

ORIGINAL RESEARCH

Evidenced-based clinical standard for the diagnosis and treatment of acute pancreatitis in adults

Estándar clínico basado en la evidencia para el diagnóstico y tratamiento de adultos con pancreatitis aguda

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Abstract

Introduction: Acute pancreatitis (AP) is one of the most common gastrointestinal diseases requiring admission to hospital and its incidence is increasing worldwide. Approximately 20% of patients develop severe AP, which is associated with risk of complications, prolonged hospitalization times, and high mortality rates.

Objective: To identify the clinical indications for the diagnosis and treatment of AP in adults by developing an evidence-based clinical standard (EBCS) in a national referral university hospital of Bogotá, Colombia.

Materials and methods: Upon formation of a development group and defining the scope and objectives of the EBCS, systematic searches were conducted between April and June 2021 in MEDLINE, EMBASE and LILACS, as well as in clinical practice guideline (CPG) developers and compilers to identify CPGs published in the last 10 years that matched the objectives and scope of this EBCS. The quality of the selected CPGs was assessed using the AGREE II instrument. Based on the selected CPGs, a preliminary EBCS (clinical algorithm and recommendations) was proposed and then validated by means of an interdisciplinary consensus (modified Delphi methodology).

Results: Five CPGs were selected. A clinical algorithm with 6 sections was defined after all members of the interdisciplinary consensus reached complete agreement: "AP diagnosis", "initial treatment and classification of AP severity", "nutritional management of patients with AP", "classification of AP etiology", "treatment of AP of biliary origin", and "management of complications associated with AP treatment". Moreover, key aspects were established for the implementation of the algorithm and the clinical recommendations, as well as for the evaluation and follow-up of their implementation, referred to as checkpoints (section 7).

Conclusion: The evidence-based clinical recommendations included in this EBCS are intended to standardize practices and actions related to the diagnosis and treatment of AP in adults in Colombia, and even in the region.

Resumen

Introducción. La pancreatitis aguda (PA) es una de las causas gastrointestinales más comunes de hospitalización y su incidencia está aumentando a nivel mundial. Aproximadamente 20% de los pacientes desarrollan PA grave, la cual se asocia con riesgo de complicaciones, tiempos prolongados de hospitalización y altas tasas de mortalidad.

Objetivo. Identificar las indicaciones clínicas para el diagnóstico y tratamiento de la PA en adultos mediante el desarrollo de un estándar clínico basado en la evidencia (ECBE) en un hospital universitario de referencia nacional de Bogotá, Colombia. Materiales y métodos. Una vez conformado el grupo desarrollador y definidos el alcance y los objetivos del ECBE, entre abril y junio de 2021 se realizaron búsquedas sistemáticas en MEDLINE, EMBASE y LILACS y en organismos desarrolladores y compiladores de guías de práctica clínica (GPC) para identificar GPC publicadas en los últimos 10 años que respondieran a dichos objetivos y alcance. La calidad de las GPC seleccionadas fue evaluada con el instrumento AGREE II. Con base en las GPC seleccionadas se desarrolló una propuesta preliminar de EBCE (algoritmo clínico y recomendaciones) que fue validada mediante un consenso interdisciplinario (metodología Delphi modificada).

Resultados: Se seleccionaron 5 GPC. Luego de lograr un acuerdo total en el consenso interdisciplinario se consolidó un algoritmo clínico de 6 secciones: "diagnóstico de PA", "tratamiento inicial y clasificación de la severidad de la PA", "manejo nutricional del paciente con PA", "clasificación de la etiología de la PA", "tratamiento de la PA de origen biliar" y "manejo de complicaciones asociadas al tratamiento de la PA" y Además, se definieron aspectos claves para la implementación del algoritmo y las recomendaciones clínicas y para la evaluación y seguimiento de su implementación, denominados como puntos de control (sección 7).

Conclusión. Las recomendaciones clínicas basadas en la evidencia incluidas en este ECBE contribuyen a estandarizar las prácticas y acciones relacionadas con el diagnóstico y tratamiento de la PA en adultos en Colombia e incluso la región.



Introduction

Worldwide, acute pancreatitis (AP) is one of the most common gastrointestinal diseases requiring hospitalization. ¹⁻³ It is characterized by sudden inflammation of the pancreas, which can occur due to various causes. ⁴ In addition to pancreas involvement, an activation of inflammatory and anti-inflammatory responses may occur in these patients, resulting in the development of systemic manifestations such as multiple organ dysfunction syndrome (MODS), a life-threatening condition. ⁵

Regarding its epidemiology, although an annual incidence of 34 cases per 100 000 people per year has been reported in high-income countries, systematic reviews such as the one carried out by Petrov *et al.* note that the incidence of AP varies worldwide, with North America and the Western Pacific regions being areas of high incidence (>34 cases per 100 000 people per year), while Europe is a region of low incidence (29 cases per 100 000 people per year). However, in the case of Europe, it has been suggested that incidence may vary across the continent, with a greater impact in Eastern and Northern Europe. Furthermore, it has been reported that the incidence of AP has been increasing in recent years. While the actual cause of this increase is unknown, the reason may be related to the increase in associated obesity rates and gallstones.

In terms of disease burden, the United States has seen a 30% increase in the number of admissions to hospital due to AP in the last decade, with an annual health care cost of 2.6 billion dollars. In the same vein, in a recent analysis, Peery *et al.* found that there were 288 220 hospitalizations due to AP in the United States in 2018, which in turn accounted for 96.35% of all admissions related to pancreatitis. Therefore, this is compelling evidence that the burden of AP is high.

AP diagnosis is based on clinical, laboratory, and imaging parameters. Gallstone pancreatitis (also known as biliary pancreatitis) is the most common cause, followed by excessive and long-term alcohol consumption (40-45% and 20-30% of cases in high-income countries, respectively). However, recent studies such as the systematic review performed by Zilio *et al.* in 2019 show that although the combined frequency of these etiologies was 42% and 21%, respectively, there are differences between regions. For example, gallstones were the cause of AP in 26%, 41%, and 68% of the cases in the United States, Europe, and Latin America, respectively, while alcohol-related AP accounted for 21%, 23%, and 5% of the cases in these three regions, respectively. In Colombia, it has been reported that obstruction of the bile duct by gallstones is also the main cause of AP (51.8-92.86% of the cases). 11-13

Other less common causes include hypertriglyceridemia, hypercalcemia, infections, dysbiosis, structural alterations of the pancreas, autoimmune diseases, trauma, and the use of a large group of drugs. In addition, it can also occur as a complication of some surgical procedures.^{3,5,7}

AP is considered a reversible and self-limited condition, with an average recovery time of 4 to 7 days. However, approximately 20% of the patients develop severe or moderately severe AP associated with local complications (peripancreatic fluid collections, pancreatic or peripancreatic tissue necrosis) and/or systemic complications (multiorgan failure syndrome),^{5,7} which, in turn, entail prolonged hospital stays, requirement for intensive care unit (ICU) admission, and a high mortality rate (20-40%).^{3,5,7}

The comprehensive care of these patients involves health professionals from several areas, namely, internal medicine, general surgery, intensive care, gastroenterology, interventional radiology, infectious diseases, clinical nutrition, nursing, and rehabilitation.

Consequently, standardizing the practices and activities related to the diagnosis and treatment of adult patients with AP is essential to reduce the variability in their management in hospital settings (emergency department, hospital wards, ICU), optimizing the use of resources and improving the quality of the care provided to this population.

In view of the above, the objective of this article is to identify the clinical indications for the diagnosis and treatment of AP in adults by developing an evidence-based clinical standard (EBCS) in a national reference university hospital in Bogotá, Colombia.

Materials and methods

This EBCS was developed in a sequential seven-phase process proposed by the Hospital Universitario Nacional de Colombia, in collaboration with the Universidad Nacional de Colombia and the Instituto de Investigaciones Clínicas (Clinical Research Institute) of the Universidad Nacional de Colombia. The phases are described below:

Formation of the development group

The development group comprised experts in internal medicine and clinical epidemiology (a methodological leader with experience in the development of clinical standards, two health professionals with experience in the development of evidence-based medicine processes, a first-year internal medicine resident, and an internal medicine specialist with experience in the treatment of patients with a diagnosis of AP), who participated in online meetings to establish the methodological, technical, and thematic guidelines for the formulation of the EBCS recommendations. Prior to agreeing to join the development group, all members completed a conflict-of-interest disclosure form.

EBCS scope definition and objectives

The EBCS scope was established based on the following elements: i) target population in which the recommendations will be used; ii) special populations on which the recommendations can be used, such as indigenous peoples, Afro-descendant communities, rural populations, etc., to ensure health equity; iii) aspect of the condition or disease to be addressed (treatment, diagnosis, prevention, follow-up, etc.); iv) aspects of the condition or disease that are beyond the scope of the recommendations; v) health care context (outpatient consultation, inpatient service, surgery service, intensive care, etc.); and vi) specialties, areas, or health services involved in the implementation and use of the recommendations.

This EBCS is intended to develop a clinical algorithm for the diagnosis and treatment of adult patients with AP admitted to a national referral university hospital in Bogotá (emergency room, general hospital ward, or ICU) based on the best available evidence. It should be noted that the EBCS does not contain recommendations for the pediatric population (<18 years of age) or pregnant women.

The recommendations included in the EBCS are aimed at healthcare workers involved in the care of adult patients with AP (general practitioners, internists, general surgeons, gastroenterologists, nutritionists, critical care doctors, infectious disease specialists, radiologists, nurses, nursing assistants, and rehabilitation professionals). Furthermore, it was established that the recommendations could also be used by health sciences students (undergraduate and graduate) who are involved in the care of these patients

during their clinical practice, their professors, and the healthcare or administrative staff of the healthcare institutions in charge of making decisions regarding the treatment and follow-up of this population.

The general and specific objectives of this EBCS were defined based on a literature review, an analysis of the care areas involved in the management of these patients, and an interdisciplinary consensus. The formulated objectives clearly and succinctly describe the purpose of the EBCS. Checkpoints and guidelines for the dissemination and implementation of the EBCS were also included in its preparation.

Systematic review of clinical practice guidelines

Systematic searches in MEDLINE, EMBASE and LILACS, as well as in clinical practice guideline (CPG) development and compiling agencies were conducted using controlled language and sensitive electronic search strategies to identify CPGs that met the stated objective and scope (Supplement 1). Searches were conducted between April 24 and June 3, 2021. The CPG screening and selection process was carried out taking into account the following eligibility criteria established by the development group:

Inclusion criteria

- CPGs on the diagnosis and treatment of AP in adult patients.
- CPGs published in English or Spanish and with full-text access.
- CPGs published within the last 10 years at the time of performing the searches.

Exclusion criteria

- CPGs with an overall quality assessment <6 according to the AGREE II instrument¹⁴ and a score <60% in the methodological rigor and editorial independence domains.
- CPGs on the diagnosis and treatment of AP in pediatric patients and pregnant women.
- CPGs on the diagnosis and treatment of chronic pancreatitis.

Evidence was screened by reviewing titles and abstracts, as well as the full text of the papers identified in the systematic searches. This process was performed independently by one of the members of the development group and the clinical leader. It was agreed that any discrepancies would be resolved by a third member (methodological leader); however, both reviewers agreed on the inclusion of the CPGs and there were no discrepancies in their decisions. The quality of the selected CPGs was assessed using the AGREE II instrument; this process was also carried out independently by two members of the development group: a clinical expert and a methodological expert.

Preliminary algorithm development

The development group used the selected CPGs to draft a preliminary proposal of the EBCS (clinical algorithm plus checkpoints [key recommendations for implementing the algorithm and clinical recommendations and for evaluating and monitoring their implementation]). To extract the evidence contained in the five selected CPGs, an information extraction table was created using a domain system. After reviewing the evidence gathered during several meetings, the development group elaborated the proposed clinical algorithm and recommendations for the diagnosis and treatment of

adult patients with AP. These recommendations included the level of evidence for each of the CPGs used to formulate the recommendation. Importantly, the level of evidence is presented following the evidence grading system used in the CPG.

Developing an interdisciplinary agreement

After identifying the health areas/services involved in the comprehensive care process of adult patients with AP, representatives of these services at the national reference university hospital where the EBCS was developed were appointed. They received the draft of the clinical algorithm for their assessment prior to attending a consensus meeting.

The consensus meeting took place in January 2022 and was attended by representatives of the following hospital care services: internal medicine, general surgery, gastroenterology, critical care, nursing, and clinical nutrition. Clinical leaders were responsible for the presentation of the preliminary algorithm, and the meeting was moderated by a research methodologist. Six sections of the EBCS (algorithm), as well as an additional section on checkpoints, were presented at the meeting. Using the modified Delphi methodology and a 1-9 Likert scale, it was possible to evaluate the level of agreement among the participants with the information presented in each section. The results of the seven polls confirmed that all participants of the interdisciplinary consensus group fully endorsed the use of the recommendations for the diagnosis and treatment of patients with AP contained in the flowcharts presented below. More detailed information on this step is available in the full text of this EBCS. ¹⁵

Final algorithm development

Once the interdisciplinary consensus was achieved, the development team met and consolidated the suggestions made at the consensus meeting and based on them, modified the preliminary algorithm of the document.

EBCS review and editing

The final activity of the process involved the revision of the document's wording and layout, resulting in the final version of the EBCS. As in the preliminary proposal, the recommendations include the level of evidence for each of the CPGs used to formulate the recommendation, and the level of evidence is presented in accordance with the evidence grading system used in each CPG.

Results

The preliminary searches retrieved 396 records. After removing duplicates (n=11), a total of 385 studies were identified, of which 365 were excluded at the title and abstract review stage. Then, out of the 20 documents that were fully read, 10 CPG were selected for quality assessment using the AGREE II instrument. Lastly, during the methodological quality assessment stage, 5 CPGs were excluded. The 5 CPGs that met the eligibility criteria and were finally included for evidence review are listed in Table 1. The evidence search, screening, and selection process is summarized in Figure 1.

Table 1. Clinical practice guidelines identified in the literature search that met the eligibility criteria for the development of the evidence-based clinical standard.

Id	CPG Title	Development group	Country or continent	Language	Year
CPG1	Pancreatitis (NICE guideline [NG104]) ¹⁶	National Institute for Health and Care (NICE)	United Kingdom	English	2018
CPG2	IAP/APA evidence-based guidelines for the management of acute pancreatitis ¹⁷	International Association of Pancreatology and American Pancreatic Association	United States and Australia	English	2013
CPG3	Japanese guidelines for the management of acute pancreatitis: Japanese Guidelines 2015 ¹⁸	Japanese Society of Hepato- Biliary-Pancreatic Surgery	Japan	English	2015
CPG4	Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence- based multidisciplinary guidelines ¹⁹	European Society of Gastrointestinal Endoscopy	Belgium	English	2018
CPG5	2019 WSES guidelines for the management of severe acute pancreatitis ²⁰	World Society of Emergency Surgery	Finland	English	2019

CPG: Clinical practice guidelines.

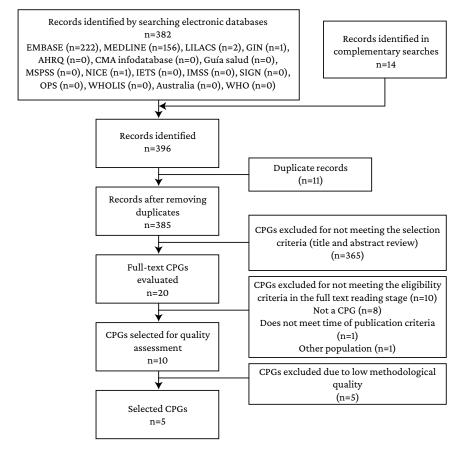


Figure 1. Systematic search for clinical practice guidelines.

Recommendations

The recommendations for diagnosing and treating patients with AP are presented using the sections of the clinical algorithm formulated by the development group based on the evidence retrieved from the selected CPGs and the opinions of the expert members of the development group, as well as the experts involved in the interdisciplinary consensus (Figure 2). The results are described below:

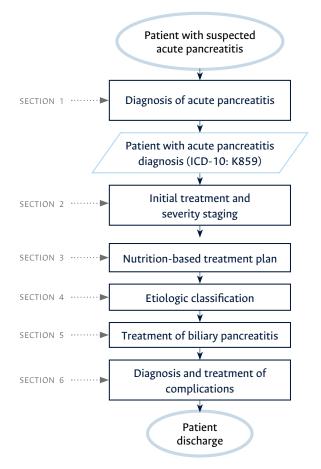


Figure 2. Flowchart for the diagnosis and treatment of adult patients with acute pancreatitis (ICD-10:K85.9).

ICD-10: International Classification of Diseases and Related Health Problems, Tenth Revision.

Section 1 - Recommendations for AP diagnosis

Context: A patient with a suspected diagnosis of AP must undergo a comprehensive initial assessment, as it will allow establishing an appropriate diagnosis and treatment during hospital stay, as well as identifying possible differential diagnoses compatible with the patient's clinical manifestations. Figure 3 illustrates the flowchart for Section 1.

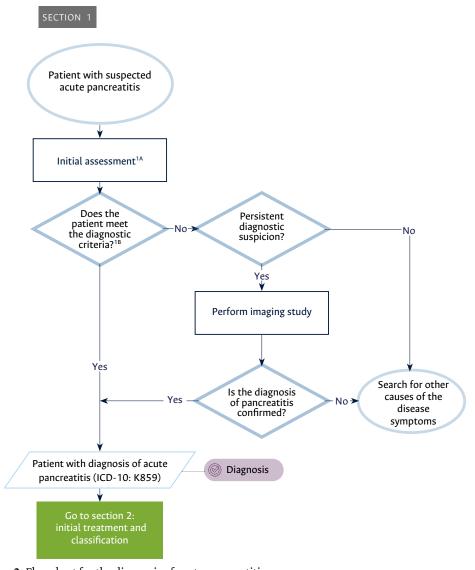


Figure 3. Flowchart for the diagnosis of acute pancreatitis. ICD-10: International Classification of Diseases and Related Health Problems, Tenth Revision.

1.A Initial approach: It has been reported that the incidence of AP worldwide varies between 14 and 50 cases per 100 000 inhabitants^{3,16} and that the main risk factors include long-term alcohol consumption, obesity, smoking, and a family history of AP.² Upon admission to the institution, the patient must:

- Be interviewed, focusing on pain characterization and medical history, and undergo a thorough physical examination.²
- Undergo a lipase test. However, if there are difficulties in accessing this test, a blood amylase test can be performed (level of evidence (LE): moderate; GRADE).¹⁸
- Undergo a hepatobiliary ultrasound (LE: low; GRADE),¹⁷ (LE: low; GRADE),¹⁸ even if this imaging study was performed at the referring institution or on an outpatient basis (expert recommendation).
- Undergo the following complementary studies: bilirubin blood test, aspartate aminotransferase blood test, alkaline phosphatase test, complete blood count, creatinine

test, blood urea nitrogen (BUN) test, sodium blood test, and potassium blood test (LE: moderate; GRADE).¹⁷

1.B Diagnostic criteria: The patient will be diagnosed with AP if two of the following criteria are met (LE: moderate; GRADE):¹⁷

- Clinical criterion: upper abdominal pain typical of AP.
- Lipase or amylase values 3 times above the upper reference limit. The amylase test has a sensitivity of 60% and specificity of 100% for the diagnosis of AP, while the sensitivity and specificity of the lipase test is 90-98% and 100%, respectively.
- Ultrasound findings (abdominal/biliary tract), abdominal computed tomography
 (CT), or abdominal magnetic resonance imaging (MRI) compatible with pancreatitis:
 imaging findings suggestive of pancreatitis include pancreatic enlargement with
 decreased echogenicity on abdominal/bile duct ultrasound; diffuse or localized
 enlargement of the pancreas and homogeneous enhancement and striation of
 peripancreatic fat on CT; and enlargement of the pancreas, increased T1 intensity, and
 suspected T1 fat deposits on MRI.

1.C Complementary imaging studies: It is suggested to carry out imaging studies that allow obtaining cross-sectional images, considering the performance of a contrast-enhanced abdominal CT scan as the first option or a contrast-enhanced MRI of the abdomen when:

- There is diagnostic uncertainty (LE: low; GRADE), ^{17,18} (LE: low or very low; GRADE). ²⁰
- It is necessary to confirm the severity of pancreatitis (LE: low; GRADE).¹⁷
- There is no clinical response to conservative treatment or clinical deterioration is evident (LE: low; GRADE).¹⁷

It should be noted that the optimal moment to perform an abdominal CT is between 72 and 96 hours after symptom onset (LE: low; GRADE). ^{17,19} Abdominal MRI may be used in patients with contraindications to contrast-enhanced CT (LE: low; GRADE). ¹⁹ After performing the selected imaging study, the diagnostic imaging criteria must be reassessed.

Section 2 - Recommendations for initial treatment and classification of AP severity

Context: Once the diagnosis of AP is confirmed, optimal management must be initiated to improve perfusion, control pain, and meet nutritional needs. Moreover, possible signs of MODS must be identified, and appropriate actions must be taken in patients who require it. Figure 4 illustrates the flowchart for Section 2.

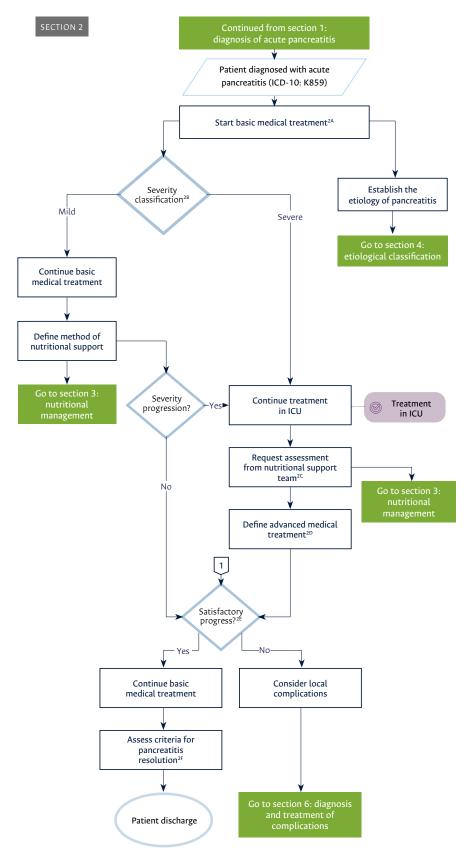


Figure 4. Flowchart for initial treatment and severity staging of acute pancreatitis. ICD-10: International Classification of Diseases and Related Health Problems, Tenth Revision; ICU: Intensive care unit.

- **2.A Basic medical treatment:** Basic medical treatment for AP patients is based on the following pillars:
- Intravenous fluid resuscitation: Early resuscitation with intravenous fluids is indicated to optimize tissue perfusion, instead of waiting for hemodynamic parameters to worsen (LE: moderate; GRADE).²⁰ Ringer's lactate infusions of 5-10/kg/hour must be administered depending on the hemodynamic status of the patient and until hemodynamic rehabilitation goals are met (LE: moderate; GRADE),¹⁷ (LE: low; GRADE),¹⁸ (LE: moderate; GRADE).¹⁹ Fluid requirements must be tailored and re-evaluated at frequent intervals. Similarly, it is important to watch out for the development of fluid overload, as rapid hemodilution has been associated with increased morbidity and mortality.^{20,21}
- Analgesia: Pain associated with AP is severe and persistent, so adequate management is required (LE: high; GRADE).¹⁷ All patients with AP must receive some type of analgesia within the first 24 hours of hospitalization to avoid compromising their quality of life, preferably hydromorphone (LE: low or very low; GRADE).²⁰ It is recommended to administer this opioid in doses of 0.2-0.6mg every 4-6 hours and titrate it depending on the patient's response and clinical course, as well as progress in pain control. It is also recommended to consider having the patient assessed by the pain and palliative care service of the hospital (expert recommendation).
- **Nutrition:** It is recommended to start oral food administration as soon as possible with a low-fat liquid diet. Subsequently and depending on tolerance, intake control, and nutritional condition of the patient, solid food must be started orally. The use of a nasogastric tube must also be considered in patients with oral intolerance, uncontrollable vomiting, and abdominal pain and distension (expert recommendation). Antibiotic prophylaxis is not recommended in patients with AP (LE: moderate; GRADE), (LE: high; GRADE). (Prophylaxis is not recommended in patients with AP (LE: moderate; GRADE).
- 2.B Classification of AP severity (Bedside index for severity in acute pancreatitis BISAP): In addition to the laboratory and imaging tests requested for the initial approach to the patient, a chest X-ray must be performed to establish the severity of the disease, given that this test is useful for detecting the presence of pleural effusion, a parameter that must be reported in the BISAP to calculate severity (expert recommendation). The mortality rate in patients with severe AP (score ≥3) varies between 5% and 20%, therefore, they must be admitted to the ICU to initiate treatment and follow-up. Moreover, in mild cases, the BISAP score must be recalculated 48 hours later to determine whether there has been an increase in the severity of the disease and whether transfer to the ICU is required for further treatment and follow-up (LE: moderate; GRADE).^{19,20} A score ≥3 predicts severity with a sensitivity and specificity of 51% and 91%, respectively. Regarding the prediction of mortality, a sensitivity of 56% and a specificity of 91% have been documented.⁵

Patients with AP and MODS must be admitted to the ICU with priority, whenever possible (LE: low; GRADE), ¹⁷ (LE: low or very low; GRADE). ²⁰

- **2.C** Nutritional support team: Once admitted to the ICU, the nutritional needs of each patient will be discussed with the nutritional support team, which is made up of the critical care physician on duty, the clinical nutritionist on duty, and the head nurse on duty and in charge of patient care (expert recommendation).
- **2.D Advanced medical care:** A treatment aimed at optimizing the parameters of organic perfusion and solving MODS must be implemented, improving basic medical treatment and defining the need to initiate specific support therapies based on each patient's condition, mainly ventilatory support, cardiovascular support, and/or renal support therapies (expert recommendation).

- **2.E Satisfactory progress of the patient's clinical condition:** A patient with a satisfactory progress of their clinical condition is defined as a patient who does not require cardiovascular, renal, or ventilatory support for more than 48 hours; shows adequate tolerance to feeding; and does not present with systemic inflammatory response syndrome for more than 48 hours (expert recommendation).
- **2.F Resolution of pancreatitis: It is considered that pancreatitis has resolved, if the patient:** shows adequate tolerance to the oral route, does not present signs of systemic inflammatory response syndrome, and reports adequate pain control (expert recommendation).

Once pancreatitis resolution is confirmed, the patient will be discharged, with warning signs and general recommendations to be considered, as well as an indication for a mandatory outpatient follow-up appointment two weeks after discharge.

Section 3 - Recommendations for nutritional management of patients with AP

Context: The nutritional management of patients with AP must take into account their baseline conditions. Accordingly, the assessment of possible food administration options must be individualized. Figure 5 illustrates the flowchart for Section 3.

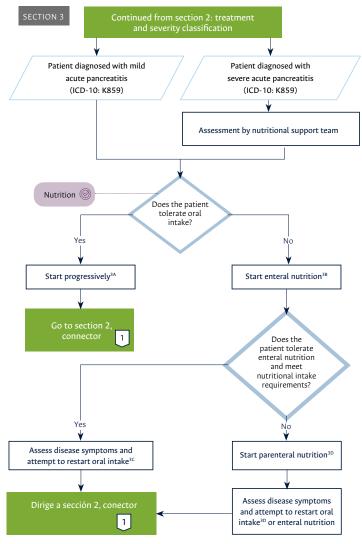


Figure 5. Flowchart for nutritional management of patients with acute pancreatitis. ICD-10: International Classification of Diseases and Related Health Problems, Tenth Revision.

3.A Progressive initiation of oral food intake: Once AP has been diagnosed, a liquid diet and, subsequently, a low-fat soft diet must be started, taking into account the patient's underlying diseases and tolerance to oral feeding (expert recommendation).

3.B Enteral nutrition: Enteral nutrition: Polymeric and low-fat enteral formula (LE: moderate; GRADE)¹⁷ must be started through nasogastric or nasojejunal tube (LE: high; GRADE)^{17,20} within 72 hours after making the diagnosis (LE: high; GRADE).¹⁶

It is suggested to initiate enteral nutrition with nasogastric tube, except in patients with hemodynamic instability. It is recommended to use the nasojejunal tube in patients with intolerance to enteral/oral feeding (LE: moderate; GRADE).¹⁹

When the use of the nasojejunal tube is considered appropriate, it is recommended to place it by endoscopy guided by a professional from the gastroenterology service (expert recommendation).

It is recommended to start enteral nutrition early to prevent intestinal failure and gastrointestinal infections (LE: high; GRADE).²⁰ It is suggested to initiate enteral nutrition by nasogastric tube in cases of intolerance to oral administration of liquids and food. The caloric intake that the patient is receiving and the actual caloric intake required must be evaluated: if the caloric intake is higher than 75% of what is required, this feeding route can continue to be used; otherwise, the nutritional support team must decide whether supplementation is required or whether it is necessary to initiate total or peripheral parenteral nutrition (expert recommendation).

- **3.C Restarting oral intake:** Oral intake may be restarted at any time once abdominal pain and gastrointestinal symptoms improve (LE: moderate; GRADE).^{17,18}
- **3.D Parenteral nutrition:** Parenteral nutrition must be initiated in patients with severe or moderate AP, in whom enteral nutrition has not been successful or in patients in whom enteral nutrition is contraindicated (LE: high; GRADE), ¹⁶ patients who require nutritional support (LE: low; GRADE), ¹⁷ patients with persistent food intolerance, or in those in whom it is not possible to achieve the required caloric intake by enteral nutrition (LE: low; GRADE: GRADE). ¹⁹

Partial or mixed parenteral nutrition must be considered to achieve the patient's caloric and protein requirements if oral feeding is not fully tolerated (LE: high; GRADE).²⁰ It is suggested to ensure an adequate route of administration for the initiation of parenteral nutrition when it is considered necessary (expert recommendation).

Section 4 - Recommendations for the classification of AP etiology

Context: Proper identification of the cause of AP and its appropriate management greatly reduce the possibility of recurrence, improving the patient's quality of life in the long term. Figure 6 illustrates the flowchart for Section 4.

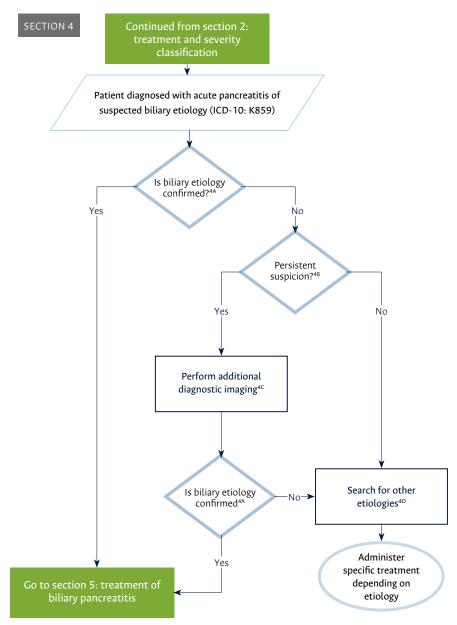


Figure 6. Flowchart for etiological classification of the patient with acute pancreatitis. ICD-10: International Classification of Diseases and Related Health Problems, Tenth Revision.

4.A AP of biliary origin: AP of biliary origin: It is considered that AP has a biliary origin when its etiology involves obstruction of the biliary tract by biliary stones or biliary sludge. It is necessary to confirm or rule out biliary etiology as a priority, since it can affect the treatment of these patients and implies a high risk of recurrence (LE: high; GRADE). **4.B Persistent suspicion of a biliary etiology:** When the following clinical signs and laboratory and imaging findings are observed, a biliary etiology must be suspected: signs such as abdominal pain, predominantly in the right hypochondrium and epigastrium, jaundice, acholia, and choluria; laboratory and imaging findings such as hyperbilirubinemia at the expense of the conjugated or direct fraction with increased levels of alkaline phosphatase,

or when hepatobiliary ultrasound findings are inconclusive (expert recommendation).

4.C Complementary imaging studies: Biliopancreatic endoscopic ultrasound (expert recommendation) and MRI cholangiopancreatography (LE: low; GRADE)¹⁷ are both imaging tests with the best results for assessing the biliary tract in patients with suspected AP of biliary origin and in whom abdominal ultrasound findings were inconclusive.

Biliopancreatic endoscopic ultrasound has a sensitivity of 97% and a specificity of 90% for the identification of a biliary etiology, while MRI cholangiopancreatography has a sensitivity of 87% and a specificity of 92%.²¹ Either test must be selected depending on availability (expert recommendation).

- **4.D Search for other etiologies:** If AP is not caused by bile duct obstruction, other possible etiologies must be actively investigated depending on the suspected cause in each patient (LE: moderate; GRADE), 16,17 (LE: low or very low; GRADE): 20
- Long-term alcohol consumption.
- Hypercalcemia: assuming >1.30mmol/L ionized calcium or >10.4mg/dL total serum calcium as the cut-off point.
- Anatomical causes: pancreas divisum, biliopancreatic tumors, associated anatomical malformations, or sphincter of Oddi dysfunction. Complementary imaging studies must be considered if one of these anatomical alterations is suspected.
- Pancreatitis secondary to the performance of procedures such as endoscopic retrograde cholangiopancreatography (ERCP) or, less frequently, endoscopic ultrasound.
- Use of medications associated with the development of pancreatitis.
- Family history.
- Microlithiasis.
- Gastrointestinal infections.
- Autoimmune diseases.
- High triglycerides: Blood levels >1 000mg/dL or >11.3mmol/L.
- Genetic causes.
- Other unknown causes.

Section 5 - Recommendations for the treatment of AP of biliary origin

Context: Given the complications and comorbidities that patients with AP of biliary origin may present, early surgical management of this type of AP is required. Figure 7 illustrates the flowchart for Section 5.

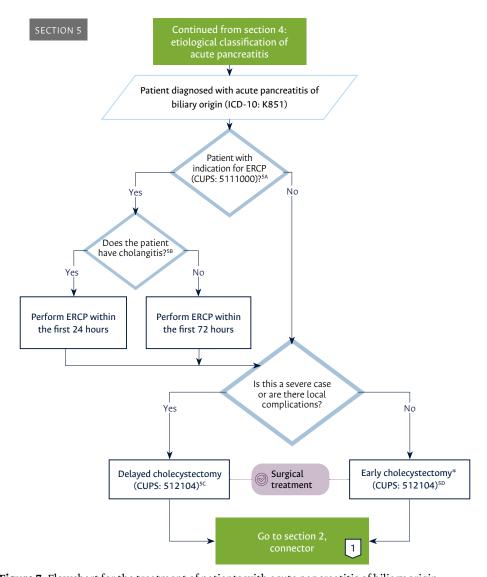


Figure 7. Flowchart for the treatment of patients with acute pancreatitis of biliary origin. ICD-10: International Classification of Diseases and Related Health Problems, Tenth Revision; ERCP: Endoscopic retrograde cholangiopancreatography; CUPS: Unique code for healthcare procedures.

- **5.A Performance of ERCP:** ERCP is indicated in patients with AP of biliary origin and any of the following conditions:
- Acute cholangitis (LE: moderate; GRADE), 18 (LE: high; GRADE). 18,19
- Confirmed choledocholithiasis (LE: moderate; GRADE).²⁰
- **5.B Priority ERCP:** This study will be considered as a priority based on the following factors:
- Patient with cholangitis: proceed within 24 hours after diagnosis (LE: low; GRADE).
- Patient with common bile duct stones: proceed within 72 hours after diagnosis (LE: moderate; GRADE).¹⁹
- **5.C Delayed cholecystectomy:** Cholecystectomy performed during hospitalization as a result of the occurrence of complications and the opinion of the general surgery service (expert recommendation).
- **5.D Early cholecystectomy:** Cholecystectomy performed within the first 24-48 hours after the onset of symptoms and signs of AP (expert recommendation). In general, laparoscopic cholecystectomy is recommended on admission in patients with mild AP caused by gallstones (LE: high; GRADE).²⁰ (LE: low; GRADE).¹⁷

Section 6 - Recommendations for the management of complications associated with AP treatment

Context: AP management has been associated with the occurrence of several complications, so their proper identification and timely treatment are critical for the adequate resolution of AP. Figure 8 illustrates the flowchart for Section 6.

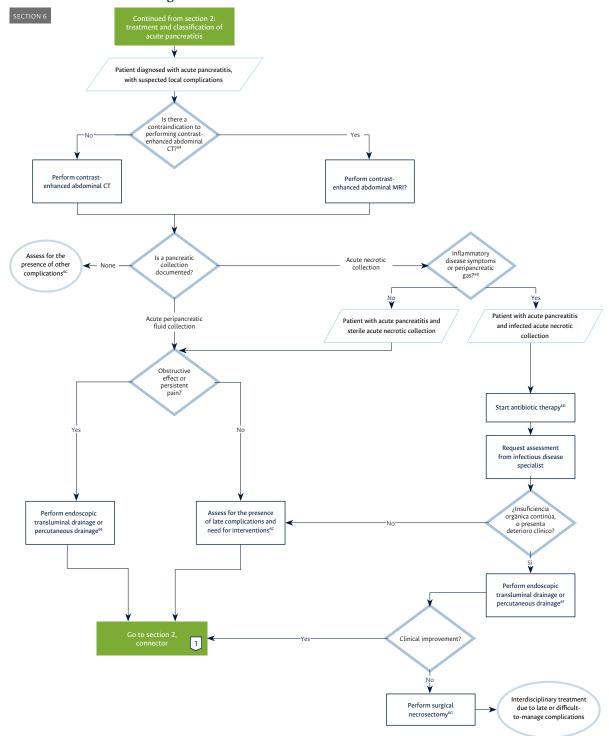


Figure 8. Flowchart for the management of complications associated with the treatment of patients with acute pancreatitis. CT: Computed tomography; MRI: Magnetic resonance imaging. Connections: 1: Go to section 2, subdivision "Satisfactory progress".

6.A Contraindications to contrast-enhanced abdominal CT: This diagnostic imaging test is contraindicated in the following cases (LE: low):¹⁷ patients who are allergic to contrast medium and patients with acute renal failure (creatinine >1.5 or an increase >30% from baseline).

Follow-up CT or MRI of the abdomen and pelvis is indicated in patients with AP if there is no clinical improvement, clinical deterioration, or, particularly, when invasive intervention is considered necessary.

6.B Predictors of infected pancreatic necrosis: It is recommended to use the following clinical signs and paraclinical findings as accurate predictors of infected pancreatic necrosis before performing fine needle aspiration biopsy (LE: low; GRADE):^{17,18}

- Persistent fever.
- Increased levels of inflammatory markers.
- Pancreatic and/or peripancreatic gas on CT or MRI of the abdomen and pelvis.
 Similarly, a procalcitonin test is recommended for the detection of infected pancreatic necrosis, as low procalcitonin levels have been reported to be strong negative predictors of this condition (LE: high; GRADE).²⁰
- **6.C** Other complications associated with AP: Some of the complications associated with AP include: abdominal compartment syndrome, ascites, intestinal ischemia, gastric motor disorders, and portal and/or splenic vein thrombosis (expert recommendation).
- **6.D Antibiotic therapy:** Antibiotic therapy is recommended for all patients with severe infected AP (LE: high; GRADE).²⁰ It should be noted that it is very unlikely that infections develop before the first week after symptom onset (expert recommendation). Antibiotic therapy should be initiated with coverage directed at Gram-positive and Gram-negative aerobes and anaerobes (LE: high; GRADE),²⁰ adapted to culture and antibiotic susceptibility testing, if available (LE: low; GRADE).¹⁹

It is also recommended to use the following empirical antibiotic treatment scheme: intravenous ampicillin sulbactam at a dose of 3 grams every 6 hours. If the clinical course is not satisfactory 48 hours after initiating treatment, it is recommended to stagger antibiotic management and use intravenous meropenem at a dose of 1 gram every 8 hours or intravenous piperacillin/tazobactam at a dose of 4.5 grams every 8 hours. If meropenem is selected and the patient has a history of biliary tract instrumentation, it is recommended to add intravenous ampicillin 2 grams every 4 to 6 hours to the treatment to cover enterococci (expert recommendation). Finally, it is suggested to request an assessment of the patient from the infectious disease department in case of an acute infected necrotic collection to define changes in the initial antibiotic therapy scheme based on the risk factors of each patient (expert recommendation).

6.E Late pancreatic collections: After 4 to 6 weeks, early collections, defined as acute peripancreatic fluid collection and acute necrotic collection, may progress to pancreatic pseudocyst or walled-off pancreatic necrosis, respectively, which are treated in case of intestinal or biliary obstruction, early satiety, disconnected pancreatic duct syndrome, or superinfection (expert recommendation).

6.F Indications for endoscopic ultrasound-guided transluminal drainage or percutaneous drainage of pancreatic collections: These interventions are indicated in the following cases (LE: high; GRADE):^{17,18}

- Peripancreatic fluid collection with signs of sepsis.
- Symptomatic pseudocyst >5cm, infected or causing biliary or gastrointestinal obstruction.
- Pancreatic necrosis with clinical or imaging signs of superinfection.

- Presence of pancreatic abscess.
- Persistent pain.

The decision of which of the two interventions to implement, including the option of surgical management, must be taken on case-by-case basis and considering the opinion of the treating services (expert recommendation):

6.G Surgical necrosectomy: If there is no improvement after percutaneous or endoscopic ultrasound-guided transluminal drainage, surgery must be performed, being the minimally invasive approach the first choice, either by retroperitoneal or anterior necrosectomy. It will be decided which of these two types of intervention will be performed depending on the characteristics of each case (LE: moderate; GRADE). 18,19

Section 7 - Checkpoints

The EBCS checkpoints, which were established considering key moments in the comprehensive care of adult patients with AP and were chosen jointly by the members of the development team based on the suggestions made at the interdisciplinary consensus meeting, are presented below:

- 1. Hepatobiliary ultrasound on admission in patients diagnosed with AP.
- 2. Admission to the ICU of patients with severe AP.
- 3. Early implementation of a feeding route (within 72 hours of symptom onset) in these patients.
- 4. Cholecystectomy in patients diagnosed with AP of biliary origin.

Implementation and updating

A multi-stage approach is proposed to implement the EBCS and evaluate adherence to these recommendations. First, an interdisciplinary team will be created, comprising members of the development group and representatives of the administrative and clinical areas of the referral university hospital who can support the implementation process; priority will be given to information technology staff. This team will be key to identifying barriers and facilitators of the implementation process.

Subsequently, two approaches will be adopted to address possible EBCS implementation actions. The first will focus on the dissemination of the clinical algorithm and its checkpoints through educational activities, such as face-to-face and pre-recorded educational talks, and dissemination using social networks and institutional billboards. The second approach will focus on developing administrative strategies that utilize information technology and electronic health record software to generate interactive prompts and reminders that are incorporated into educational activities.

Finally, the assessment of adherence to the EBCS will include three components: i) assessment of EBCS knowledge; ii) assessment of adherence using administrative information sources; and iii) evaluation of impact (clinical, financial, and patient-reported) through additional studies in priority areas of the hospital. The implementation process will take place in stages other than those of the development process, thereby allowing the identification of the best implementation solutions for this EBCS.

The EBCS will be updated in accordance with the stipulated institutional processes. To this end, the development group has set a time limit of 3 to 5 years for updating the EBCS, taking into account various critical aspects: i) the volume of evidence currently available, ii) the availability of new evidence that may have an impact on the comprehensive care

of patients with AP, iii) the quality of the evidence available at the time of EBCS development, and iv) the availability of institutional resources for the implementation and updating of the standard.

Conclusions

The evidence-based clinical recommendations included in this EBCS are intended to standardize practices and actions related to the diagnosis and treatment of adult patients with AP in Colombia, and even the region. In this sense, the algorithm and clinical recommendations presented here aim to optimize the use of resources and improve the quality of care provided to this population and, therefore, their health outcomes. Finally, it is worth noting that this document can also be used as an educational tool in undergraduate and postgraduate studies for health professionals involved in the care of patients with this condition.

Conflicts of interest

None stated by the authors.

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Supplement 1. Search strategy reporting tables

Databases: Medline

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Compilers: Guidelines International Network (GIN)

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Search date range	Last 10 years
Language restrictions	None
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Compilers: CMA infodatabase

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Language restrictions	None
Other restrictions	None
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References obtained	0
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Compilers: Guía Salud España

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Date of search	24/04/2021
Search date range	Last 10 years
Language restrictions	None
Other restrictions	None
Search strategy	Pancreatitis, Pancreatitis aguda, Acute pancreatitis
References obtained	0
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Developers: Ministerio de Salud y Protección Social (MSPSS)

Search strategy	Clinical practice guidelines
Developer	MSPSS
Platform	MSPSS
Date of search	24/04/2021
Search date range	Last 10 years
Language restrictions	None
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Developers: National Institute for Health and Clinical Excellence- (NICE)

Search strategy	Clinical practice guidelines
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Developers: Instituto de Evaluación Tecnológica en Salud (IETS)

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Developers: Instituto Mexicano del Seguro Social (IMSS)

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Developers: Scottish Intercollegiate Guidelines Network (SIGN)

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Developers: WHOLIS

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Search strategy	Clinical practice guidelines
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Developers: World Health Organization (WHO)

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Developer	WHO
Platform	WHO
Date of search	24/04/2021
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