Minimally invasive treatment of pancreatic necrosis

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Abstract

AIM: To systematically review these minimally invasive approaches to infected pancreatic necrosis.

METHODS: We used the MEDLINE database to investigate studies between 1996 and 2010 with greater than 10 patients that examined these techniques. Using a combination of Boolean operators, reports were retrieved addressing percutaneous therapy (341 studies), endoscopic necrosectomy (574 studies), laparoscopic necrosectomy via a transperitoneal approach (148 studies), and retroperitoneal necrosectomy (194 studies). Only cohorts with at least 10 or more patients were included. Non-English papers, letters, animal studies, duplicate series and reviews without original data were excluded, leaving a total of 27 studies for analysis.

RESULTS: Twenty-seven studies with 947 patients total were examined (eight studies on percutaneous approach; ten studies on endoscopic necrosectomy; two studies on laparoscopic necrosectomy via a transperitoneal approach; five studies on retroperitoneal necrosectomy; and two studies on a combined percutaneous-retroperitoneal approach). Success rate, complications, mortality, and number of procedures were outcomes that were included in the review. We found that most published reports were retrospective in nature, and thus, susceptible to selection and publication bias. Few reports examined these techniques in a comparative, prospective manner.

CONCLUSION: Each minimally invasive approach though was found to be safe and feasible in multiple reports. With these new techniques, treatment of infected pancreatic necrosis remains a challenge. We advocate a multidisciplinary approach to this complex problem with treatment individualized to each patient.

Key words: Acute pancreatitis; Pancreatic abscess; Pancreatic necrosis; Necrosectomy; Laparoscopic necrosectomy

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INTRODUCTION

Most cases of acute pancreatitis are self-limited and resolve without serious complications. However, severe acute pancreatitis is associated with the development of potentially life-threatening complications including pancreatic necrosis and pancreatic abscess. The 1992 international consensus conference held in Atlanta established uniform terminology for acute pancreatitis and its complications. According to the Atlanta Classification, pancreatic necrosis refers to diffuse or focal areas of nonviable pancreatic parenchyma, typically associated with peripancreatic fat necrosis, whereas pancreatic abscess is defined as a circumscribed intra-abdominal col-
lecion of pus, usually in proximity to the pancreas arising as a consequence of acute pancreatitis or pancreatic trauma\(^5\). Treatment for pancreatic necrosis has evolved considerably over the past decade with respect to both the timing of intervention and the development of alternatives to traditional open necrosectomy.

Pancreatic necrosis may be sterile or infected. The prognosis (with or without intervention) is much worse for infected than sterile necrosis. Historically, early surgical intervention was considered mandatory for cases of suspected infection. The 2002 International Acute Pancreatitis (IAP) guidelines recommended early fine-needle aspiration to discriminate between sterile and infected pancreatic necrosis, with continued non-operative management for stable or improving patients with sterile necrosis but surgical intervention for those with documented infection\(^5\). The traditional surgical approach to infected necrosis was open necrosectomy with the goals of wide drainage of all infected compartments and complete removal of all necrotic tissue with the placement of drains for continuous postoperative closed lavage. Frequently, repeat laparotomy was needed to ensure complete debridement\(^5\). Historically, open necrosectomy was associated with substantial morbidity and rates of perioperative mortality that exceeded 50% in some reports\(^5\), although mortality in some contemporary series has been 11% or lower\(^2\).

Because various studies showed high mortality with early operation for severe necrotizing pancreatitis, the IAP recommended avoidance of surgical intervention within the first 14 d after onset unless there was progressive multiple organ failure and clinical deterioration. Subsequent studies suggested that morbidity and mortality can be further reduced if operation is delayed beyond 28-30 d\(^3\), presumably because the extended interval allows sufficient demarcation between normal and necrotic tissue, thereby reducing the risk of inciting overwhelming postoperative septic and systemic inflammatory responses, as well as the risk of intraoperative injury to surrounding organs and hemorrhage.

In addition to the open approach for pancreatic necrosis and abscess, the last two decades have brought about alternative “minimally-invasive” techniques. Percutaneous drainage of infected pancreatic necrosis has been shown to be safe and effective in highly-selected patients\(^8\), but multiple procedures are often needed, and adjunctive treatment is often required.

Gagner\(^9\) first described minimally invasive surgical treatment of necrotizing pancreatitis in 1996, including laparoscopic retroperitoneal, retroperitoneoscopic, and transgastric procedures. Over the past 15 years, a number of other minimally invasive surgical, endoscopic, and radiological approaches to drain and debride pancreatic necrosis have been described. These alternatives appear to be feasible and safe, although comparisons among approaches have been difficult due to small numbers, lack of uniform reporting criteria, and varying degrees of operator dependence. The advent of some of these alternatives has led to reconsideration of some of the fundamental tenets of open surgical necrosectomy, particularly with respect to the timing and completeness of debridement. In this report, we review current techniques of minimally invasive pancreatic necrosectomy.

### MATERIALS AND METHODS

A literature search was performed of the MEDLINE database from April 1996 to November 2010 for each of four techniques well described for minimally invasive necrosectomy: percutaneous therapy (341 studies), endoscopic necrosectomy (574 studies), laparoscopic necrosectomy \textit{via} a transperitoneal approach (148 studies), and retroperitoneal necrosectomy (194 studies). Only cohorts with at least 10 or more patients were included. Non-English papers, letters, animal studies, duplicate series and reviews without original data were also excluded.

For percutaneous drainage, a search was conducted using subject headings: “percutaneous”, “drainage”, “pancreatic necrosis”, and “necrotizing pancreatitis” with the aid of Boolean operators. There were 341 initial hits in MEDLINE. After exclusion using the above-mentioned criteria, eight studies were included in this review.

For endoscopic necrosectomy, a search was conducted using subject headings: “endoscopic”, “endotherapy”, “drainage”, “pancreatic necrosis”, and “necrotizing pancreatitis” with the aid of Boolean operators. There were 574 initial hits in MEDLINE. After exclusion using the above-mentioned criteria, ten studies were included in this review.

For laparoscopic necrosectomy \textit{via} a transperitoneal approach, a search was conducted using subject headings: “laparoscopic”, “minimally invasive”, “necrosectomy”, “pancreatic necrosis”, and “necrotizing pancreatitis” with the aid of Boolean operators. There were 148 initial hits in MEDLINE. After exclusion using the above-mentioned criteria, two studies were included in this review.

For retroperitoneal necrosectomy, a search was conducted using subject headings: “laparoscopic”, “minimally invasive”, “retroperitoneal”, “necrosectomy”, “pancreatic necrosis” and “necrotizing pancreatitis” with the aid of Boolean operators. There were 194 initial hits in MEDLINE. After exclusion using the above-mentioned criteria, five studies were included in this review.

### RESULTS

#### Percutaneous therapy

The results of the literature search for percutaneous therapy for pancreatic necrosis are summarized in Table 1. Technique was similar throughout the studies, access to the area of necrosis was obtained utilizing ultrasound and/or computed tomography to place percutaneous drains ranging in size from 10 to 28 French drains. Afterward, saline flushes were often used every 8 h.
Eight studies included 286 patients ranging from 10 to 80 patients. There were six retrospective case series, one prospective case series, and one randomized controlled trial. In the randomized control trial, percutaneous drainage was used as part of the minimally invasive "step-up" approach, in which a retroperitoneal necrosectomy was necessary in 65% of patients. This technique is further described later in the Results section under "combined approach".

One hundred and twenty seven of 286 (44%) patients had successful percutaneous therapy and did not subsequently require surgical necrosectomy. Mortality was reported in 58 of 286 patients (20.2%). Complications were reported in 80 of 286 patients (28%) and included multiple organ failure, respiratory failure, renal failure, pancreatic fistula, new-onset diabetes, pseudocyst, and use of pancreatic enzymes.

**Endoscopic necrosectomy**

The results of the literature search for endoscopic necrosectomy for pancreatic necrosis are summarized in Table 1. Ten studies, all retrospective, included 352 patients ranging from 13 to 93 patients.

Two hundred and seventy four of 352 (78%) patients had successful endoscopic necrosectomy therapy and did not subsequently require surgical necrosectomy. Mortality was reported in 20 of 352 patients (5.6%). Complications were reported in 100 of 352 patients (28%) and included bleeding, fever, gallbladder puncture, hypotension, deep-vein thrombosis/pulmonary embolism, peritonitis, Clostridium difficile colitis, perforation of necrosis into abdominal cavity, pneu-moperitoneum, migration of stent into cyst, post-endoscopic retrograde cholangiopancreatography, fistula, bowel obstruction, and air embolism. Median follow up was reported as 5.7 mo to 43 mo.

The specific technique varied among the reports. Usually, a therapeutic or pediatric gastroscope or a videoduodenoscope was used. Endoscopic ultrasound was used often to locate the necroma cavity and guide initial access. Transmural drainage was then usually performed followed by dilation and irrigation of the debris. This was accomplished most often via the stomach, although the duodenum was used in approximately 10%-50% of these patients. The size of the endoscopic cystgastro-
tomy was typically 1.5 cm to 2.0 cm. Endoscopic biopsy forceps and baskets was used to remove solid debris into the stomach, allowing it to be eliminated by digestion and peristalsis. Multiple pigtal stents were left in place to maintain cystgastrostomy patency, and often a nasocystic tube was left in place for post-procedure irrigation. On average, 3.2 endoscopic debridement procedures were necessary to achieve resolution of necrosis.

**Laparoscopic necrosectomy**

The results of the literature search for laparoscopic necrosectomy for pancreatic necrosis are summarized in Table 1. Two studies included 29 patients ranging from 10 to 19 patients\(^{(28,29)}\). Each was a retrospective study.

Twenty-three of 29 (79%) patients had successful laparoscopic necrosectomy therapy and did not subsequently require open necrosectomy. Mortality was reported in 3 of 29 patients (10.3%). Complications were reported in only the study by Parekh\(^{(28)}\) and included *Clostridium difficile* infection, reintubation, central line infection, delirium tremens, pseudomonas pneumonia, and minor wound complications. The study also notes 11 patients were diagnosed with a pancreatic fistula. Thus the complication rate was calculated as 11 of 19 patients (58%). Zhu et al\(^{(29)}\) did not report complications of the procedure, only mortality. Median follow up was not available for either study.

Parekh\(^{(28)}\) described using three ports for access: a hand access device and two standard laparoscopic ports. Access to the retroperitoneum was obtained either through an infracolic approach or through the greater omentum between the stomach and colon. Gentle finger dissection was used for debridement and several drains were left for postoperative drainage. Four patients that were referred to the service were not considered for a laparoscopic approach because two patients had ileus and anasarca, and two patients had gastrointestinal perforations from prior interventions at other hospitals.

Zhu et al\(^{(29)}\) described using at least four standard ports, and going through the gastrocolic ligament to approach the pancreas. A fan retractor was used to elevate the stomach for exposure. Four to six drainage tubes were used for postoperative drainage. Selection criteria were not described.

**Retroperitoneal necrosectomy**

The results of the literature search for endoscopic necrosectomy for pancreatic necrosis are summarized in Table 1.

Five studies included 197 patients ranging from 10 to 137 patients\(^{(17,30,33)}\). There were three retrospective studies\(^{(17,30,31)}\) and two prospective case series\(^{(32,33)}\). 173 of 197 (88%) patients had successful retroperitoneal necrosectomy therapy and did not subsequently require open necrosectomy. Mortality was reported in 33 of 197 patients (17%). Complications were reported in 90 of 197 patients (46%) and included colonic fistula\(^{(11)}\), gastric perforation\(^{(31)}\), duodenal perforation\(^{(31)}\), enteric fistula\(^{(30)}\), bleeding\(^{(17,30,33)}\), pseudocyst\(^{(17,30,33)}\), pancreatic fistula\(^{(17)}\), incisional hernia\(^{(17)}\), myocardial infarct\(^{(30)}\), cerebrovascular event\(^{(90)}\), biliary stricture\(^{(90)}\), pulmonary embolus\(^{(30)}\), colonic necrosis\(^{(30)}\), hepatic portal/superior mesenteric/splenic vein thrombosis\(^{(30)}\), *Clostridium difficile* infection\(^{(90)}\), residual abscess\(^{(31)}\), pneumonia\(^{(31)}\), respiratory and liver failure\(^{(33)}\), and gastric ileus\(^{(33)}\).

Technique varied among the five studies. Gambiez et al\(^{(33)}\) described using a short lumbotomy (6 cm in length) centered on the 12th rib. The spleen and descending colon (or ascending colon if on right side) were mobilized anteriorly and pancreas was accessed without violating the peritoneum. A 23 cm mediastinoscope was used for direct vision. Necrotic areas were removed with blunt dissection using a suction metal tube. A tube drain was left to facilitate later drainage. Similarly, Castellanos et al\(^{(33)}\) described a left translumbar approach. However, the group used a flexible endoscope for access followed by flushing and aspiration under direct guidance.

Chang et al\(^{(33)}\) described using a 5 cm skin incision below the costal margin, followed by blunt dissection. A Yankauer sucker was then used for probing the abscess cavity and/or removing necrotic discharge.

Raraty et al\(^{(30)}\) described first placing a 12F pigtail catheter under CT-guidance. After moving the patient to the operating room, the catheter was exchanged over a guide wire with serial dilators to 30F size. A nephroscope was then used for access, and a metal forceps used for piecemeal removal. Two drains were placed for irrigations. Carter et al\(^{(30)}\) used a similar technique with the nephroscope but also used a flexible endoscope for direct access.

**Combined approach**

Based on anecdotal success of percutaneous radiological and endoscopic necrosectomy used as primary therapy with avoidance of open necrosectomy, an increasing number of reports have utilized combinations of non-surgical approaches to treat pancreatic necrosis. A prospective randomized multicenter trial called the Minimally Invasive Step Up Approach Versus Maximal Necrosectomy in Patients with Acute Necrotising Pancreatitis (PANTER) was recently performed in the Netherlands\(^{(11)}\). After the diagnosis of necrotizing pancreatitis or infected pancreatic necrosis was made, patients were randomly assigned to either a “step-up” approach or open necrosectomy. The step-up approach consisted of percutaneous drainage or endoscopic drainage, followed by a minimally invasive retroperitoneal necrosectomy if necessary. A video-assisted retroperitoneal debridement (VARD) with postoperative lavage was then performed three days after if there was no clinical improvement. Major complications or death occurred in 31 of 45 patients after open necrosectomy (69%) vs 17 of 43 patients after the step-up approach (40%) (risk ratio with the step-up approach, 0.57; 95% CI, 0.38 to 0.87; *P* = 0.006). About 35% of patients in the step up group were successfully able to be managed with percutaneous drainage only\(^{(11)}\).
Similar to the PANTER Trial, there is also a recent, prospective multicenter, single-arm study based out of the University of Washington. Percutaneous drainage was used as initial treatment for infected pancreatic necrosis. If there was a 75% reduction in size based on follow-up scan 10 d later, the remainder of their treatment would be percutaneous drains alone. If patients did not have a 75% reduction they were treated with a VARD. Twenty-three percent of patients were treated with percutaneous drains only. Sixty percent of patients were treated with a “minimally invasive intervention” (drains with or without VARD). Mortality at 30 d was 2.5%.

The results of these two studies are summarized in Table 1.

DISCUSSION

Infected pancreatic necrosis and pancreatic abscess are serious complications of severe acute pancreatitis. However, the last two decades have demonstrated much innovation and variety in minimally invasive techniques. These new techniques can potentially lower the significant morbidity and mortality of these complications. The less invasive approach can potentially keep an infection compartmentalized, specifically avoiding contamination of virgin spaces, such as the peritoneal cavity. It may reduce systemic inflammatory and septic response as a consequence of a major open operation and release of infected necrosis.

The percutaneous approach to infected pancreatic necrosis has been shown to be safe and feasible in multiple retrospective case series. It is significant to note, 44% of patients in the studies reviewed did not need surgical therapy. Conclusions are limited, however, since the studies are retrospective and small. We limited our review to include only studies that examined 10 or greater patients. Selection criteria was also not often reported and thus, it may be difficult to predict which subset of patients would most benefit from percutaneous drainage alone. In addition, repeat procedures were often needed, ranging from 1 to 12 procedures in the above-mentioned studies. What has become increasingly popular is the combination of percutaneous technique combined with a VARD as mentioned in the PANTER trial and the Horvath study. These studies not only confirmed that there is a subgroup of patients that can benefit from percutaneous drainage alone but also examined a combined technique in a prospective fashion with a relatively larger amount of patients.

The endoscopic approach to necrosectomy has also been shown to be safe and feasible with an acceptable procedure-related morbidity. The endoscopic ultrasound has allowed this approach to evolve allowing a better definition of the fluid collection and surrounding vasculature. The approach can also be used in poor risk surgical candidates. However, this technique though is not available at all institutions and often there is a need for repeated procedures for maximal drainage. Furthermore, not all pancreatic abscesses and pancreatic necrosis are accessible via a transgastric or transduodenal approach. Like percutaneous drainage alone, often repeat procedures are needed.

Laparoscopic necrosectomy may provide better access to fluid collections not amenable to endoscopic approach. This may facilitate a more thorough debridement of the cavity. The laparoscopic approach has also been demonstrated to be safe in several small case series. In the two studies reported 23 of 29 (79%) patients did not require an open necrosectomy. As previously discussed, these are highly selected patients: these were likely stable patients that were able to tolerate pneumoperitoneum. Morbidity still exists in this approach including enterocutaneous and pancreatic fistulas.

Similar to the laparoscopic approach, retroperitoneal necrosectomy has been shown to be effective in select patients: 173 of 197 (88%) patients did not need an open necrosectomy. The approach has the theoretical advantage of not having transmission of intraperitoneal infection from the necrotic area compared to laparoscopy. This technique allows access to areas not accessible via endoscopy and the potential to remove all necrotic tissue from the area.

Because of their relatively rare presentation, reports on these minimally invasive approaches to pancreatic necrosis and abscess have mostly small numbers of patients and are mostly retrospective in nature. Selection and publication bias is inherent in these studies and the low morbidity and mortality demonstrated in these studies have to be interpreted as such. There is also a significant amount of heterogeneity and variety of technique within each type of different approach.

In addition, several studies utilize a combined technique using percutaneous drainage first followed by endoscopic, laparoscopic, or retroperitoneal necrosectomy. Percutaneous drainage likely temporizes the patient in early phases of infected necrosis.

In the future, we look for more prospective studies that use definitions as laid out clearly by the Atlanta classification. Several of the above studies do not strictly adhere to those classifications. Furthermore, complications, specifically major ones including pancreatic or enteric fistula and major hemorrhage should separately be reported. Additionally, some studies do not report the amount of days from presentation to time of necrosectomy. It is well-accepted now that a delay of 28 d between onset of symptoms and intervention can potentially lower morbidity and mortality.

Up until recently, there has been no comparison of results between open necrosectomy and these minimally invasive techniques. The only randomized control trial to date comparing a minimally invasive approach versus an open approach is the PANTER trial recently published. The minimally invasive approach is actually a “step-up” approach in which the first step is either a percutaneous or endoscopic transgastric approach. A VARD procedure was then performed if those approaches were unsuccessful or if the patient did not clinically improve in 72 h. The step-up approach reduced the rate of the
comprise end point of major complications or death. In addition, the step-up approach yielded less incisional hernias and new-onset diabetes. The authors hypothesize that in open necrosectomy, there is potentially viable pancreatic parenchyma that is unintentionally debrided leading to diabetes as a late complication. This is potentially the reason why other minimally invasive techniques have shown good outcomes.

It is important to note that the PANTER trial is not a direct comparison between open necrosectomy and minimally invasive necrosectomy, rather a comparison between treatment strategies. Perhaps this is a better model moving forward in contrast to doing direct comparisons between open necrosectomies or among the different types of minimally invasive approaches. It is likely that these pancreatic fluid collections are amenable to multiple approaches.

Complications of severe acute pancreatitis remain a complex problem to treat. We advocate a multidisciplinary approach with interventional radiologists, gastroenterologists, intensivists, and hepatobiliary surgeons at tertiary care centers. Since comparison data is limited, the minimally invasive approach should be based on location of lesion and individual patient presentation. Challenges moving forward will be learning curves, technology improvements, and product cycles of new techniques. This report provides a brief overview of the evolving minimally invasive approaches as alternatives to open necrosectomy.

**COMMENTS**

**Background**

A variety of minimally invasive approaches have been described for treatment of infected pancreatic necrosis and pancreatic abscess.

**Research frontiers**

Early, open necrosectomy for infected pancreatitis was the traditional mainstay of surgical therapy for these critically ill patients. Current practice has shifted toward, with intervention ideally delayed for a minimum of two and preferably four weeks from the onset of illness. Moreover, various minimally invasive surgical, endoscopic, and percutaneous drainage/debridement strategies have emerged as alternatives to open operation.

**Innovations and breakthroughs**

This systematic review summarized studies published between 1996 and 2010 with greater than 10 patients. The quality of these published reports is limited by their retrospective design, selection bias, and possible publication bias.

**Applications**

Treatment algorithms for infected pancreatic necrosis should be multidisciplinary, reflective of local expertise and experience, and tailored to the individual presenting circumstances of each patient.

**Terminology**

Pancreatic necrosectomy refers to the debridement and drainage of necrotic pancreatic and peripancreatic tissue.

**Peer review**

An exhaustive review of the literature leading to the best summary of minimally invasive surgical approaches to infected pancreatic necrosis.

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