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Is Early or Late Surgical Intervention More Beneficial in Acute Necrotizing Pancreatitis?

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Abstract

Objective: Infective necrotizing pancreatitis is widely accepted as a surgical disease, but the appropriate timing of surgical intervention is controversial. Some authors prefer early surgery, while most consensus and guidelines agree that late surgery has more benefit. We reviewed our institutional experience in the surgical management of necrotizing pancreatitis, focusing on the results of early and late surgical intervention.

Materials and Methods: Data for patients with necrotizing pancreatitis who underwent surgical intervention between July 1996 and June 2004 were analyzed. According to the timing of surgical intervention, they were subdivided into the early group (≤14 days after disease onset, 7 patients) and late group (>14 days after disease onset, 11 patients).

Results: Patients in the early surgery group had more operations (mean, 3.86 *vs.* 1.36; $p=0.0342$) and a higher mortality rate (42.8% *vs.* 0%; $p=0.043$) compared to the late surgery group.

Conclusion: Our experience was that late surgery for necrotizing pancreatitis can lead to a lower mortality rate and is more beneficial to patients, which is in agreement with most consensus and guidelines. [*Tzu Chi Med J* 2008;20(4):286–290]

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1. Introduction

According to the Atlanta consensus in 1993, acute pancreatitis can be allocated into the mild or severe type [1]. Eighty percent of patients have mild acute pancreatitis and this type is less complicated. Conversely, severe acute pancreatitis (in about 10–25% of patients) is a relatively more fatal form, with a mortality of approximately 30–40% [2,3]. Surgeons need to consider candidates who may need surgical intervention. Most consensus and published guidelines agree that sterile necrotizing pancreatitis should be managed conservatively and surgical treatment should be preserved for infective cases [4,5]. However, the timing of surgery for necrotizing pancreatitis remains controversial [6]. In this retrospective study, we reviewed our experience of the surgical treatment of necrotizing pancreatitis in a small medical center in eastern Taiwan, with a focus on the most appropriate timing of intervention.

Table 1 — Comparison of early and late groups*

	Early	Late	*p*
Number of patients	7	11	
Gender (male/female)	7/0	8/3	0.245
Age (yr)	42.1 (30–72)	32.7 (20–46)	0.089
Etiology			
Alcohol-related	2	5	
Hyperlipidemia	0	3	
Both alcohol-related and hyperlipidemic	3	2	
Post-traumatic	2	0	
Biliary	0	1	
Ranson score	4 (1–6)	3.1 (0–5)	0.299
Number of operations	3.86 (1–11)	1.36 (1–3)	0.034†
Preoperative organ failure‡	4 (57.1%)	3 (27.3%)	0.335
Hospital stay (survivors)	68.75 (31–112)	80.5 (29–155)	0.614
Morbidity	6 (85.7%)	7 (67.3%)	1.000
Mortality	3 (42.8%)	0	0.043†

*Data presented as *n*, mean (range), or *n* (%); †$p<0.05$; ‡number of patients who developed organ failure preoperatively.

2. Materials and methods

The records of consecutive patients with a diagnosis of acute pancreatitis admitted to Buddhist Tzu Chi General Hospital from July 1996 to June 2004 were obtained from the computerized database of the hospital. The search was according to the International Classification of Diseases-9 (ICD-9) code for acute pancreatitis (code 577.0).

From the resultant cohort, subsequent restriction focused on patients who underwent surgical debridement, necrosectomy or pancreatectomy. Their medical records were reviewed, and those whose diagnosis was not necrotizing pancreatitis were excluded. The diagnosis of necrotizing pancreatitis was based on preoperative abdominal computed tomography (CT) features (a non-enhanced pancreatic parenchyma of more than 3 cm or more than 30% of the parenchyma in an enhanced CT scan) or intraoperative findings. The etiology of acute pancreatitis was defined in each patient. These patients were further subdivided into two groups: those who received their first surgical intervention ≤ 14 days after disease onset (early group), and those who underwent surgical intervention > 14 days (late group) after disease onset. The decision to proceed to surgical exploration was judged by the individual attending surgeon, basically according to bacteriological results of fine-needle aspiration (FNA) or deterioration of the clinical course in spite of aggressive intensive care. The following variables were obtained in each group: age, gender, Ranson score, preoperative organ failure status, number of operations, and morbidity and mortality rate. The length of hospital stay (LOS) was determined in patients who survived. We then compared survivors and nonsurvivors with the same variables in the early and late groups.

Statistical analysis of variables between the early and late groups was made using Student's unpaired *t* test and Fisher's exact test when appropriate. Probabilities ≤0.05 were considered significant.

3. Results

Overall, there were 329 patients with a diagnosis of acute pancreatitis identified from July 1996 to June 2004, with a total of 18 patients who underwent surgical intervention (surgical debridement, necrosectomy or pancreatectomy) for necrotizing pancreatitis, which accounted for 5.4% of this cohort. The mean age of the patients was 36.38 years (range, 20–72 years), and the male-to-female ratio was 5:1. The etiologies of acute pancreatitis were alcohol-related in seven patients (38.9%), hyperlipidemia in three patients (16.7%), both alcohol-related and hyperlipidemia in five patients (27.8%), post-traumatic in two patients (11.1%), and biliary in one patient (5.5%) (Table 1). Surgery was performed in 16 of the 18 patients because they were considered infective according to the results of FNA. In the remaining two patients, one had surgery due to persistent fever although the FNA culture was negative. The other patient had hemoperitoneum and was in a state of shock. The preoperative microbiological results of those who received FNA preoperatively showed that 12 patients had polymicrobial (75%) infection and four patients had monomicrobial (25%) infection. *Escherichia coli* was cultured in four patients, and it was cultured most frequently. The morbidity rate for all patients was 83.3% (15 of 18 patients), and the mortality rate was 16.7% (3 of 18 patients). The most common complication was wound infection (Table 2).

There were seven and 11 patients in the early and late groups, respectively. Patient data are shown in Table 1. The differences in age, gender, Ranson score, preoperative organ failure, LOS and morbidity were not significant. However, the mean number of operations (3.86 *vs.* 1.36) and the mortality rate (42.8% *vs.* 0%) were all significantly higher in the early group ($p=0.034$ and $p=0.043$, respectively) (Table 1).

4. Discussion

Acute pancreatitis is a medical disease most of the time, and it usually resolves uneventfully. Most deaths occur in patients with severe acute pancreatitis, which is usually a clinical manifestation of pancreatic necrosis [1]. The clinical course of severe acute pancreatitis can be divided into two phases. The first phase encompasses the first 2 weeks and has the features of systemic inflammatory response syndrome (SIRS). The release of proinflammatory mediators contributes to the pathogenesis of SIRS-associated pulmonary, cardiovascular, and renal insufficiency. The second phase is accompanied by local or systemic infectious complications, and the incidence of infection in pancreatic necrosis is about 30–70% [5,7]. This distinction also explains the differences in causes of death as time progresses, that is, multiorgan failure due to SIRS in the early stage and sepsis in the late stage.

Table 2 — Postoperative complications

	Early (*n*)	Late (*n*)	Total (*n*)
Wound infection	3	5	8
Sepsis	4	1	5
Residual abscess	1	3	4
Colon perforation	3	1	4
Enterocutaneous fistula	0	3	3
Acute renal failure	1	0	1
Acute respiratory distress syndrome	1	0	1
Splenic pseudoaneurysm	1	0	1
Ventral hernia	1	0	1
Choledochocutaneous fistula	1	0	1
Pancreatic fistula	1	0	1

There is not much debate concerning conservative treatment with aggressive intensive care as long as the necrosis is sterile. Surgical intervention should be undertaken when infective necrosis is confirmed [2–5,7–16], although some reports on nonoperative management of infective necrotizing pancreatitis have been published recently [17,18]. Other indications for surgical treatment include intestinal infarction or perforation, exsanguinating hemorrhage, and abdominal compartment syndrome [2,19–23].

The most conflicted issue is the timing of surgical intervention for infective necrotizing pancreatitis. This can be classified into early or late intervention. The rationale for early intervention is that infected necrosis tends to have a greater extent of necrosis, a greater number of organ failures and an increased mortality rate. Surgical or radiologic intervention that provides adequate debridement or drainage to control the necrosis can eradicate the cause of organ failures. Failure to do so may result in 100% mortality. Those who support late intervention claim that the demarcation of viable and nonviable tissue is clearer in the late stage and can lead to less trauma to normal pancreatic tissue and decrease surgical mortality. The amount of remaining pancreatic parenchyma strongly influences the quality of long-term results with regard to endo- and exocrine pancreatic function [24]. Furthermore, most patients respond to intensive care treatment and surgery can be avoided [3,5,6].

There is no clear definition of what constitutes early and late intervention. In the series published, the definition of *early intervention* was as short as 3 days and as long as 14 days (Table 3). The results of published series are not identical. Three series concluded that late surgery decreased mortality [25–27], while another three series concluded that mortality was not statistically different between early and late surgery, although it was actually higher in the early surgery group [28–30]. In a prospective, randomized study, Mier et al compared patients who underwent their first operation within 48–72 hours of onset with those who had surgery at least 12 days later. Although the difference in mortality rate (58% in the early group *vs.* 27% in the late group) did not reach statistical significance, the odds ratio for mortality was 3.4 times

Table 3 — Published series on surgical timing for necrotizing pancreatitis

Authors (year) [Ref.]	Patients (early/late)	Timing (early/late)	Mortality (early/late)	Significance
Mier et al (1997) [28]	25/11	<3d/>12d	56%/27%	No
Takeda et al (1998) [29]	110/69	≤14d/>14d	27.3%/27.5%	No
Hungness et al (2002) [30]	14/11	≤14d/>14d	29%/18%	No
Yang et al (2002) [26]	16/38	<3d/>3d	37.5%/10.5%	Yes
Hartwig et al (2002) [25]	30/32	<3d/>3d	53%/22%	Yes
Besselink et al (2007) [27]	16/11 26	≤14d/15–29d >30d	75%/45% 8%	Yes

higher in the early group, which led them to stop the study due to the high mortality in the early surgery group [28]. In another retrospective review, Hungness et al found that patients debrided early had a trend toward higher mortality (29% *vs.* 18%) and experienced a higher number of major complications ($p<0.05$) [30]. Takeda et al found that there was no difference in mortality between patients who had early surgery (≤14 days) and those who had late surgery (>14 days) (27.3% *vs.* 27.5%) [29]. In a recent retrospective study, Besselink et al demonstrated that the mortality was even lower when surgery was performed after 30 days (8% *vs.* 75% in the 1–14-day group and 45% in the 15–29-day group; $p<0.001$) [27]. We used 14 days as a cut-off according to International Association of Pancreatology guidelines [5]. In our study, patients in the late surgery group had fewer operations and a lower mortality rate compared to those in the early surgery group ($p=0.034$ and $p=0.043$, respectively).

One of the reasons for the high mortality in surgical patients with necrotizing pancreatitis is that surgery results in major trauma to patients. In this era of minimally invasive surgery, this impact may be decreased. There are some data concerning this technique, but it has not yet been accepted as standard procedure [6,31–33].

In conclusion, we found that surgery more than 14 days after disease onset can result in decreased mortality compared to surgery before 14 days. This result coincides with most consensus and guidelines.

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