

ACG Clinical Guideline: Management of Acute Pancreatitis

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Abstract

This guideline presents recommendations for the management of patients with acute pancreatitis (AP). During the past decade, there have been new understandings and developments in the diagnosis, etiology, and early and late management of the disease. As the diagnosis of AP is most often established by clinical symptoms and laboratory testing, contrast-enhanced computed tomography (CECT) and/or magnetic resonance imaging (MRI) of the pancreas should be reserved for patients in whom the diagnosis is unclear or who fail to improve clinically. Hemodynamic status should be assessed immediately upon presentation and resuscitative measures begun as needed. Patients with organ failure and/or the systemic inflammatory response syndrome (SIRS) should be admitted to an intensive care unit or intermediary care setting whenever possible. Aggressive hydration should be provided to all patients, unless cardiovascular and/or renal comorbidities preclude it. Early aggressive intravenous hydration is most beneficial within the first 12–24 h, and may have little benefit beyond. Patients with AP and concurrent acute cholangitis should undergo endoscopic retrograde cholangiopancreatography (ERCP) within 24 h of admission. Pancreatic duct stents and/or postprocedure rectal nonsteroidal anti-inflammatory drug (NSAID) suppositories should be utilized to lower the risk of severe post-ERCP pancreatitis in high-risk patients. Routine use of prophylactic antibiotics in patients with severe AP and/or sterile necrosis is not recommended. In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis may be useful in delaying intervention, thus decreasing morbidity and mortality. In mild AP, oral feedings can be started immediately if there is no nausea and vomiting. In severe AP, enteral nutrition is recommended to prevent infectious complications, whereas parenteral nutrition should be avoided. Asymptomatic pancreatic and/or extrapancreatic necrosis and/or pseudocysts do not warrant intervention regardless of size, location, and/or extension. In stable patients with infected necrosis, surgical, radiologic, and/or endoscopic drainage should be delayed, preferably for 4 weeks, to allow the development of a wall around the necrosis.

Introduction

Acute pancreatitis (AP) is one of the most common diseases of the gastrointestinal tract, leading to tremendous emotional, physical, and financial human burden (1,2). In the United States, in 2009, AP was the most common gastroenterology discharge diagnosis with a cost of 2.6 billion dollars (2). Recent studies show the incidence of AP varies between 4.9 and 73.4 cases per 100,000 worldwide (3,4). An increase in the annual incidence for AP has been observed in most recent studies. Epidemiologic review data from the 1988 to 2003 National Hospital Discharge Survey showed that hospital admissions for AP increased from 40 per 100,000 in 1998 to 70 per 100,000 in 2002. Although the case fatality rate for AP has decreased over time, the overall population mortality rate for AP has remained unchanged (1).

There have been important changes in the definitions and classification of AP since the Atlanta classification from 1992 (5). During the past decade, several limitations have been recognized that led to a working group and web-based consensus revision (6). Two distinct phases of AP have now been identified: (i) early (within 1 week), characterized by the systemic inflammatory response syndrome (SIRS) and/or organ failure; and (ii) late (>1 week), characterized by local complications. It is critical to recognize the paramount importance of organ failure in determining disease severity. Local complications are defined as peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocysts, and walled-off necrosis (sterile or infected). Isolated extrapancreatic necrosis is also included under the term necrotizing pancreatitis; although outcomes like persistent organ failure, infected necrosis, and mortality of this entity are more often seen when compared to interstitial pancreatitis, these complications are more commonly seen in patients with pancreatic parenchymal necrosis (7). There is now a third intermediate grade of severity, moderately severe AP, that is characterized by local complications in the absence of persistent organ failure. Patients with moderately severe AP may have transient organ failure, lasting <48 h. Moderately severe AP may also exacerbate underlying comorbid disease but is associated with a low mortality. Severe AP is now defined entirely on the presence of persistent organ failure (defined by a modified Marshall Score) (8).

We first discuss the diagnosis, etiology, and severity of AP. We then focus on the early medical management of AP followed by a discussion of the management of complicated disease, most notably pancreatic necrosis. Early management focuses on advancements in our understanding of aggressive intravenous hydration, which when applied early appears to decrease morbidity and mortality (9,10). The evolving issues of antibiotics, nutrition, and endoscopic, radiologic, surgical, and other minimally invasive interventions will be addressed.

A search of MEDLINE via the OVID interface using the MeSH term “acute pancreatitis” limited to clinical trials, reviews, guidelines, and meta-analysis for the years 1966–2012 was undertaken without language restriction, as well as a review of clinical trials and reviews known to the authors were performed for the preparation of this document. The GRADE system was used to grade the strength of recommendations and the quality of evidence (11). An explanation of the quality of evidence and strength of the recommendations is shown in Table 1. Each section of the document presents the key recommendations related to the section topic, followed by a summary of the supporting evidence. A summary of recommendations is provided in Table 2.

Table 1. GRADE system of quality of evidence and strength of recommendation	
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of the effect is very uncertain.

Table 2. Summary of recommendations	
Diagnosis	
1.	The diagnosis of AP is most often established by the presence of two of the three following criteria: (i) abdominal pain consistent with the disease, (ii) serum amylase and/or lipase greater than three times the upper limit of normal, and/or (iii) characteristic findings from abdominal imaging (strong recommendation, moderate quality of evidence).
2.	Contrast-enhanced computed tomographic (CECT) and/or magnetic resonance imaging (MRI) of the pancreas should be reserved for patients in whom the diagnosis is unclear or who fail to improve clinically within the first 48–72 h after hospital admission (strong recommendation, low quality of evidence).
Etiology	
3.	Transabdominal ultrasound should be performed in all patients with acute pancreatitis (strong recommendation, low quality of evidence).
4.	In the absence of gallstones and/or history of significant history of alcohol use, a serum triglyceride should be obtained and considered the etiology if >1,000 mg/dl (conditional recommendation, moderate quality of evidence).
5.	In a patient older than 40 years, a pancreatic tumor should be considered as a possible cause of acute pancreatitis (conditional recommendation, low quality of evidence).
6.	Endoscopic investigation in patients with acute idiopathic pancreatitis should be limited, as the risks and benefits of investigation in these patients are unclear (conditional recommendation, low quality of evidence).
7.	Patients with idiopathic pancreatitis should be referred to centers of expertise (conditional recommendation, low quality of evidence).
8.	Genetic testing may be considered in young patients (<30 years old) if no cause is evident and a family history of pancreatic disease is present (conditional recommendation, low quality of evidence).
Initial assessment and risk stratification	
9.	Hemodynamic status should be assessed immediately upon presentation and resuscitative measures begun as needed (strong recommendation, moderate quality of evidence).
10.	Risk assessment should be performed to stratify patients into higher- and lower-risk categories to assist triage, such as admission to an intensive care setting (conditional recommendation, moderate quality of evidence).
11.	Patients with organ failure should be admitted to an intensive care unit or intermediary care setting whenever possible (strong recommendation, low quality of evidence).

Table 2. Summary of recommendations <i>continued</i>	
Initial management	
12.	Aggressive hydration, defined as 250-500 ml per hour of isotonic crystalloid solution should be provided to all patients, unless cardiovascular and/or renal comorbidities exist. Early aggressive intravenous hydration is most beneficial the first 12–24 h, and may have little benefit beyond (strong recommendation, moderate quality of evidence).
13.	In a patient with severe volume depletion, manifest as hypotension and tachycardia, more rapid repletion (bolus) may be needed (conditional recommendation, moderate quality of evidence).
14.	Lactated Ringer’s solution may be the preferred isotonic crystalloid replacement fluid (conditional recommendation, moderate quality of evidence).
15.	Fluid requirements should be reassessed at frequent intervals within 6 h of admission and for the next 24–48 h. The goal of aggressive hydration should be to decrease the blood urea nitrogen (strong recommendation, moderate quality of evidence).
ERCP in acute pancreatitis	
16.	Patients with acute pancreatitis and concurrent acute cholangitis should undergo ERCP within 24 h of admission (strong recommendation, moderate quality of evidence).
17.	ERCP is not needed in most patients with gallstone pancreatitis who lack laboratory or clinical evidence of ongoing biliary obstruction (strong recommendation, low quality of evidence).
18.	In the absence of cholangitis and/or jaundice, MRCP or endoscopic ultrasound (EUS) rather than diagnostic ERCP should be used to screen for choledocholithiasis if highly suspected (conditional recommendation, low quality of evidence).
19.	Pancreatic duct stents and/or postprocedure rectal nonsteroidal anti-inflammatory drug (NSAID) suppositories should be utilized to prevent severe post-ERCP pancreatitis in high-risk patients (conditional recommendation, moderate quality of evidence).
The role of antibiotics in acute pancreatitis	
20.	Antibiotics should be given for an extrapancreatic infection, such as cholangitis, catheter-acquired infections, bacteremia, urinary tract infections, pneumonia (strong recommendation, high quality of evidence).
21.	Routine use of prophylactic antibiotics in patients with severe acute pancreatitis is not recommended (strong recommendation, moderate quality of evidence).
22.	The use of antibiotics in patients with sterile necrosis to prevent the development of infected necrosis is not recommended (strong recommendation, moderate quality of evidence).
23.	Infected necrosis should be considered in patients with pancreatic or extrapancreatic necrosis who deteriorate or fail to improve after 7–10 days of hospitalization. In these patients, either (i) initial CT-guided fine needle aspiration (FNA) for Gram stain and culture to guide use of appropriate antibiotics or (ii) empiric use of antibiotics without CT FNA should be given (strong recommendation, low quality of evidence).
24.	In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis, such as carbapenems, quinolones, and metronidazole, may be useful in delaying or sometimes totally avoiding intervention, thus decreasing morbidity and mortality (conditional recommendation, low quality of evidence).

Table 2. Summary of recommendations <i>continued</i>	
25.	Routine administration of antifungal agents along with prophylactic or therapeutic antibiotics is not recommended (conditional recommendation, low quality of evidence).
Nutrition in acute pancreatitis	
26.	In mild AP, oral feedings can be started immediately if there is no nausea and vomiting, and abdominal pain has resolved (conditional recommendation, moderate quality of evidence).
27.	In mild AP, initiation of feeding with a low-fat solid diet appears as safe as a clear liquid diet (conditional recommendations, moderate quality of evidence).
28.	In severe AP, enteral nutrition is recommended to prevent infectious complications. Parenteral nutrition should be avoided unless the enteral route is not available, not tolerated, or not meeting caloric requirements (strong recommendation, high quality of evidence).
29.	Nasogastric delivery and nasojejunal delivery of enteral feeding appear comparable in efficacy and safety (strong recommendation, moderate quality of evidence).
The role of surgery in acute pancreatitis	
30.	In patients with mild AP, found to have gallstones in the gallbladder, a cholecystectomy should be performed before discharge to prevent a recurrence of AP (strong recommendation, moderate quality of evidence).
31.	In a patient with necrotizing biliary AP, in order to prevent infection, cholecystectomy is to be deferred until active inflammation subsides and fluid collections resolve or stabilize (strong recommendation, moderate quality of evidence).
32.	The presence of asymptomatic pseudocysts and pancreatic and/or extrapancreatic necrosis do not warrant intervention, regardless of size, location, and/or extension (strong recommendation, moderate quality of evidence).
33.	In stable patients with infected necrosis, surgical, radiologic, and/or endoscopic drainage should be delayed preferably for more than 4 weeks to allow liquefaction of the contents and the development of a fibrous wall around the necrosis (walled-off necrosis) (strong recommendation, low quality of evidence).
34.	In symptomatic patients with infected necrosis, minimally invasive methods of necrosectomy are preferred to open necrosectomy (strong recommendation, low quality of evidence).
AP, acute pancreatitis; CT, computed tomography; ERCP, endoscopic retrograde cholangiopancreatography; MRCP, magnetic resonance cholangiopancreatography.	

Table 3. Definitions of severity in acute pancreatitis: comparison of Atlanta and recent revision	
Atlanta criteria (1993)	Atlanta Revision (2013)
Mild acute pancreatitis	Mild acute pancreatitis
Absence of organ failure	Absence of organ failure
Absence of local complications	Absence of local complications
Severe acute pancreatitis	Moderately severe acute pancreatitis
1. Local complications AND/OR	1. Local complications AND/OR
2. Organ failure	2. Transient organ failure (< 48 h)
GI bleeding (> 500 cc/24 hr)	Severe acute pancreatitis
Shock – SBP ≤ 90 mm Hg	Persistent organ failure > 48 h ^a
PaO ₂ ≤ 60%	
Creatinine ≥ 2 mg/dl	
GI, gastrointestinal; SBP, systolic blood pressure.	
^a Persistent organ failure is now defined by a Modified Marshal Score (6,8)	

Table 4. Clinical findings associated with a severe course for initial risk assessment ^a
<i>Patient characteristics</i>
Age >55 years (53,57)
Obesity (BMI >30 kg/m ²) (68)
Altered mental status (69)
Comorbid disease (53)
<i>The systemic inflammatory response syndrome (SIRS) (6,53,54,70,71) Presence of >2 of the following criteria:</i>
– pulse >90 beats/min
– respirations >20/min or PaCO ₂ >32 mm Hg
– temperature >38 °C or <36 °C
– WBC count >12,000 or <4,000 cells/mm ³ or >10% immature neutrophils (bands)
<i>Laboratory findings</i>
BUN >20 mg/dl (63)
Rising BUN (63)
HCT >44% (62)
Rising HCT (62)
Elevated creatinine (72)
<i>Radiology findings</i>
Pleural effusions (73)
Pulmonary infiltrates (53)
Multiple or extensive extrapancreatic collections (67)
BMI, body mass index; BUN, blood urea nitrogen; HCT, hematocrit; WBC, white blood cell.
^a The presence of organ failure and/or pancreatic necrosis defines severe acute pancreatitis.

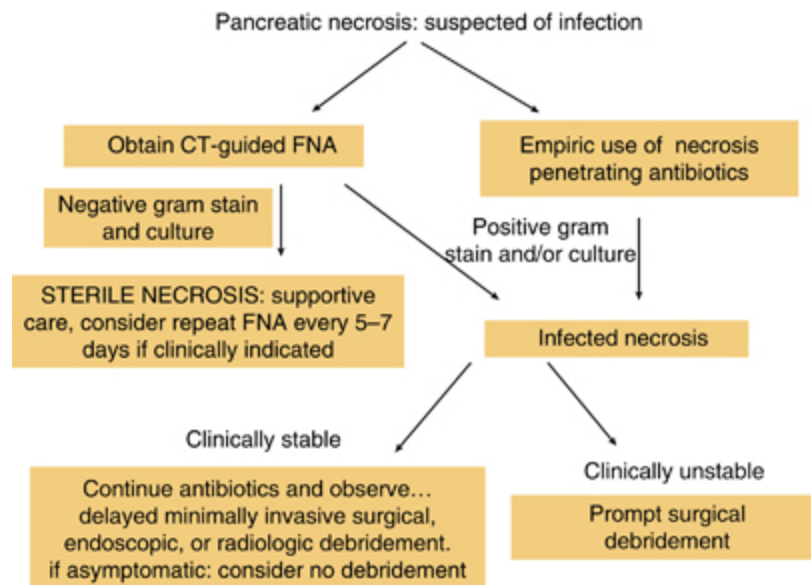


Figure 1. Management of pancreatic necrosis when infection is suspected. Infected necrosis should be considered in patients with pancreatic or extrapancreatic necrosis who deteriorate or fail to improve after 7–10 days of hospitalization. In these patients, either (i) initial computed tomography-guided fine needle aspiration (CT FNA) for Gram stain and culture to guide use of appropriate antibiotics or (ii) empiric use of antibiotics without CT FNA should be given. In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis may be useful in delaying intervention, thus decreasing morbidity and mortality. In stable patients with infected necrosis, surgical, radiologic, and/or endoscopic drainage should be delayed by preferably 4 weeks to allow the development of a wall around the necrosis (walled-off pancreatic necrosis).