

PANCREAS ALERTS

Gastrointest Endosc 2004; 60:557-61.
(PMID: 15472678)

Endoscopic transpancreatic papillary septotomy for inaccessible obstructed bile ducts: Comparison with standard pre-cut papillotomy.

Catalano MF, Linder JD, Geenen JE.

St Luke's Medical Center. Milwaukee, Wisconsin, USA.

Access to the pancreatic or the bile duct is paramount to the success of diagnostic and therapeutic ERCP. Selective cannulation may be difficult because of the small size of the papilla and anatomic factors such as peripapillary diverticulum and gastrectomy with Billroth-II anastomosis. Currently, one of the techniques for gaining access in such cases is the pre-cut technique with a catheter that has a thin wire at the tip (needle knife). A less well-described pre-cut technique involves initial cannulation of the pancreatic duct with a "traction-type" papillotome and then incision through the "septum" toward the bile duct. The aim of this randomized trial was to compare the success and the complication rates of needle-knife sphincterotomy and transpancreatic sphincterotomy in achieving cannulation of an otherwise inaccessible bile duct. Sixty-three consecutive patients with inaccessible bile ducts underwent pre-cut sphincterotomy either by needle-knife sphincterotomy (n=34) or transpancreatic septotomy (n=29). In patients with an accessible pancreatic duct who undergo needle-knife sphincterotomy, a short (2-3 cm) stent (5F-7F) was placed in the pancreatic duct to act as a guide and to reduce the risk of post-procedure pancreatitis. All patients were hospitalized overnight for observation after pre-cut sphincterotomy. The outcomes measured were success rate and complications. Indications for pre-cut sphincterotomy were the following: suspected choledocholithiasis, 11 patients (17.5%);

obstructive jaundice with negative CT findings, 19 patients (29.2%), or with positive CT findings, 13 patients (20.6%); abdominal pain with elevated biochemical tests of liver function, 15 patients (23.8%); and miscellaneous, 5 patients (7.9%). In 55 of 63 (87%) patients, the bile duct was selectively cannulated after pre-cut sphincterotomy. On a pre-protocol basis, the bile duct was cannulated in 29 of 29 (100%) patients randomized to transpancreatic septotomy sphincterotomy and 26 of 34 (77%) patients who underwent needle-knife sphincterotomy (P=0.01). There were 7 complications, including bleeding (n=2) and acute pancreatitis (n=5). Complications were less frequent in the transpancreatic septotomy sphincterotomy group (1/29; 3.5%) compared with the needle-knife sphincterotomy group (6/34; 17.7%). The authors concluded that transpancreatic pre-cut sphincterotomy can be performed with a high degree of success in patients with inaccessible obstructed bile ducts. Compared with standard needle-knife sphincterotomy, transpancreatic septotomy sphincterotomy has a significantly higher rate of bile duct cannulation and a lower complication rate.

Gastrointest Endosc 2004; 60:544-50.
(PMID: 15472676)

Does prophylactic pancreatic stent placement reduce the risk of post-ERCP acute pancreatitis? A meta-analysis of controlled trials.

Singh P, Das A, Isenberg G, Wong RC, Sivak MV, Agrawal D, Chak A.

Division of Gastroenterology, University Hospitals of Cleveland. Cleveland, Ohio, USA.

Impaired drainage of the pancreatic duct is one of the possible triggers for post-ERCP acute pancreatitis. The aim of this meta-

analysis was to determine whether temporary stent placement across the main pancreatic-duct orifice lowers the frequency of post-ERCP acute pancreatitis in patients at high risk for this complication. Two reviewers systematically identified prospective studies that (1) compared the risk of post-ERCP acute pancreatitis in patients with pancreatic stent placement vs. no stent placement and (2) included patients at high risk of developing this complication. Studies were assessed for methodologic quality and variations in execution and design. Frequency and severity of post-ERCP acute pancreatitis were the primary outcomes evaluated. Results Five trials involving 481 patients were selected. Of the 481, 55 (11.4%) patients developed pancreatitis after ERCP. Patients in the no stent group had 3-fold higher odds of developing pancreatitis compared with the stent group. Number needed to treat analysis showed that one in every 10 patients could be expected to benefit from pancreatic-duct stent placement. The authors concluded that prophylactic temporary stent placement across the main pancreatic-duct orifice reduces the risk of post-ERCP acute pancreatitis in patients at risk for developing this complication.

Mol Cancer 2004; 3:26.
(PMID: 15469605)

Molecular regulation of pancreatic stellate cell function.

Jaster R.

Department of Medicine, Division of Gastroenterology, Medical Faculty, University of Rostock. Rostock, Germany.

Until now, no specific therapies are available to inhibit pancreatic fibrosis, a constant pathological feature of chronic pancreatitis and pancreatic cancer. One major reason is the incomplete knowledge of the molecular principles underlying fibrogenesis in the pancreas. In the past few years, evidence has been accumulated that activated pancreatic

stellate cells are the predominant source of extracellular matrix proteins in the diseased organ. Pancreatic stellate cells are vitamin A-storing, fibroblast-like cells with close morphological and biochemical similarities to hepatic stellate cells (also known as Ito-cells). In response to profibrogenic mediators such as various cytokines, pancreatic stellate cells undergo an activation process that involves proliferation, exhibition of a myofibroblastic phenotype and enhanced production of extracellular matrix proteins. The intracellular mediators of activation signals, and their antagonists, are only partially known so far. Recent data suggest an important role of enzymes of the mitogen-activated protein kinase family in pancreatic stellate cell activation. On the other hand, ligands of the nuclear receptor peroxisome proliferator-activated receptor gamma stimulate maintenance of a quiescent pancreatic stellate cell phenotype. In the future, targeting regulators of the pancreatic stellate cell activation process might become a promising approach for the treatment of pancreatic fibrosis.

Trop Gastroenterol 2004; 25:69-72.
(PMID: 15471319)

Micronutrient antioxidant intake in patients with chronic pancreatitis.

Bhardwaj P, Thareja S, Prakash S, Saraya A.

Department of Gastroenterology and Human Nutrition Unit, All India Institute of Medical Sciences. New Delhi, India.

Increased oxidative stress has been postulated to be an important mechanism in the pathophysiology of chronic pancreatitis. Micronutrient deficiency may increase the oxidative stress as they assist in free radical clearance. The present study was undertaken to assess the intake of micronutrients, i.e. vitamins E and C, carotene, selenium, copper, zinc, manganese, magnesium, sulphur, riboflavin, methionine and choline in patients with chronic pancreatitis. All consecutive

patients with chronic pancreatitis attending the Pancreas Clinic at the All India Institute of Medical Sciences were enrolled in the study. The usual dietary intake was estimated by the 24-hour dietary recall method and food frequency questionnaire. Dietary restrictions, if any, were also noted. The micronutrient intake of patients not on any nutritional supplements (n=75, 65 males and 10 females, mean age 31.06 +/- 10.64 years) was compared with age- and sex- matched healthy controls (n=75). The micronutrients were calculated as per the Nutritive value of Indian Foods given by the National Institute of Nutrition, Indian Council of Medical Research, India and the US dietary intake guidelines as applicable. It was found that the Body Mass Index of patients was significantly lower than that of healthy controls. The total intake in terms of calorie was lower in patients when compared to controls. The dietary intake of vitamin E, riboflavin, choline, magnesium, copper manganese and sulfur was significantly lower than that of controls as well as the Recommended Dietary Allowance. Dietary intake of selenium and vitamin C was within the limits of the Recommended Dietary Allowance but was lower than that of controls, while the intake of carotene was similar in both the groups and met the Recommended Dietary Allowance. We conclude that patients with chronic pancreatitis had significantly decreased micronutrient intake owing to diet modification due to pain. Micronutrient deficiency might contribute to increased oxidative stress in these patients.

Diagn Cytopathol 2004; 31:313-8.
(PMID: 15468134)

Diagnosis of nonprimary pancreatic neoplasms by endoscopic ultrasound-guided fine-needle aspiration.

Mesa H, Stelow EB, Stanley MW, Mallery S, Lai R, Bardales RH.

Department of Pathology, University of Minnesota. Minneapolis, Minnesota, USA.

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a proven modality for the diagnosis of primary pancreatic neoplasms. We describe our experience in diagnosing nonprimary pancreatic tumors by endoscopic ultrasound-guided fine-needle aspiration. Cytology files were searched for all endoscopic ultrasound-guided fine-needle aspiration of the pancreas for the period 2000-2002. All cases diagnosed as neoplasms were selected and those diagnosed as nonprimary pancreatic tumors were reviewed and analyzed. One hundred ninety-one of 468 cases were diagnosed as neoplasms. Eleven of these cases were diagnosed as nonprimary pancreatic tumors (2.4% of all diagnoses and 5.7% of all neoplasms). The diagnoses were supported by clinical history (n=7), cytological findings (n=11), cell block histology (n=11), cell block immunohistochemistry (n=6), and flow cytometry (n=1). The authors concluded that endoscopic ultrasound-guided fine-needle aspiration is a safe and minimally invasive method for the diagnosis of nonprimary pancreatic neoplasms. Evaluation of clinical history, cytomorphology, and ancillary techniques, especially those applied to cell block material, are essential for accurate diagnoses.

Int J Cancer 2004; 112:184-9.
(PMID: 15352029)

Selenoprotein P, as a predictor for evaluating gemcitabine resistance in human pancreatic cancer cells.

Maehara S, Tanaka S, Shimada M, Shirabe K, Saito Y, Takahashi K, Maehara Y.

Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University. Fukuoka, Japan.

Gemcitabine is a new standard chemotherapeutic agent used in the treatment of pancreatic cancer, but the mechanisms of gemcitabine sensitivity are still controversial. In our study to determine a mechanism that

regulates gemcitabine sensitivity, we carried out molecular analysis on the susceptibility of the pancreatic cancer cells. Using a gemcitabine-sensitive pancreatic cancer cell line KLM1, we established a resistant cell line KLM1-R exhibiting a 20-fold IC50-value (the concentration of gemcitabine causing 50% growth inhibition). Microarray analysis of genes showed specific expression of selenoprotein P, one of the anti-oxidants, in the KLM1-R cell line but not in the KLM1 cell line. Administration of selenoprotein P inhibited the gemcitabine-induced cytotoxicity in the pancreatic cell lines. The levels of intracellular reactive oxygen species were increased in the KLM1 cells by gemcitabine, but selenoprotein P suppressed the gemcitabine-induced reactive oxygen species levels. Furthermore interferon-gamma suppressed the expression of selenoprotein P mRNA and increased intracellular reactive oxygen species level, leading to the recovery of the gemcitabine sensitivity in KLM1-R. These results suggest a novel mechanism that selenoprotein P reduces the intracellular reactive oxygen species levels, resulting in the insusceptibility to gemcitabine.

MMWR Morb Mortal Wkly Rep 2004; 53:918-20.
(PMID: 15470324)

State-specific trends in chronic kidney failure. United States, 1990-2001.

No Authors listed.

*Centers for Disease Control and Prevention (CDC).
Atlanta, Georgia, USA.*

Kidney disease is the ninth leading cause of death in the United States. Approximately 19 million U.S. adults have chronic kidney disease, and an estimated 80,000 persons have chronic kidney failure diagnosed annually. Major causes of chronic kidney failure are diabetes mellitus and hypertension, which account for approximately 60% of new cases. To assess national and state-specific trends in the prevalence of chronic kidney failure during 1990-2001, Centers for Disease

Control and Prevention analyzed data from the United States Renal Data System. This report summarizes the results of that analysis, which indicated that the prevalence of chronic kidney failure in the United States increased 104% during 1990-2001. Treating and controlling risk factors and screening persons at high risk for chronic kidney failure are key steps that health-care providers and public health practitioners can take to reverse the upward trend in this disease.

Int J Cancer 2004; 111:813-8.
(PMID: 15300792)

Poly(ADP-ribosylation) inhibitors: promising drug candidates for a wide variety of pathophysiologic conditions.

Beneke S, Diefenbach J, Burkle A.

*Molecular Toxicology Group, University of Konstanz.
Konstanz, Germany.*

Poly(ADP-ribose) polymerases are involved in many aspects of regulation of cellular functions. Using NAD⁺ as a substrate, they catalyse the covalent transfer of ADP-ribose units onto several acceptor proteins to form a branched ADP-ribose polymer. The best characterised and first discovered member of this multiprotein family is PARP-1. Its catalytic activity is markedly stimulated upon binding to DNA strand interruptions, and the resulting polymer is thought to function in chromatin relaxation as well as in signalling the presence of damage to DNA repair complexes and in regulating enzyme activities. Moderate activation of PARP-1 facilitates the efficient repair of DNA damage arising from monofunctional alkylating agents, reactive oxygen species or ionising radiation, but severe genotoxic stress leads to rapid energy consumption and subsequently to necrotic cell death. The latter aspect of PARP-1 activity has been implicated in the pathogenesis of various clinical conditions such as shock, ischaemia-reperfusion and diabetes. Inhibition of ADP-ribose polymer formation has been shown to be effective, on

the one hand, in the treatment of cancer in combination with alkylating agents by suppressing DNA repair and thus driving tumour cells into apoptosis, and on the other hand it appears to be a promising drug target for the treatment of pathologic conditions involving oxidative stress. In view of the

existence of several members of the PARP family in mammalian cells, one has to be aware of possible side effects but also of a wide spectrum of potential clinical applications, which calls for the development of more specific inhibitors.
