Acute Pancreatitis and Indications for Intervention: a Surgeon's View

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ABSTRACT

Acute pancreatitis is one of the most common gastrointestinal disorders requiring urgent hospitalization worldwide. It is a highly unpredictable disease with a wide range of clinical courses. Most attacks of acute pancreatitis are mild to moderate and resolve spontaneously, but about 10% of patients will develop severe acute pancreatitis. Uncomplicated acute pancreatitis is a one-week disease. Failure to recover or the persistence of local and systemic signs of pancreatic inflammation beyond the first week are signs that a complication may be brewing. Recognizing the natural course of severe acute pancreatitis is necessary in multidisciplinary approach. Only a small subset of necrotizing pancreatitis patients will require emergent surgery in less than four weeks from the onset of acute pancreatitis for organ failure and acute decompensation due to an intra-abdominal catastrophe. The strategy of postponing surgical intervention beyond four weeks from the onset of acute pancreatitis was implemented in the treatment algorithm several years ago. Surgical removal of pancreatic necrosis can be achieved by open or minimally invasive approach. Necrosectomy can be performed at once or in a staged manner (open-staged or closed-continuous lavage). These methods do not compare with, but rather complement other techniques. In general, surgical intervention should be done – if at all – at a late stage after the onset of pancreatitis.

INTRODUCTION

The incidence of acute pancreatitis (AP) varies considerably throughout the world, with a reported annual incidence of 13–45 cases per 100.000 persons (1). Gallstones and alcohol misuse are long-established risk factors, but several new causes have emerged. Ninety percent of patients will have a mild form of interstitial edematous pancreatitis, and most of them will resolve spontaneously. However, about 10% of patients will develop severe AP. In the United States alone, AP leads to 270.000 hospital admissions annually, and inpatient costs exceed 2.5 billion dollars (2). The mortality reaches up to 30% in patients that develop pancreatic necrosis and suffer a severe course (3).

The natural course of the disease has two stages: the early toxic/hypovolemic phase, and the late septic phase. Hypovolemia and organ failure caused by excessive fluid sequestration and the release of biologically active compounds dominate the early phase in the first

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two weeks. During the late course, local and systemic septic complications are the main findings (4).

Recognizing the natural course of severe AP in a multidisciplinary approach has become the standard of care and decreased the mortality to about 20% during the past 20 years. Beside improved intensive care management and progress in interventional drainage, postponing surgical interventions from early necrosectomy to delayed operation had a beneficial effect on the outcome of these patients (5). Consequently, recent guidelines recommended that invasive intervention (i.e., percutaneous catheter drainage, endoscopic transluminal drainage or necrosectomy) should be delayed where possible until at least four weeks after initial presentation to allow the collection to become 'walled-off.' But regardless of the time from the onset of AP and the presence of necrosis, patients with intra-abdominal catastrophes (hemorrhage, visceral ischemia, perforation, abdominal compartment syndrome) require immediate intervention (6).

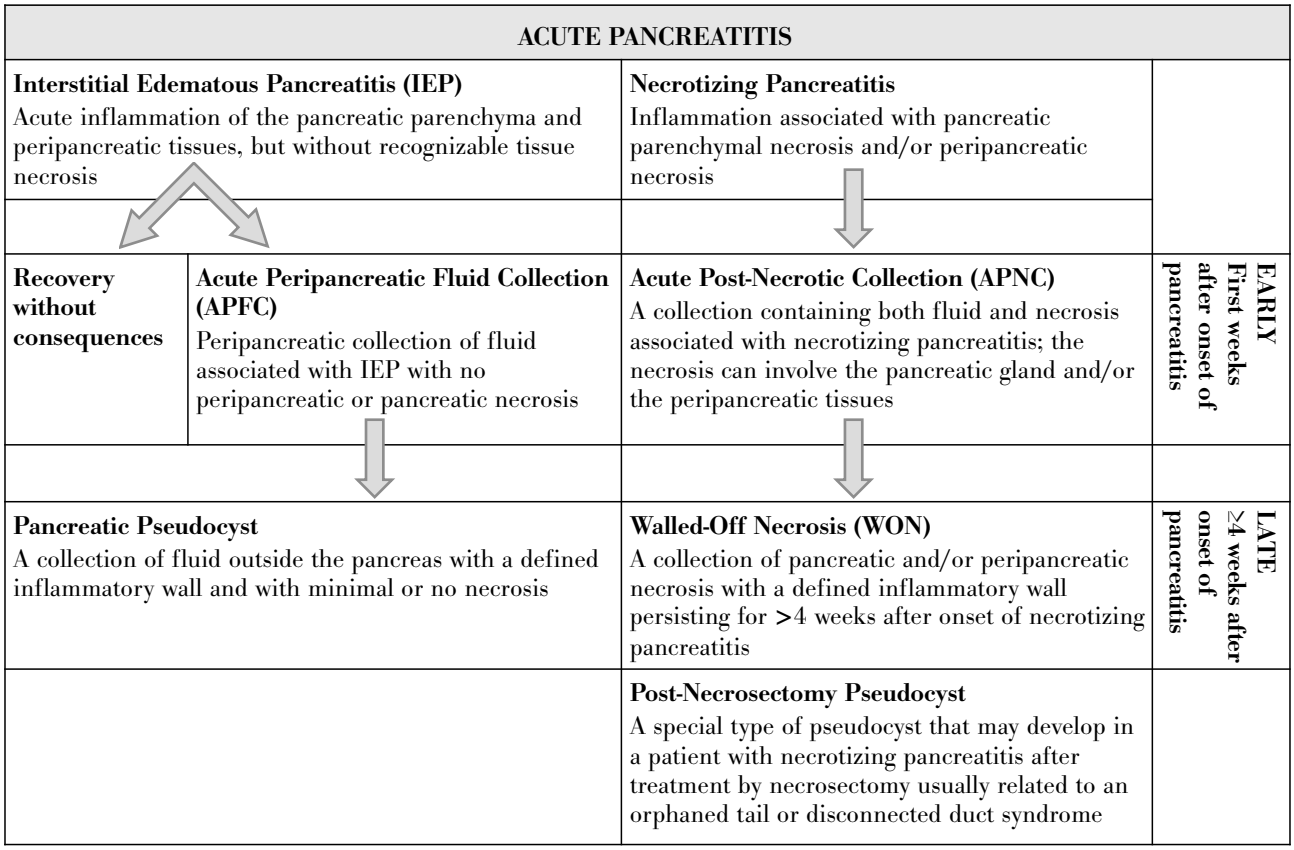
NATURAL COURSE OF THE DISEASE

Ninety percent of patients will have a mild form of interstitial edematous pancreatitis, but about 10% will develop severe AP. According to the Revised Atlanta Classification, AP can be subdivided into two types: interstitial edematous pancreatitis and necrotizing pancreatitis. In the Revised Atlanta Classification, clear definitions of pancreatic and peripancreatic collections are made (7, 8).

Interstitial edematous pancreatitis usually resolves within the first week. Some patients will develop acute peripancreatic fluid collections (APFC) that will resolve with medical support alone or will go on to develop a pancreatic pseudocyst. Pancreatic pseudocyst presents as a delayed (usually four weeks) complication of interstitial edematous pancreatitis with a well-defined wall and devoid of solid material.

The subject of this article concerns those patients who develop necrotizing pancreatitis. These patients

Figure 1. Natural course of acute pancreatitis



develop APNC involving necrosis of the pancreatic parenchyma and the peripancreatic tissue, the pancreatic parenchyma alone, or the peripancreatic tissue alone. When APNC persists beyond four weeks from the onset of pancreatitis, the term walled-off necrosis (WON) can be applied. These terms represent morphologic abnormalities noted on contrast-enhanced CT scan that are used for classification purposes and to guide treatment (Figure 1).

When treating patients with necrotizing pancreatitis, it is important to be cognizant of the time from onset of symptoms since recent data demonstrates that delayed intervention leads to lower morbidity and mortality rates. Over a four-week period, APCs evolve: the peripancreatic tissue inflammation subsides, the tissue within the collection demarcates into viable and non-viable components, and the perimeter of the collection matures into the defined wall of WON. A distinction should also be made between sterile and infected necrosis since the presence of infection means a different prognosis, natural history, and approach to treatment. Patients with sterile WON will usually resolve over time without any intervention. In fact, a percutaneous drain should not be placed into sterile collections unless there is a very good indication since it will iatrogenically infect the collection after a short time and complicate the patient's management. A small subset of patients with sterile WON will require pancreatic necrosectomy either because of persistent symptoms such as anorexia, early satiety, vomiting, pain, fever, or failure to thrive. All patients with WON who become infected require treatment with parenteral antibiotics in combination with effective drainage/necrosectomy (9, 10).

INFECTION

Infection develops in 30–70% of patients with necrotizing pancreatitis and accounts for more than 80% of deaths from AP. The risk of infection increases with the amount of pancreatic glandular necrosis and the time from the onset of AP, peaking at three weeks. Infection is presumed when there is gas present in the WON on CT scan. It is also diagnosed definitively with an image-guided fine needle aspiration (FNA) showing positive Gram stain and culture. Since patients carry a significant risk of converting from sterile to infected tissue over time, patients should be followed closely, and an FNA performed if clinically indicated with a change in abdominal pain, fever, or leukocytosis. Since FNA has a false negative rate of about 10%, a negative FNA may be repeated after appropriate intervals, such as 5–7 days, if a clinical suspicion of infection persists. FNA has a low iatrogenic infection rate along with a high sensitivity and specificity (10).

However, according to evidence-based guidelines, routine percutaneous FNA of peripancreatic collections to detect bacteria is not indicated, because clinical signs (i.e., persistent fever, increasing inflammatory markers) and imaging signs (i.e., gas in peripancreatic collections) are accurate predictors of infected necrosis in the majority of patients. Although the diagnosis of infection can be confirmed by FNA, there is a risk of false-negative results (6). According to an international expert survey, none of the experts use FNA routinely, 85% selectively and 15% never (11).

INDICATIONS AND TIMING FOR INTERVENTION

Once the patient is determined to be infected, they require complete external drainage or face a near 100% mortality. While deciding amongst percutaneous, endoscopic, video-assisted, laparoscopic or open surgical options, a percutaneous drain should be placed within 24 hours of a diagnosis of infection to initiate external drainage (12). Once a percutaneous drain has been placed, the catheters should be upsized every 3–4 days to an 18–20-French goal. A CT is repeated about two weeks after the first drain was placed. If the patient has a remaining large collection and at least four weeks have elapsed since onset of disease, plans are made for surgery. In general, surgery for APNC should be delayed until the WON phase due to lower morbidity and mortality. While waiting for this safer time, sepsis control can be temporized with percutaneous drains and when necessary, the addition of parenteral antibiotics. Careful attention must be paid to

the protein and calorie requirements in these patients which are very high. Most patients are unable to consume their total caloric needs, and almost all will require supplemental enteral or parenteral nutrition and close monitoring of their nutritional status with serum markers. Enteral nutrition (nasogastric or nasojejunal) is the preferred route when tolerated since it has been shown to be associated with significant decreases in the risk of pancreatitis associated morbidity and mortality (13).

But regardless of the presence of necrosis, a small subset of severe pancreatitis patients will require emergency surgery for organ failure and acute decompensation due to an intra-abdominal catastrophe such as haemorrhage, visceral ischemia, perforation, and abdominal compartment syndrome. Acute decompensation is most often due to a reactivation of the systemic inflammatory response or a non-surgical source of infection. Because of this, intensive support should be given for 24–48 hours along with a search for the cause, but if an intra-abdominal catastrophe is suspected the patient will need an emergency laparotomy (14).

INDICATIONS FOR SURGERY

- Severe AP with APFC or APNC, less than four weeks from the onset of pancreatitis, with organ failure and suspected intra-abdominal catastrophe unresponsive to 24–48 hours of intensive support.
- WON, by definition greater than four weeks from the onset of necrotizing pancreatitis, that is:
  - infected; with infection documented by gas seen in the collection on contrast-enhanced CT scan or with a positive FNA or
  - sterile but symptomatic.

PREOPERATIVE PLANNING AND SURGICAL APPROACHES TO NECROSECTOMY

There are many excellent surgical options for pancreatic debridement (15). Transgastric endoscopic methods and percutaneous drains can also be used as primary or adjunctive methods.

Percutaneous drainage (PD) of pancreatic necrosis involves placement of single or multiple catheters that are used for irrigation and drainage of retroperitoneum. Surgical intervention can be postponed, and even the need for surgical necrosectomy can be eliminated in many patients. Over the past two decades, PD has been increasingly utilized to stabilize critical patients both as 'a bridge to surgery' and sometimes as definitive therapy. The preferred route for PD is retroperitoneal approach through the flank because it avoids enteric leaks and dissemination of infected material into the peritoneal cavity. Also, a retroperitoneal approach for PD allows the tract to be used as guidance for retroperitoneal surgical video-assisted retroperitoneal necrosectomy (VARD). PD is beneficial especially as a prelude to definitive necrosectomy or when combined with another modality of treatment. However, PD is technically not adequate or feasible when retroperitoneal hemorrhage, bowel necrosis, duodenal/biliary obstruction further complicates ANP. One of the drawbacks, when PD is used alone, is also limited ability to remove necrotic debris (16).

Advances in technology and instrumentation allow the use of minimally invasive techniques which lessen the surgical stress in an already compromised patient. Minimally invasive methods are increasingly being used for operative necrosectomy in patients with infected WON with open necrosectomy reserved for patients who fail minimal access techniques or require an emergent exploration.

Several minimally invasive techniques have been developed. Despite small variations in the different techniques applied, they have in common that infected necrosis of the retroperitoneum is accessed under endoscopic visualization with subsequent necrosectomy and lavage. The techniques involve either intraoperative dilatation of a percutaneous drain tract, which was created by US- or CT-guidance preoperatively, or a direct approach of the infection with a retroperitoneoscope. Depending on the location of the infectious tissue,

access can be gained from the left or the right flank and over one or more routes (17).

In general, access to debridement involves retroperitoneal or transperitoneal approach by open or minimally invasive surgery.

The most popular surgical minimally invasive retroperitoneal debridement methods are:
- step-up approach consisting of PD followed by VARD,
- percutaneous necrosectomy and sinus tract endoscopy, and
- minimal access retroperitoneal pancreatic necrosectomy (MARPN).

The minimally invasive transperitoneal debridement method is laparoscopic debridement.

Methods for open transperitoneal or retroperitoneal debridement are:
- necrosectomy followed by continuous postoperative lavage,
- conventional drainage with placement of standard surgical drains and reoperation as needed,
- open management technique with necrosectomy followed by scheduled re-laparotomies through an open abdomen (laparostomy and system of a continuous negative pressure), and
- open retroperitoneal approach through the base of the 12th rib.

The techniques described here will be the minimally invasive methods. Open retroperitoneal approach through the base of the 12th rib followed by continuous postoperative lavage is the open method upon which a majority of these minimally invasive surgical techniques are based.

The step-up approach and VARD technique was described by Horvath et al. which now has phase I feasibility, phase II safety and efficacy, and phase III randomized controlled data supporting its use (18–20). The phase III results from the Dutch PANTER trial have provided strong data in support of the step-up approach. In this randomized controlled trial, patients with infected pancreatic or peripancreatic tissue were randomized to either open necrosectomy or minimally invasive step-up approach. Patients randomized to the step-up arm had a lower rate of incidence of postoperative organ failure, a lower rate of major complications, and a lower risk of death. Postoperatively, the step-up arm had fewer incisional hernias, less diabetes, less exocrine insufficiency with the need for pancreatic enzyme supplementation, and lower healthcare utilization and medical costs. Also, surgical intervention (other than drain placement) was avoided in one-third of patients in the step-up arm (20).

Once the patient with WON is determined to be infected, a percutaneous drain is placed. If this drain is not effective, a VARD will be needed. The patient will need a minimum of one percutaneous drain placed into the collection from the flank, to be used as an intraoperative guide. When doing the VARD procedure, the surgeon follows the path of this drain through the retroperitoneum and into the collection. Even if another drain is already in place, it is important for the interventional radiologist to place a drain as close as possible to the left mid-axillary line just under the costal margin for operative guidance. The position of this drain inside the collection and its location to nearby anatomical structures will be used by the surgeon to guide operative debridement. A VARD technique involves a small subcostal incision followed by placement of a port. Through port, a video scope is inserted. Necrosectomy is achieved with irrigation, hydrodissection and different instruments which are inserted directly through the wound (10).

Percutaneous necrosectomy and sinus tract endoscopy

The method was first described by Carter et al. (21). Sinus tract endoscopy involves intraoperative dilatation of the percutaneous drain tract followed by irrigation, lavage, and suction using a flexible or rigid endoscope (22).

Percutaneous necrosectomy

Percutaneous necrosectomy starts with insertion of an 8-French pigtail catheter into the cavity of retroperitoneal necrotic collection, the surgeon having carefully selected a path that will allow subsequent dilatation. A path of choice is to enter the area of infected necrosis between the lower pole of the spleen and the splenic flexure. In predominately right-sided pancreatic head necrosis, they used a path through the gastrocolic omentum, anterior to the duodenum. However, this results in a more technically difficult necrosectomy and prevents dependent postoperative drainage. The catheter is secured, and the patient is transferred to the operating room. With the patient under general anesthesia, access to the infected cavity is maintained using a guidewire, over which the catheter tract is then dilated to 30-French using graduated dilators and radiologic guidance. This allows a 30-French special guidewire to be inserted. An operating nephroscope that allows intermittent irrigation and suction with a 4 mm working channel is then passed along the special guidewire into the infected cavity. Piecemeal removal of solid material (necrosectomy) is then performed using soft grasping forceps through the working channel by repeatedly passing the instrument into the cavity until all loose necrotic tissue is removed. Finally, a drain is passed into the cavity to allow high volume continuous postoperative lavage (500 mL/hour).

Sinus tract endoscopy

This method is used in patients with a previous primary debridement, either at open laparotomy or after the above technique, in whom residual sepsis is suspected. In the operating room and under general anesthesia, the previously sited drain or drains are removed. Either flexible or a rigid endoscopic system is used, depending on the suspected amount of residual necrosis. Sinus tract endoscopy using a flexible endoscope is tedious, and only small fragments of necrotic tissue can be removed with each pass of the endoscope. However, the advantage is access to pockets of necrosis which can be limited when using rigid endoscopic systems. For flexible endoscopy, each tract is dilated to 45-French using a balloon dilator. A flexible endoscope is then passed through the skin opening. Irrigation and suction allows fluid collection to be cleared, and residual solid necrotic tissue or adherent slough can be teased away using a variety of endoscopic instruments. At the end of the procedure, a tube drain is placed in the cavity, after which lavage begins again.

Minimal access retroperitoneal pancreatic necrosectomy

This method was described by Rarity et al. Under CT-guidance a 12-French pigtail catheter was inserted into the infected cavity. After moving the patient to the operating room, the catheter was exchanged over a guide wire with serial dilators to 30-French size. A nephroscope was then used for access, and metal forceps used for piecemeal removal. Two drains were placed for irrigations (23). The same group has shown significant benefits for a minimal access approach including fewer complications and deaths compared with open necrosectomy (24).

Laparoscopic debridement

Laparoscopic debridement is performed with laparoscopic visualization followed by necrosectomy through separate ports. Laparoscopic debridement through transperitoneal route has gained little acceptance because of the risk of disseminating retroperitoneal infection into the peritoneal cavity. There have been only a few case series related to the laparoscopic approach. Parekh 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 the greater omentum between the stomach and colon. Gentle finger dissection was used for debridement, and several drains were left for postoperative drainage (25). Zhu et al. described using at least four standard ports, and going through the gastrocolic ligament to approach the pancreas. A special retractor was used to elevate the stomach for exposure. Many drainage tubes were used for postoperative lavage (26).

The laparoscopic approach may be theoretically suitable late in the course of the disease for patients with WON who has to undergo simultaneous cholecystectomy. However, it should be undertaken only by highly experienced minimally invasive surgeons.

CHOLECYSTECTOMY

All patients with pancreatitis should have a US of the gallbladder performed. If gallstones or sludge are present, a cholecystectomy should be planned. Patients undergoing VARD should have a laparoscopic cholecystectomy within six months following complete resolution of the peripancreatic collections and inflammatory process. Patients undergoing a transperitoneal open or laparoscopic necrosectomy may have a cholecystectomy attempted at the time of their surgery; however, it may not be possible to perform a safe cholecystectomy when there is a large amount of necrosis because of significant inflammation in the portal vein.

POSTOPERATIVE LAVAGE

With both the minimally invasive and open necrosectomy procedures, postoperative lavage can be performed. Saline or Ringer's lactate is continuously infused in through a percutaneous drain at about 100-200 mL/hour and passively drains out through other drains. Postoperative lavage is continued for up to five days or until the effluent is clear. Following the lavage period, all drains are opened to gravity drainage. A CT scan is first obtained two weeks postoperatively to evaluate the collections. Criteria for drain removal include all the following:

- complete resolution of retroperitoneal collections on contrast-enhanced CT scan,
- drain outputs of 10mL/day or less, and
- absence of elevated amylase levels in the drain effluent.

COMPLICATIONS

The main complications of pancreatic necrosectomy include:

- perioperative hemorrhage,
- enteric fistulas (including gastric, small bowel, and large bowel),
- pancreatic fistulas, most often from a disconnected duct ('orphaned tail'),
- incisional hernias, and
- pancreatic endocrine and exocrine insufficiency.

Bleeding occurs if vessels traversing the cavity are debrided or disrupted or by using the suction device too aggressively. Structures traversing the cavity that do not easily fracture with gentle blunt pressure are blood vessels unless proven otherwise and should be left undisturbed. If significant hemorrhage is detected, the first step is to tightly pack the retroperitoneal wound and wait. This is often sufficient to stop most bleeding and to gain hemodynamic stability. Adjunctive use of angiographic embolization should also be strongly considered. Dissection of the indurated and inflamed tissues of the retroperitoneum is discouraged as this will frequently result in further hemorrhage. The distorted anatomy also makes routine exposure techniques extremely difficult. If packing does not quickly control bleeding in VARD, there should be a low threshold for performing an open laparotomy with retroperitoneal packing followed by angiographic embolization.

Visceral injury to the left colon during VARD is best avoided by accessing the retroperitoneum under direct vision and utilizing preoperatively placed drainage catheters as a digital manual road-map into the cavity. Blunt finger dissection also facilitates safe entry into the cavity, minimizing the risk of visceral injury. Despite careful technique, patients will still develop enteric fistulas. Fistulas may require prolonged PD, but almost all fistulas will close without surgery. Patience is required since most enteric fistulas will not close until all collections are drained, and the patient is anabolic and has a normal serum albumin which may take months. Most pancreatic fistulae can also be

treated with patience and PD. Persistent pancreatic fistulas are treated with a distal pancreatectomy of the orphaned tail (10, 27).

IS NECROSECTOMY OBSOLETE FOR INFECTED NECROTIZING PANCREATITIS?

Necrosectomy has been a mainstay of surgical procedures for infected necrotizing pancreatitis. Currently, the management of necrotizing pancreatitis has undergone a paradigm shift toward minimally invasive techniques for necrosectomy, obviating the need for open necrosectomy in most cases (28). There is increasing evidence that minimally invasive approaches are associated with improved outcomes over traditional open necrosectomy (18–28). A recent international multidisciplinary consensus conference emphasized the superiority of minimally invasive approaches over standard open surgical approaches (9).

Recently, however, increasing evidence on the efficacy of endoscopic technique shows good outcomes when treating walled-off necrotizing pancreatitis without a necrosectomy (29). Moreover, a simple PD can eliminate the need for necrosectomy in many patients. The success of these drainage-only procedures raises the question of whether necrosectomy is obsolete. With further refinement of the drainage procedures, a paradigm shift from necrosectomy to drainage might be inevitable (30).

CONCLUSIONS

The treatment of necrotizing pancreatitis has undergone significant advances. Many lessons have been learned from the stalwart work done by surgeons in the past century. Changes over that time include improved intensive care, a move toward delayed surgery to after four weeks from the onset of symptoms, and the use of percutaneous drains and other minimal access techniques. With these advances, patients are experiencing a much lower morbidity and mortality than in the past. 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.

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