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TOPIC HIGHLIGHT

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Surgical and interventional management of complications caused by acute pancreatitis

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Abstract

Acute pancreatitis is one of the most common gastrointestinal disorders worldwide. It requires acute hospitalization, with a reported annual incidence of 13 to 45 cases per 100000 persons. In severe cases there is persistent organ failure and a mortality rate of 15% to 30%, whereas mortality of mild pancreatitis is only 0% to 1%. Treatment principles of necrotizing pancreatitis and the role of surgery are still controversial. Despite surgery being effective for infected pancreatic necrosis, it carries the risk of long-term endocrine and exocrine deficiency and a morbidity and mortality rate of between 10% to 40%. Considering high morbidity and mortality rates of operative necrosectomy, minimally invasive strategies are being explored by gastrointestinal surgeons, radiologists, and gastroenterologists. Since 1999, several other minimally invasive surgical, endoscopic, and radiologic approaches to drain and debride pancreatic necrosis have been described. In patients who do not improve after technically adequate drainage, necrosectomy should be performed. When minimal invasive management is unsuccessful or necrosis has spread to locations not accessible by endoscopy, open abdominal surgery is recommended. Additionally, surgery is recognized as a major determinant of outcomes for acute pancreatitis, and there is general agreement that patients should undergo surgery in the late phase of the disease. It is important to consider multidisciplinary management, considering the clinical situation and the comorbidity of the patient, as well as the surgeons experience.

Key words: Severe acute pancreatitis; Complications; Necrosectomy; Percutaneous drainage; Endoscopy; Laparoscopy

Core tip: The surgery and its timing are contentious regarding treatment of severe acute pancreatitis and related complications. Many studies showed that "early" open surgery has been accompanied often by higher mortality and morbidity rates, and should be the next step in treating severe acute pancreatitis complications, when minimally invasive management fails. In this review article, current treatment options and results are discussed.

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INTRODUCTION

Acute pancreatitis (defined as the acute nonbacterial inflammatory condition of the pancreas) is derived from early activation of digestive enzymes inside acinar cells, with varying compromising of the gland itself, nearby tissues, and other organs. It is well known that several situations develop into acute pancreatitis, but the mechanisms and how those mechanisms develop the disease remain

unclear. Why do some individuals develop edematous pancreatitis and others develop a more severe necrotic pancreatitis? Knowledge regarding pancreatitis pathogenesis may have important implications in prevention and treatment of the disorder. If the early events that generate the inflammatory process are understood - and if pro- and anti-inflammatory factors that modulate the severity of the disease are known - treatment can be implemented so the process will not happen or possible associated complications will be minimized[1].

Acute pancreatitis is one of the most common gastrointestinal disorders requiring acute hospitalization worldwide, with a reported annual incidence of 13 to 45 cases per 100000 persons[2]. In the United States, it is the third most common gastrointestinal disorder requiring acute hospitalization[3]. In the United States alone, acute pancreatitis leads to 270000 hospital admissions annually and in-patient costs exceeding 2.5 billion dollars[4].

It is rare in childhood but may occur at any age (according to recent publications[5,6], median age, 55-58 yr). Acute biliary pancreatitis is more common in women, and alcoholic pancreatitis is more common in middle-aged men[6].

Although most patients with acute pancreatitis recover without sequelae, between 10% to 20% will have a more complicated clinical course with higher risks of morbidity and mortality[7]. Severe acute pancreatitis (SAP) requires prolonged hospitalization, frequently including a stay in the intensive care unit (ICU) because of organ dysfunction[8].

Severe pancreatitis is associated with a mortality of 15% to 30%, whereas mortality from mild pancreatitis is only 0% to 1%, and organ failure is the most important determinant of mortality in acute pancreatitis. However, in approximately 30% of patients with necrotizing pancreatitis, a secondary necrotic infection occurs, mostly 3 to 4 wk after the onset of necrotizing pancreatitis[9]. If left untreated, mortality of infected necrosis approaches 100%[3,10]. Initial treatment of SAP is primarily medical, and these patients require intensive organ support[11,12]. Surgery for SAP is a morbid procedure associated with complications in 34% to 95% of patients, and mortality in 11% to 39%[13,14]. Surgery may lead to long-term pancreatic insufficiency[14,15]. The high mortality rate encountered with surgery reflects the hazards of operating on critically ill septic patients, often with multiorgan failure[16].

Surgery and its timing are the focus of contention when treating SAP. Decades ago, some experts used laparotomy in the early phase of SAP to debride and drain the retroperitoneal infected necrosis[17,18]. However, studies have shown that "early" surgery is often accompanied by higher mortality[19,20], and several studies also have shown that there is success with some SAP patients with retroperitoneal infected necrosis, conservatively managed without high-risk surgical intervention; therefore, many experts advocated delayed surgery[20,21]. In recent decades, higher mortality rates during early surgery resulted from those SAP cases that underwent traditional laparotomy (which may cause severe trauma) to debride and drain the retroperitoneal infected necrosis[22]. After several studies showed that high mortality rates for severe necrotizing pancreatitis came with early surgery, the 2002 International Acute Pancreatitis guidelines recommended avoiding surgical intervention during the first 14 d after onset, unless there was progressive multiple organ failure and clinical deterioration. Subsequent studies have suggested that morbidity and mortality rates can be reduced further if surgery is delayed beyond 28 to 30 d[9], because the extended interval allows sufficient demarcation between normal and necrotic tissue, reducing the risk of inciting overwhelming postoperative septic and systemic inflammatory responses, and the risk of intraoperative injury to surrounding organs and hemorrhage[23].

Faced with high morbidity and mortality rates of operative necrosectomy, minimally invasive strategies are being increasingly explored by gastrointestinal surgeons, radiologists, and gastroenterologists[24]. As technical ability and endoscopic tools have gradually become more precise, the mortality rates of patients with severe pancreatitis have improved, and there are fewer complications compared to those having open debridement treatment[25]. Percutaneous catheter drainage (PCD), endoscopic transgastric procedures, and a minimally invasive approaches all have been proposed as alternatives to open necrosectomy[16]. When minimal invasive management is unsuccessful or necrosis has spread to locations not accessible by endoscopy, open abdominal surgery is recommended[25].

CLASSIFICATION AND SCORING

The Atlanta Classification system for acute pancreatitis came about as a result of the Atlanta Symposium of 1992, and, despite there being some confusion over definitions, it has been a practical aid for health care providers[11]. Since then, with improvements in the understanding of organ failure and necrotizing pancreatitis, and in diagnostic tools, some revisions have been made through a working group consultation with eleven international pancreatic societies[26]. The fourth draft, in current use, contains a clinical assessment of severity and the previous confusing definitions concerning local complications have been further clarified. The criteria for the diagnosis of acute pancreatitis, the differences between the two forms (*i.e.*, interstitial edematous pancreatitis and necrotizing pancreatitis), the three categories of severity of acute pancreatitis (mildly acute, moderately severe acute, and severe acute)[27,28], and the morphology observed in diagnostic images of pancreatic and peripancreatic collections brought about by complications are now more clearly set out.

Criteria to help in classifying severity are the presence of transient organ failure (that which is present for less than 48 h), persistent organ failure (continuing for more than 48 h), and local (such as, peripancreatic fluid or acute necrotic collections) or systemic complications (such

as exacerbations of underlying comorbidities related to the acute pancreatitis)[29-31].

Scoring systems

Attempts to define objective criteria for assessing disease severity and prognosis were pioneered in the 1970s by Ranson *et al*[32] and Blamey *et al*[33]. The 2 scoring systems include basic laboratory data and clinical variables obtained 48 h after hospital admission. In subsequent years, these scoring systems have found widespread application and have undergone numerous modifications. Several large studies have shown a close correlation between advanced age and nonsurvival in acute pancreatitis[34-36]. Advanced age often is associated with comorbidities (*e.g.*, cardiovascular disease, diabetes, and overall decreased biological resistance)[36], and therefore, increases risk of fatal outcome. Comorbidities have been included in multiple parameter scoring systems such as the Acute Physiology and Chronic Health Examination (APACHE) Ⅱ system, the most widely used index for early risk stratification[37]. Although more recent iterations of this scoring system have been developed, the advantages of the APACHE Ⅱ are its familiarity, its objective nature, and its ability to be calculated at any time during a patient's hospital stay. Use of the APACHE Ⅱ in clinical practice has several important limitations (*e.g.*, the requirement for multiple parameters and an online calculator - versions of which are widely available on the Internet)[38]. As a result, several additional scoring systems have been developed for bedside application.

A more recent scoring system developed for use during the first 24 h of admission to the hospital is the Bedside Index of Severity in Acute Pancreatitis[7]. This system was derived using data from 17992 patients and validated on a population of 18256 patients in the United States. This 5-factor scoring system has a similar accuracy as the APACHE Ⅱ for predicting death in the initial retrospective study and in several subsequent prospective cohort studies[39]. The Bedside Index of Severity in Acute Pancreatitis is a simplified scoring system that can be applied easily in the earliest phases of acute pancreatitis helping identify those patients with an increased risk of death.

DEFINITION AND COMPLICATIONS

Defining the severity of acute pancreatitis

There are three good reasons for defining the severity of acute pancreatitis: the first being diagnosing those patients who may need aggressive early treatment in cases of severe acute form; the second is the identification of patients who may need to be transferred to a specialist care unit; and the third is that placing these patients into sub-groups according to particular complications will aid the specialists to whom they are transferred[26].

Mild acute pancreatitis

Patients without organ failure or complications are classified as having mild acute pancreatitis. They are usually discharged at an early stage, do not need pancreatic imaging, and death as a result of the disease is extremely uncommon[40].

Moderately severe acute pancreatitis

This is diagnosed when transient organ failure, local complications (such as prolonged abdominal pain, leukocytosis, or fever caused by peripancreatic collections, or if the patience can not feed normally), or systemic complications (such as when coronary artery disease or chronic lung disease is made worse as a result) are present. This form of the disease can resolve itself without treatment (when transient organ failure or acute fluid collection is involved) or specialist care may be needed (when extensive sterile necrosis is present, but organ failure is not). The chance of death as a result of this form is lower than in cases of the severe acute form[27].

Severe acute pancreatitis

This is diagnosed when there is persistent single or multiple organ failure, resulting from systemic inflammatory response syndrome caused by cytokine cascades at an early stage[30,31,41,42], which can complicate the pancreatitis, lead to other complications, and increase the risk of death (a 36% to 50% mortality rate), commonly due to infected necrosis, if this is in the first few days of the disease[31,41,42].

One systematic review into deaths caused by necrosis in the absence of organ failure (11% of patients) resulted in a four tier grading of severity being proposed[28], while two large Dutch studies came up with a figure of 6%[43,44]. The differences in morphological characteristics of local complications and their different treatments need to be determined to prevent mortality.

Necrotizing pancreatitis

Necrosis, which affects between 5% and 10% of patients, generally involves both the pancreas and peripancreatic tissue, although sometimes just the peripancreatic tissue, and, even more rarely, only the pancreatic parenchyma.

With patients who have peripancreatic necrosis, as in those with interstitial edematous pancreatitis, the pancreas enhances normally on contrast-enhanced computed tomography, but morbidity is increased and intervention rates are higher[40,45,46]. The progression of both pancreatic and peripancreatic necrosis varies, remaining solid or liquefying, becoming infected or remaining sterile, persisting for a long time or gradually disappearing.

Infected pancreatic necrosis

Both forms of necrosis can become infected, but the majority of evidence shows no certain correlation between its extent, the risk of infection, and its duration, although it is not common in the first week[9,43]. Its diagnosis is crucial as antibiotic and other necessary treatments need to be applied as soon as possible[47]. If computed tomography (CT) scans show up extraluminal gas in the pancreas or peripancreatic tissue, or if biopsies detect

bacteria and/or fungi on Gram stains and cultures, then infection is highly likely[48]. Signs of suppuration may also be evidence of liquefaction and will increase over time. Despite the first version of the Atlanta Classification defining a localized collection of purulent material without significant necrotic material as a pancreatic abscess, the term was found to be unhelpful and is not used in the revised version. Secondary infections have been found to increase the the chances of morbidity and death[49].

Acute pancreatitis complications

Defining organ failure: Organ failure in the respiratory, cardiovascular, and renal systems is defined using the modified Marshall scoring system: a score of two or more for one of these systems is sufficient[50]. This system is preferred over the Sepsis-related Organ Failure Assessment scoring system, used in critical care units, as it is easier to use and gives objective results, although both systems could be used to help stratify the severity of organ failure[51].

Defining local complications: The original Atlanta Classification was useful because it recognized the differences between uncomplicated interstitial pancreatitis and acute pancreatitis with local complications[11]. Local complications (such as acute peripancreatic fluid collection, pancreatic pseudocyst, acute necrotic collection, walled-off necrosis, gastric outlet dysfunction, splenic and portal vein thrombosis, and colonic necrosis) and their clinical consequences are now better understood and described. Signs that these problems may be present are persistent abdominal pain, secondary serum pancreatic enzyme activity increases, organ dysfunction getting worse, and symptoms of sepsis (*i.e.*, fever, white blood cell increases, *etc.*), although imaging may be necessary for correct diagnosis[26].

The definitions of pancreatic fluid collections are based on the revised Atlanta classification by the Acute Pancreatitis Classification Working Group and are described as follows: (1) Acute peripancreatic fluid collections (APFC): these are not connected to necrosis, occur in the first four weeks of acute pancreatitis, are entirely liquid, found in or near the pancreas, and have no fibrous wall or granulation tissue. Those which resolve themselves or have no symptoms need no treatment and are not classed as severe acute pancreatitis; (2) Pseudocyst: a collection of pancreatic juice, containing no solid necrotic material, enclosed by a wall of fibrous or granulation tissue resulting from acute pancreatitis, pancreatic trauma, or chronic pancreatitis. They are a result of the main pancreatic duct or its intrapancreatic branches being disrupted in the absence of pancreatic parenchymal necrosis and causing pancreatic juice to leak persistently and collect, usually after the first month; (3) Infected pseudocyst: this contains purulent liquid with no solid necrotic material (although there may be other solid debris) and can be diagnosed by following the patient's clinical course or through the presence of gas on CT scans; (4) Post-necrotic pancreatic/peripancreatic fluid collections (PNPFC): fluid collections associated with necrotizing pancreatitis, containing fluid and necrotic tissue, which over the course of weeks, evolve into a necrotic fluid collection with liquid and solid debris; and (5) WON: these are formed because of encapsulation of the PNPFC over time in a thickened wall of fibrous or granulation tissue without an epithelial lining at the interface of necrotic tissue, generally maturing after the first month of necrotizing pancreatitis. Walled-off necrosis, resulting from necrotic pancreatic parenchyma and/or necrotic peripancreatic tissue, can be sterile or infected, and there can be many of them, sometimes in locations distant from the pancreas[52]. Walled-off necrosis helps to distinguish the necrotic tissue from the parenchyma, thereby lessening the chances of bleeding and the loss of vital tissue during surgery, although this can result in pancreatic exocrine and endocrine deficiency[53,54].

Bradley *et al*[55] suggested a conservative approach to sterile pancreatic necrosis, although the Acute Pancreatitis Classification Working Group found that patients may continue to be ill even when there was no infection[26,55]. Secondary infection, which usually occurs two to four weeks after primary infection, commonly results in sepsis, multi-organ failure, and patient mortality[56]. High Ranson's and APACHE-Ⅱ scores are good indicators of the possibility of death, and even those with severe sterile necrosis have a high mortality rate if their overall health is not good.

Defining systemic complications

Systemic complications are classed as those arising from already existent complaints, such as coronary artery disease, or chronic lung disease, made worse by the acute pancreatitis. The Acute Pancreatitis Classification Working Group made a distinction between these and persistent organ failure, the latter being the main feature of the severe acute form.

TREATMENT

Management of infected pancreatic necrosis

Pancreatic necrosis surgery, the principles of which were laid out by Moynihan in 1925[57], involves isolating the pancreas from the abdominal cavity and cellular fat spaces, and draining the amassed peripancreatic fluid. The aim is to check the sepsis and control the release of pro-inflammatory mediators. The combination of debriding the necrotic tissue and removing retro-peritoneal debris and exudate is carried out in order to preserve the organ. Four principle surgical methods are recommended: (1) being necrosectomy alongside open packing[58]; (2) being planned, staged relaparotomies with repeated lavage[21]; (3) being closed continuous lavage of the lesser sac and retro-peritoneum[59]; and (4) being closed packing[60].

These days, the third method is most often used to remove post-operative residual pancreatic necrosis as it has the lowest rate of morbidity[24,53]. Surgery has the pos-

sibility of saving the patient's life, but it carries a high risk of morbidity and mortality, between 4% and 10%, and possible long-term endocrine and exocrine deficiency[25]. In addition, timing of surgery has been increasingly recognized as a major determinant of outcome in acute pancreatitis, and there is general agreement that patients must undergo operation in the late phase of the disease. However, the definition of late differs between studies[53,61]. It has been reported that mortality from necrotizing pancreatitis can be reduced by avoiding surgical therapy or by postponing surgery until the late stage of the disease[62].

Despite the availability of several clinical (Ranson criteria, acute physiology and chronic health evaluation Ⅱ score, and APACHE Ⅱ) and radiologic grading systems (Balthazar scoring system, modified computerized tomography severity index), there is no consensus on accurately predicting the best treatment strategy and outcome after acute necrotizing pancreatitis[63-65].

The treatment principles of necrotizing pancreatitis and the role of surgery remain controversial. In the 1990s, more than 60% of patients with the disease were treated surgically[18]. In 1991, Bradley and Allen defined pancreatic necrosis as the principal determinant of survival in acute pancreatitis, but they recommended conservative treatment of sterile necrosis in selected cases[55]. Guidelines of the International Acute Pancreatitis recommend doing a fine-needle aspiration biopsy in patients with necrotizing pancreatitis and signs of sepsis. Once fine-needle aspiration biopsy-proven infection of necrosis has been shown, it is considered an indication for surgery[53].

Recent reports have shown that a subset of patients with SAP developing infected fluid collection, pancreatic necrosis, or pancreatic abscess can be managed by PCD[66]. It was hypothesized that simple drainage with regular-bore (12- to 14-Fr) percutaneous catheters is an effective therapeutic option. This recommendation is based on the premise that is not necessary to remove all necrotic tissue to successfully treat patients with infected pancreatic necrosis. By performing drainage of infected fluid under pressure, the clinical condition might improve and the necrotic tissue may successfully be dealt with by the patient's immune system. The goal of drainage has been to remove infected fluid rather than the necrosis[67]. However, PCD used for infected pancreatic necrosis has been criticized for its poor ability to remove solid debris.

Percutaneous drainage is usually performed under computed tomography, whereas sonographically controlled PCD rarely has been reported[68]. The success rate of percutaneous catheter drainage in infected pancreatic necrosis varies and ranges from 0% to 78%[43,69]. van Baal *et al*[70] reported a meta-analysis, which included 384 patients from 11 studies, of PCD as a primary treatment for necrotizing pancreatitis. Surgical necrosectomy could be avoided in 56% of the patients and the overall mortality rate was 17%. However, infected necrosis was confirmed in only 71% of the patients.

In a recent report, authors aimed to identify factors that led to surgical intervention after initial management with PCD, and also to identify a subgroup of patients where PCD alone would be effective. Twenty-seven patients (38.5%) underwent surgery after initial PCD. Indications for surgical intervention were ongoing sepsis not controlled by interventional radiologic management. In that study, percutaneous catheter drainage achieved sepsis reversal in 62% of patients and complete recovery was achieved without surgical intervention in 48% of patients[16].

Gagner first described minimally invasive surgical treatment of necrotizing pancreatitis in 1996, including laparoscopic retrocolic, retroperitoneoscopic, and transgastric procedures[71]. Over the past 15 years, several other minimally invasive surgical, endoscopic, and radiologic approaches for draining and debriding pancreatic necrosis have been described[23].

A literature search of the MEDLINE database from April 1996 to November 2010 was performed for each of the 4 techniques for minimally invasive necrosectomy: 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. Twenty-seven studies with 947 patients were examined (8 studies on percutaneous approach; 10 studies on endoscopic necrosectomy; 2 studies on laparoscopic necrosectomy *via* a transperitoneal approach; 5 studies on retroperitoneal necrosectomy; and 2 studies on a combined percutaneous retroperitoneal approach). Finally, the authors advocated a multidisciplinary approach with interventional radiologists, gastroenterologists, intensivists, and hepatobiliary surgeons at tertiary care centers. They concluded that because the comparison data are limited, the minimally invasive approach should be based on location of lesion and individual patient presentation[23].

A prospective, randomized, multicenter trial called the Minimally Invasive Step Up Approach Versus Maximal Necrosectomy in Patients with Acute Necrotizing Pancreatitis (PANTER) was performed in the Netherlands[43]. After diagnosing necrotizing pancreatitis or infected pancreatic necrosis, patients were randomly assigned to either a step-up approach or 2 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 performed 3 d 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%). About 35% of patients in the step-up group could be managed with percutaneous drainage only[43].

Similar to the PANTER Trial, there also is a recent, prospective multicenter, single-arm study from the University of Washington. Percutaneous drainage was used

as an initial treatment for infected pancreatic necrosis. If there was a 75% reduction in size based on a 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 (*i.e.*, drains with or without a VARD). Mortality at 30 d was 2.5%. The percutaneous approach to infected pancreatic necrosis has been shown to be safe and feasible in multiple retrospective case series. It is noteworthy that 44% of patients reviewed in the studies did not need surgical therapy. What has become increasingly popular is combined percutaneous technique with a VARD as mentioned in the PANTER trial and the Horvath study[72]. These studies not only confirmed a subgroup of patients that can benefit from percutaneous drainage alone but also examined a combined technique in a prospective manner with a relatively larger amount of patients.

Retroperitoneal laparoscopic debridement drainage (RLDD) for treating retroperitoneal infected necrosis in SAP has been rarely reported, and there has been no report regarding comparison of curative efficacy between RLDD and laparotomy. This study showed that RLDD (a minimally invasive procedure) has obvious advantages for treating SAP retroperitoneal infected necrosis. It is safe and effective when done early and can prevent systemic inflammatory response syndrome from progressing further[22].

The overall message of these studies is that in patients who do not improve after adequate drainage, necrosectomy should be performed next. The percutaneous drain, together with the computed tomography scan, can be used as a roadmap for (minimally invasive) necrosectomy. Percutaneous (or transgastric) drainage should be the first intervention, and the indication for drainage should be the same as for surgical necrosectomy[3].

Direct endoscopic necrosectomy (DEN) is a minimally invasive treatment introduced recently for treating infected WON[73]. Using DEN, a stoma is created endoscopically between the enteric lumen and the walled-off fluid collection, allowing insertion of an endoscope into the fluid collection, which allows for an endoscopic necrosectomy. Current data suggest that DEN is a less invasive and less risky alternative to open surgical necrosectomy for managing infected WON and infected pseudocyst with solid debris[74].

Two large, multicenter, retrospective studies demonstrated that necrosis managed using direct transluminal endoscope techniques resulted in a positive prognosis and a high success rate at the beginning[75,76]. Nevertheless, all of the current endoscopic techniques have inherent limitations (*e.g.*, risk of air embolism, endoscopically uncontrollable bleeding, and inadequate drainage through multiple plastic stents) together with early occlusion of the fistulous tract. To overcome these difficulties, Hritz and associates demonstrated a successful method of endoscopic transluminal necrosectomy - a combination of the temporary placement of a self-expanding metal stent into the fistulous tract and daily irrigations of the necrotic cavity with a high-flow water-jet system using a flush knife[77].

Percutaneous techniques, including VARD, need open necrosectomy in a high proportion of patients, and mortality is around 20%[3]. It is now well recognized that most sterile collections do not require intervention (at least in the early phase of disease), and that mortality and morbidity rates after an intervention are time dependent, falling to almost 0% by the stage of a sterile WON. The indication for early intervention for infected necrosis is limited to sepsis control, and there is increasing consensus within this group that some form of minimally invasive approach may enhance outcomes. Conventional management of late pancreatic collections was by open pancreatic cystgastrostomy, but with developments in interventional radiology, therapeutic endoscopy, and minimal access surgery, new techniques have been used as alternatives to this approach[78]. While all have proven to be feasible in small cohort series, there is little evidence to the relative benefits of one method over another for managing APFC[79,80].

Laparoscopic cystgastrostomy (LCG) is used in mature symptomatic collections. It facilitates complete drainage of the collection with a minimal requirement for re-intervention. It also allows simultaneous management of gallstones. Laparoscopic cystgastrostomy should allow a wide debridement of the cyst cavity with the advantages of a minimally invasive approach. Open cystogastrostomy (OCG) is used when an intervention is required on additional intra-abdominal pathology (*e.g.*, enteric stricture or fistula) or where collection anatomy precludes other approaches. Laparoscopic cystgastrostomy allows larger collections to be managed by a one-step intervention, and the solid necrosis to be more effectively drained. Importantly, definitive management of gallstones can be achieved. However, the concept that endoscopic ultrasound (EUS)-guided drainage (the least invasive approach) may be of most benefit in fluid predominant collections requires evaluation within a study format, as experience has shown some APFC with significant necrosis may resolve completely using this approach only. Optimal management of collections with intermediate (size and fluid content) characteristics is not clear, and there may be clinical equipoise regarding whether a laparoscopic or endoscopic cystgastrostomy should be used as the preferred approach. A well-conducted, randomized, controlled study is required to determine which method is most effective in this particular group of patients[78].

In summary, standard treatment for infected pancreatic necrosis is open or laparoscopic surgical drainage. However, on occasions, percutaneous drainage may work well. As recommended by the International Association of Pancreatology Clinical Guideline, drainage should be effectively established when the patient is septic. A step-by-step treatment is proposed by which percutaneous or

endoscopic drainage should be established first and then necrosectomy with drainage through a minimally invasive retroperitoneal access. When this method was compared with open surgery, it offered several advantages including the chance to avoid surgery in some patients, fewer complications, and lower cost[45,53,70].

The alternatives to open surgery should be considered, mainly in frail and critical patients who would not tolerate more aggressive surgery. In clinical practice, it is important to consider the importance of a multidisciplinary management, considering the clinical situation and comorbidity of the patient and the experience of the personnel.

Pancreatic duct breaking: Generally this is produced in the context of pancreatic necrosis because of erosion of the duct. In cases of necrosis, complete or partial pancreatic duct breaking occurs in about 60% of cases. To assess this situation, wirsungography by using computed tomography, nuclear magnetic resonance (spectroscopy), or endoscopic retrograde cholangiopancreatography can be performed. This latter method may be associated with placing a stent, which will favor definitive resolution. Nutritional support and potent antisecretors (*e.g.*, octreotide) should be associated. Collections can be removed by percutaneous or endoscopic drainage. Successful fistula sealing is described using cyanoacrylate or fibrin[81]. If other treatments fail (which is common) surgery is indicated. However, in cases of complete duct rupture, it is rarely successful to access the residual duct in the pancreatic tail. In such cases, a distal pancreatic resection may be curative. Otherwise, internal drainage through a pancreatic-digestive anastomosis, may be necessary[1].

Pancreatic pseudocyst

According to several retrospective studies, the incidence of a pseudocyst after acute pancreatitis varies depending on the definition and methods of detecting a pseudocyst. The incidence ranges from 5% to 16%, and is reported as being higher in patients with underlying chronic pancreatitis[82-84].

Treatment of pancreatic pseudocysts: Fluid collections that appear during disappear spontaneously in 40% to 50% of cases. In about 10% to 15% of cases, these collections persist and become encapsulated, generating pancreatic pseudocysts. A true pancreatic pseudocyst (*i.e.*, without an epithelial lining; the counterpart would be a pancreatic cyst) takes at least 4 to 6 wk from the beginning of symptoms to be encapsulated by a wall formed by inflammatory fibrosis of the adjacent tissues. Few studies have documented the natural evolution of pancreatic pseudocysts. It has been thought that pancreatic pseudocysts more than 6 cm in diameter, or those that persisted for more than 6 wk, should be operated on[1] despite some studies showing that 50% of those which had no symptoms or were smaller than 10 cm resolved of their own accord[84]. It also has been shown that about half of all pancreatic pseudocysts can be solved spontaneously; thus, the attitude has shifted toward a more conservative approach.

Asymptomatic pancreatic pseudocysts may be followed for periods of 6 mo or longer if they do not grow, become symptomatic, or present complications (*e.g.*, hemorrhage, infection, or mechanical compromise of adjacent organs). In these situations, percutaneous, endoscopic, or surgical drainage should be considered. It depends on several factors: patients' general status, size, number, and location of pseudocysts, communication (or not) with the main pancreatic duct, solid necrosis inside (or not), and possible complications[1].

Despite almost 50% of pseudocysts resolving themselves, the remainder can become symptomatic or infected, and may rupture, hemorrhage, develop vascular thrombosis, or obstruct nearby viscera, resulting in the need for some kind of medical intervention[85,86].

A ruptured pseudocyst, if it causes hemorrhaging in the digestive tract, will need immediate treatment, while if it occurs in the peritoneal cavity, it can lead to peritonitis or hemorrhagic shock requiring emergency exploratory surgery[25].

Kim *et al*[84] report spontaneous resolution, including disappearance and a size decrement, was achieved in 71.6% of cases despite the higher proportion of underlying chronic pancreatitis, and there was no significant difference in spontaneous resolution rate between acute and acute-on-chronic pancreatitis groups. Therefore, the wait-and-see policy for more than 4 to 6 wk may be feasible, unless the pseudocysts are associated with symptoms or complications. Although there have been differing results concerning spontaneous resolution of pseudocysts according to the study, size, detection time, and cause of the underlying pancreatic disease were reported as predictive factors[87-89]. The presence of an underlying chronic pancreatitis, an alcoholic cause, and a long interval from symptom onset until admission are risk factors for a pseudocyst, and a single lesion is a predictor of spontaneous resolution[84].

Percutaneous drainage should be avoided in cases of hemorrhage or pancreatic ascites. Surgical treatment (mainly by internal drainage) is reserved for patients in whom percutaneous or endoscopic treatment has failed, those with complications from chronic pancreatitis, those with multiple or giant pseudocysts, or when malignancy cannot be ruled out[90,91].

Hemorrhage or pseudoaneurysm

Hemorrhagic complications: Hemorrhagic complications of acute pancreatitis are fortunately rare; however, they may present in a diversity of forms. Sometimes, upper or lower gastrointestinal bleeding occurs because of gastroduodenitis secondary to adjacent inflammation, bleeding peptic ulcer, pseudocyst rupture into the digestive tract, or drainage of a pseudoaneurysm through the Wirsung duct. In severe cases of acute pancreatitis, bleeding may occur due to intra- or retroperitoneal erosion of

the vessels of the celiac trunk, mainly the splenic artery. Diagnosis may be established by angiography or angio-computed tomography. Angiography, besides identifying the bleeding point, sometimes allows embolization that may stop bleeding. If this method fails, definitive treatment must be surgery[92].

Ischemic complications (either local or related to remote vascular events) and venous or arterial complications - specifically splanchnic thrombosis and associated varices - are a major cause of morbidity and mortality[93]. The reported frequency of pulmonary embolism in acute pancreatitis is rare. The thrombohemorrhagic complications in pancreatitis play a tremendous part in developing its most severe forms and fatal outcomes. Early recognition and investigation of thromboembolism is imperative because accurate diagnosis and timely radiologic interventional procedures reduce mortality. Early treatment with intravenous heparin or thrombolysis is effective. Vascular filter insertion may be a life-saving measure for such patients[94].

Pseudoaneurysm

Pseudoaneurysm is a rare but potentially fatal complication of acute pancreatitis. The risk of rupture is as high as 37%[95]. The arteries involved include, in order of frequency, the splenic (40%), gastroduodenal (20%), pancreaticoduodenal (20%), gastric (5%), and hepatic (2%)[96]. The pathogenetic mechanism is secondary to degradation of the vessel wall by pancreatic enzymes released from a destroyed pancreatic duct, resulting in a primary formation of a pseudoaneurysm or rupture of the vessel into a pre-existing pseudocyst, which then converts into a pseudoaneurysm. Pseudoaneurysms present symptoms such as gastrointestinal bleeding (60%), abdominal pain (50%), and splenomegaly or pulsatile abdominal tumors (5%), and spontaneous regression also have been reported[97,98].

Generally developing intracystically, they are usually diagnosed *via* angiography, which is used for locating and treating with embolization (with a high technical success rate of 93%-100%, and low 24 h and 30 d re-bleeding rates - 4% and 17%, respectively, Kalva *et al*[99]), but it should also be borne in mind when a pancreatitis patient is undergoing a CT scan. Gonzalez *et al*[100] have also demonstrated that lipiodol with n-butyl cyano-acylate injected using endo-ultrasonography can be successful. If these techniques are not successful or if re-bleeding occurs, then surgery is required[25].

Necrotizing pancreatitis and pseudocysts involving the pancreatic tail appear to predispose patients to splenic complications[101]. The incidence of pseudocyst extension into the spleen has been estimated at around 1%. Erosion of noncystic pancreatic inflammation occurs less commonly[102,103]. In a series of 500 patients with chronic pancreatitis, splenic complications were found in 11 patients (2.2%), four of whom presented with splenic rupture. Five patients had intrasplenic pseudocysts and 2 had intrasplenic subcapsular hematomas[104]. A series of 159 CT scans performed on 100 consecutive patients with acute pancreatitis found splenic infarcts in 10 patients and subcapsular hemorrhage in 2 patients[105]. Another series of 238 patients with pancreatic pseudocysts found 14 patients (5.9%) with splenic parenchymal involvement[106].

Management of patients with subcapsular hematomas and/or splenic parenchymal pseudocysts is by conservative approach, percutaneous drainage, or surgery[106]. The hemodynamically unstable patient with splenic rupture or hemoperitoneum requires emergency laparotomy and either splenectomy or distal pancreatosplenectomy, which can reduce the risk of pancreatic leak or fistula formation[104,106]. In hemodynamically stable patients, the decision for intervention should be based on clinical parameters rather than computed tomography imaging alone. A clinically stable patient with improving symptoms and resolving clinical signs can be managed conservatively with the intent of splenic conservation. Follow-up is by serial ultrasound or computed tomography scans, which can show spontaneous regression. Time for resolution varies from 1 wk to 4 mo depending on the severity of the underlying pancreatitis[107].

Chylous ascites

Pancreatitis is a rare cause of chylous ascites formation. It is believed that either lymph may actually leak through destroyed lymphatics because of pancreatic enzyme erosion or that chylous accumulation results from exudation of chyle, caused by the obstruction of lymphatic channel flow secondary to severe inflammatory changes that take place in the retroperitoneal space surrounding the pancreas[108]. Most cases involve chronic pancreatitis, though acute pancreatitis also has been recognized as the causative reason, with the first such report dating to 1984[109]. Since that time, only a few cases of chylous ascites secondary to acute pancreatitis have been documented. In almost all, the presence of chyle into the peritoneal cavity was discovered some time after the episode of pancreatitis, usually days or weeks[108]. However, Khan *et al*[110] reported a case of acute hyperlipidemic pancreatitis (with normal serum amylase) that presented with acute chylous peritonitis and was treated conservatively. Smith *et al*[111] operated on a patient with relapsing pancreatitis and acute chylous ascites formation caused by a clinical resemblance with appendicitis.

Therapeutic choices may vary in accordance with the underlying pathology.

Thorough lavage of the abdomen and adequate drainage is an excellent treatment modality for acute chylous peritonitis, because resolution of chylous ascites usually occurs within the next few days. However, successful conservative treatment also has been reported[112]. Conservative treatment requires proper preoperative diagnosis, which is often difficult because of the exceptional rarity of this condition and its resemblance to other surgical urgencies that call for immediate laparotomy. Long-term fasting, supported by total parenteral nutrition, frequently offers resolution. Alternatively, a high-protein low-fat diet

is effective at reducing the amount of chyle produced. Administration of octreotide is controversial[108].

In summary, the mortality rate for severe acute pancreatitis stands at between 15% and 30%, while if the between 5% and 10% of patients with parenchyma or peripancreatic necrosis are left untreated and it becomes infected, the mortality rate can be as high as 100%. The surgical methods and its timing are contentions regarding treatment of severe acute pancreatitis. Many studies showed that early surgery often was accompanied by higher mortality and morbidity rates. Faced with high morbidity and mortality rates of operative necrosectomy, minimally invasive strategies are being explored by gastrointestinal surgeons, radiologists, and gastroenterologists. In cases where there are severe acute pancreatitis complications, minimally invasive treatment is unsuccessful, or if there is widespread necrosis in locations not easily reached using other techniques, then traditional open surgery is strongly recommended.

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