Conservative treatment of necrotizing pancreatitis improves outcome

Recent evidence suggests a conservative approach for infected necrotizing pancreatitis, but reliable outcome data in daily practice are scarce. Van Santvoort and colleagues describe the outcome of conservative and interventional treatment in 397 patients with necrotizing pancreatitis at 202 hospitals. Treatment was highly protocolized, as described in the PROPATRIA and PANTER trials. The primary outcome was mortality during index admission. Secondary outcome measures were organ failure, infection, and mortality of patients. The authors used their well-validated PANTER trial. The primary outcome was mortality during index admission. Secondary outcome measures were organ failure, infected necrosis, and mortality of patients. Overall mortality was 15% (93/639). Complete conservative treatment (no drainage procedures) was performed in 397 patients (62%), with an overall mortality of 7%. Mortality in patients with organ failure treated conservatively (N = 63) was 37%, and mortality in patients with infected necrosis (N = 11) treated conservatively was 0%. In the remaining 242 patients (38%), one or more interventions were performed. Overall, these patients were sicker on admission, and developed organ failure (73%) and infected necrosis (78%). Overall mortality in patients undergoing intervention was 27%. The longer the time between admission and intervention, the lower the risk of mortality: 0 to 14 days, 56%; 14 to 29 days, 26%; >29 days, 15%. The results were unchanged when adjusted for baseline prognostic factors. Mortality was extremely high (78%) after emergency laparotomy for suspected bowel ischaemia or abdominal compartment syndrome. A total of 208 patients (33%) underwent an intervention for infected necrosis. The longer the time between admission and intervention, the lower the risk of complications. A total of 130 patients (63%) underwent catheter drainage as the first intervention (overall mortality: 7%) and 45 (35%) were successfully treated without further necrosectomy. Those who needed additional necrosectomy had a mortality of 22%. Mortality of patients with a necrosectomy as the first intervention was 18%. Complications were greater in patients undergoing laparotomy compared to video-assisted retroperitoneal debridement and endoscopic transmural necrosectomy. Fewer complications occurred in patients undergoing catheter drainage as the first intervention than in patients undergoing primary necrosectomy (42% vs 64%, p = 0.003). Organ failure and mortality were higher in patients with pancreatic necrosis than in patients with peripancreatic necrosis alone. Infected necrosis was diagnosed in 202 patients (32%) at a median of 26 days, with a higher incidence in patients with pancreatic necrosis (47%) compared to peripancreatic necrosis alone (16%). Overall mortality with infected necrosis was 20%.

This is an extremely important cohort study providing further evidence for a conservative/minimally invasive approach for infected necrotizing pancreatitis. Although infected pancreatic necrosis remains an indication for intervention, a few patients may be treated with antibiotics alone. Patients with infected necrosis also benefit from postponing intervention and minimally invasive techniques. One-third can be treated with percutaneous catheter drainage only. Mortality remains high in those with multiple organ failure and patients after emergency laparotomy.


Nebulized anticoagulants limit pulmonary coagulopathy but not bacterial clearance or inflammation in Pseudomonas pneumonia

Several lines of evidence suggest that disturbed alveolar fibrin turnover is a feature of pneumonia that compromises pulmonary integrity and function. Anticoagulants may therefore improve outcome of pneumonia by improving bacterial clearance and reducing inflammation. Due to systemic side effects, local administration of anticoagulants seems preferable. Cornet and colleagues investigated the local and systemic effects of nebulized anticoagulants in pneumonia.

The authors used their well-validated Pseudomonas aeruginosa pneumonia model in rats. The animals were randomized to local nebulized treatment with placebo, rh-APC, plasma-derived AT III, heparin, or danaparoid. Healthy animals without pneumonia served as control. Measurements included cell numbers in lavage fluid, bacterial quantification in lungs and blood, coagulation parameters in lungs and blood, cytokines and chemokines in lungs, and lung histopathology. Pseudomonas aeruginosa pneumonia was associated with local activation of coagulation and inhibition of fibrinolytic activity. Rh-APC in particular, but also plasma-derived AT III and danaparoid, reduced BALF TATc. The ratio of TATc to AT was reduced by all anti-
Levosimendan improves human diaphragm function

Impaired force generation of the respiratory muscles is present in patients with COPD, congestive heart failure, and critical illness. The pathophysiology includes muscle atrophy and contractile protein dysfunction. Although often multifactorial, prolonged weaning from mechanical ventilation could benefit from pharmacological improvement of diaphragm function. Doorduin and colleagues investigated the effects of levosimendan (a calcium sensitizer) on the contractile function of the human diaphragm in healthy human volunteers. As such, the results of this study are intriguing and could have far-reaching consequences. However, further research is essential to show that the same results can be obtained in critically ill patients during weaning. Finally, a randomized controlled trial in difficult-to-wean patients would be necessary to prove that levosimendan may actually decrease the time spent on the ventilator. Until then, levosimendan cannot be recommended for this patient category.


ICU-acquired delirium has an impact on long-term cognitive functioning

ICU-acquired delirium is associated with increased acute morbidity and mortality, and may also have an effect on long-term outcome. Van de Boogaard and colleagues investigated health-related quality of life (HRQoL), including self-reported cognitive functioning, in ICU survivors with and without delirium at a median of 18 months after discharge.

The authors included all discharged patients who had a complete delirium screening during their ICU stay. Delirium screening was performed with the CAM-ICU three times a day. Several measures were taken to improve the quality of the delirium diagnosis. Patients with delirium were divided into three subtypes: hyperactive, hypoactive, and mixed alternating type. At a median of 18 months, discharged patients received an HRQoL questionnaire, including the Short Form-36 (SF-36), the Dutch Checklist Individual Strength (CIS), and the Cognitive Failure Questionnaire (CFQ). There were 1,292 ICU survivors, of whom 272 patients (21%) suffered from delirium during their ICU stay. A total of 915 (71%) returned the questionnaire (171 delirious - 744 non-delirious). After adjustment for covariates, patients with delirium had no significant difference in SF-36 and CIS scores compared to patients without delirium. However, patients with delirium reported more pronounced cognitive failure on the CFQ. The duration of delirium was weak (r = 0.21), but significantly correlated with the dimension memory of the CFQ. Patients with a hypoactive form of delirium had significantly better mental health than patients with a hyperactive or mixed alternating type.

This study confirms the deleterious long-term effects of ICU-acquired delirium on cognitive functioning. Interventions aimed at reducing ICU-acquired delirium may therefore have important long-term effects. This study also suggests that besides preventing delirium, reducing its duration may also be important. The relationship with the development of dementia is intriguing, and should be further explored.


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Impaired force generation of the respiratory muscles is present in patients with COPD, congestive heart failure, and critical illness. The pathophysiology includes muscle atrophy and contractile protein dysfunction. Although often multifactorial, prolonged weaning from mechanical ventilation could benefit from pharmacological improvement of diaphragm function. Doorduin and colleagues investigated the effects of levosimendan (a calcium sensitizer) on the contractile function of the human diaphragm in healthy volunteers.

They enrolled 30 healthy volunteers instrumented with a multielectrode oesophageal catheter with two balloons to measure diaphragm electromyographic activity (EMGdi) and oesophageal (Pes) and gastric (Pga) pressure. Cervical magnetic stimulation of the phrenic nerves was performed to measure twitch transdiaphragmatic pressure (Pdi). Inspiratory loading tasks were performed before and after administration of levosimendan or placebo. There was a significant decrease in Pdi after loaded breathing in the placebo group, but not in the levosimendan group. Levosimendan improved neuromechanical efficiency of the diaphragm (Pdi/EMGdi) by 21%, whereas neuromechanical efficiency was not affected in the placebo group. Respiratory effort sensation was not affected by levosimendan.

This study shows that levosimendan may restore diaphragm contractility in healthy human volunteers. As such, the results of this study are intriguing and could have far-reaching consequences. However, further research is essential to show that the same results can be obtained in critically ill patients during weaning. Finally, a randomized controlled trial in difficult-to-wean patients would be necessary to prove that levosimendan may actually decrease the time spent on the ventilator. Until then, levosimendan cannot be recommended for this patient category.