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American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis

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This document presents the official recommendations of the American Gastroenterological Association (AGA) on the initial management of acute pancreatitis (AP). The guideline was developed by the AGA's Clinical Practice Guideline Committee and approved by the AGA Governing Board. It is accompanied by a technical review that is a compilation of the clinical evidence from which these recommendations were formulated.[1]

AP is an inflammatory condition of the pancreas that can cause local injury, systemic inflammatory response syndrome, and organ failure. Worldwide, AP is a common gastrointestinal condition that is associated with substantial suffering, morbidity, and cost to the health care system. In the United States, AP is a leading cause of inpatient care among gastrointestinal conditions: >275,000 patients are hospitalized for AP annually, at an aggregate cost of >$2.6 billion per year.[2] The incidence of AP ranges from 5 to 30 cases per 100,000, and there is evidence that the incidence has been rising in recent years.[3–5] The overall case fatality rate for AP is roughly 5%, and is expectedly higher for more severe disease.[6] Patients with AP frequently experience abdominal pain, nausea, and vomiting, and the condition negatively impacts quality of life.[7] The most common causes of AP remain gallstones and alcohol, which together comprise 80% of cases; the remainder of cases are due to less common causes, including drug reactions, pancreatic solid and cystic malignancies, and hypertriglyceridemia.[8]

The diagnosis of AP requires at least 2 of the following features: characteristic abdominal pain; biochemical evidence of pancreatitis (ie, amylase or lipase elevated >3 times the upper limit of normal); and/or radiographic evidence of pancreatitis on cross-sectional imaging.[9] Presentations of AP occur along a clinical spectrum, and can be categorized as mild, moderately severe, or severe, based on the recent revised Atlanta classification.[9] Most cases of AP (around 80%)[10] are mild, with only interstitial changes of the pancreas without local or systemic complications. Moderately severe pancreatitis is characterized by transient local or systemic complications or transient organ failure (<48 hours), and severe AP is associated with persistent organ failure.[9] Necrotizing pancreatitis is characterized by the presence of pancreatic and/or peripancreatic necrosis, and is typically seen in patients with moderately severe or severe AP. Severity of disease factors into several of the recommendations in this guideline. There are 2 overlapping phases of AP, early and late. The early phase of AP takes place in the first 2 weeks after disease onset, and the late phase can last weeks to months thereafter.[9]

In this guideline, we address the initial management of AP within the first 48−72 hours of admission. We focus on the initial management of AP, as this is the period when management decisions can alter the course of disease and duration of hospitalization. The management of AP has evolved slowly during the preceding 100 years. However, emerging evidence challenges many of the long-held management paradigms in AP regarding the benefit of antibiotics, the timing and mode of nutritional support, and the utility and timing of endoscopic retrograde cholangiopancreatography (ERCP) and cholecystectomy. Therefore, we sought to evaluate the sum of the evidence for these and other important questions regarding the management of AP.

Because of the focus on initial treatment of AP, certain questions pertaining to late complications of AP (eg, management of pancreatic fluid collections) are beyond the scope of this guideline. Additionally, because this guideline focuses on the management of AP, we will not address diagnostic questions, such as the use of laboratory tests or radiographic studies to establish the diagnosis of AP.

The guideline was developed utilizing a process outlined elsewhere.[11] Briefly, the AGA process for developing clinical practice guidelines incorporates Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology[12] and best practices as outlined by the Institute of Medicine.[13] GRADE methodology was utilized to prepare the background information for the guideline and the technical review that accompanies it.[1] Optimal understanding of this guideline will be enhanced by reading applicable portions of the technical review. The guideline

Abbreviations used in this paper: AGA, American Gastroenterological Association; AP, acute pancreatitis; CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HES, hydroxyethyl starch; OR, odds ratio; RCT, randomized controlled trial.

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Table 1. Quality of Evidence Categories

Quality of evidence	Interpretation
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

panel and the authors of the technical review met face to face on July 18, 2017, to discuss the findings from the technical review. The guideline authors subsequently formulated the recommendations. Although the quality of the evidence (Table 1) was a key factor in determining the strength of the recommendations (Table 2), the panel also considered the balance between benefit and harm of interventions, patients' values and preferences, and resource utilization. The recommendations are summarized in Table 3.

Recommendation 1A. In patients with AP, the AGA suggests using goal-directed therapy for fluid management. *Conditional recommendation, very low quality evidence.*
Comment: The AGA makes no recommendation whether normal saline or Ringer's lactate is used.

Fluid therapy to prevent hypovolemia and organ hypoperfusion is a long-established cornerstone of the initial management of AP. However, the evidence basis for fluid therapy in AP is relatively weak. In the technical review, a total of 7 randomized trials were identified pertaining to fluid resuscitation, with 4 primarily addressing the role of goal-directed targeted therapy.[1] Goal-directed therapy is generally defined as the titration of intravenous fluids to specific clinical and biochemical targets of perfusion (eg, heart rate, mean arterial pressure, central venous pressure, urine output, blood urea nitrogen concentration, and hematocrit). Use of goal-directed therapy has been shown to lower mortality in sepsis,[14] a condition with physiologic similarities to AP. Compared to non-targeted therapy, goal-directed therapy did not result in significantly improved mortality, prevention of pancreatic necrosis, or decrease in the rate of persistent multiple organ failure. In this context, though there was not clear randomized controlled trial (RCT)–level evidence of benefit, the panel issued a conditional recommendation suggesting the use of judicious goal-directed fluid therapy vs other methods. However, the panel recognized that overly aggressive fluid therapy can be associated with harms in AP, including respiratory complications and abdominal compartment syndrome.[15,16] The overall quality of the evidence was very low due to the inconsistency among reported outcome measures (especially the lack of differentiation between transient and persistent organ failure), the small number of RCTs, outcome assessment (detection bias), and lack of blinding (performance bias). The lack of RCT evidence addressing the optimal initial rate, volume, and duration of fluid resuscitation in AP rendered the panel unable to make specific recommendations in this regard.

Regarding the use of Ringer's lactate vs normal saline as the optimal fluid solution for resuscitation, the panel could not make a recommendation based on the low quality of evidence. The 2 RCTs specifically addressing this topic used surrogate markers of severity and did not focus on

Table 2. Interpretation of Strength of Recommendation Categories

Strength of recommendation	Wording in the guideline	For the patient	For the clinician
Strong	"The AGA recommends…"	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	Most individuals should receive the recommended course of action. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.
Conditional	"The AGA suggests…"	The majority of individuals in this situation would want the suggested course of action, but many would not.	Different choices will be appropriate for different patients. Decision aids may be useful in helping individuals in making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision.
No recommendation	"The AGA makes no recommendation…"		The confidence in the effect estimate is so low that any recommendation is speculative at this time

AGA SECTION