

Pancreatic Necrosis

Results of Necrosectomy, Packing, and Ultimate Closure Over Drains

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Objective

The treatment of pancreatic necrosis at a tertiary referral center was reviewed to effect better patient outcome.

Summary Background Data

Pancreatic necrosis is a devastating disease that leads to death in 10% to 50% of cases. Infected necrosis is particularly deadly because 80% of deaths from necrosis are due to infection or its complications. Therapeutic strategies center on aggressive support of organ systems and prevention and treatment of infectious complications.

Methods

Records of all patients who underwent pancreatic necrosectomy from 1990 to 1996 at Emory University Hospital were reviewed. Patients with infected necrosis were debrided as soon as the diagnosis was made. Reoperation for completion necrosectomy with ultimate closure over lavage catheters was performed as necessary.

Results

Of the 244 patients admitted with acute pancreatitis in the study period, 50 underwent pancreatic debridement. The mean age was 52 years, and 74% of patients were transferred from other institutions. Eighty-four percent of patients had infected necrosis, and all patients underwent sequential debridement with eventual closure over drains. Organ failure occurred in 72% of cases, and the overall mortality rate was 12%. The mean length of stay was 54 days.

Conclusions

The management of pancreatic necrosis demands the allocation of extensive resources. An aggressive operative strategy of multiple debridements with ultimate closure over drains can lead to a low mortality rate in patients with this complex disease, but the determination of when to explore patients with sterile necrosis remains difficult.

Pancreatic necrosis is the most devastating complication of acute pancreatitis. Management of this complex disease has improved dramatically over the past decade, and mortality rates are regularly reported in the range of 20% instead of the 50% to 70% range reported in the 1970s.¹⁻³ Despite this improvement, 80% of deaths from acute pancreatitis evolve from infectious complications of pancreatic and peripancreatic necrosis.

The steps available and necessary in the effective management of acute pancreatitis are becoming well

standardized. The clinical features, laboratory diagnosis, radiographic findings, and even prognostic assessment are usually straightforward even in severe cases. Moreover, the consensus is that patients with infected necrosis should undergo debridement.

Several controversies remain. Deciding when to operate on patients with sterile necrosis remains difficult.⁴⁻⁶ Debridement with immediate closure over drains, debridement with open or semi-open packing, and staged debridement with closure over irrigation drains are the three most widely reported methods of operative management. Each method has advantages, and results vary widely.^{2,3,7} Patient outcome after recovery from the episode of necrosis depends on many variables, and longitudinal follow-up is critical to determine whether the management was effective.

This study was undertaken to assess the treatment of

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Table 1. EVALUATION OF SEVERITY OF ACUTE PANCREATITIS

Criteria for Organ System Failure	
Organ System	Criteria
Cardiovascular	Mean arterial pressure ≤ 50 mm Hg. Need for volume loading and/or vasoactive drugs to maintain systolic blood pressure above 100 mm Hg. Heart rate ≤ 50 beats min^{-1} . Ventricular tachycardia/fibrillation. Cardiac arrest. Acute myocardial infarction.
Pulmonary	Respiratory ≤ 5 min^{-1} of ≤ 50 min^{-1} . Mechanical ventilation for 3 or more days or fraction of inspired oxygen (F_{iO_2}) > 0.4 and/or positive end-expiratory pressure > 5 mm Hg.
Renal	Serum creatinine ≥ 280 $\mu\text{mol L}^{-1}$ (3.5 mg. dl^{-1}). Dialysis/ultrafiltration.
Neurologic	Glasgow coma scale ≤ 6 (in the absence of sedation).
Hematological	Hematocrit $\leq 20\%$. Leukocyte count $\leq 0.3 \times 10^9 \text{ L}^{-1}$. Thrombocyte count $\leq 50 \times 10^9 \text{ L}^{-1}$. Disseminated intravascular coagulation.
Hepatic	Total bilirubin level ≥ 51 $\mu\text{mol L}^{-1}$ (3 mg. dl^{-1}) in the absence of hemolysis. Serum glutamic-pyruvic transaminase $> 100 \text{ UL}^{-1}$
Gastrointestinal	Stress ulcer necessitating transfusion of more than 2 units of blood per 24 hrs. Acalculous cholecystitis. Necrotizing enterocolitis. Bowel perforation.

Criteria for organ system failure in acute pancreatitis after Tran and Cuesta, *Am J Gastroenterol* 87:604–608, 1992.

pancreatic necrosis at a tertiary referral center to assess and improve patient outcomes.

MATERIALS AND METHODS

The records of all patients who underwent exploration and debridement for pancreatic necrosis at Emory University Hospital from 1990 through 1996 were reviewed. Demographic data were tabulated. Data concerning the course of illness were evaluated including etiology, length of stay, (intensive care unit and ward), time to and number of debridements, and days receiving ventilator support. Multiple organ failure scores were evaluated by the criteria of Tran and Cuesta and modified for acute pancreatitis (Table 1).⁸ The diagnosis of pancreatic necrosis was confirmed by bolus contrast computed tomography (CT) scan. The Balthazar scheme was used to grade the scans.⁹ Two patients had grade B scans, one patient had a grade C scan, whereas the remainder had grade D or E scans, comprising a fluid collection (D) or collections (E). Necrosis or gas in the pancreas or peripancreatic tissues was present in all scans, but the percent of necrosis was not estimated, which makes the combined scoring system impossible to use. Whether the necrotic material was infected was determined by culture of fine-needle aspirates or of material obtained at debridement. Ultimate pancreatic function and sequelae of the necrosis were analyzed. Intermediate follow-up of at least 12 months was performed for all available patients. Length of stay and survival data were analyzed by Fisher's exact test.

Operative Treatment

The decision to proceed with debridement was based primarily on the presence of infection. When gas was seen in the pancreas or peripancreatic tissues, or organisms were cultured from aspirated material, debridement was per-

formed. In the absence of proven infection, patients underwent debridement if other complications developed (e.g., obstruction or bleeding) or if the patient exhibited a persistent systemic inflammatory response syndrome (SIRS) despite negative cultures or in the face of persistent organ dysfunction despite maximal hemodynamic and nutritional support. Timing of surgical intervention in such patients was widely variable and purely at the discretion of the individual surgeon.

Exploration was undertaken by a generous midline or chevron incision. The lesser sac was entered by the gastrocolic omentum by its division with clamps and ties. This approach was preferred because the inframesocolic space is usually uninvolved by the peripancreatic necrosis and infection and is left isolated if possible. All necrotic tissue is debrided unless it is densely adherent to vital structures (e.g., superior mesenteric vein, superior mesenteric artery, duodenum), and all spaces shown by CT scan to be involved are opened and debrided. This may require opening the left or right paracolic gutters, the pararenal spaces, the retroperitoneum into the pelvis, or the gastrohepatic omentum. High-volume and warm 0.9% NaCl irrigation is performed. Splenectomy was occasionally required if the splenic artery and vein were thrombosed or if splenic abscesses were present. Complete debridement was not always possible during this first exploration. Some patients were too unstable hemodynamically to tolerate a long procedure. Necrotic material was sometimes too densely adherent to vital structures to safely remove. Some patients became cold and coagulopathic, making complete debridement unsafe. In such cases, Mikulicz pads were packed in all debrided spaces, and the patient closed in a temporary fashion. The patient was returned to the operating room in 24 to 48 hours, at which time the packs were removed and further debridement was performed. The process was repeated if necessary, and at the time of the final debridement, adjunctive proce-

dures were performed if necessary (e.g., cholecystectomy, gastrostomy, feeding jejunostomy, colostomy, duodenal intubation, pyloric exclusion, colostomy, ileostomy or splenectomy). Whether one or multiple debridements are needed, triple-lumen sump drains (Davol) are placed into the debrided spaces for postoperative irrigation and suction. The drains were irrigated with 0.9% sodium chloride (NaCl) and connected to continuous low-wall suction until there was no particulate matter in the effluent. The irrigation was then discontinued, and the drains remained on suction until there was minimal output. When a CT scan or sinogram showed complete collapse of the cavities and the volume of drainage remained low, the triple-lumen sump catheters were replaced with red rubber catheters (26–30 French) that were subsequently downsized to 14 to 16 French and gradually withdrawn.

RESULTS

Of 224 patients admitted to Emory University Hospital with the diagnosis of acute pancreatitis, 50 underwent debridement. Twenty-seven (54%) patients were men and 23 (46%) were women. Because the hospital is a tertiary referral center for Georgia, South Carolina, eastern Alabama, and northern Florida, 74% of the patients were first admitted to other hospitals and later transferred to Emory (mean, 13.8 days; range, 1–80 days).

The etiology of pancreatitis was gallstones in 21 patients (42%), idiopathy in 11 patients (22%), alcoholism in 7 patients (14%), hyperlipidemia in 4 patients (8%), endoscopic retrograde cholangiopancreatography induced in 3 patients (6%), steroid use in 3 patients (6%), pancreas divisum in 2 patients (4%), and trauma in 1 patient (2%). Forty-two patients (84%) had infected necrosis, whereas 8 patients (16%) had sterile necrosis at the time of surgery.

Forty (80%) patients were discharged home, 4 (8%) were discharged to rehabilitation facilities, and 6 (12%) died. Of the six patients who died, three underwent chronic steroid therapy. Three of the six patients had infected necrosis, whereas three had sterile necrosis. The mortality rate for patients with infected necrosis was 3 of 42 or 7%, whereas the mortality rate of those with sterile necrosis who underwent surgery was 3 of 8 or 42% ($p < 0.05$ compared with infected necrosis).

Treatment

The average time of the first debridement from the initial hospitalization was 27 days (range, 1–134 days) and from hospitalization at Emory was 14.5 days (range, 1–120 days). Twenty-six patients required single debridements, whereas 24 required from 2 to 13 debridements. All redebridements were performed in the operating room. The average intensive care unit (ICU) stay was 23.2 days (range, 0–119 days), whereas the average ward stay was 27 days (range, 8–124 days), and the average total stay in the 44 discharged

Table 2. LENGTH OF STAY AS RELATED TO ORGAN DYSFUNCTION

Condition (No. of Patients)	Mean \pm SEM (days)	Range (days)
Sepsis or SIRS (22)	93 \pm 31	35–186
Multiple Organ Failure (19)	95 \pm 34	27–186
Acute respiratory distress syndrome (12)	115 \pm 20	65–186
No organ failure (14)	38 \pm 15	9–122* ($p < 0.05$)

SIRS = systemic inflammatory response syndrome (At least two of the following; 1) oral temperature $>38^{\circ}\text{C}$; 2) respiratory rate of >20 breaths/min or $\text{PaCO}_2 <32$ torr; 3) heart rate >90 beats/min; 4) leukocyte count of $>12,000/\mu\text{L}$ or 10% bands.

* Compared with patients in other groups.

Length of stay as related to organ dysfunction in 44 patients surgically treated for pancreatic necrosis, who were alive at discharge from hospital.

patients was 54 days (range 9–186 days). Most patients were treated initially with total parenteral nutrition. After debridement, enteral feeding was attempted either orally or by a nasogastric or jejunostomy feeding tube. Average time to full enteral nutrition was 28 days (range, 1–155 days).

Organ Dysfunction

Twenty-five patients (50%) exhibited multiple-organ dysfunction, whereas 11 others (22%) exhibited dysfunction of a single organ system. Of the 36 patients with organ dysfunction, hepatic (75%), pulmonary (67%), cardiac (42%), renal (31%), and hematologic (31%) were most often affected, whereas the gastrointestinal (17%) and neurologic (8%) systems were involved less often. Fifty-six percent of patients exhibited microbial sepsis or SIRS (at least two of the following: 1) oral temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$; 2) respiratory rate of >20 breaths per minute or $\text{PaCO}_2 <32$ torr; 3) heart rate >90 beats per minute; or 4) leukocyte count of $>12,000/[\text{L}$ or 10% bands]), and 32% had radiographic and clinical evidence of adult respiratory distress syndrome. Of patients with organ dysfunction, 28 (78%) had single or multiple-organ dysfunction before surgery, whereas 22% developed organ dysfunction after surgery.

The average multiple organ failure score in the 44 patients who survived was 1.7, whereas in the 6 patients who died, the mean MOF score was 4.0. Organ failure was associated with increased length of stay (Table 2). Patients with multiple organ failure had an average length of stay of 95 ± 34 days (range, 27–186 days), whereas patients with adult respiratory distress syndrome as the manifestation of pulmonary failure had a average stay of 115 ± 20 days (range, 65–186 days). (Note that the shortest hospital stay for any patient with adult respiratory distress syndrome was 65 days.) Conversely, patients with no organ dysfunction had a significantly shorter length of stay, with an average of 38 ± 15 days (range, 9–122 days) ($p < 0.05$).

Table 3. THIRTY-TWO COMPLICATIONS IN 23 PATIENTS REQUIRING READMISSION TO HOSPITAL FOLLOWING DISCHARGE AFTER PANCREATIC NECROSECTOMY

Complication	Number	%
Abscess (intraabdominal)	6	26
Pseudocyst	6	26
Infection (biliary stent, pyelonephritis empyema, wound)	6	26
Fistulae (pancreatico-colo-cutaneous, pancreatic, enteric, gastric)	4	17
Diabetes	3	13
Cholelithiasis	2	9
Pancreatic duct stricture	2	9
Acute pancreatitis	1	4
Congestive heart failure	1	4
Bowel obstruction	1	4

Complications and Outcome

Fistulae from the pancreas, (defined as elevated amylase in the effluent of a pancreatic or peripancreatic drain) were always present. Octreotide was not used routinely in the treatment of these fistulas. Although gastric, colonic, or duodenal fistulae were unusual (16%), 32 of 44 (72%) patients discharged had elevated amylase from remaining drains. Two patients with pancreas fistulas underwent diversion ileostomies. Both patients underwent partial colectomy and ileostomy reversals after 4 and 6 months when the fistulas had closed. One of these two patients died of complications of sepsis. Only one pancreaticocutaneous fistula required operative closure 8 months after discharge. Pancreatic endocrine (34%), exocrine (32%), or endocrine and exocrine (16%) insufficiency was present during hospitalization in the 44 surviving patients.

Twenty-three (55%) of the survivors were readmitted to Emory University Hospital after discharge. Pancreatic complications were common, and pseudocyst and abscess was often seen (Table 3). Of the 23 patients readmitted with complications, 10 patients required reoperation (Table 4).

Follow-up

Thirty patients were available for follow-up in November 1997. The median time, from original presentation to last follow-up was 40 months (mean, 43; range, 12–93 months). Four additional patients had died, only one of whom (mentioned above) died of complications related to her pancreatitis. Twelve patients (40%) had endocrine insufficiency, whereas seven patients (23%) had exocrine insufficiency. Only four patients (13%) had endocrine and exocrine insufficiency as a result of their necrosis. Seventy-three percent ate a diet modified for pancreatic endocrine or exocrine insufficiency. Twelve patients (40%) drank ethanol before

their necrosis, whereas only 2 (7%) currently drink ethanol. Only 17 patients were employed outside the home before debridement, of these, 8 have returned to work, and 2 who retired. Twenty-five patients (83%) have returned to what they considered to be completely normal activity levels.

DISCUSSION

The management of patients who have pancreatic necrosis is challenging. The patients are typically ill for an extended period and require numerous medical, surgical, radiologic, and nutritional interventions if they are to survive.^{12,13} The patients in this study represent approximately 2700 patient days in the hospital and more than 1100 ICU days. The physician, nurse, and ancillary service resources allocated to these patients are daunting. Though much of their care was standardized, numerous issues arose that led us to question our methods and practices.

The terminology associated with pancreatic necrosis and acute pancreatitis is more standardized since the international symposium in Atlanta in 1992.¹⁴ The wider application of the suggested terminology pertaining to acute pancreatitis, severe pancreatitis, necrosis, infected necrosis, and pancreatic abscess is to be applauded. The importance of this system is that radiographic criteria are combined with organ function to determine the category of disease, and if the terminology is consistently and widely used, comparisons can be more easily made among institutions and between studies. Terms such as “phlegmon” and “hemorrhagic pancreatitis” continue to appear in publications and medical records and although descriptive, do not allow for comparison of data.

The multiple organ failure scoring system was used for the comparison of patients in this study. The system was not used in a prospective manner, but was useful in comparing

Table 4. OPERATIVE AND NONOPERATIVE RADIOLOGIC OR ENDOSCOPIC INTERVENTIONS IN 23 PATIENTS WHO WERE READMITTED AFTER BEING DISCHARGED FROM THE HOSPITAL

Operations in 23 readmitted patients	
Abscess drainage	3
Cholecystectomy	2
Wound complication (debridement, hernia, infected mesh)	2
Fistula excision/closure	2
Pseudocyst drainage	1
Total:	10
Nonoperative procedures in 23 readmitted patients	
CT guided abscess drainage	3
CT guided pseudocyst drainage	3
Percutaneous biliary stent placement	1
Endoscopic pancreatic stent placement	1
Total:	8

Table 5. MORTALITY IN COLLECTED SERIES OF PATIENTS WITH INFECTED NECROSIS COMPARED BY THE METHOD OF OPERATIVE TREATMENT

Treatment	No. of Patients	Deaths	Mortality
Conventional (ref. 18,19,20)	76	32	42.1
Open/Semi Open (ref. 3,21,22,23)	113	24	21.2
Closed/lavage (2,24,25 present)	163	27	16.6

the level of illness among patients. The patients who recovered had an average multiple organ failure score of 1.7, whereas those who died had a significantly greater average score of 4.0. However, nine patients with MOF scores of 4 or 5 survived, and one patient with an MOF score of 2 died. The multiple organ failure score was found to be beneficial early in the disease process in that it was easily obtainable on a daily basis, contained only objective data, was much easier to use than the APACHE II,¹⁵ and was useful beyond the 48-hour period — a shortcoming of the Ranson or Imrie criteria.^{13,16}

The results of three operative techniques have been well documented (Table 5). The results of “conventional therapy” in which the necrosus is debrided and the patient is closed over drains was described by Altemeyer and Alexander²⁶ and has been reported for 3 decades. The therapy was originally proposed in 1963 and still has some adherents. Using this technique, reoperation is required in 30% to 40% of patients. Even when aggressive use is made of imaging studies, a high index of suspicion is maintained and reoperation is employed, the mortality rate remains in the range of 40%.

In open or semiopen treatment, the debridements are initially performed in the operating theater and followed by repeated open dressing changes every 24 to 48 hours in the ICU setting. The abdomen is left to close by secondary intention, and the overall results of this therapy in several series showed a decreased mortality rate compared with conventional treatment, though this is not uniformly the case.¹⁷ One disadvantage of this therapy is the relatively high rate of fistula formation and bleeding from the repeated dressing changes. These complications can be decreased by the use of a nonadherent gauze material placed between the abdominal packs and the tissue surfaces.

The preferred method at Emory and in several other recent series was described herein. The results of repeated debridements followed by closure over lavage catheters has lowered the mortality rate in many institutions to below 20%. Moreover, the rate of enteric fistula formation and bleeding complications is low, and the need for late reoperations is decreased. Our results closely parallel those

described by Rau et al.,² who reported 52 patients with infected necrosis treated similarly. Length of stay in the hospital ICU and mortality rates were similar. The rate of recurrent abscess (18%) and pseudocyst (18%) formation were somewhat lower in our series, for unclear reasons.

The timing of pancreatic debridement if infected necrosis is proven is not controversial. The debridement should proceed as quickly as possible to prevent further complications of sepsis or organ failure. Most patients in this study exhibited SIRS or sepsis. Patients with SIRS and no documented organisms in the pancreatic necrosus by aspiration were managed with antibiotic coverage and hemodynamic and respiratory support. Patients with sepsis (SIRS and documented infection) and bacterial growth in pancreatic aspirates were urgently debrided. We group SIRS and sepsis patients together; however, because their ICU treatment is essentially identical.

The time required for the necrotic material to be clearly delineated and differentiated from surrounding healthy tissue is unclear, although some authors report that it takes at least 1 week for the demarcation to occur.^{6,7} A prospective study examined whether operating at an interval shorter or longer than 2 weeks benefited the patient.¹⁷ The authors concluded that patients debrided more than 2 weeks from the onset of their disease had a better outcome, although the mortality rate in both of their groups (56% and 27%) was greater than that reported in other recent series. Certainly, if the patient remains stable and infection does not supervene, an added period of stability and resolution of the acute inflammatory process can only be of benefit to the patient. There was no difference in the outcome of our 14 patients who were debrided at less than 2 weeks when compared with those 36 patients debrided later than 2 weeks from the onset of pancreatitis.

The decision to operate on patients with sterile necrosis is a difficult one. Opinions vary on whether debridement should be undertaken based on the amount of necrotic pancreas and peripancreatic tissue or whether debridement should only be performed if patients fail to improve or deteriorate despite ICU therapy. In 1992, Rattner and Warsaw reported a policy of debriding sterile necrosis at approximately 3 weeks if symptoms persisted. The mortality rate in their sterile and infected groups was equivalent. In a follow-up from this group (Meeting of the American Hepato-Biliary Association November 9, 1996), Fernandez-del Castillo et al. reported a series of 54 patients in which 40% had sterile necrosis. Surgery was performed for deterioration despite ICU treatment and signs of ongoing sepsis. The mortality rate in the series was 7.4%, but the authors raised the question of whether the surgery may have been avoided in a significant number of these patients. Rau et al.⁴ reported a series of 172 patients who had sterile necrosis. One hundred five of these patients went to surgery based on failure to respond to ICU therapy within the first week. They concluded that most patients with sterile pancreatic necrosis respond to ICU treatment. Increasing organ

complications despite intensive care was the only clear indication for exploration. Bradley has written extensively on the subject of sterile necrosis and reported that debridement is rarely necessary. He advocated waiting 4 to 5 weeks to operate if symptoms persist in sterile necrosis.^{6,27}

Uomo et al.⁵ reported a series of 199 patients with pancreatic necrosis. One hundred sixty-nine were patients with sterile necrosis, of whom 23 (14%) underwent debridement. The mortality rate was lower (9.5% vs. 23.5), in the non-operated group, and in the surgical group, the mortality rate was higher in the infected group (33%) than in the sterile group (22%). Eighty-six percent of patients with sterile necrosis were managed nonoperatively, and whether the 14 patients who died would have benefited is unclear.

In this series, the mortality rate for patients explored with sterile necrosis was significantly higher than that for those with infected necrosis. However, the meaning of these data are unclear because the numbers for sterile necrosis were small in our review. The denominator of patients with significant sterile necrosis who did not proceed to surgery is unknown. However, it is our feeling that most patients with sterile necrosis should not be debrided and will only benefit from necrosectomy if they continue to deteriorate despite aggressive organ support, are unable to start oral or enteral nutrition because of compression symptoms or have recurrent inflammatory symptoms despite pancreatic rest.

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Discussion

DR. LARRY C. CAREY (Tampa, Florida): This is a big experience with a difficult problem, and I think it is representative of the fact that there is a little room for encouragement. We have traditionally said that patients who get into this fix and require operations for infected pancreatic necrosis can expect three operations and 3 months in the hospital, and John and his group have it down to two operations and 2 months in the hospital. So we are gaining on it.

It is still a bad problem, and the difficulty is frequently associated with trying to figure out when to operate on patients who don't have demonstrated infection, because the indications seem a little less certain than when you can prove that there are bacteria in this infected necrotic tissue.

I have three questions I would like to ask the authors.

How many of your patients had had previous attempts at radiologic drainage? We couldn't assimilate 50 patients in the entire state of Florida with necrotic pancreatic problems that somebody hadn't stuck a needle or a catheter in before we got to see them. So I am curious about whether you have the same problem in Atlanta.