PANCREAS ALERTS

Cardiol Res Pract 2012; 2012:191807.
(PMID: 22195286)

Hemodynamic changes during a deep inspiration maneuver predict fluid responsiveness in spontaneously breathing patients.

Préau S, Dewavrin F, Soland V, Bortolotti P, Colling D, Chagnon JL, *et al.*

Service de Réanimation Polyvalente, Centre Hospitalier Jean Bernard. Valenciennes, France.

The authors hypothesized that the hemodynamic response to a deep inspiration maneuver (DIM) indicates fluid responsiveness in spontaneously breathing (SB) patients. Consecutive nonintubated patients without mechanical ventilation, considered for volume expansion (VE) were enrolled. The authors assessed hemodynamic status at baseline and after VE. They measured radial pulse pressure (PP) using an arterial catheter and peak velocity of femoral artery flow (VF) using continuous Doppler. Changes in PP and VF induced by a DIM (ΔPPdim and ΔVFdim) were calculated in 23 patients. ΔPPdim and ΔVFdim eqial to, or greater than, 12% predicted responders to VE with sensitivity of 90% and specificity of 100%. In a restricted population of SB patients with severe sepsis or acute pancreatitis, ΔPPdim and ΔVFdim are accurate indices for predicting fluid responsiveness. These results should be confirmed in a larger population before validating their use in current practice.

Gut Liver 2011; 5:513-20.
(PMID: 22195252)

Heat shock proteins and autophagy in rats with cerulein-induced acute pancreatitis.

Kim JN, Lee HS, Ryu SH, Kim YS, Moon JS, Kim CD, *et al.*

Division of Gastroenterology, Department of Internal Medicine, Seoul Paik Hospital, Inje University College of Medicine. Seoul, South Korea.

Heat shock proteins (HSPs) protect rats from cerulein-induced acute pancreatitis (AP) by preventing the subcellular redistribution of cathepsin B and the activation of trypsinogen. Autophagy plays a critical role in the secretion of digestive enzymes and triggering of cerulein-induced AP via the colocalization of trypsinogen and lysosomes. Therefore, using a rat cerulein-induced AP model, the authors investigated whether HSPs prevent AP by regulating autophagy. Twelve hours after fed standard laboratory chow and water, the experimental groups (cerulein, water-immersion (WI)-cerulein and heat-shock (HS)-cerulein) and the control groups (control, WI, and HS) received one intraperitoneal injection of cerulein (50 μg/kg) or saline, respectively. All of the rats were sacrificed at 6 hours after injection. The severity of the AP was assessed based on the serum amylase level and the histological and electron microscopy findings. Western blotting was also performed for HSP60/70 and LC3B-II. WI and HS induced HSP60 and HSP70, respectively. The induced HSP60/70 effectively prevented the development of cerulein-induced AP. Autophagy developed in the rats with cerulein-induced AP and was documented by the expression of LC3-II and electron microscopy findings. The WI-stressed rats and HS-treated rats did not develop cerulein-induced autophagy. HSPs exert protective effects against cerulein-induced AP in rats by inhibiting autophagy.

Am J Gastroenterol 2011; Dec 20.
(PMID: 22186977)

A comparative evaluation of radiologic and clinical scoring systems in the early prediction of severity in acute pancreatitis.

Bollen TL, Singh VK, Maurer R, Repas K, van Es HW, Banks PA, Mortele KJ.

Division of Abdominal Imaging and Intervention, Department of Radiology, Brigham and Women's Hospital, Harvard Medical School. Boston, MA, USA.

The early identification of clinically severe acute pancreatitis (AP) is critical for the triage and treatment of patients. The aim of this study was to compare the accuracy of computed tomography (CT) and clinical scoring systems for predicting the severity of AP on admission. Demographic, clinical, and laboratory data of all consecutive patients with a primary diagnosis of AP during a two-and-half-year period was prospectively collected for this study. A retrospective analysis of the abdominal CT data was performed. Seven CT scoring systems (CT severity index (CTSI), modified CT severity index (MCTSI), pancreatic size index (PSI), extrapancreatic score (EP), "extrapancreatic inflammation on CT" score (EPIC), "mesenteric oedema and peritoneal fluid" score (MOP), and Balthazar grade) as well as two clinical scoring systems: Acute Physiology, Age, and Chronic Health Evaluation (APACHE)-II and Bedside Index for Severity in AP (BISAP) were comparatively evaluated with regard to their ability to predict the severity of AP

on admission (first 24 h of hospitalization). Clinically severe AP was defined as one or more of the following: mortality, persistent organ failure and/or the presence of local pancreatic complications that require intervention. All CT scans were reviewed in consensus by two radiologists, each blinded to patient outcome. The accuracy of each imaging and clinical scoring system for predicting the severity of AP was assessed using receiver operating curve analysis. Of 346 consecutive episodes of AP, there were 159 (46%) episodes in 150 patients (84 men, 66 women; mean age, 54 years; age range, 21-91 years) who were evaluated with a contrast-enhanced CT scan (n=131 episodes) or an unenhanced CT scan (n=28 episodes) on the first day of admission. Clinically severe AP was diagnosed in 29/159 (18%) episodes; 9 (6%) patients died. Overall, the Balthazar grading system (any CT technique) and CTSI (contrast-enhanced CT only) demonstrated the highest accuracy among the CT scoring systems for predicting severity, but this was not statistically significant. There were no statistically significant differences between the predictive accuracies of CT and clinical scoring systems. The predictive accuracy of CT scoring systems for severity of AP is similar to clinical scoring systems. Hence, a CT on admission solely for severity assessment in AP is not recommended.

Pancreas 2011; Dec 13.
(PMID: 22158076)

Cyclosporin A, but not FK506, induces osmotic lysis of pancreas zymogen granules, intra-acinar enzyme release, and lysosome instability by activating K^+ channel.

Lee WK, Braun M, Langeluddecke C, Thevenod F.

Institute of Physiology and Pathophysiology, University of Witten/Herdecke. Witten, Germany.

The immunosuppressant tacrolimus (FK506) has improved pancreas allograft survival compared with cyclosporin A (CsA), possibly because of reduced acute pancreatitis following ischemia-reperfusion injury. Ion permeabilities in zymogen granule (ZG) membranes, including a KCNQ1 K channel, promote hormone-stimulated enzyme secretion. The authors investigated whether a differential modulation of ZG and lysosomal ion permeabilities and enzyme secretion by CsA/FK506 contributes to pancreatitis. Rat ZGs and lysosomes were isolated by gradient centrifugation, ion permeabilities assayed by osmotic lysis, and single-channel currents recorded in a planar lipid bilayer. Amylase release was measured in permeabilized acini and lysosomal cathepsin B release detected by immunoblotting. CsA (1-10 μM), but not FK506, enhanced ZGs osmotic lysis by selectively increasing K permeability up to 5-fold. Zymogen granule membrane K channels showed about 2-fold increased single-channel open probability with CsA only. Cyclosporin A selectively increased basal (about 2-fold), but not cholecystokinin-octapeptide (1 nM)-induced amylase secretion in K medium only. Cyclosporin A (5 μM), but not FK506, increased cathepsin B release from lysosomes. Cyclosporin A selectively opens the ZG K channel and induces cathepsin B release from lysosomes, which cause increased in situ lysis of ZGs and may aggravate or fuel acute allograft pancreatitis following hypoxia-reperfusion injury.

Gut Liver 2011; 5:521-6.
(PMID: 22195253)

The Rosemont criteria can predict the pain response to pancreatic enzyme supplementation in patients with suspected chronic pancreatitis undergoing endoscopic ultrasound.

Zubarik R, Ganguly E.

Division of Gastroenterology, The University of Vermont. Burlington, VT, USA.

The Rosemont classification system was designed to standardize the endosonographic assessment of chronic pancreatitis. To determine whether the Rosemont classification system can predict the response to pancreatic enzyme supplementation in patients undergoing endoscopic ultrasound (EUS) evaluation of suspected chronic pancreatitis. Sixty-five patients were included with abdominal pain undergoing endosonography for suspected chronic pancreatitis were included. Patients completed a questionnaire for evaluation of their abdominal pain. Group 1 (n=13) had EUS findings consistent with or suggestive of chronic pancreatitis. Group 2 (n=45) had EUS findings that were normal or indeterminate in the Rosemont classification system. Patients were given pancreatic enzyme supplementation and then given a follow-up pain questionnaire for a mean of 37 days subsequent to EUS regarding the change in pain. Group 1 patients were more likely to have a response to pancreatic enzymes (62% *vs*. 24%, P=0.012) and a decrease in their pain scale ratings (2.62 *vs*. 0.29, P=0.01). Computed tomography findings of chronic pancreatitis and narcotic use did not predict the response to pancreatic enzyme supplementation. The individual Rosemont criteria of hyperechoic foci with shadowing (P=0.03), lobularity (P=0.02), and stranding (P=0.001) were associated with improvement of pain after treatment. The Rosemont classification system can identify patients who are more likely to have improvement in abdominal pain after treatment with pancreatic enzyme supplementation.

J Gastroenterol 2011; Dec 21.
(PMID: 22183858)

Risk factors for pancreatic stone formation in autoimmune pancreatitis over a long-term course.

Maruyama M, Arakura N, Ozaki Y, Watanabe T, Ito T, Yoneda S, *et al.*

Department of Gastroenterology, Shinshu University School of Medicine. Matsumoto, Japan.

Autoimmune pancreatitis (AIP) has the potential to progress to a chronic state that forms pancreatic stones. The aim of this study was to clarify the risk factors underlying pancreatic stone formation in AIP. Sixty-nine patients with AIP who had been followed for at least 3 years were enrolled for evaluation of clinical and laboratory factors as well as computed tomography and endoscopic retrograde cholangiopancreatography findings. During the course of this study, increased or *de novo* stone formation was seen in 28 patients, who were defined as the stone-forming group. No stones were observed in 32 patients, who were defined as the non-stone-forming group. Nine patients who had stones at diagnosis but showed no change during the course of this study were excluded from our cohort. Univariate analysis revealed no significant differences in clinical or laboratory factors associated with AIP-specific inflammation between the two groups. However, pancreatic head swelling (P=0.006) and narrowing of both Wirsung's and Santorini's ducts in the pancreatic head region (P=0.010) were significantly more frequent in the stone-forming group. Furthermore, multivariate analysis identified Wirsung and Santorini duct narrowing at diagnosis as a significant independent risk factor for pancreatic stone formation (OR 4.4, P=0.019). A primary risk factor for pancreatic stone formation in AIP was narrowing of both Wirsung's and Santorini's ducts, which most presumably led to pancreatic juice stasis and stone development.

Clin Chem 2011; Dec 22.
(PMID: 22194634)

Serum microRNA expression profile as a biomarker in the diagnosis and prognosis of pancreatic cancer.

Liu R, Chen X, Du Y, Yao W, Shen L, Wang C, *et al.*

Tianjin Medical University Cancer Institute and Hospital, Key Laboratory of Cancer Prevention and Therapy. Tianjin, China.

Detection of pancreatic cancer (PaC), particularly at early stages, remains a great challenge owing to lack of specific biomarkers. We sought to identify a PaC-specific serum microRNA (miRNA) expression profile and test its specificity and sensitivity as a biomarker in the diagnosis and prognosis of PaC. The authors obtained serum samples from 197 PaC cases and 158 age- and sex-matched cancer-free controls. The authors screened the differentially expressed serum miRNAs with Illumina sequencing by synthesis technology using pooled serum samples followed by RT-qPCR validation of a large number of samples arranged in multiple stages. They used risk score analysis to evaluate the diagnostic value of the serum miRNA profiling system. To assess the serum miRNA-based biomarker accuracy in predicting PaC, the authors performed additional double-blind testing in 77 PaC cases and 52 controls and diagnostic classification in 55 cases with clinically suspected PaC. After the selection and validation process, 7 miRNAs displayed significantly different expression levels in PaC compared with controls. This serum 7-miRNA-based biomarker had high sensitivity and specificity for distinguishing various stages of PaC from cancer-free controls and also accurately discriminated PaC patients from chronic pancreatitis (CP) patients. Among the 7 miRNAs, miR-21 levels in serum were significantly associated with overall PaC survival. The diagnostic accuracy rate of the serum 7-miRNA profile was 83.6% in correctly classifying 55 cases with clinically suspected PaC. Tese data demonstrate that the serum 7-miRNA-based biomarker can serve as a novel noninvasive approach for PaC diagnosis and prognosis.

Cancer Epidemiol Biomarkers Prev 2011; Dec 22.
(PMID: 22194529)

Coffee, tea and sugar-sweetened carbonated soft drink intake and pancreatic cancer risk: a pooled analysis of 14 cohort studies.

Genkinger J, Li R, Spiegelman D, Anderson KE, Albanes D, Bergkvist L, *et al.*

Epidemiology, Mailman School of Public Health. New York, NY, USA.

Coffee has been hypothesized to have pro- and anti-carcinogenic properties, while tea may contain anti-carcinogenic compounds. Studies assessing coffee intake and pancreatic cancer risk have yielded mixed results, while findings for tea intake have mostly been null. Sugar-sweetened carbonated soft drink (abbreviated as SSB) intake has been associated with higher circulating levels of insulin, which may promote carcinogenesis. Few prospective studies have examined SSB intake and pancreatic cancer risk; results have been heterogeneous. In this pooled analysis from 14 prospective cohort studies, 2,185 incident pancreatic cancer cases were identified among 853,894 individuals during follow-up. Multivariate (MV) study-specific relative risks (RR) and 95% confidence intervals (CI) were calculated using Cox proportional hazards models and then pooled using a random effects model. No statistically significant associations were observed between pancreatic cancer risk and intake of

coffee (MVRR=1.10, 95% CI=0.81-1.48 comparing more than 900 g/day to 0 g/day; 237 g equal about 8 oz), tea (MVRR=0.96, 95% CI=0.78-1.16 comparing more than 400 g/day to 0 g/day; 237 g equal about 8 oz) or SSB (MVRR=1.19, 95% CI=0.98-1.46 comparing more than 250 g/day to 0 g/day; 355 g equal about 12 oz) (test for between-studies heterogeneity P>0.05). These associations were consistent across levels of sex, smoking status and body mass index. When modeled as a continuous variable, a positive association was evident for SSB (MVRR=1.06, 95% CI=1.02-1.12). Overall, no associations were observed for intakes of coffee or tea during adulthood and pancreatic cancer risk. Although the authors able to examine modest intake of SSB, there was a suggestive, modest positive association for risk of pancreatic cancer for intakes of SSB.

Autoimmune Dis 2012; 2012:251730.
(PMID: 22195277)

How does age at onset influence the outcome of autoimmune diseases?

Amador-Patarroyo MJ, Rodriguez-Rodriguez A, Montoya-Ortiz G.

Center for Autoimmune Diseases Research (CREA), School of Medicine and Health Sciences, Universidad del Rosario. Bogotá, Colombia.

The age at onset refers to the time period at which an individual experiences the first symptoms of a disease. In autoimmune diseases (ADs), these symptoms can be subtle but are very relevant for diagnosis. They can appear during childhood, adulthood or late in life and may vary depending on the age at onset. Variables like mortality and morbidity and the role of genes will be reviewed with a focus on the major autoimmune disorders, namely, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), multiple sclerosis (MS), type 1 diabetes mellitus (T1D), Sjögren's syndrome, and autoimmune thyroiditis (AITD). Early age at onset is a worst prognostic factor for some ADs (i.e., SLE and T1D), while for others it does not have a significant influence on the course of disease (i.e., SS) or no unanimous consensus exists (i.e., RA and MS).

PLoS One 2011; 6:e27670.
(PMID: 22194788)

Socioeconomic status and incident type 2 diabetes mellitus: data from the Women's Health Study.

Lee TC, Glynn RJ, Peña JM, Paynter NP, Conen D, Ridker PM, *et al.*

Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital. Boston, MA, USA.

The authors prospectively examined whether socioeconomic status (SES) predicts incident type II diabetes (diabetes), a cardiovascular risk equivalent and burgeoning public health epidemic among women. Participants include 23,992 women with Hb(A1c) levels less than 6% and no CVD or diabetes at baseline followed from February 1993 to March 2007. SES was measured by education and income while diabetes was self-reported. Over 12.3 years of follow-up, 1,262 women developed diabetes. In age and race adjusted models, the relative risk of diabetes decreased with increasing education (less than 2 years of nursing, 2 to less than 4 years of nursing, bachelor's degree, master's degree, and doctorate: 1.0, 0.7 (95% confidence interval (CI), 0.6-0.8), 0.6 (95% CI, 0.5-0.7), 0.5 (95% CI, 0.4-0.6), 0.4 (95% CI, 0.3-0.5); P(trend)<0.001). Adjustment for traditional and non-traditional cardiovascular risk factors attenuated this relationship (education: P(trend)=0.96). Similar associations were observed between income categories and diabetes. In conclusion, advanced education and increasing income were both inversely associated with incident diabetes even in this relatively well-educated cohort. This relationship was largely explained by behavioral factors, particularly body mass index.