

**ORIGINAL PAPERS**

Immunohistochemical Assessment of Angiogenesis in Primary Hepatocellular Carcinoma

*Adrian Săftoiu<sup>1</sup>, Tudorel Ciurea<sup>1</sup>, Monica Baniță<sup>2</sup>, Claudia Georgescu<sup>3</sup>, Violeta Comănescu<sup>3</sup>, Ion Rogoveanu<sup>1</sup>, Florin Gorunescu<sup>4</sup>, Ion Georgescu<sup>5</sup>*

Pain in Chronic Pancreatitis: Assessment and Relief Through Treatment

*Andrada Seicean, Mircea Grigorescu, Marcel Tanțău, Dan L. Dumitrașcu, Diana Pop, Teodora Mocan*

Cost-Effectiveness of Endoscopically Placed Stents in the Palliation of Locally Advanced Esophageal Carcinoma

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Overlap Syndrome between Autoimmune Hepatitis and Primary Biliary Cirrhosis Complicated by Hepatocellular Carcinoma

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Gastrocolic Fistula Secondary to Nonsteroidal Anti-Inflammatory Drugs Abuse in a Cirrhotic Patient

*Konstantinos Mimidis<sup>1</sup>, Vassilios Papadopoulos<sup>1</sup>, Panagiotis Katsinelos<sup>1</sup>, Savvas Deftereos<sup>2</sup>, Dimitrios Filippou<sup>1</sup>, Georgios Kartalis<sup>1</sup>*

Hydatid Disease Cured by Minimally Invasive Therapy

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**TECHNIQUE**

Endoscopic Ultrasound Guided Fine Needle Aspiration Biopsy in the Diagnosis of

## Pancreatic Masses

Mariana Jinga<sup>1</sup>, Cristian Gheorghe<sup>2</sup>, Marius Dumitrescu<sup>1</sup>, Liana Gheorghe<sup>2</sup>, Tudor Nicolaie<sup>1</sup>

## CLINICAL IMAGING

### Liver Angioscintigraphy: Clinical Applications

Mircea Dragoteanu, Sabin O. Cotul, Cecilia Pîgleșan, Ștefan Tamaș

## ORIGINAL PAPERS

# Immunohistochemical Assessment of Angiogenesis in Primary Hepatocellular Carcinoma

Adrian Săftoiu<sup>1</sup>, Tudorel Ciurea<sup>1</sup>, Monica Baniță<sup>2</sup>, Claudia Georgescu<sup>3</sup>, Violeta Comănescu<sup>3</sup>, Ion Rogoveanu<sup>1</sup>, Florin Gorunescu<sup>4</sup>, Ion Georgescu<sup>5</sup>

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Abstract

**Background.** Primary hepatocellular carcinoma (HCC) is characterized by the presence of angiogenesis, which is necessary for tumor growth, progression and distant metastasis. Vascular endothelial growth factor (VEGF) is clearly expressed in HCC, in variable degrees as a function of differentiation and vascularisation.

**Aim.** To assess angiogenesis in HCC, by means of immunohistochemical analysis of the expressions of VEGF.

**Method.** Immunohistochemical techniques were performed on the samples obtained by ultrasound-guided liver biopsies or intraoperative biopsies, in 32 patients with HCC.

**Results.** Positive expression of VEGF was always observed in the extracellular matrix of portal tracts of the non-neoplastic or tumor areas (extra- and intranodular areas of HCC patients). VEGF was not expressed inside the hepatocytes of extranodular non-neoplastic areas of the patients with HCC. However, we did find positive reactions for VEGF inside the tumor hepatocytes in 34.38% of the HCC patients. The difference between VEGF expression for the patients with poor and undifferentiated HCC as compared with moderate and well-differentiated HCC was statistically significant ( $P < 0.05$ ).

**Conclusion.** Our study demonstrated an increased VEGF expression in tumor hepatocytes, which progressed with the dedifferentiation of HCC. VEGF expression was always present in the extracellular matrix, supporting the hypothesis of paracrine activation of VEGF at the level

of tumor stroma. Consequently, increased VEGF expression might be responsible for the activation of angiogenesis in HCC.

**Key words**

Hepatocellular carcinoma - angiogenesis - vascular endothelial growth factor - immunohistochemistry

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## Pain in Chronic Pancreatitis: Assessment and Relief Through Treatment

Andrada Seicean, Mircea Grigorescu, Marcel Tanțău, Dan L. Dumitrașcu, Diana Pop, Teodora Mocan

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Abstract

**Aim.** To assess two scores of pain used in chronic pancreatitis, to analyse the morphological factors identified by imaging techniques and the extrinsic factors involved in causing pain and in pain evolution during treatment.

**Patients and methods.** Pain was assessed by means of a unidimensional numeric scale and a multidimensional Mc Gill score in 50 patients with chronic pancreatitis. We prospectively followed up 28 patients over a period of 17 months.

**Results.** Pain assessment by means of the two scores was statistically comparable. The multidimensional score correlated with the presence of Wirsung stenoses in the univariate analysis and with Wirsung stenoses and their diameter in the multivariate one. The smokers had a smaller rate of pain relief during the treatment. In cases with more morphological changes of severe chronic pancreatitis, pain relief was lower than in cases with fewer changes.

**Conclusions.** The Mc Gill score is more appropriate for the quantitative assessment of pain. Smoking reduces the chances of pain relief under treatment. Duct stenoses and Wirsung diameter have the best correlation with pain intensity. The severe chronic pancreatitis changes are negative predictive factors for pain relief under treatment.

**Key words**

Chronic pancreatitis - pain - scores of pain - endoscopic therapy - surgery

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# Cost-Effectiveness of Endoscopically Placed Stents in the Palliation of Locally Advanced Esophageal Carcinoma

Gabriel Dimofte<sup>1</sup>, Felicia Crumpei<sup>2</sup>, Liviu Trifina<sup>1</sup>, Simona Nicolescu<sup>1</sup>, Dan Leanca<sup>3</sup>

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Abstract

## Abstract

The study assessed 50 consecutive patients presenting advanced esophageal carcinoma, in order to evaluate the cost-effectiveness of endoscopic palliation of dysphagia. Cases were divided into groups according to the type of therapy: Group A - surgical resections; Group B - gastrostomy, jejunostomy, surgical bypass or no palliation; Group C - endoscopic palliation. A retrospective study analysed early mortality, length of hospital stay and cost of therapy. Mean postoperative survival was within the expected limits in the endoscopically treated group (3-6 months), and in the non-resected group, while resected patients showed a very high early mortality and no long term survivals. Costs were significantly smaller in Group C as compared with Group A, with shorter hospital stay and better palliation. We conclude that endoscopically placed stents represent a cost effective palliation for advanced esophageal carcinoma and medical authorities should consider covering the expenses required by such procedures.

## Keywords

Esophageal cancer - survival - stent - palliation

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## REVIEWS

# Correlation between Cholestasis and Infection

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Bucharest

Abstract

## Abstract

This is an overview of cytokine-induced cholestasis, justified by the insufficient knowledge of this frequent type of cholestasis. In the presence of an infectious agent a systemic and intrahepatic production of proinflammatory cytokines results (TNF- $\alpha$ , IL-1 $\beta$ , IL-6 etc.), stimulated by microbial lipopolysaccharides. In patients having systemic infections, the liver has several major functions: source of the inflammatory cytokines produced as a response to

*infection and a target of these inflammation mediators. The inflammatory cytokines interfere with the activity of both the sinusoidal and canalicular transporting systems. One of the potential consequence of this process is the appearance of cholestasis. An infection can lead to cholestasis despite the absence of direct invasion of the liver by the infectious agent. Particularly the cholestasis produced when the infection generating agent is not located in the liver (sepsis or extrahepatic infections) has been emphasized. The clinical aspect of the diseases associated with this type of cholestasis and the effects of anti-infectious therapy on cholestasis are presented. Cytokine-induced cholestasis represents a common pathogenic path for several diseases: hepatites that present with an intrahepatic cholestatic pattern (viral, ethanol-induced, NSAID-induced), but also many other infections, which are sometimes overlooked because of the lack of clinical signs. When a preexistent liver disease is present, the cholestasis incidence is higher. In this latter condition, ignorance of this possible mechanism of cholestasis will lead to misdiagnosis and unnecessary tests, sometimes expensive and useless.*

#### **Keywords**

*Cholestasis - bacterial infection - cytokines - lipopoly-saccharides - bile acids*

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## **Microenteropathy; the entity of the new millennium. Overview of the Second Asian Symposium on Coeliac Disease, October 18-21, 2003, Tehran**

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### **CASE REPORTS**

## **Overlap Syndrome between Autoimmune Hepatitis and Primary Biliary Cirrhosis Complicated by Hepatocellular Carcinoma**

*Liana Gheorghe<sup>1</sup>, Speranța Iacob<sup>1</sup>, Nicolae Bolog<sup>2</sup>, Adriana Stoicescu<sup>1</sup>, Iuliana Pârvueșcu<sup>1</sup>, Irinel Popescu<sup>3</sup>*

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**Abstract**

*The risk of hepatocellular carcinoma superimposed in the evolution of autoimmune hepatitis or primary biliary cirrhosis is low, even in patients with long-standing cirrhosis. We report a case of hepatocellular carcinoma occurring in a 46 year old woman with liver cirrhosis following overlap syndrome between autoimmune hepatitis and primary biliary cirrhosis, routinely followed while on the waiting list for liver transplantation. The patient had combined biochemical (elevated aminotransferases, alkaline phosphatase and  $\gamma$ -glutamyl-transpeptidase in the range of 2-3 times above the upper limit of the normal) and serological (anti-smooth muscle antibody > 1/80 and anti-mitochondrial antibody anti-M2 > 1/40) criteria of autoimmune hepatitis and primary biliary cirrhosis.*

*Hepatocellular carcinoma was diagnosed in the setting of chronic liver disease by the combination of two concordant imaging technics (Doppler ultrasound and magnetic resonance imaging) showing a hepatic nodule with arterial hypervascularization and elevated serum levels of  $\alpha$ -fetoprotein up to 950 ng/ml. Liver transplantation is the best treatment both for the solitary nodule less than 5 cm and underlying autoimmune cirrhosis. Using the new Model for End-Stage Liver Disease allocation system our patient was placed in a prior position for liver transplantation (MELD 29). Unfortunately, a sudden fulminant liver failure complicated with intravascular disseminated coagulopathy was fatal for our patient while awaiting liver transplantation.*

**Keywords**

*Autoimmune hepatitis - overlap syndrome - hepatocellular carcinoma - liver transplantation*

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## Gastrocolic Fistula Secondary to Nonsteroidal Anti-Inflammatory Drugs Abuse in a Cirrhotic Patient

*Konstantinos Mimidis<sup>1</sup>, Vassilios Papadopoulos<sup>1</sup>, Panagiotis Katsinelos<sup>1</sup>, Savvas Deftereos<sup>2</sup>, Dimitrios Filippou<sup>1</sup>, Georgios Kartalis<sup>1</sup>*

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Abstract

**Abstract**

*Gastrocolic fistula is rarely described in the literature. It has been associated with a variety of diseases and recently with benign gastric ulcers related to the use of nonsteroidal anti-inflammatory drugs (NSAIDs<sup>1</sup>). The present case represents the first report of gastrocolic fistula due to NSAIDs in a cirrhotic patient. This is in keeping with the established knowledge that cirrhotic patients constitute a high-risk group of patients when treated with NSAIDs<sup>1</sup>. Review of the literature shows that this condition warrants a complete diagnostic work-up to exclude more*

*ominous underlined diseases.*

**Keywords**

*Gastrocolic fistula - nonsteroidal anti-inflammatory drugs - cirrhosis - hepatic encephalopathy*

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## Hydatid Disease Cured by Minimally Invasive Therapy

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*Abstract*

**Abstract**

*Hydatid disease is relatively frequently encountered in general surgery services (4-5% of the total operated cases). The association of the hepatic and pulmonary localizations is quite common, but the involvement of more organs is rare. The asymptomatic rupture of the hydatid cyst in the peritoneal cavity is exceptional.*

*We present the case of a 69-year old female patient who was hospitalized in the 1st Surgical Clinic for irritative dry cough, loss of weight (4 kg in the last 3 months), fatigue, itching and dyspnea. She had been hospitalized in a department of internal medicine for respiratory symptoms when, during X-ray investigation, an opacity was observed, which was suggestive for a pulmonary hydatid cyst. The abdominal ultrasound revealed a multiple hydatid localization (liver, spleen, lower right abdominal quadrant and hypogastrium) and the patient was sent to our clinic. The patient was treated with albendazole 10 mg/kg/day for 10 days before surgery. Surgery was performed by a minimally invasive approach, first by thoracoscopy and, in the same operative session, the other hydatid localizations were approached by laparoscopy. The parasiticide treatment was continued about 3 months after surgery, when the patient was hospitalized again in order to cure the splenic hydatid cyst. Postoperative evolution was complicated by a biliary fistula which resolved spontaneously in 10 days after the intervention. The postoperative hospital stay was 14 days.*

*This case was unusual because of the paucity of symptoms in spite of the multiple abdominal cysts and because it was cured by a modern, minimally invasive approach.*

**Key words**

*Hydatid disease - hepatic hydatid cyst - pulmonary hydatid cyst - minimally invasive therapy - thoracoscopy - laparoscopy - albendazole - percutaneous technique*

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## TECHNIQUE

# Endoscopic Ultrasound Guided Fine Needle Aspiration Biopsy in the Diagnosis of Pancreatic Masses

*Mariana Jinga<sup>1</sup>, Cristian Gheorghe<sup>2</sup>, Marius Dumitrescu<sup>1</sup>, Liana Gheorghe<sup>2</sup>, Tudor Nicolaie<sup>1</sup>*

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*Abstract*

### **Abstract**

*Endoscopic ultrasound (EUS) represents a highly sensitive method for the detection of pancreatic masses. When available, EUS-guided fine needle aspiration (FNA) is the best technique for the diagnosis and staging of pancreatic cancer due to its ability to obtain tissue for diagnosis. The standardized indications for pancreatic EUS-FNA comprise the definite diagnosis of malignancy and histopathological confirmation of adenocarcinoma before surgical resection, chemo/radiotherapy, or celiac plexus neurolysis. The technique of performing EUS-FNA is described in detail, from the visualization of the target lesion and adequate placement of the transducer to allow optimal needle access, to needle penetration and sampling of the targeted lesion.*

*We report a series of 9 patients who underwent EUS-FNA and shortly review the indications, technique, results and impact of EUS-FNA on the management of these patients..*

### **Key words**

*Endoscopic ultrasound - fine needle aspiration - pancreatic cancer*

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## CLINICAL IMAGING

# Liver Angioscintigraphy: Clinical Applications

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*Abstract*

### **Abstract**

*Liver angioscintigraphy (LAS) is a radio-isotope method for the investigation of liver perfusion and its alteration in various hepatic diseases. It measures the arterial and portal venous*

fractions of total liver blood flow. The percentage of liver blood flow supplied by hepatic artery is estimated mathematically by the hepatic perfusion index (HPI), normally between 25% and 40%.

The decrease of portal blood flow in liver cirrhosis is compensated („buffer” mechanisms) by increased arterial supply, with higher HPI value. For a patient with chronic liver disease, HPI over 50% suggests arterialization of hepatic perfusion, guiding the diagnose to liver cirrhosis. Splenic curve is completing the diagnostic informations of the hepatic curve. Corroborated with per rectal scintigraphy and liver SPECT, LAS offers a good hemodynamic staging of chronic inflammatory liver diseases.

Malignant tumors (primitive or metastases) increase the arterial supply of the liver and decrease the portal flow, HPI being over 50% (currently 65%-90%). Benign tumors do not change portal/arterial liver blood flow ratio. SPECT or non-scintigraphic morphological investigations increase the diagnostic value of LAS for primitive liver tumors. Liver cancer occurring on cirrhosis is a limitative factor for LAS.

Hepatic metastases increase the arterial perfusion (and HPI value) very quickly, before their size allows morphologic imaging diagnosis. LAS is therefore an early method to diagnose liver metastases being especially used in colorectal cancer.

Other clinical applications of LAS are: follow up of liver toxicity of drugs, evaluation of portal vein permeability, post surgery follow up of the liver tumor patients.

**Key words**

*Liver angioscintigraphy - hepatic blood flow - hepatocellular carcinoma - cirrhosis*

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