth, respiratory distress syndrome, intrauterine death in the third trimester and a possible cerebral damage. Early diagnosis and prednisone treatment have allowed an improvement of the neonatal outcome in the following pregnancies.

### **Keywords**

Intrahepatic cholestasis - pregnancy - premature birth - pruritus.

## **Persistent Diarrhea**

*Michael Sackmann<sup>1</sup>, Viola Vehling<sup>1</sup>, Klaus - D. Schmidt<sup>1</sup>, Ulrich von Streitberg<sup>2</sup>, Gerhard Seitz<sup>2</sup>*

### **Abstract**

A 63-year-old man presented with massive diarrhea and weight loss. This was preceded by nonspecific symptoms for three years, which resembled sarcoidosis. By duodenal biopsy, the diagnosis of Whipples disease was confirmed. Antibiotic treatment resulted in rapid and complete disappearance of signs and symptoms.

### **Key words**

Whipple disease - diarrhea - sarcoidosis

## **Isolated Ampullary Adenoma Causing Biliary Obstruction**

*Salvatore Greco<sup>1</sup>, Andrea Cassinotti<sup>1</sup>, Alessandro Massari<sup>1</sup>, Ilaria Bossi<sup>2</sup>, Emilio Trabucchi<sup>3</sup>, Gabriele Bianchi Porro<sup>1</sup>*

### **Abstract**

This is an interesting case of an isolated ampullary adenoma causing biliary obstruction that required surgical excision. We describe a patient who presented with a six month history of recurrent attacks of typical biliary pain radiating from the right upper quadrant of the abdomen to the back, nausea and vomiting, which we attributed to a large pedunculated tubulovillous adenoma. Abdominal ultrasound and endoscopic ultrasonography provided useful information in the diagnostic assessment of ampullary adenoma. Sporadic duodenal adenomas are an increasingly recognized condition in those with familial adenomatous polyposis syndromes as well as sporadic cases.

### **Keywords**

Sporadic duodenal adenoma intestinal ultrasound - endoscopic ultrasonography (EUS) - radical surgery.

# **Double-Balloon Endoscopy in the Diagnosis and Treatment of Hemorrhage from Retrovalvular Angiodysplasias**

*Soeresh Jarbandhan, W.M. van der Veer, Chris J.J. Mulder*

## **Abstract**

Acute rectal blood loss is a common problem that occurs most often in the elderly. The majority of the cases are caused by diverticular bleeding, while angiodysplasias account for about 8% of cases with gross rectal blood loss. Angiodysplasias in the colon are most often located in the caecum. They can cause severe colonic bleeding, sometimes even requiring multiple transfusions. Treatment of bleeding colonic angiodysplasias is usually done with argon plasma coagulation (APC). We describe two cases of elderly patients who presented with rectal blood loss, in whom gastroduodenoscopy and colonoscopy had not revealed a bleeding focus. Both patients were referred to our hospital for retrograde double balloon endoscopy as it was suspected that the bleeding focus was located in the distal small bowel. The flexible double-balloon endoscope allowed a better and easier inspection of the caecum and the ileocaecal valve (ICV). In both cases a large angiodysplasia was found on the back of the ICV. After treatment with APC the bleeding stopped and the haemoglobin levels remained within the normal range.

## **Keywords**

Double-balloon endoscopy - colon angiodysplasia - lower gastrointestinal bleeding.

# Endoscopic Repair of a Complete post-Radiation Esophageal Obstruction

*Thomas Giever<sup>1\*</sup>, Klaus Gottlieb<sup>2\*</sup>, Anders Merg<sup>3</sup>*

## **Abstract**

We describe a 64-year-old man with squamous cell carcinoma of the esophagus who presented with an obstruction of the esophagus following radiation therapy and chemotherapy. Initial upper gastrointestinal barium swallow studies showed a complete stoppage of the barium column, not unlike that of a congenital esophageal atresia. Therapeutic endoscopy was performed using a two-endoscope, two-operator system that reestablished patency of the esophagus. Repeated endoscopy was then used to continue esophageal dilation with eventual placement of a permanent stent. A video and a comprehensive review of the literature regarding combined antegrade-retrograde dilation techniques used to date are also provided.

## **Key words**

Esophageal carcinoma - obstruction - combined antegrade-retrograde dilatation - endoscopy.

## **Tissue Specific MR Contrast Media Role in the Differential Diagnosis of Cirrhotic Liver Nodules**

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### **Abstract**

State-of-the-art magnetic resonance (MR) imaging using tissue specific contrast media facilitates detection and characterization in most cases of hepatic nodules. According to the currently used nomenclature, in liver cirrhosis there are only two major types of hepatocellular nodular lesions: regenerative lesions and dysplastic or neoplastic lesions. The purpose of this clinical imaging review is to provide information on the properties of tissue-specific MR contrast agents and on their usefulness in the demonstration of the pathologic changes that take place at the level of the hepatobiliary and reticuloendothelial systems during the carcinogenesis in liver cirrhosis.

### **Keywords**

Liver cirrosis - carcinogenesis - magnetic resonance imaging - tissue specific contrast media.

## **Colon Capsule Endoscopy: a New Method of Investigating the Large Bowel**

*Silviu Iobagiu, Lidia Ciobanu, Oliviu Pascu*

### **Abstract**

Using the same principles as small bowel capsule endoscopy, a new wireless device has been developed to explore the colon. Colon capsule endoscopy (CCE) is a safe and non-invasive method in visualizing the entire large bowel mucosa. A special preparation of the digestive tract is necessary to ensure the cleanliness of the colon and the progression of the capsule. CCE acquires images with a very good quality and accuracy. The actual experience confirms the possibility of using CCE as a method for screening colorectal polyps and cancer.

### **Key words**

Colon - colon capsule - colonoscopy - screening