

PANCREAS ALERTS

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Organ microcirculatory disturbances in experimental acute pancreatitis. A role of nitric oxide.

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Microcirculatory disturbances are important early pathophysiological events in various organs during acute pancreatitis. The authors aimed to investigate an influence of L-arginine (nitric oxide substrate) and N(G)-nitro-L-arginine (L-NNA, nitric oxide synthase inhibitor) on the organs' microcirculation in caerulein-induced experimental acute pancreatitis. Acute pancreatitis was induced by 4 intraperitoneal caerulein injections. The microcirculation of pancreas, liver, kidney, stomach, colon and skeletal muscle was measured by laser Doppler flow meter. Serum interleukin 6 and hematocrit levels were analyzed acute pancreatitis resulted in a significant drop of all examined organs' micro perfusion. L-arginine administration improved the microcirculation: in pancreas, liver, kidney, colon, and skeletal muscle, and lowered hematocrit level. L-NNA treatment (2x25 mg/kg) caused aggravation of oedematous acute pancreatitis to necrotizing one, increased IL-6 and hematocrit levels. Further reduction of blood perfusion was noted in stomach only. The authors concluded that L-arginine administration has a positive influence on organ microcirculatory disturbances accompanying experimental Cn-induced acute pancreatitis and nitric oxide

inhibition aggravates the course of pancreatitis.

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Ablation of phosphoinositide 3-kinase-gamma reduces the severity of acute pancreatitis.

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Using mice lacking PI3Kgamma, the authors studied the function of this enzyme in vivo in two different models of acute pancreatitis. The disease was induced by supramaximal concentrations of cerulein and by feeding mice a choline-deficient/ethionine-supplemented diet. Although the secretive function of isolated pancreatic acini was identical in mutant and control samples, in both models, genetic ablation of PI3Kgamma significantly reduced the extent of acinar cell injury/necrosis. In agreement with a protective role of apoptosis in pancreatitis, PI3Kgamma-deficient pancreata showed an increased number of apoptotic acinar cells, as determined by terminal dUTP nick-end labeling and caspase-3 activity. In addition, neutrophil infiltration within the pancreatic tissue was also reduced, suggesting a dual action of PI3Kgamma, both in the triggering events within acinar cells and in the subsequent neutrophil recruitment and activation. Finally, the lethality of the choline-deficient / ethionine - supplemented diet-induced pancreatitis was significantly reduced in mice lacking PI3Kgamma. The

authors concluded that inhibition of PI3Kgamma may be of therapeutic value in acute pancreatitis.

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Recurrence of acute gallstone pancreatitis and relationship with cholecystectomy or endoscopic sphincterotomy.

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The authors aimed to determine the prevalence of recurrence of gallstone pancreatitis, its clinical features, and the presence of prognostic factors of recurrence. From January 1, 2000 to August 31, 2003, 233 patients admitted with acute gallstone pancreatitis were prospectively studied. Patients were divided into two groups: recurrent and nonrecurrent group. Clinical, analytical, radiological, prognostic parameters, and severity (Atlanta criteria) were assessed, along with the performance of cholecystectomy or endoscopic sphincterotomy. Clinical features of recurrence were analyzed. Two hundred and eighty-six attacks were identified. Forty-two patients (18.2%) recurred, suffering 53 recurrent attacks, which took place within 30 days in 23.3%. Patients who did not undergo surgery after the first attack had 31-fold risk of recurrence ($P < 0.001$). In patients not operated, recurrence was more frequent if endoscopic sphincterotomy was not performed (37.04% vs. 0%, $P = 0.019$). Among patients with surgical risk, none who recurred underwent endoscopic sphincterotomy, compared with 27.9% of those who did not recur. Patients in the nonrecurrent group underwent cholecystectomy within the first 30 days or endoscopic sphincterotomy more frequently (31.2% vs. 7.3%, $P = 0.001$). The authors concluded that recurrence of gallstone

pancreatitis is a frequent event. Delay of cholecystectomy implies an increased risk of recurrence. Endoscopic sphincterotomy could be an acceptable option to prevent recurrence in patients who are not candidates for surgery or who do not desire to undergo cholecystectomy.

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Serum antibody to carbonic anhydrase II in patients with chronic viral hepatitis: a review of its prevalence in liver diseases.

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Serum antibody to carbonic anhydrase II (CA II) has been reported in patients with autoimmune pancreatitis and its related autoimmune liver diseases. To evaluate its diagnostic significance, the authors studied serum antibodies to CA II and also CA I in patients with chronic viral hepatitis by enzyme-linked immunosorbent assay and reviewed its prevalence previously reported in patients with liver diseases. Anti-CA II antibody was detected in 5 of 20 patients with chronic hepatitis type C (25%, $P < 0.05$ versus normal controls), 2 of 10 patients with chronic hepatitis type B (20%, not significant versus normal controls), and 1 of 30 normal controls (3%). Anti-CA I antibody was detected in 3 of 20 patients with chronic hepatitis type C (15%, not significant versus normal controls). Anti-CA II antibody has previously been reported as being associated with a variety of liver diseases, including primary biliary cirrhosis with or without anti-mitochondrial antibody, autoimmune hepatitis and chronic hepatitis type C. These findings suggest less significance of anti-CA II antibody for the diagnosis of autoimmune pancreatitis and its hepatic involvements than as having been reported. However, the

pathogenetic role of the antibody remains uncertain.

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Dynamic contrast-enhanced MRI of the pancreas: initial results in healthy volunteers and patients with chronic pancreatitis.

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The authors aimed to characterize pancreatic perfusion in volunteers and patients with chronic pancreatitis by dynamic contrast-enhanced MRI. Pancreatic enhancement after bolus injection of Gd-DTPA with a three-dimensional ultrafast partial-Fourier radiofrequency spoiled gradient-echo acquisition was examined prospectively. An acquisition volume of the pancreatic parenchyma was obtained every 4.2 seconds during a single breath-hold in 31 volunteers and 19 patients with chronic pancreatitis. The authors calculated the wash-in rate and a newly defined parameter, the "time-to-inflow deceleration". Significant differences in the time-to-inflow deceleration and wash-in rate were found for the head and body of the pancreas: the time-to-inflow deceleration was 22.4 ± 4.4 sec and 23.5 ± 6.1 sec in the pancreatic head and body of the healthy volunteers, and 29.8 ± 8.6 sec and 29.4 ± 3.8 sec in patients with chronic pancreatitis. The wash-in rate was 96 ± 37 sec⁻¹ and 101 ± 27 sec⁻¹ in controls, and 62 ± 17 sec⁻¹ and 75 ± 27 sec⁻¹ in chronic pancreatitis. Chronic pancreatitis can be identified by semiquantitative changes on dynamic contrast-enhanced-MRI. Whether dynamic contrast-enhanced-MRI of the pancreas can be used to detect early chronic pancreatitis remains to be validated.

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A prospective comparison of the yield of EUS in primary vs. recurrent idiopathic acute pancreatitis.

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It is uncertain whether EUS should be performed after a single episode of idiopathic pancreatitis vs. recurrent episodes or if clinical factors can predict positive EUS findings. Consecutive patients with a single episode of idiopathic pancreatitis or with recurrent episodes underwent EUS (with analysis of bile for bilirubinate and cholesterol crystals, when possible). The diagnostic yield was compared for patients with a single episode of idiopathic pancreatitis and recurrent episodes (stratified by cholecystectomy status). Predictors of positive EUS findings were sought. EUS was considered "positive" if it identified any possible cause of pancreatitis other than chronic pancreatitis. A total of 370 patients were studied (246 no-cholecystectomy group [134 single episode of idiopathic pancreatitis, 112 recurrent episodes] and 124 post-cholecystectomy group [67 single episode of idiopathic pancreatitis, 57 recurrent episodes]). Overall, EUS yielded a positive finding in 29.2%. For patients in the no-cholecystectomy group, positive EUS findings were not significantly more frequent in those with a single episode of idiopathic pancreatitis vs. those with recurrent episodes (31.3% vs. 32.1%; P=0.89). In the post-cholecystectomy group, the yield was not significantly different for single episode of idiopathic pancreatitis (29.9%) vs. recurrent episodes (17.5%) (P=0.15). Chronic pancreatitis was the only abnormality identified in 30.9% of patients in the no-cholecystectomy group vs. 26.6% of those in the post-cholecystectomy group (P=0.24). It was the most common abnormality found in

all 4 subgroups (range 16.4-42.0%) and was approximately twice as frequent in patients with recurrent episodes vs. a single episode of idiopathic pancreatitis (no-cholecystectomy: 42.0% vs. 21.6%, P=0.0008; post-cholecystectomy: 38.6% vs. 16.4%, P=0.008). Analysis of bile revealed crystals in 38/80 (47.5%) patients in whom it could be performed. Patients with positive EUS findings tended to be older. The authors concluded that in patients with idiopathic pancreatitis, the yield of EUS is not significantly different after an initial attack or after recurrent attacks. Therefore, it is reasonable to perform EUS after an initial attack of idiopathic acute pancreatitis, especially in older patients.

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A cost-minimization analysis of alternative strategies in diagnosing pancreatic cancer.

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Several modalities currently exist for tissue confirmation of suspected pancreatic cancer prior to therapy. Since there is a paucity of cost-minimization studies comparing these different biopsy modalities, we analyzed costs and examined effectiveness of four alternative strategies for diagnosing pancreatic cancer. A decision analysis model of patients with suspected pancreatic cancer was constructed. The authors analyzed costs, failure rate, testing characteristics, and complication rates of four commonly employed diagnostic modalities: 1) computerized tomography or ultrasound-guided fine-needle aspiration (CT/US-FNA), 2) endoscopic retrograde cholangiopancreatography with brushings (ERCP-B), 3) Endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNA), and 4) laparoscopic surgical biopsy. If the

first attempt with a particular modality failed, a different modality was employed to identify the most preferable secondary biopsy strategy. This analysis identifies EUS-FNA as the preferred initial modality for the diagnosis of pancreatic cancer. Resultant expected costs and strategies in decreasing optimality include: 1) EUS-FNA (1,405 dollars), 2) ERCP-B (1,432 dollars), 3) CT/US-FNA (3,682 dollars), and 4) surgery (17,711 dollars). If a patient presents with obstructive jaundice, decision analysis modeling resulted in a total expected costs of 1,970 dollars if ERCP-B is successful at the time of biliary stent placement. Additional analyses to identify the preferred follow-up modality after a failed alternative method showed that EUS-FNA is the preferred secondary modality if any of the other three modalities failed first, in both the setting of and absence of obstructive jaundice. One- and two-way sensitivity analysis of the variables shows unchanged results over an acceptable range. The authors concluded that this cost-minimization study illustrates that EUS-FNA is the best initial and the preferred secondary alternative method for the diagnosis of suspected pancreatic cancer. In addition to local expertise and availability, costs and diagnostic yield should be considered when choosing an optimal diagnostic strategy.

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MDCT cholangiography with volume rendering for the assessment of patients with biliary obstruction.

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The authors sought to evaluate the diagnostic utility of MDCT cholangiography with volume rendering in the evaluation of patients with suspected biliary tree obstruction. MDCT was performed in 34 patients who were thought to have biliary obstruction.

Portal venous phase scanning was initiated 70 sec after the IV infusion of 150 mL of contrast agent, and no cholangiographic contrast agent was administered. Three-dimensional MDCT cholangiographic images were produced using volume rendering. ERCP was performed in 26 patients, and percutaneous transhepatic cholangiography (PTC) was performed in five patients; 17 patients underwent biopsy or surgery. The findings on MDCT cholangiography were compared with those of ERCP, PTC, biopsy, or surgery. The correct diagnosis was made on MDCT cholangiography for 14 (93%) of the 15 patients with a biliary stone and in 16 (94%) of the 17 patients with malignant biliary obstruction. Microlithiasis in one patient could not be detected on MDCT cholangiography. One patient with polypoid adenocarcinoma and one patient with normal findings were incorrectly diagnosed with a biliary stone on the basis of MDCT cholangiography. In one of the two patients with a benign stricture, the stricture was incorrectly diagnosed as malignant. For the diagnosis of biliary stone, sensitivity and specificity of MDCT cholangiography were 93% and 89%, respectively. For the diagnosis of malignant obstruction, sensitivity and specificity were both 94%. The accuracy of the technique for the diagnosis of the cause of biliary obstruction was 83.3%. The authors concluded that MDCT cholangiography with volume rendering is a noninvasive and fast imaging technique with high sensitivity and specificity for the diagnosis of the cause of biliary tree obstruction. It is a promising diagnostic tool for the assessment of patients with bile duct obstructions.

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Intraductal papillary mucinous neoplasms of the pancreas: CT patterns of recurrence and multiobserver performance in detecting recurrent neoplasm after surgical resection.

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The purposes of this study were to describe the CT appearance of recurrent intraductal papillary mucinous neoplasms of the pancreas after surgical resection and estimate the performance of CT in detecting recurrent neoplasms. A single unblinded reviewer characterized the presence and appearance of recurrent intraductal papillary mucinous neoplasms on 66 CT scans of 17 patients with proven recurrence, noting location and appearance of recurrent neoplasm. These results were summarized in tabular format and shown to three blinded observer. The observers then evaluated one postoperative CT examination from every patient at our institution who underwent surgical removal of intraductal papillary mucinous neoplasms (n=45) for the presence or absence of local or distant recurrence. The unblinded reviewer found 11 cases of local recurrence. Extrapancreatic local recurrences tend to have solid components (5/6), tend to be located adjacent to the resection margin (5/6), and may exhibit vascular invasion (2/6). Intrapancreatic neoplasms are usually cystic (4/5). Nine patients had distant metastases. Prospective sensitivity for recurrent tumor ranged from 76% (13/17) to 94% (16/17). Sensitivity for local recurrence ranged from 55% (6/11) to 82% (9/11). Specificity ranged from 79% (22/28) to 96% (27/28). Interobserver agreement for predicting recurrence was moderate to substantial (kappa=0.51-0.65). The authors concluded that locally recurrent intraductal papillary mucinous neoplasms of the pancreas tend to be either extrapancreatic and solid at the resection margin or intrapancreatic and cystic. CT can detect most recurrent intraductal papillary mucinous neoplasms of the pancreas with moderate to substantial interobserver agreement.