Association of Extent and Infection of Pancreatic Necrosis With Organ Failure and Death in Acute Necrotizing Pancreatitis

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Background & Aims: **Organ failure is the usual cause of death in acute necrotizing pancreatitis. Our objective was to study whether the extent and infection of pancreatic necrosis correlate with organ failure and mortality.** ***Methods:*** **All consecutive patients with acute pancreatitis were prospectively studied. They underwent a detailed clinical and investigative evaluation. Pancreatic necrosis, diagnosed on a computed tomography scan, was graded as <30%, 30%–50%, and >50% necrosis and characterized as either sterile or infected. Logistic regression analysis was done to find out the association of the extent and infection of pancreatic necrosis with organ failure and mortality.** ***Results:*** **Of 276 patients (mean age, 41.25 years; 172 men), 104 had pancreatic necrosis: 30 had <30% necrosis, 37 had 30%–50% necrosis, and 37 had >50% necrosis; 74 had sterile necrosis, and 30 had infected necrosis. Of them, 37 (35%) patients developed organ failure. Two significant factors were associated with the development of organ failure, the extent of necrosis (<30% necrosis vs 30%–50% necrosis: *P* = .03; odds ratio [OR], 5.82; 95% confidence interval [CI], 1.15–29.45; <30% necrosis vs >50% necrosis: *P* = .0004; OR, 18.86; 95% CI, 3.75–94.92) and infected pancreatic necrosis (*P* = .02; OR, 3.29; 95% CI, 1.17–9.24). The overall mortality was 22%. Infected pancreatic necrosis (*P* = .006; OR, 4.99; 95% CI, 1.56–16.02) and Acute Physiology, Age, and Chronic Healthy Evaluation II score (*P* = .004; OR, 1.28; 95% CI, 1.08–1.52) were 2 independent predictors of mortality.** ***Conclusions:*** **Extent of necrosis and infected pancreatic necrosis were associated with the development of organ failure in patients with acute necrotizing pancreatitis. Infected pancreatic necrosis was the most significant predictor of mortality.**

Acute necrotizing pancreatitis (ANP), a severe form of pancreatitis, occurs in 9%–20% of all patients with acute pancreatitis and is associated with significant morbidity and mortality.[1–3] The course of severe acute pancreatitis is often complicated by the development of organ failure.[4,5] Organ failure, especially multiorgan failure, is the usual cause of death in such patients with ANP.[3,6] Interstitial (non-necrotizing) acute pancreatitis is usually not associated with organ failure and takes a milder course with spontaneous resolution in the majority.[6] The mechanisms of local tissue injury leading to pancreatic necrosis and systemic injury manifesting as organ failure are intimately linked and involve recruitment and activation of neutrophils, production of various cytokines and vasoactive substances, and activation of inflammatory pathways.[7,8] Thus, there could be an association between the extent of pancreatic necrosis and the development of organ failure, both of which might depend on the severity of the inflammatory process. However, there are contradictory reports in the literature regarding the association of the extent of pancreatic necrosis with organ failure and mortality.[9–12] Although some studies have shown a definite association between the extent of pancreatic necrosis and organ failure,[9,10] other studies have not found this so.[11,12] Whether infection of the pancreatic necrosis modulates the development of organ failure is also not clear.[9,12] The objective of the present study was to investigate prospectively whether the extent and infection of the pancreatic necrosis are associated with the development of organ failure and mortality.

Methods

All consecutive patients with acute pancreatitis admitted under the gastroenterology services of our hospital, a tertiary care referral center, were included in the study. The diagnosis of acute pancreatitis was made in the presence of suggestive clinical features, increased serum amylase level (>2 times the upper limit of normal), and evidence of acute pancreatitis on imaging studies, ie, abdominal ultrasonography and/or computed tomography (CT) scan. A dynamic contrast-

Abbreviations used in this paper: ANP, acute necrotizing pancreatitis; APACHE II, Acute Physiology, Age, and Chronic Health Evaluation II; CECT, contrast-enhanced computed tomography; CI, confidence interval; CT, computed tomography; FNA, fine-needle aspiration; OR, odds ratio.

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Table 1. Demographic Profile of Patients at Admission

Total number of patients (n)	276
Male, female	172, 104
Age (*y*, mean ± SD) (range)	41.25 ± 13.68 (15–80)
Duration of disease before admission (*days*, mean ± SD) (range)	7.74 ± 13.88 (1–110)
Duration of hospital stay (*days*, mean ± SD) (range)	17.81 ± 17.87 (2–191)

SD, standard deviation.

enhanced computed tomography (CECT) scan of the abdomen was done by using a helical CT machine with rapid acquisition of images. This was done in patients with acute pancreatitis usually at the end of first week except in patients with clinically mild pancreatitis who improved with conservative treatment within the first week of the onset of acute pancreatitis. CECT scan was also done at the time of admission if the diagnosis of acute pancreatitis was not certain. It was repeated during the course of the illness if the clinical condition of the patient so warranted, eg, assessing the CT signs of acute pancreatitis if the patient's condition was deteriorating and looking for the development of complications such as pseudocyst and abscess, especially if any intervention such as drainage or surgical treatment was contemplated.

Pancreatic Necrosis

Pancreatic necrosis was diagnosed as non-enhancing (nonviable) areas of pancreas on a CECT scan. The amount of pancreatic necrosis was graded as <30%, 30%–50%, and >50% (massive). A CT severity score was calculated according to Balthazar et al.[13] An experienced consultant radiologist interpreted and reported the CT findings.

Pancreatic necrosis was characterized as sterile or infected. Infected pancreatic necrosis was suspected if there was evidence of sepsis in the form of development of fever and/or increased leukocytosis in a patient with necrotizing pancreatitis. The diagnosis of infected pancreatic necrosis was made when pancreatic necrotic tissue showed presence of bacteria on Gram stain or when it grew an organism on culture. It was cultured for aerobic, anaerobic, and fungal organisms. Pancreatic tissue was obtained by either a fine-needle aspiration (FNA) done under ultrasonography guidance or at surgery. The FNA was performed in the second or third week of the illness. FNA was repeated in the following week if the first FNA was negative and the signs of sepsis persisted. The mean and median durations of time from the onset of symptoms until FNA were 16.73 and 14 days, respectively. In patients with suspected infected pancreatic necrosis, presence of extraintestinal gas in the pancreatic bed on a CT scan was taken as other evidence of infected necrosis. Other causes of fever were also looked for, eg, cholangitis, intravenous line sepsis, and chest infection; appropriate cultures of blood and fluids such as bile (if available), sputum, and urine, and other material such as an intravenous catheter were obtained periodically.

Organ Failure

Organ failure was defined according to Atlanta classification[14] as follows: respiratory failure (partial pressure of arterial oxygen [paO_2], <60 mm), acute renal failure (serum creatinine, >2.0 mg/dL), cardiovascular failure (systolic blood pressure, <90 mm Hg any time during the course of acute pancreatitis), or severe gastrointestinal bleeding (>500 mL/24 h).

Severity of Acute Pancreatitis

The severity of acute pancreatitis was defined by at least one of the following criteria: (1) clinical: presence of one or more organ failures as defined above[14]; (2) Acute Physiology, Age, and Chronic Health Evaluation II (APACHE II) score: an APACHE II score of >8.[15]

Management

All patients were managed according to a predefined management protocol. They were treated conservatively with nil by mouth, analgesics, intravenous fluids, and supportive treatment. Antibiotics were prescribed if (1) patients had infected necrosis, (2) there was documented infection such as cholangitis, (3) patients had severe ANP, and (4) patients had signs of sepsis in the form of fever and leukocytosis even in absence of documented infection, provided the fever (temperature >38°C) persisted for more than 2 days.[16] The antibiotics chosen were according to the culture and sensitivity report whenever available. In the absence of a sensitivity report, a combination of cefotaxime, amikacin, and metronidazole was used initially. We changed this combination to ceftazidime, ofloxacin, and metronidazole in the year 2000 after we found that the infecting organisms were sensitive to these antibiotics in our patients with acute pancreatitis.[17] In patients with mild pancreatitis, oral feeding was resumed soon after abdominal pain subsided. Feeding was started with clear liquids. In patients with severe pancreatitis, a nasojejunal tube was placed and enteral feeding started unless the patient had severe ileus or active gastrointestinal bleeding, in which case parenteral nutrition was instituted. The calorie intake was increased gradually to 2000–3000 Kcal/day. Patients with clinically severe acute pancreatitis were treated in an intensive care unit, and all possible organ support systems were utilized including ventilatory support, vasopressors, and dialysis as and when required. Patients with biliary obstruction, as evidenced by abnormal liver function test results and biliary ductal dilata-

Table 2. Etiology of Acute Pancreatitis

Etiology	n (%)
Biliary	123 (44.6)
Alcohol	49 (17.7)
Post-ERCP	16 (5.8)
Miscellaneous	19 (6.9)
Idiopathic	69 (25)
Total	276 (100)

n, number of patients; ERCP, endoscopic retrograde cholangiopancreatography.