PANCREAS ALERTS

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Coupled plasma filtration adsorption combined with continuous veno-venous hemofiltration treatment in patients with severe acute pancreatitis.

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Background. Severe acute pancreatitis (SAP) still has a high mortality rate. Coupled plasma filtration adsorption (CPFA) and continuous veno-venous hemofiltration (CVVH) are two extracorporeal blood purification techniques. The authors hypothesized that CPFA combined with CVVH could preferentially improve prognosis and suppress clinical manifestations of SAP. **Methods.** In this observational cohort study, 25 patients with SAP were enrolled, in which 12 received CPFA plus CVVH treatment (group 1), and 13 received CVVH therapy (group 2). All the patients underwent a successive 10-day intervention. Clinical indicators were detected before or after the intervention and the results were compared between the two groups. The feasibility and the survival rate were evaluated on day 28. **Results.** Compared with group 2, oxygenation index (PaO_2/FiO_2), mean arterial pressure, serum amylase, and blood urine nitrogen showed significant differences (all $P<0.01$) and serum TNF-α, IL-1β, IL-6 were reduced and IL-10 was elevated with time in group 1 (all $P<0.01$). Liver functions, electrolyte, and acid-base balance did not show significant difference before and after the 10-day treatment with CPFA plus CVVH compared with CVVH ($P>0.05$). No therapy-related adverse reactions were noted in both groups. Twenty-eight-day survival rate of group 1 was higher than that in group 2 (11/12, 91.7% *vs.* 7/13, 53.8%; $P<0.05$). **Conclusions.** CPFA combined with CVVH was an effective and safe method for treatment of SAP patients, the mechanism being related to its effect on regulating the level of cytokines and serum amylase.

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Probiotic treatment with Probioflora in patients with predicted severe acute pancreatitis without organ failure.

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Background. The authors previously demonstrated that probiotic prophylaxis did not prevent infectious complications in patients with predicted severe pancreatitis but unexpectedly increased the risk of bowel ischemia and mortality. The suggestion that these negative findings are only observed in the presence of organ failure at the start of probiotic treatment has not been confirmed. **Methods.** In a retrospective analysis, all patients with predicted severe acute pancreatitis without initial organ failure admitted to a medium care facility of a teaching hospital in Prague from January 2003 to December 2010 were included. All patients routinely received probiotic treatment with Probioflora. Total parenteral nutrition (TPN) was routinely started and shifted toward total enteral nutrition. Infectious complications, mortality and the incidence of bowel ischemia were recorded. **Results.** Ninety-nine consecutive patients (mean age 56 years) were included. Infectious complications occurred in 42 patients (42%), consisting of bacteraemia (n=40), pneumonia (n=11) and infected necrosis (n=11). Bowel ischemia was detected in two patients (2%). Overall mortality was 8%. **Conclusion.** In this retrospective study no apparent positive or negative impact of probiotic treatment with Probioflora was demonstrated when administered to patients with predicted severe acute pancreatitis without initial organ failure.

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Melatonin attenuates acute pancreatitis-associated lung injury in rats by modulating interleukin 22.

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Aim of the study. To investigate whether therapeutic treatment with melatonin could protect rats against acute pancreatitis and its associated lung injury. **Methods.** Seventy-two male Sprague-Dawley rats were randomly divided into three groups: the sham operation (SO), severe acute pancreatitis (SAP), and melatonin treatment (MT) groups. Acute pancreatitis was induced by infusion of 1 mL/kg of sodium taurocholate (4% solution) into the biliopancreatic duct. Melatonin (50 mg/kg) was administered 30 min before pancreatitis was induced, and the severity of pancreatic and pulmonary injuries was evaluated 1, 4 and 8 h after induction. Serum samples were collected to measure amylase activities, and lung tissues were

removed to measure levels of mRNAs encoding interleukin 22 (IL-22) and T helper cell 22 (Th22), as well as levels of IL-22. **Results.** At each time point, levels of mRNAs encoding IL-22 and Th22 were significantly higher (P<0.001) in the MT group than in the SAP group (0.526±0.143 *vs*. 0.156±0.027, respectively, here and throughout, after 1 h; 0.489±0.150 *vs*. 0.113±0.014 after 4 h; 0.524±0.168 *vs*. 0.069±0.013 after 8 h, 0.378±0.134 *vs*. 0.122±0.015 after 1 h; 0.205±0.041 *vs*. 0.076±0.019 after 4 h; 0.302±0.108 *vs*. 0.045±0.013 after 8 h, respectively) and significantly lower (P<0.001) in the SAP group than in the SO group (0.156±0.027 *vs*. 1.000±0.010 after 1 h; 0.113±0.014 *vs*. 1.041±0.235 after 4 h; 0.069±0.013 *vs*. 1.110±0.213 after 8 h, 0.122±0.015 *vs*. 1.000±0.188 after 1 h; 0.076±0.019 *vs*. 0.899±0.125 after 4 h; 0.045±0.013 *vs*. 0.991±0.222 after 8 h, respectively). The mean pathological scores for pancreatic tissues in the MT group were significantly higher (P<0.01) than those for samples in the SO group (1.088±0.187 *vs*. 0.488±0.183 after 1 h; 2.450±0.212 *vs*. 0.469±0.242 after 4 h; 4.994±0.184 *vs*. 0.513±0.210 after 8 h), but were significantly lower (P<0.01) than those for samples in the SAP group at each time point (1.088±0.187 *vs*. 1.969±0.290 after 1 h; 2.450±0.212 *vs*. 3.344±0.386 after 4 h; 4.994±0.184 *vs*. 6.981±0.301 after 8 h). The severity of SAP increased significantly (P<0.01) over time in the SAP group (1.088±0.187 *vs*. 2.450±0.212 between 1 h and 4 h after inducing pancreatitis; and 2.450±0.212 *vs*. 4.994±0.184 between 4 and 8 h after inducing pancreatitis). **Conclusion.** Melatonin protects rats against acute pancreatitis-associated lung injury, probably through the upregulation of IL-22 and Th22, which increases the innate immunity of tissue cells and enhances their regeneration

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Effect and cost of treatment for acute pancreatitis with or without gabexate mesylate: A propensity score analysis using a nationwide administrative database.

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Background. Despite a lack of evidence, gabexate mesylate (GM) is routinely used for the treatment of acute pancreatitis (AP) in some countries. The present study examined the effect and cost of GM for AP treatment using the Japanese Diagnosis Procedure Combination database. **Methods.** The authors performed a propensity score analysis to compare in-hospital mortality, length of stay (LOS), and total costs between patients with AP treated with GM and those without GM in 2010. **Results.** The authors identified 2,483 patients treated with GM and 890 patients without GM. Overall, 77% of the patients treated with GM were nonsevere AP cases. The propensity-matched 707 pairs showed no significant difference between GM users and nonusers in inhospital mortality or median length of stay in non-severe AP (1.0% *vs*. 1.2%, P=0.789; 10 *vs*. 10 days, P=0.160) and severe AP (8.4% *vs*. 5.0%, P=0.438; 12 *vs*. 14 days, P=0.487) cases. Total costs were significantly different between the GM users and the nonusers in non-severe AP cases (US$ 4,982 *vs*. US$ 4,373, P<0.001), but not in severe AP cases (US$ 6,605 *vs*. US$ 6,490, P=0.764). **Conclusions.** Using GM for non-severe AP cannot be justified because of higher costs without significant effects. Gabexate mesylate use is also not justifiable for severe AP because it does not reduce mortality or length of stay

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Similar efficacies of biliary, eith or without pancreatic sphincterotomy in treatment of idiopathic recurrent acute pancreatitis.

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Background. The role of sphincter of Oddi manometry (SOM) in the management of patients with idiopathic recurrent acute pancreatitis requires clarification. The authors evaluated the therapeutic effects of endoscopic sphincterotomy in patients with recurrent acute pancreatitis and the prognostic significance of pancreatic sphincter dysfunction (SOD). **Methods.** The authors performed a randomized trial of endoscopic retrograde cholangiopancreatography with SOM for patients with idiopathic recurrent acute pancreatitis. Patients with pancreatic SOD (n=69) were assigned randomly to groups that received only biliary sphincterotomy (BES) or a combination of biliary and pancreatic sphincterotomy (DES); patients who underwent normal SOM (n=20) were assigned randomly to groups that received BES or a sham surgery. The primary outcome was incidence of recurrent acute pancreatitis during the follow-up period (minimum, 1 year; maximum, 10 years). The authors also determined the incidence of chronic pancreatitis and analysed factors associated with recurrence of acute pancreatitis. **Results.** Among the 69 patients with SOD, 48.5% who received BES and 47.2% who received DES had recurrent acute pancreatitis (95% confidence interval: -22.3 to 24.9; P=1.0). In patients with normal SOM (n=20), 27.3% of those who received BES and 11.1% of those who received the sham surgery, had recurrent acute pancreatitis (95%

confidence interval: -49.5 to 17.2; P=0.59). Overall, 16.9% of subjects developed chronic pancreatitis during a median follow-up period of 78 months (interquartile range: 35-108 months). The odds of recurrent acute pancreatitis during follow-up evaluation were significantly greater among patients with SOD than those with normal SOM (unadjusted hazard ratio: 3.5; 95% confidence interval: 1.07-11.4; P<0.04), and remained so after adjusting for potential confounders (hazard ratio: 4.3; 95% confidence interval: 1.3-14.5; P<0.02). **Conclusions.** Among patients with pancreatic SOD, DES and BES have similar effects in preventing recurrence of acute pancreatitis. Pancreatic SOD is an independent prognostic factor, identifying patients at higher risk for recurrent acute pancreatitis. Clinical Trials Registration: Clinicaltrials.gov (NCT01583517).

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Expression of the antiapoptotic protein BAG3 is a feature of pancreatic adenocarcinoma and its overexpression is associated with poorer survival.

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Background. Pancreatic ductal adenocarcinoma (PDAC) is one of the most deadly cancers, being the fourth leading cause of cancer-related deaths. Long-term survival reaching 15% is achieved in less than 5% of patients who undergo surgery, and median survival is only 6 months in those with inoperable lesions. A deeper understanding of PDAC biologic characteristics as well as novel prognostic markers are therefore required to improve outcomes. **Methods.** Herein the authors report that BAG3, a protein with recognized anti-apoptotic activity, was expressed in 346 PDACs analysed, but was not expressed in the surrounding non-neoplastic tissue. **Results.** In a cohort of 66 patients who underwent radical resection (R0), survival was significantly shorter in patients with high BAG3 expression (median: 12 months) than in those with low BAG3 expression (median: 23 months) (P=0.001). Furthermore, the authors report that BAG3 expression in PDAC-derived cell lines protects from apoptosis and confers resistance to gemcitabine, offering a partial explanation for the survival data. **Conclusion.** These results indicate that BAG3 has a relevant role in PDAC biology, and suggest that BAG3 expression level might be a potential marker for prediction of patient outcome.