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Evidence-Based Management of Gallstone Pancreatitis

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Keywords

• Gallstone pancreatitis • Biliary pancreatitis • Same-admission cholecystectomy
• Endoscopic retrograde cholangiopancreatography (ERCP)

Key points

- Acute gallstone pancreatitis remains a common cause for hospitalization and readmissions and continues to impose a significant health care burden in the United States.
- Although the management of acute gallstone pancreatitis depends on its severity, the accuracy and utility of predictive models and laboratory markers remain limited.
- Multiple randomized trials and metaanalyses support early (within 2 weeks), same-admission laparoscopic cholecystectomy to prevent gallstone-related complications after gallstone pancreatitis.
- Earlier cholecystectomy during index admission for mild gallstone pancreatitis (within 24–72 hours) is feasible and decreases length of stay, but studies are underpowered to determine the effect on complications.
- Gallstone pancreatitis often requires multidisciplinary coordination between surgery, critical care, gastroenterology, and radiology, especially for patients with complicated presentations or severe or necrotizing pancreatitis.

INTRODUCTION

Acute pancreatitis is one of the most common causes for hospitalization and for readmissions in the United States. In 2014, acute pancreatitis was the third most common diagnosis for patients admitted to the hospital with a

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gastrointestinal illness, accounting for approximately 280,000 cases and costing $2.6 billion [1]. Gallstones and alcohol are the 2 most common causes of acute pancreatitis, although the prevalence of other causes and associated diseases, such as tobacco use and hyperlipidemia, has increased over time [2].

Gallstone or biliary pancreatitis, like other causes of acute pancreatitis, is characterized by severe epigastric pain and is often associated with nausea and vomiting. In 1992, the Atlanta classification was developed by expert consensus to standardize terminology relating to acute pancreatitis. The 2012 update, or the revised Atlanta classification, is currently used for the diagnosis of acute pancreatitis, which includes 2 of 3 of the following features:

1. Abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back);
2. Serum lipase activity (or amylase activity) at least 3 times greater than the upper limit of normal;
3. Characteristic findings of acute pancreatitis on contrast-enhanced computed tomography or MRI [3].

Gallstones should be suspected as the cause of acute pancreatitis in the setting of a prior history of biliary colic or other gallstone-related complications or if there is a finding of gallstones or sludge on right upper-quadrant ultrasound. Elevated liver function tests in the setting of acute pancreatitis support gallstones as the cause, but normal liver function tests do not rule out gallstone pancreatitis because of the low sensitivity. Similarly, a dilated biliary tree on imaging supports the diagnosis of gallstone pancreatitis, but the absence does not rule it out.

STRATIFICATION AND PREDICTION OF SEVERITY OF ACUTE GALLSTONE PANCREATITIS

The revised Atlanta classification (Table 1) describes 2 types of acute pancreatitis (interstitial edematous pancreatitis and necrotizing pancreatitis) and 3 levels of severity (mild, moderate, and severe) [3]. Mortality increases with each severity class. In addition, 4 types of peripancreatic fluid collections are described (Fig. 1).

More recently, the American Association for the Surgery of Trauma (AAST) developed an alternative classification system for acute pancreatitis. This system is one of several developed for emergency general surgery (EGS)

Table 1
Revised Atlanta classification for severity of acute pancreatitis

	Mild	Moderate	Severe
Organ failure	No	Resolving <48 h (transient organ failure)	Persistent >48 h
Local or systemic complications	No	Without persistent organ failure	Single or multiple organ failure

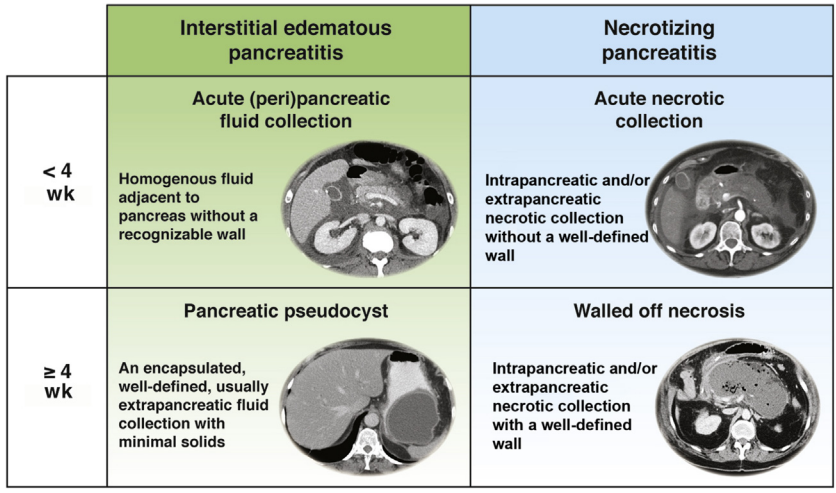

Fig. 1. Types of fluid collections associated with interstitial edematous pancreatitis and necrotizing pancreatitis based on the revised Atlanta criteria. (*From* Trikudanathan G, Wolbrink DRJ, van Santvoort HC, et al. Current concepts in severe acute and necrotizing pancreatitis: An evidence-based approach. *Gastroenterology.* 2019;156(7):1994-2007 e3; with permission.)

conditions; it uses clinical, imaging, operative, and pathologic criteria to grade acute pancreatitis (Table 2) [4]. In a single-center retrospective study, the accuracy of the AAST EGS grades for predicting mortality was noninferior to the revised Atlanta classification system [5]. Furthermore, increasing AAST EGS grades for acute pancreatitis correlated with hospital and intensive care unit length of stay and readmissions.

Because the management and outcomes vary with severity, multiple scoring systems and models have been developed to predict the severity of acute pancreatitis:

- Combination of clinical and laboratory parameters: Ranson criteria, modified Glasgow score, APACHE II, Bedside Index for Severity in Acute Pancreatitis (BISAP)
- Imaging-guided severity indices: Computed Tomography Severity Index, Balthazar score
- Single laboratory parameters: C-reactive protein, blood urea nitrogen (BUN), cortisol
- Cytokines and adipokines: interleukin-13/interferon-γ ratio [6], adiponectin, visfatin, resistin [7,8]
- Adhesion molecules: E and P selectins [9]

Most of the models are not specific to gallstone pancreatitis. In fact, very few studies have evaluated the prognostic ability of markers specifically in gallstone pancreatitis versus other types of acute pancreatitis. One study determined that neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio predict severity

Table 2
American Association for the Surgery of Trauma emergency general surgery grades for acute pancreatitis

AAST grade	Description	Clinical criteria	Imaging criteria (CT findings)	Operative criteria	Pathologic criteria
I	Acute edematous pancreatitis	Midepigastric abdominal pain and tenderness; elevated amylase or lipase	Pancreatitis without phlegmon, necrosis, peripancreatic fluid collection or abscess	Edematous pancreas	N/A
II	Pancreatic phlegmon or peripancreatic fluid collection or hemorrhage	Midepigastric abdominal pain and tenderness; elevated amylase or lipase	Phlegmon or peripancreatic fluid collection or hemorrhage	Pancreatic phlegmon or peripancreatic fluid collection	N/A
III	Sterile pancreatic necrosis	Midepigastric abdominal pain and tenderness; elevated amylase or lipase	Pancreatic necrosis without extraluminal air or abscess	Pancreatic necrosis without purulence or abscess	Gram stain and culture of necrosis negative for organisms
IV	Infected pancreatic necrosis or abscess	Severe midepigastric abdominal pain and tenderness; elevated amylase or lipase	Pancreatic necrosis with extraluminal air or abscess	Pancreatic necrosis with purulence or abscess	Gram stain and culture of necrosis or abscess positive for organisms
V	Extrapancreatic extension of pancreatic necrosis involving adjacent organs, such as colonic necrosis	Severe diffuse midepigastric abdominal pain and tenderness; elevated amylase or lipase	Extrapancreatic extension of necrosis involving adjacent organs, such as colonic necrosis	Involvement or necrosis of adjacent organs	Involvement or necrosis of resected adjacent organs

Data from Tominaga GT, Staudenmayer KL, Shafi S, et al. The American Association for the Surgery of Trauma grading scale for 16 emergency general surgery conditions: Disease-specific criteria characterizing anatomic severity grading. *J Trauma Acute Care Surg*. 2016;81(3):593-602.

for acute gallstone pancreatitis but not for acute alcoholic pancreatitis [10]. This marker, like many others, lacks widespread acceptance. Potential barriers to the uptake of novel biomarkers include lack of external validation, lack of evaluation in improving outcomes, low accuracy, need for laboratory resources, and costs [11]. Even the more widely used prognostic scores, such as Ranson and BISAP, have limited accuracy [12]. Ultimately, the test of any prognostic model or biomarker is whether changes in management based on predicted severity improve outcomes.

MEDICAL MANAGEMENT

The mainstays of medical management of acute pancreatitis, regardless of cause, remain fluid resuscitation, nutritional support, and analgesia.

Fluid resuscitation

Acute pancreatitis as a disease causes a massive inflammatory response leading to third spacing and hypovolemia. As a result, appropriate fluid resuscitation is a major cornerstone in the treatment of acute pancreatitis. Crystalloids are the recommended fluid choice [13,14], with lactated Ringers being preferred over normal saline. A recent systematic review and metaanalysis reported that lactated Ringers resulted in less persistent systemic inflammatory response syndrome (SIRS) at 24 hours than normal saline but that there was no mortality difference [15].

Guidelines and consensus statements differ in their recommended initial bolus and infusion rates of crystalloid resuscitation [13,14]. Proponents of early aggressive fluid resuscitation cite faster clinical improvement. In a randomized trial of aggressive (20 mL/kg bolus followed by 3 mL/kg/h) versus standard hydration (10 mL/kg bolus followed by 1.5 mg/kg/h) in the initial management of acute pancreatitis, an aggressive fluid strategy was associated with less SIRS and a higher rate of clinical improvement at 36 hours [16]. However, criticisms of this trial include the choice of indicators of clinical improvement (decreased hematocrit, BUN, and creatinine levels) and the lack of generalizability owing to a relatively young mean age (44 years) of the patients [17].

Opponents of an aggressive fluid strategy have focused on the harms of excessive fluid resuscitation. Observational studies have suggested that greater than 4 L of fluid within the first 24 hours in patients with acute pancreatitis is associated with new onset and persistent organ failure [18,19]. In addition, 2 randomized controlled trials (RCTs) reported that rapid fluid resuscitation was associated with increased mortality as well as increased need for mechanical ventilation, abdominal compartment syndrome (ACS), and sepsis [20,21].

Intraabdominal hypertension (IAH) and ACS are known complications of acute pancreatitis and are associated with worse outcomes [22]. The incidence ranges from 59% to 84% for IAH and 25% to 56% for ACS [22]. Although the pathophysiology may be related to the underlying inflammation, excessive amount or rate of fluid administration may also be contributory [21]. Nonoperative interventions for IAH and ACS include measures to increase abdominal

compliance (adequate analgesia, sedation, and mechanical ventilation), to decrease abdominal distention (nasogastric and colonic decompression, promotility agents), and to drain excessive fluid (percutaneous drain placement). Surgical intervention consists of decompressive laparotomy. However, it is unknown what the optimal treatment is for acute pancreatitis-related ACS. An RCT, the DECOMPRESS trial, aims to enroll 100 patients who will be randomized to decompressive laparotomy with temporary abdominal closure or percutaneous puncture with placement of an abdominal catheter [23].

Currently, guidelines conditionally recommend use of goal-directed fluid resuscitation in acute pancreatitis, although the body of evidence is limited [14,24]. The recommendation for goal-directed therapy in acute pancreatitis is conditional because of known concern for risk of development of ACS or respiratory complications with overly aggressive fluid resuscitation. However, the ideal target parameters have not been defined. For example, use of laboratory values, such as BUN, to guide resuscitation has not been shown to be effective [25]. Furthermore, there is very little evidence supporting goal-directed fluid resuscitation over any other method of resuscitation when examining reduction in multisystem organ failure or pancreatic necrosis. A randomized trial comparing a protocolized fluid resuscitation strategy using a noninvasive cardiac monitor versus standard care and that will measure clinical outcomes and resource utilization is currently underway [26].

Nutritional support

Early enteral feeding is generally recommended. The concept of bowel rest used to be universally accepted, with the justification that enteral feeding continued to stimulate the pancreas and worsen the disease process. A review of 11 RCTs for the American Gastroenterological Association (AGA) Institute Guideline comparing early to delayed feeding demonstrated significantly increased rates of peripancreatic necrosis, multiple organ failure, and necrotizing pancreatitis with delayed feeding [24,27]. In addition, Zhang and colleagues [28] reviewed 8 trials comparing early oral refeeding to traditional feeding strategies for mild acute pancreatitis and determined that there was no increase in symptoms of abdominal pain or nausea and vomiting and a reduced length of stay with oral refeeding. Another metaanalysis suggested that early enteral feeding is preferred over no diet for both mild to moderate and severe acute pancreatitis [29]. Thus, guidelines recommend early enteral feeding if feasible within the first 24 hours [13,24,30]. The difficulty comes when at times these patients are not tolerant of enteral feeding, in which case, it is recommended to place a nasogastric or nasoenteric feeding tube to begin feeding even if at a low volume amount [24,30].

Metaanalyses comparing nasogastric and nasojejunal feeds have primarily been conducted in severe acute pancreatitis [31,32]. Another network metaanalysis compared nasogastric feeds, nasojejunal feeds, and total parenteral nutrition (TPN) [33]. A network metaanalysis is a method by which multiple treatments can be compared using both direct and indirect comparisons across

RCTs using a common comparator. This analysis suggested that nasogastric feeds is the preferred route, and TPN is the least preferred route for preventing infectious complications [33].

Analgesia

Guidelines pertaining to management of pain in acute pancreatitis are limited, and most guidelines do not provide any specific recommendations [13,24]. A 2013 Cochrane Review of 5 RCTs comparing opioids with other analgesics suggested that there was no difference in the risk of pancreatitis complications or clinically serious adverse events with opioids [34]. A systematic review from the same year evaluated 8 RCTs comparing different analgesics for acute pancreatitis did not identify a preferred medication [35]. A recently published trial evaluated an enhanced recovery pathway in mild acute pancreatitis; the enhanced recovery group received nonopioid analgesia, patient-directed oral intake, and early ambulation versus opioid analgesia and physician-directed diet [36]. The enhanced recovery group had a shorter time to refeeding. Further outcomes were not assessed. Future trials should focus on other nonopioid regimens.

ENDOSCOPIC AND SURGICAL MANAGEMENT OF ACUTE GALLSTONE PANCREATITIS

Routine endoscopic retrograde cholangiopancreatography in gallstone pancreatitis

Current guidelines from the American Society for Gastrointestinal Endoscopy (ASGE) [37] and the AGA Institute [24] recommend against the routine use of endoscopic retrograde cholangiopancreatography (ERCP) in gallstone pancreatitis. This recommendation is based on older RCTs; no new RCTs have been conducted since the last 2012 Cochrane Review comparing early ERCP to conservative management for acute gallstone pancreatitis [38]. The Cochrane Review demonstrated no benefit to early ERCP in terms of mortality or local and systemic adverse events. Although initial RCTs suggested that early ERCP was beneficial in severe but not mild acute gallstone pancreatitis, the review failed to demonstrate a subgroup difference. Therefore, routine early ERCP is not recommended for gallstone pancreatitis. However, early ERCP within 48 hours is recommended for patients with cholangitis or biliary obstruction from choledocholithiasis [37].

Management of common bile duct stones in acute gallstone pancreatitis

In the absence of cholangitis, there are 4 strategies that are commonly used for the management of common bile duct (CBD) stones in patients with acute gallstone pancreatitis and normal anatomy:

1. Preoperative ERCP followed by laparoscopic cholecystectomy
2. Laparoscopic cholecystectomy with laparoscopic common bile duct exploration (LCBDE)
3. Laparoscopic cholecystectomy with intraoperative ERCP
4. Laparoscopic cholecystectomy with postoperative ERCP

Laparoscopic cholecystectomy with either LCBDE or intraoperative ERCP are referred to as 1-step approaches. With the latter approach, when CBD cannulation during ERCP is facilitated by placement of a guide wire through the cystic duct into the duodenum, this is also known as the rendezvous technique. The success of 1-step approaches depend on available laparoscopic and endoscopic expertise, ability to clear the duct intraoperatively, and need for a choledochotomy (which has a higher complication rate) during LCBDE. Limitations to widespread implementation of 1-step procedures include lack of appropriate expertise and issues related to operating room time and/or logistics [39].

The most recent 2019 ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis does not state that 1 approach should be used over another. Rather, the guideline states that preoperative or postoperative ERCP or laparoscopic treatment should be performed depending on local surgical and endoscopic expertise [37]. On the other hand, a 2019 systematic review and network metaanalysis of 20 trials comparing the 4 strategies for any gallstone-related indication recommended the rendezvous approach [40]. In this analysis, laparoscopic cholecystectomy with intraoperative ERCP was identified to have the highest probability of being successful, being safest, and reducing hospital length of stay. Laparoscopic cholecystectomy with LCBDE had the highest probability of decreasing overall bleeding, operative time, and costs. However, laparoscopic cholecystectomy with LCBDE had the highest risk of biliary leaks. Of note, there was significant heterogeneity related to the success rate for laparoscopic CBDE across trials, likely because of differences in the year of publication, the country in which the trial was conducted, and the characteristics of the patients enrolled. This heterogeneity suggests that local factors, such as available expertise and resources, may affect outcomes and that decisions should be context dependent.

ERCP in the setting of prior bariatric surgery is not specifically addressed by the ASGE guidelines on choledocholithiasis and has not been studied specifically with regards to acute gallstone pancreatitis. The difficulty arises in accessing the ampulla after a Roux-en-Y gastric bypass. There are multiple strategies that can be used, including but not limited to deep enteroscopy-assisted ERCP [41], spiral enteroscopy-ERCP [41], laparoscopy-assisted ERCP and EUS-directed transgastric ERCP [42], or gastric access temporary for endoscopy [43].

The role of endoscopic sphincterotomy in the management of acute gallstone pancreatitis

Guidelines recommend laparoscopic cholecystectomy during index admission for mild acute gallstone pancreatitis and delayed cholecystectomy for severe acute gallstone pancreatitis [14,44,45]. However, in patients who are considered to be high risk for complications during surgery, such as owing to comorbidities, endoscopic sphincterotomy has been proposed as definitive management. In addition, endoscopic sphincterotomy has been proposed as

a temporizing maneuver before interval cholecystectomy in patients with peripancreatic fluid collections. There are no randomized trials comparing endoscopic sphincterotomy alone to cholecystectomy as definitive therapy for prevention of recurrent pancreatitis. However, large observational studies may provide insights regarding the comparative effectiveness of these therapies. An analysis of adult hospitalizations for gallstone pancreatitis in the 2010 to 2014 National Readmissions Database found that cholecystectomy had the strongest protective effect against readmissions [46]. Among patients who did not receive a cholecystectomy, ERCP was associated with lower all-cause and pancreatitis-related readmissions, even in cases of severe pancreatitis. Based on best available evidence, cholecystectomy should be performed if possible, even if endoscopic sphincterotomy has been performed, to prevent future recurrences and readmissions. However, ERCP with endoscopic sphincterotomy may be a reasonable option in patients with prohibitive surgical risks.

Timing of cholecystectomy after mild acute gallstone pancreatitis

Early (<2 weeks from admission) or same-admission versus delayed (>2 weeks after discharge)

Multiple trials have been performed evaluating the optimal timing of laparoscopic cholecystectomy after gallstone pancreatitis. The rationale for performing early or same-admission cholecystectomy is for prevention of recurrent pancreatitis and gallstone-related complications. The rationale for delaying cholecystectomy is to allow inflammation to fully resolve to decrease the risk of operative complications and conversion to open. There have been several recent (2018–2019) systematic reviews and metaanalyses focused on early versus delayed cholecystectomy (Table 3); they all have different definitions for early cholecystectomy and include studies of differing methodologic quality [47–50]. Nonetheless, these metaanalyses all report similar conclusions: early cholecystectomy is associated with decreased length of stay, readmissions, and gallstone-related complications. They all report no significant difference in operative time or conversion to open.

Early (24–72 hours) versus control (clinical and laboratory normalization) during same admission

More recent studies have proposed even earlier cholecystectomy for mild gallstone pancreatitis. Several observational studies have suggested that early cholecystectomy during index admission for mild gallstone pancreatitis, defined as within 48 to 72 hours regardless of resolution of clinical symptoms and laboratory values, is safe and shortens hospital stay [51–54]. In addition, there have been 3 RCTs comparing early versus later same-admission or control cholecystectomy (after clinical resolution and with downtrending laboratory values) for patients with mild gallstone pancreatitis.

1. Aboulian and colleagues [55] randomized 50 out of a planned 100 patients with mild gallstone pancreatitis to early (within 48 hours of admission) versus control laparoscopic cholecystectomy. They demonstrated a shorter length of stay with

Table 3
Systematic reviews and metaanalyses of early versus delayed cholecystectomy (2018 and 2019)

Authors, year	Number of studies	Number of patients	Early	Late	Outcomes
Yang et al [48], 2018	3 RCTs 10 retrospective	2291	Within 14 d after admission	Not defined	Total complications (odds ratio [OR] 0.45, 0.33–0.61) Readmissions (OR 0.11, 0.07–0.19) Conversion to open (OR 1.26, 0.88–1.78) Length of stay (−2.46, −3.47–1.44)
Lyu et al [47], 2018	15 RCTs	1669	Within 7 d of presentation	6 wk after conservative treatment	Bile duct injury (risk ratio [RR] 0.79, 0.23–2.79) Total complications (RR 0.90, 0.58–1.39) Conversion to open (RR 0.94, 0.74–1.21) Operation time (9.29 min, −0.41–18.98) Length of stay (−3.07 d, −3.98–2.16)
Lyu et al [50], 2018	4 RCTs 7 retrospective	1833	During index admission	Not defined	Biliary-related complications (RR 0.128, 0.42–3.86) Postoperative complications (RR 1.06, 0.067–1.69) Conversion to open (RR 1.24, 0.78–1.97) Length of stay (−2.08, −3.17–−0.99)

Zhong et al [49], 2019	5 RCTs 14 retrospective	2639	Within 2 wk after admission	Not defined	Intraoperative complications (RR 1.46, 0.88–2.41) Postoperative complications (RR 0.81, 0.58–1.14) Conversion to open (RR 1.00, 0.75–1.33) Operative time (1.60, 1.36–4.56) Length of stay (−2.01 d, −3.15–−0.87) Gallstone-related events (0.17, 0.07–0.44) Lower ERCP usage (0.83, 0.71–0.97)
Moody et al [62], 2019	5 RCTs	629	During index admission	At least 2 wk after discharge	Biliary complications requiring readmission (RR 0.17, 0.09–0.33) Intraoperative complications (OR 0.58, 0.17–1.92) Postoperative complications (0.78, 0.38–1.62) Conversion to open (OR 1.47, 0.63–3.42)

Data from Refs. [47–50,62].

early cholecystectomy without an increase in conversion or postoperative complication rates. However, this trial was stopped early and was underpowered to detect a significant difference in adverse outcomes.

2. Mueck and colleagues [56] randomized 97 patients without a strong suspicion for CBD stones to early (within 12–24 hours) versus control laparoscopic cholecystectomy with intraoperative cholangiogram. They reported a faster time to surgery, shorter 30-day length of stay (to include readmissions), and fewer ERCPs in the early group. Complication rates were not statistically different (6% vs 2%, $P = .61$). However, on Bayesian analysis, there was a 72% probability of increased complications, albeit largely minor. In addition, they noted limited ability to accurately predict the severity of acute pancreatitis using the BISAP score.
3. Riquelme and colleagues [57] randomized 52 out of a planned 100 patients regardless of CBD stone risk to early (within 72 hours from admission) versus delayed laparoscopic cholecystectomy. Early cholecystectomy was associated with decreased length of stay. There were no differences in ERCP or in postoperative complications. The study was terminated at interim analysis secondary to having met their predefined stopping point with regards to a difference in length of stay.

Given the current evidence, there appear to be patients with mild acute pancreatitis in whom early laparoscopic cholecystectomy, even within 24 hours, can be done safely. However, widespread adoption is not recommended at this time given limitations in current predictive models and insufficient power to determine if there is an increase in complications. All 3 RCTs used different scoring systems to predict severity of pancreatitis: Ranson criteria, BISAP, and revised Atlanta classification with SIRS. Failure to identify correctly severe pancreatitis could lead to a higher rate of complications and conversion to open.

Management of necrotizing gallstone pancreatitis

The AGA recently published a Clinical Practice Update reviewing the best available evidence on pancreatic necrosis, regardless of cause [30]. The update provides 15 best practice advice points that include the need for multidisciplinary care coordination and referral to a tertiary-care center as appropriate. The update describes supportive care, avoidance of prophylactic antibiotics, and optimization of nutrition. In addition, there is an included algorithm for the management of pancreatic necrosis requiring debridement (Fig. 2). Debridement within the early acute phase of pancreatitis (within the first 2–4 weeks) should be avoided if possible secondary to increased morbidity and mortality. Intervention in the late phase ($\geq$2–4 weeks) is indicated for patients with infected necrosis or persistent organ dysfunction and failure to thrive. Multiple approaches are available for the management of infected necrosis, including but not limited to percutaneous, endoscopic, or laparoscopic transgastric, or open debridement. In addition, a combination approach using percutaneous drainage followed by videoscopic retroperitoneal debridement or step-up approach can also be used.

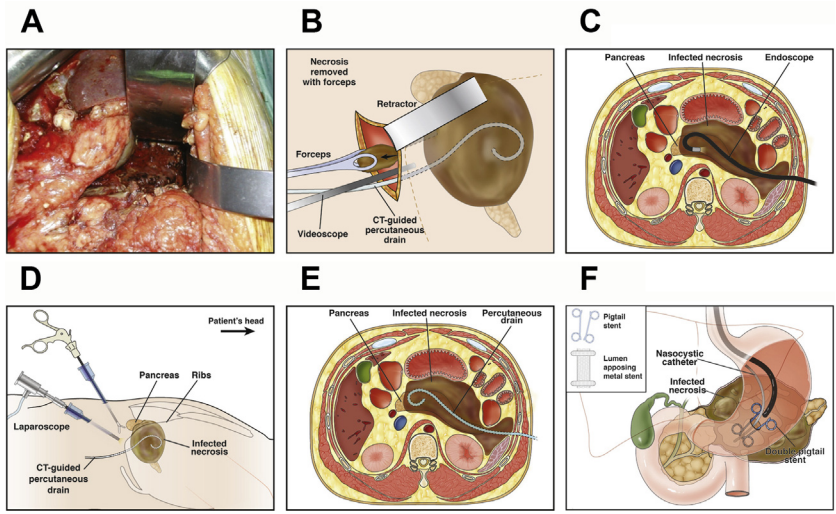

Fig. 2. Interventions for necrotizing pancreatitis. (*A*) Open surgical necrosectomy. (*B*) VARD. (*C*) Sinus tract endoscopy. (*D*) Laparoscopic necrosectomy. (*E*) Percutaneous catheter drainage. (*F*) Endoscopic transluminal necrosectomy. CT, computed tomography. (*From* Trikudanathan G, Wolbrink DRJ, van Santvoort HC, et al. Current concepts in severe acute and necrotizing pancreatitis: An evidence-based approach. *Gastroenterology.* 2019;156(7):1994-2007 e3; with permission.)

Since the publication of a multicenter RCT (PANTER) in 2010, the step-up approach for necrotizing pancreatitis has been increasingly used. The step-up approach or video-assisted retroperitoneal debridement (VARD) is a minimally invasive technique that begins with percutaneous drain placement for necrotizing pancreatitis followed by a minimally invasive retroperitoneal necrosectomy. Patients who underwent the step-up approach versus open necrosectomy had less multiple-organ failure, incisional hernias, and new-onset diabetes, but no difference in mortality [58]. The 2020 AGA Clinical Practice Update on the management of pancreatic necrosis suggests that best practice is that "minimally invasive operative approaches to the debridement of acute necrotizing pancreatitis are preferred to open surgical necrosectomy when possible, given lower morbidity" [30]. However, the update also notes that open necrosectomy still has a role in the modern management of acute necrotizing pancreatitis, particularly for cases whereby less invasive techniques are not feasible.

Future advances

Many advances have been made in the management of acute gallstone pancreatitis, and as a result, mortality has decreased over time [2]. Currently, the mainstays of management are supportive, such as fluid and nutritional optimization. However, a better understanding of the pathogenesis of acute

pancreatitis, such as from animal models, is needed in order to develop novel therapeutic strategies [59]. Challenges also remain regarding the accurate and early prediction of severity in order to optimize treatment. Future predictive strategies may incorporate machine learning [60], proteomic or genomic patterns [61], or other biomarkers in order to deliver individualized prognoses for the severity of acute pancreatitis. In addition, less invasive strategies continue to evolve in the management of complicated gallstone pancreatitis, such as due to persistent choledocholithiasis in the setting of prior bariatric surgery or due to development of peripancreatic fluid collections. Although available large databases allow evaluation of the comparative effectiveness of novel management strategies, multicenter, pragmatic trials are still needed to inform patient-centered care of patients with acute gallstone pancreatitis.

Disclosure

The authors have nothing to disclose.

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