

GUIDELINE OPEN ACCESS

AEG-AESPANC-OPGE-SIED-SPG Ibero-Latin American Guidelines on Acute Pancreatitis (iLATAM-AP)

Karina Cárdenas-Jaén^{1,2}  | Lucía Guilbert^{1,2}  | Emma Martínez-Moneo³ | Carla Mancilla⁴ | Miguel Bispo⁵ | Pedro Moutinho-Ribeiro⁶ | Rodrigo Mansilla⁷  | Andreia Rei⁸ | Ana García García de Paredes^{9,10,11} | Antonio López-Serrano^{12,13} | Bruno Rosa¹⁴ | Claudia Sánchez-Marín^{15,16} | Daniel de la Iglesia¹⁷  | Edson Guzmán-Calderon^{18,19,20} | Eduardo Rodrigues-Pinto⁶  | Eva Marín-Serrano²¹  | Fabio Ausania²²  | Fauze Maluf-Filho²³ | Guido Villagómez²⁴ | Humberto Cristino²⁵ | Isabel Pascual-Moreno²⁶ | José A. Gonzalez²⁷ | José M. Ramia^{2,28} | João Lopes-Delgado²⁹ | Lucas Granero^{30,31}  | Mario Peláez-Luna^{32,33} | María Francisco³⁴  | Natalia Corzo-Zamora³⁵ | Ricardo Río-Tinto⁵ | Rómulo D. Vargas³⁶ | Sandra Basso³⁷  | Susana Lopes⁶ | Susana Marques⁵ | William Manzanares³⁸  | Zoltán Berger³⁹ | Irene Carrillo⁴⁰  | José Joaquín Mira-Solves⁴⁰  | Alberto Espino⁴¹ | Adriana Cowdin⁴² | Alejandro Piscoya⁴³  | Alexandra Fernandes⁴⁴ | Noelia Rodríguez-Ferreiro⁴⁵ | Neftalí Jara Pérez-López^{1,2} | Beatriz Valero⁴⁶ | Enrique de-Madaria^{1,2,11,47} 

Correspondence: Enrique de-Madaria (enriquedemadaria@gmail.com)

Received: 17 September 2025 | **Revised:** 20 January 2026 | **Accepted:** 12 February 2026

Keywords: acute pancreatitis | consensus | GRADE | guidelines | ibero-Latin American | management | Portuguese | Spanish

ABSTRACT

Introduction: Acute pancreatitis (AP) is a major cause of gastrointestinal hospitalizations worldwide. Although typically self-limiting, up to one-third of cases develop complications associated with increased morbidity and mortality. Despite recent advances that have improved outcomes, clinical heterogeneity necessitates updated, evidence-based guidance. In addition, there remains a need to improve the implementation of evidence-based recommendations across Ibero-Latin American countries by bringing together diverse scientific societies and regional experts to enhance applicability and the dissemination of best practices. This guideline offers comprehensive recommendations for both mild and complicated AP diagnosis and management.

Methods: Questions on AP management were addressed by expert teams comprising one coordinator and four pancreatology specialists from the Iberian Peninsula and Latin America. For each question, a systematic review was conducted using PubMed, Embase, and the Cochrane Library, focusing on randomized controlled trials and systematic reviews published between January 1979 and March 2024 in English, Spanish, or Portuguese. In the absence of high-quality evidence, the search was expanded to include observational studies. Recommendations were formulated using the GRADE system and submitted to an expert panel for consensus; unresolved questions were revised and resubmitted until consensus was reached.

Results: Twenty evidence-based recommendations were developed, addressing key aspects of AP management, including definitions, diagnostic criteria, etiological assessment, initial management, management of local complications, splanchnic vein thrombosis, abdominal compartment syndrome, indications for intensive care admission, antibiotic use, early endoscopic

Abbreviations: ALP, alkaline phosphatase; ALT, alanine aminotransferase; AP, acute pancreatitis; APACHE II, Acute Physiology and Chronic Health Examination II; AST, aspartate aminotransferase; BISAP, Bedside Index for Severity in Acute Pancreatitis; CI, confidence interval; CRP, C-reactive protein; CT, computed tomography; DBC, determinant-based classification; DPDs, disconnected pancreatic duct syndrome; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; GGT, gamma-glutamyl transferase; HR, hazard ratio; HTG, hypertriglyceridemia; IAH, intra-abdominal hypertension; IAP, intra-abdominal pressure; ICU, intensive care unit; IL, interleukin; IPN, infected pancreatic necrosis; LAMS, lumen-opposed metal stent; MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging; NSAIDs, nonsteroidal anti-inflammatory drugs; OF, organ failure; PEI, pancreatic exocrine insufficiency; PERT, pancreatic enzyme replacement therapy; PPPC, pancreatic and/or peripancreatic collections; RAC, Revised Atlanta Classification; RAP, recurrent acute pancreatitis; RCT, randomized clinical trial; RR, relative risk; SIRS, systemic inflammatory response syndrome; TG, triglyceride; TNF, tumor necrosis factor; TUS, transabdominal ultrasound; WON, walled-off necrosis.

The first two authors Co-first authors.

This article has been translated into Portuguese and Spanish. The Portuguese version is available in Supporting Information S2; the Spanish version is available in Supporting Information S3.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2026 The Author(s). *United European Gastroenterology Journal* published by Wiley Periodicals LLC on behalf of United European Gastroenterology.

retrograde cholangiopancreatography, timing of cholecystectomy, strategies for detecting choledocholithiasis, and the management of pancreatic function insufficiency. Each recommendation included a statement, the level of evidence, the strength of the recommendation, and a summary of the supporting evidence.

Conclusion: The iLATAM guidelines are the first Ibero-Latin American clinical practice guidelines for AP. They provide evidence-based recommendations integrating medical, endoscopic, and surgical approaches, with the aim of promoting consistent, high-quality care across diverse healthcare settings.

Trail Registration: In alignment with international standards for transparency and methodological rigor, the methodological protocol for this guideline was registered in PROSPERO (International Prospective Register of Systematic Reviews) on July 23, 2022 (Registration ID: CRD42022345788).

1 | Introduction

Acute pancreatitis (AP) is a leading cause of gastrointestinal-related hospital admissions worldwide, with an incidence exceeding 34 cases per 100,000 person-years [1] and a documented average annual percent change of 3.07% (95% CI, 2.30%–3.84%) between 1961 and 2016 [2]. In the United States, AP accounted for more than 378,000 emergency department visits and 263,000 hospitalizations in 2021, ranking third among gastrointestinal diagnoses and generating costs exceeding \$12.8 billion [3]. While most cases are mild, up to one-third develop local or systemic complications with mortality up to 50% in the case of persistent or multiple organ failure [4, 5]. These data highlight the clinical and economic impact of AP, underscoring the need for standardized, evidence-based care.

Advances in understanding the pathophysiology, diagnosis, and treatment of AP have improved outcomes [6]; however, disease heterogeneity and the expansion of therapeutic options necessitate updated guidance. Moreover, several studies have reported suboptimal adherence to international AP guidelines across Ibero-Latin American countries [7, 8]. This guideline responds to the need for improving the implementation of evidence-based recommendations across Ibero-Latin American countries by bringing together diverse national scientific societies and local experts, many of whom are not represented in existing international AP guidelines, to enhance regional applicability and dissemination of best practices.

2 | Materials and Methods

This is the first Ibero-Latin American guideline on AP management. It was developed by a multidisciplinary panel of experts from the Iberian Peninsula (Spain and Portugal) and Latin America, with institutional support from the Spanish Association of Gastroenterology (AEG), Spanish Association of Pancreatology (AESPANC), the Portuguese Society of Gastroenterology (SPG), The Panamerican Gastroenterology Organization (OPGE) and the Interamerican Society of Gastrointestinal Endoscopy (SIED), and funding provided by AEG, through a competitive research grant (AEG grant from the Pancreas and Bile Duct 2022). In alignment with international standards for transparency and methodological rigor, the methodological protocol for this guideline was registered in PROSPERO (International Prospective Register of Systematic Reviews) on July 23, 2022 (Registration ID: CRD42022345788). Methodological support was provided by

experts in healthcare quality and patient safety (JJM and IC), who advised on guideline structure, evidence appraisal processes, and consensus methodology.

2.1 | Organizational Structure and Clinical Question Formulation

The study had two general coordinators (KCJ and EdM) and six team coordinators (KCJ, CM, MB, PMR, EMM, and RM). A first draft of the questions to be addressed in these guidelines was shared with the full panel of participants. Using an online platform, each participant rated the appropriateness of the questions on a 0–10 scale and suggested changes or proposed new questions. A total of 20 key clinical questions (appropriateness 9 or 10) addressing the diagnostic, therapeutic, and follow-up aspects of AP were agreed upon. Each question was assigned to a dedicated working team composed of one team coordinator and four physicians (including specialists in gastroenterology, surgery, internal medicine, and intensive care medicine), with experience in the management of AP and research in that field (Supporting Information S1).

A patient representative of Latin American origin from a recognized patient organization (The National Pancreas Foundation) participated in all the stages of these guidelines (AC). This patient representative reviewed the questions to be addressed and the draft recommendations, contributed experiential insights reflecting patient priorities, and participated in the Delphi voting rounds. This contribution ensured that patient-centered perspectives were incorporated.

In addition, to facilitate implementation, uptake, and wider dissemination across Ibero-American settings, the guideline has been translated into Spanish and Portuguese; these versions are provided as Supporting Information S2 and S3.

2.2 | Literature Search and Study Selection

For each clinical question, a structured, comprehensive literature search was conducted in PubMed, Embase, and the Cochrane Library. These were framed as PICO questions for the search where appropriate. The search included studies published from January 1979 to March 2024 in English, Spanish, or Portuguese. Priority was given to randomized controlled trials (RCTs) and systematic reviews. In the absence of high-quality evidence, the inclusion criteria were expanded to include

observational studies with at least 20 participants. A qualitative risk-of-bias assessment was performed for all studies contributing to each clinical question. Given the marked heterogeneity in study designs, populations, and outcome measures across the available evidence, the use of a single standardized tool was not considered appropriate. Instead, risk of bias was evaluated across key methodological domains and studies with significant methodological flaws, inconsistent results, or indirect evidence were excluded. Search terms and further methodological information can be found in Supporting Information S1.

A formal cost-effectiveness analysis was beyond the scope of this guideline; however, several pragmatic considerations related to resource availability and the regional healthcare context were incorporated by the panel into the formulation of recommendations, particularly those involving advanced diagnostic modalities or higher levels.

2.3 | Data Extraction and Quality Assessment

Each team member independently reviewed the literature and extracted data into a standardized Excel template comprising three evidence Tables: (1) RCTs and systematic reviews, (2) observational studies, and (3) diagnostic or prognostic studies. Extracted variables included study design, population characteristics, interventions, outcomes, and key findings. Risk of bias was assessed qualitatively, with particular attention to non-blinded or non-randomized studies.

2.4 | Evidence Synthesis and Recommendation Development

Each question team synthesized the evidence through structured discussion. For each clinical question, a technical summary report was developed, containing:

- The structured clinical question
- A recommendation statement
- The level and strength of evidence using the GRADE system (Grading of Recommendations, Assessment, Development and Evaluation) [9] (Supporting Information S1)
- A concise summary of supporting evidence “Remarks”
- Full bibliographic references (Author, Journal, Year, PMID)

The expert panel then submitted recommendations to a structured voting process in a dedicated Delphi consensus platform. Statements that did not reach consensus (< 80%) in the initial round were revised and resubmitted for reevaluation. At the end, all questions had more than 80% agreement. Internal documentation of the whole consensus process was maintained and recorded.

Although a formal Evidence to Decision framework [10] was not applied systematically, key Evidence to Decision domains, including resource use, accessibility, feasibility, and equity, were

considered during guideline development. Given the heterogeneity of healthcare systems across Ibero-Latin American settings, several recommendations were intentionally framed to allow flexibility according to local availability of diagnostic tools, specialized procedures, and levels of care. This pragmatic approach aimed to maximize applicability and support equitable implementation across diverse clinical environments.

2.5 | Use of Artificial Intelligence and Reporting Standards

This guideline was developed in accordance with the AGREE II (Appraisal of Guidelines for Research & Evaluation II) recommendations [11] to ensure methodological rigor and transparency. ChatGPT-4 (OpenAI, San Francisco, CA, USA) was used exclusively to assist with language editing and grammar refinement of the manuscript's English version. All scientific content, interpretation, and final approval of the text were performed by the authors.

3 | Results (Clinical Questions and Guideline Recommendations—Table 1)

3.1 | Key Clinical Questions

3.1.1 | Q1. What is the Definition of Acute Pancreatitis?

3.1.1.1 | Statement and GRADE.

- Acute pancreatitis (AP) is an acute inflammation of the pancreas with several etiologies. Most patients experience a mild inflammatory process limited to the pancreas, whereas approximately one third develop pancreatic necrosis and/or peripancreatic or distant organ involvement resulting in a moderate severe to severe disease course. This yields a wide clinical spectrum, ranging from self-limited abdominal pain to local or systemic complications associated with significant morbidity and potential mortality. *Strong recommendation, moderate quality evidence.*

3.1.1.2 | Remarks. The pancreas integrates two glandular systems: endocrine, secreting hormones like insulin and glucagon for glycemic control, and exocrine, producing pancreatic juice for digestion [12]. Damage to acinar cells, caused by ductal hypertension, luminal acidification, or toxic metabolites, initiates a cascade that leads to cell injury and pancreatitis [12, 13]. This cellular damage results in persistently elevated intracellular calcium levels, which subsequently increase mitochondrial permeability and lead to loss of membrane potential, thereby impairing ATP generation [14–18]. Endoplasmic reticulum oxidative stress worsens injury by inhibiting autophagy [19, 20], while blocked zymogen exocytosis granules (inactive enzymes) trigger the premature intrapancreatic trypsinogen activation and autodigestion [19–22].

In most patients, these mechanisms remain self-limited, resulting in mild disease confined to the pancreas. However, in a subset of patients, sustained acinar cell injury and

dysregulated inflammatory signaling amplify local damage and promote systemic inflammatory response syndrome (SIRS), and organ failure may ensue [21–24]. The progression from mild to moderate or severe AP, occurs in about one third of patients [5].

3.1.2 | Q2. How to Diagnose AP? What is the Role of Imaging Studies?

3.1.2.1 | Statement and GRADE.

- The diagnosis of AP requires at least two of the following three criteria: (i) abdominal pain consistent with pancreatitis (epigastric, band-like, radiating to the back), (ii) serum amylase and/or lipase activity > 3 times the upper limit of the normal value or (iii) characteristic imaging findings. *Strong recommendation, moderate quality evidence.*
- The diagnosis is primarily clinical-analytical, with imaging studies reserved for cases with atypical signs or symptoms that raise diagnostic doubt. *Strong recommendation, low-quality evidence.*

3.1.2.2 | Remarks. The classic AP diagnostic criteria have been used for decades and were reaffirmed in the 2012 Revised Atlanta Classification [4]. According to this definition, radiological studies are unnecessary when typical symptoms and labs are present, but are required otherwise [4].

Laboratory parameters for the AP diagnosis include the measurement of serum lipase or amylase levels, or determining urinary trypsinogen-2 [25, 26]. Amylase has pancreatic and salivary isoforms, but is also secreted by other organs (ovary, intestine), so elevations may occur in non-pancreatic illnesses. In AP, amylase rises 6 h after symptom onset, peaks at 48 h, and remains elevated 5–7 days [25, 26]. Lipase increases approximately 4 h after symptom onset, peaks at 24 h, and remains elevated for 8–14 days [25, 26]. Elevated urinary trypsinogen (> 50 ng/mL) has proven useful in diagnosing AP [27–29]. Lipase levels rise predominantly in AP, making it a theoretically more specific marker, but all serum/urine methods show comparable sensitivity (~70%) and specificity (~90%) in an appropriate clinical context [26–29].

Transabdominal ultrasound (TUS) is commonly used as the initial imaging modality due to its accessibility, low cost, and ability to detect gallstones [30, 31]. However, its sensitivity to confirm pancreatitis is limited; therefore, cross-sectional imaging is preferred when diagnostic uncertainty exists. In this setting, contrast-enhanced CT is the technique of choice due to its speed, availability, and accuracy. Contrast-enhanced CT also stages severity and assesses complications; however, for this purpose, it is preferable to wait at least 72 h from pain onset [30–36]. Magnetic Resonance Imaging (MRI), while more sensitive for subtle findings and necrosis, is limited by cost, availability, and scan time. Thus, it is less suitable initially but valuable in selected cases, such as contrast allergy or pregnancy [30–36].

3.1.3 | Q3. How Should Etiology Be Assessed?

3.1.3.1 | Statement and GRADE.

- *Initial Evaluation:* Etiology should be assessed in all patients. The essential workup includes personal and family history, with an emphasis on biliopancreatic pathologies, toxic habits and medications, physical examination, blood tests (with liver profile, triglycerides, and calcium), and TUS within the first 24–48 h of admission. *Strong recommendation, low-quality evidence.*
- *Additional tests:* If the etiology remains unknown, additional tests are advised during follow-up, even for a first episode. This phase should include a second TUS and laboratory tests. If the results are inconclusive, endoscopic ultrasound (EUS) is recommended; where highly available, EUS may replace the second TUS. Magnetic resonance cholangiopancreatography (MRCP), preferably secretin-enhanced when available, may be used as an alternative or complementary examination in cases where EUS is negative or unavailable. Pancreas-protocol contrast-enhanced CT is a fallback option if EUS/MRI are inaccessible, though it is less accurate and should also be considered to rule out pancreatic malignancy in patients over 50 years of age without an identified etiology, and even in younger patients with other risk factors. Endoscopic retrograde cholangiopancreatography (ERCP) is not recommended due to its invasiveness and associated adverse events. *Strong recommendation, low-quality evidence.*
- *Genetic and Immunological Testing in idiopathic recurrent AP:* Genetic and immunological testing are not recommended after a first episode of AP; their use is reserved for recurrent idiopathic cases or when specific clinical indications exist, such as suspected autoimmune disease, young age, or family history of pancreatic diseases. *Strong recommendation, low-quality evidence* (Figure 1).

3.1.3.2 | Remarks. Globally, the most common causes of AP are gallstones (42%; 95% confidence interval (CI) 39%–44%), alcohol consumption (21%; 95% CI 17%–25%), and idiopathic etiology (18%; 95% CI 15%–22%) [37]. Hypertriglyceridemia ranks third among identifiable causes, accounting for 4%–10% of cases [38]. In Latin America, biliary etiology is even more frequent, responsible for 50%–83% of all cases [37].

Etiological assessment requires a thorough anamnesis and examination. Certain factors can suggest specific etiologies: the combination of female sex, age > 58 years, and serum alanine aminotransferase (ALT) elevation over three times (≥ 150 U/L) suggests a biliary etiology [39–43]; long-term alcohol abuse, in the absence of other identifiable causes, points to an alcohol-related etiology [44]; chylous serum with triglyceride (TG) levels exceeding 500–1000 mg/dL indicates hypertriglyceridemia-related (HTG) etiology [45].

A second TUS can enhance lithiasis detection [46, 47], increasing diagnosis rates from 66% to 83% [46, 47]. When combined with elevated ALT levels, accuracy further increases

TABLE 1 | Summary of key clinical questions and evidence-based recommendations.

Clinical question	Evidence-based answer Recommendation	Grade Evidence level
What is the definition of acute pancreatitis?	AP is a sudden inflammation of the pancreas that can range from mild cases to more severe forms with necrosis and systemic complications, presenting a wide clinical spectrum with significant risk of morbidity and mortality.	Strong recommendation; moderate quality evidence
How is acute pancreatitis diagnosed? What is the role of imaging studies?	- Diagnosis of acute pancreatitis requires at least two of three criteria: Typical abdominal pain, elevated serum pancreatic enzymes (more than 3 times the upper limit of normality), or characteristic imaging. - It is mainly a clinical and laboratory diagnosis; imaging is used when presentation is atypical.	Strong recommendation; moderate quality evidence Strong recommendation; low-quality evidence
How should the etiology of acute pancreatitis be assessed?	- Initial assessment includes clinical history, physical examination, liver profile, triglycerides, calcium, and abdominal ultrasound. Contrast-enhanced CT is recommended if malignancy is suspected. - If the cause is unclear, follow-up may include repeat ultrasound, labs, EUS and/or MRCP; contrast-enhanced CT is a secondary option. - Genetic and/or immunological testing may be considered for recurrent idiopathic cases.	Strong recommendation; low-quality evidence Strong recommendation; low-quality evidence Strong recommendation; low-quality evidence
What is the definition of acute idiopathic pancreatitis? What is the definition of acute recurrent pancreatitis?	- Idiopathic AP is defined as AP with no identifiable cause after thorough history, lab workup, and at least one advanced imaging test (EUS and/or MRCP). - RAP is defined as two or more distinct AP episodes, separated by over 3 months of complete resolution.	Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence
How should pancreatitis secondary to hypertriglyceridemia be diagnosed and managed?	- Diagnosis: Levels > 1000 mg/dL confirm AP cause if no other etiology is found; > 500 mg/dL indicates high likelihood. - Treatment: Lower TG levels rapidly with fasting and insulin; blood purification may be considered if TG > 5000 mg/dL. - Start oral fibrates once feeding resumes.	Strong recommendation; moderate quality evidence Strong recommendation; low-quality evidence Conditional recommendation; low-quality evidence
How should the severity of acute pancreatitis be classified? How can severity be predicted early in the course of disease?	- Severity of acute pancreatitis should be classified using Revised Atlanta Classification, based on OF and local and systemic complications. - For early prediction, BISAP and persistent SIRS are recommended due to their simplicity despite limited accuracy.	Strong recommendation; moderate quality evidence Strong recommendation; low-quality evidence
Which patients with acute pancreatitis should be admitted to an intensive care unit?	Early ICU admission is recommended for patients with OF unresponsive to initial resuscitation or with IPN and systemic	Strong recommendation; moderate quality evidence

(Continues)

TABLE 1 | (Continued)

Clinical question	Evidence-based answer Recommendation	Grade Evidence level
	compromise. Patients with persistent (> 48 h) single or multiple OF should also be managed in the ICU.	
What type and rate of fluid resuscitation should be used in acute pancreatitis?	- Intermediate care admission is recommended for predicted severe AP (BISAP ≥ 3, persistent SIRS), isolated organ failure responsive to treatment, or early IAH. If unavailable, close monitoring is advised. - Moderate fluid resuscitation (1.5 mL/kg/h) is recommended, with optional 10 mL/kg bolus in hypovolemic patients. - Lactated Ringer's solution is preferred due to potential anti-inflammatory benefits.	Strong recommendation; moderate quality evidence Strong recommendation; high-quality evidence Strong recommendation; moderate quality evidence
How should pain be managed in acute pancreatitis?	- Pain management should be multimodal, using NSAIDs and/or opioids based on pain severity and patient factors. - Mild cases may respond to NSAIDs and paracetamol, while moderately severe to severe pain may require strong opioids or epidural analgesia, with gradual de-escalation.	Strong recommendation; moderate quality evidence Strong recommendation; moderate quality evidence
What is the role of antibiotic therapy in the management of acute pancreatitis?	- Antibiotics are not recommended prophylactically in necrotizing pancreatitis; use only for confirmed or suspected bacterial infections. If needed, use high-dose broad-spectrum antibiotics. - Procalcitonin can guide antibiotic use.	Strong recommendation; high-quality evidence Strong recommendation; moderate quality evidence
When should prophylaxis for deep vein thrombosis and pulmonary embolism be indicated in acute pancreatitis?	- Antifungals should be used only if fungal infection is suspected or confirmed. - Pharmacological thromboprophylaxis is recommended in moderate/severe AP or in case of high thrombotic risk without bleeding risk. - It is not routinely advised in mild AP. - Mechanical methods may be used if bleeding risk is high, switching to pharmacological once safe.	Strong recommendation; low-quality evidence Strong recommendation; low-quality evidence Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence
How should nutritional support be managed in acute pancreatitis? When and how should oral feeding be restarted?	- Early oral feeding (< 24–48 h) is recommended in all cases if tolerated; in mild AP, it may be started immediately with a soft or solid diet. - If oral intake is not tolerated after 3–4 days, initiate enteral nutrition via nasogastric tube (or nasojejunal tube if gastric outlet obstruction is present); reserve parenteral nutrition for when all other routes fail.	Strong recommendation; moderate quality evidence Strong recommendation; moderate quality evidence
What are the indications for early ERCP in acute pancreatitis?	Urgent ERCP (≤ 24 h) is recommended in acute cholangitis complicating AP.	Strong recommendation; high-quality evidence

(Continues)

TABLE 1 | (Continued)

Clinical question	Evidence-based answer Recommendation	Grade Evidence level
How should abdominal compartment syndrome be diagnosed and managed?	- In patients with choledocholithiasis without acute cholangitis, ERCP can be delayed, as early intervention does not improve outcomes. - IAH is defined as IAP > 12 mmHg; abdominal compartment syndrome is defined as IAP > 20 mmHg with new onset OF. - ICU patients with AP should undergo IAP monitoring; management includes medical measures (sedation, nasogastric and rectal tubes, prokinetics), percutaneous drainage, and even decompressive laparotomy if abdominal compartment syndrome persists.	Conditional recommendation; moderate quality evidence Strong recommendation; moderate quality evidence Strong recommendation; moderate quality evidence
How should DPDS be diagnosed and managed?	- MRCP is recommended as the first-line diagnostic modality for suspected DPDS; secretin-enhanced MRCP is preferable, when available, due to its higher diagnostic sensitivity. Besides, amylase measurement in drained fluid helps detect DPDS. - Endoscopic transluminal drainage is favored over ERCP in complete duct disruption. - Long-term plastic stent placement is advised in symptomatic cases. - MRCP is recommended before stent removal to assess duct integrity. - Surgical timing in DPDS is unclear; a step-up approach is generally preferred, reserving surgery for refractory cases	Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence Strong recommendation; low-quality evidence Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence
How should sterile and infected (peri) pancreatic collections be diagnosed and managed?	- Contrast-enhanced CT is effective for diagnosing PPPC, while MRI provides superior characterization of their contents when necessary. - Broad-spectrum antibiotic therapy should be reserved for confirmed or suspected infections, with prophylactic use not recommended. - When intervention is required, delaying it for at least 4 weeks is preferred. - Percutaneous drainage is indicated when early drainage (< 4 weeks) is needed, endoscopy or surgery is not feasible, collections are inaccessible by other means or as a combination treatment with endoscopic drainage. - Endoscopic drainage and/or necrosectomy is preferred when technically feasible	Conditional recommendation; low-quality evidence Strong recommendation; high-quality evidence Strong recommendation; high-quality evidence Strong recommendation; moderate quality evidence Strong recommendation; high-quality evidence

(Continues)

TABLE 1 | (Continued)

Clinical question	Evidence-based answer Recommendation	Grade Evidence level
How should (peri)pancreatic vein thrombosis and left-sided portal hypertension be managed?	- Minimally invasive surgical necrosectomy is recommended if percutaneous or endoscopic approaches fail. - Therapeutic anticoagulation may be considered in acute portal vein thrombosis, multi-vessel splanchnic vein thrombosis, or progressive splenic vein thrombosis. - Thrombophilia testing is recommended post-acute episode to guide recurrence risk and treatment duration. - Treatment involves LMWH followed by oral anticoagulants for 3–6 months; discontinue after resolution or absent recanalization, except in thrombophilia. - Current evidence does not support beta-blockers or endoscopic therapy for primary or secondary bleeding prevention in left-sided non-cirrhotic portal hypertension.	Strong recommendation; high-quality evidence Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence
When should cholecystectomy be performed in patients with biliary acute pancreatitis?	- In mild AP, laparoscopic cholecystectomy should be performed during the index hospitalization. - In moderately severe to severe cases, cholecystectomy should be delayed until 8 weeks post-discharge or after resolution of local complications.	Strong recommendation; moderate quality evidence Conditional recommendation; low-quality evidence
When and how should choledocholithiasis be ruled out in acute pancreatitis?	- In mild or predicted severe AP without cholangitis but with persistent cholestasis or duct dilation, testing may be delayed up to 1 week if the patient is clinically stable. If cholestasis resolves and ducts are non-dilated, no further testing is needed. - In mild biliary ap with high suspicion choledocholithiasis scheduled for early cholecystectomy, preoperative biliary exploration is advised when one of the following criteria are met: - bilirubin > 70 $\mu\text{mol/L}$ (4 mg/dL) - common bile duct > 6 mm with bilirubin 30–70 $\mu\text{mol/L}$ (1.75–4 mg/dL) - signs of cholangitis. - MRCP or EUS should be used in uncertain cases due to their high accuracy to detect lithiasis.	Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence Strong recommendation; low-quality evidence
When and how should pancreatic exocrine and endocrine insufficiency be assessed and managed following acute pancreatitis?	- Assessment of pancreatic function is recommended in patients with necrotizing AP, alcoholic etiology, recurrent forms, patients undergoing necrosectomy or with metabolic risk factors. - Fecal elastase is suitable for PEI screening, while endocrine function should be evaluated with fasting glucose, HbA1c, and/or C-peptide.	Conditional recommendation; low-quality evidence Conditional recommendation; low-quality evidence

(Continues)

TABLE 1 | (Continued)

Clinical question	Evidence-based answer Recommendation	Grade Evidence level
	Empirical PERT may be considered, when resuming oral feeding, in extensive necrosis or necrosectomy and in patients with symptoms of maldigestion.	Conditional recommendation; low-quality evidence
	Treatment includes PERT for PEI and standard diabetes therapy for endocrine insufficiency.	Conditional recommendation; low-quality evidence
	Follow-up is advised at 3, 6, and 12 months, and then every 6–12 months if dysfunction persist, through laboratory and clinical monitoring.	Conditional recommendation; low-quality evidence

Abbreviations: AP, acute pancreatitis; BISAP, bedside index for severity in acute pancreatitis; CT, computed tomography; DPDS, disconnected pancreatic duct syndrome; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; HbA1c, glycated hemoglobin; IAH, intra-abdominal hypertension; IAP, intra-abdominal pressure; ICU, intensive care unit; IPN, infected pancreatic necrosis; LMWH, low molecular weight heparin; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography; NSAIDs, non-steroidal anti-inflammatory drugs; OF, organ failure; PEI, pancreatic exocrine insufficiency; PERT, pancreatic enzyme replacement therapy; PPC: pancreatic or peripancreatic collection; RAC, revised atlanta classification; RAP, recurrent acute pancreatitis; SIRS, systemic inflammatory response syndrome; TG, triglycerides.

How should etiology be assessed?

First step - On admission

- Anamnesis
 - Toxic habits (alcohol intake, smoking, drugs of abuse)
 - Personal and family history of biliopancreatic diseases
 - Comorbidities, recent infections, autoimmune diseases, constitutional syndrome, surgeries, medical procedures or abdominal trauma
- Blood tests
 - Liver tests (ALT, AST, ALP, GGT, bilirubin)
 - Calcium
 - Triglycerides
- Transabdominal ultrasound
- Consider abdominal contrast-enhanced CT if pancreatic cancer alarm symptoms are present



Second step - Follow-up (starting 4 weeks after AP)

- Second transabdominal ultrasound and blood test
- EUS and/or MRCP (secretin-enhanced if available)
- Consider contrast-enhanced CT with pancreas protocol in those cases in which EUS and/or MRI/MRCP are not available. Patients over 50 years and not proven etiology should undergo cross-sectional image to rule out malignancy.



Third step – Recurrent IAP

- Consider IgG4 determination
 - Elevation of this alone is not diagnostic of autoimmune pancreatitis. It must be interpreted carefully alongside other suggestive clinical, radiological and histological findings
- Conduct genetic testing
 - If etiology remains unknown, especially in younger patients or those with a family history of pancreatic diseases

FIGURE 1 | Algorithm for etiological diagnosis. ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CT, computed tomography; EUS, endoscopic ultrasound; GGT, gamma-glutamyl transferase; MRCP, magnetic resonance cholangiopancreatography; MRI, magnetic resonance imaging.

to 87% [46, 47]. EUS demonstrates high sensitivity and specificity (> 90%) in detecting microlithiasis, biliary sludge, and small (< 2 cm) biliopancreatic and periampullary lesions, providing an etiological diagnosis in over 30% of idiopathic cases [48–62]. It can replace the second TUS if readily available; otherwise, it can be performed afterward. A meta-analysis revealed that EUS has higher diagnostic accuracy than MRCP (64% vs. 34%) in the etiological diagnosis of presumed idiopathic AP [55]. EUS should be performed 4–6 weeks post-episode, when inflammation subsides, to improve diagnostic accuracy

[63]. Conversely, secretin-MRCP may be superior to EUS in patients with anatomical alterations of the biliopancreatic duct system or those who have undergone cholecystectomy and complement the results from EUS [64–67]. Some studies suggest that MRCP with neostigmine stimulation may be an alternative to secretin-MRCP, offering comparable stimulation of pancreatic juice production and enhanced visualization of the ductal system, but limited evidence precludes any definitive recommendation [68, 69]. Secretin is not widely available in many regions targeted by this guideline and is associated with a higher

cost. Consequently, MRCP without secretin is an appropriate and pragmatic alternative and is generally far more accessible than EUS in most Latin American countries.

Contrast-enhanced CT should not be used routinely for etiological assessment during the acute phase; rather, its role is limited to cases with clear clinical suspicion of associated pancreatic malignancy or as a fallback diagnostic option when EUS or MRCP are unavailable, particularly in patients over 50 years of age without an identified cause or in younger patients with additional risk factors [42, 43].

Isolated IgG4 elevation has low sensitivity (64%) and high specificity (93%) for type 1 autoimmune pancreatitis [70]. It is not diagnostic on its own; other clinical, radiologic, and histologic criteria should be considered alongside. Therefore, routine IgG4 testing is not recommended except in cases of recurrent AP or when clinical or imaging features raise suspicion for autoimmune disease [47, 71].

Genetic testing for *PRSS1*, *SPINK1*, *CFTR*, *CTRC*, *CLDN2*, and *CPA1* is not indicated after a first episode of acute pancreatitis (AP). It is, however, recommended in cases of idiopathic recurrent AP or in high-risk individuals, such as patients under 35 years of age, who often have distinct etiological profiles [72–74], and/or family history of pancreatic disease [75, 76].

We acknowledge that access to advanced imaging modalities and specialized endoscopic or diagnostic procedures, varies across different Ibero-Latin American regions and may not be available. Therefore, their use should be adapted to local resource availability.

3.1.4 | Q4. What is the Definition of Idiopathic Acute Pancreatitis? What is the Definition of Recurrent Acute Pancreatitis?

3.1.4.1 | Statements and GRADE.

- Idiopathic AP is defined as AP with no identifiable cause after a comprehensive diagnostic workup, including clinical history, laboratory tests, and TUS to exclude common biliary, toxic, and metabolic causes, as well as at least one advanced imaging modality (EUS and/or MRCP), as outlined in prior recommendations. *Weak recommendation, low-quality evidence.*
- Recurrent acute pancreatitis (RAP) is defined as two or more well-documented separate attacks of AP, with complete clinical resolution for more than 3 months between them. *Weak recommendation, low-quality evidence.*

3.1.4.2 | Remarks. AP should not be classified as idiopathic without a complete and thorough diagnostic evaluation, previously discussed. This evaluation must include at least one advanced diagnostic technique, such as EUS or MRCP [47, 54, 55, 57, 77, 78]. When access to these techniques is limited, a contrast-enhanced CT may serve as an alternative, though its diagnostic accuracy in determining etiology is lower. While

recent evidence advocates performing both EUS and MRCP in case of EUS negativity because of their complementary diagnostic value, limited access—especially to EUS—in many Latin American settings led the panel to agree that performing at least one advanced imaging test is a pragmatic and feasible approach.

RAP occurs in approximately 10%–30% of patients after a first AP episode [47, 54, 55, 57, 77–79]. In some cases, RAP progresses to chronic pancreatitis during follow-up [77]. Current recommendations for evaluating patients with RAP vary; however, a comprehensive assessment using advanced imaging is essential. If radiological studies yield negative results and RAP persists, further tests including measurement of IgG4 levels and genetic analysis are recommended [55, 77, 78]. Emerging evidence suggests that many patients with idiopathic AP and RAP may possess complex genetic predispositions [80, 81]. In this context, we recommend implementing the diagnostic algorithm outlined in the preceding question.

3.1.5 | Q5. How Should Pancreatitis Secondary to Hypertriglyceridemia Be Diagnosed and Managed?

3.1.5.1 | Statement and GRADE.

- In the AP setting, TG levels should be measured at admission. TG levels above 1000 mg/dL or grossly lipemic serum in the absence of alcohol abuse or other etiologies should be considered the definitive cause of AP. In the absence of other etiology, levels > 500 mg/dL should raise a high suspicion of causality. *Strong recommendation, moderate quality evidence.*
- Rapid reduction of TG levels below 1000 mg/dL should be obtained based on conventional therapies, including fasting and insulin treatment. *Strong recommendation, low-quality evidence.*
- Blood purification methods may be considered in individual cases with very high TG levels (> 5000 mg/dL) not responding to insulin, but studies showing improved outcomes are lacking. *Strong recommendation, moderate quality evidence.*
- Oral fibrates should be started once oral feeding is possible, as maintenance therapy is advised to prevent recurrence. *Weak recommendation, low-quality evidence.*

3.1.5.2 | Remarks. HTG is the third most frequent identifiable cause of AP [38]. A well-defined threshold for classifying HTG as the etiology of AP has not been firmly established; however, it is widely accepted that triglyceride levels exceeding 1000 mg/dL should be considered a significant causal factor for AP. Alcohol increases TG levels and must be considered. In a retrospective cohort of 129 patients with severe HTG (TG > 1000 mg/dL), 20% of them presented at least one attack of AP [82]. Another retrospective study on 95 patients referred to a lipid control program with TG > 1772 mg/dL found 15.8% had a history of AP compared to none in 91 patients with TG 886–1772 mg/dL, suggesting a

low risk of AP when TG levels are < 1772 mg/dL [83]. Nonetheless, in a large population study, the adjusted hazard ratio (HR) for AP was 3.20 (95% CI 1.99–5.16) in a group with TG levels > 500 mg/dL when compared with a group with TG levels < 150; there was 4% increase in AP for every 100 mg/dL increase in TG concentration [84]. In a prospective cohort of 116,550 patients followed 6.7 years, the HR of AP increased progressively with rising TG levels: HR 2.3 (95% CI, 1.3–4.0; 5.5 events/10,000 person-years) for TG 177–265 mg/dL to HR of 8.7 (95% CI, 3.7–20.0; 12 events/10,000 person-years) for individuals with TG > 443 mg/dL [85].

Although it has not been proven that rapid reduction of TG levels improves the prognosis of HTG-induced AP, specific treatments aim to prevent the ongoing damage induced by free fatty acids and hyperviscosity. While no RCTs have evaluated fasting or insulin therapy, both have proven effective and safe in observational studies, with insulin infusion adding glycemic control in diabetic patients. A case-control series comparing fasting to insulin infusion showed both approaches reduced TG levels < 1000 mg/dL by day three, with no significant differences and minimal risk of hypoglycemia, even in non-diabetics [86]. A retrospective analysis of 77 patients with HTG-induced AP (74% with diabetes mellitus) receiving intravenous insulin showed that half of them reached TG < 1000 mg/dL in 36 h [87]. The insulin doses reported in the published evidence vary depending on whether the patient had pre-existing diabetes (0.1 UI/kg/h) or not (1–2 UI/kg/day) and are typically adjusted by body weight and close clinical and biochemical monitoring [87]. The role of heparin, alone or in combination with insulin, remains controversial. In two small-sample studies, it was associated with increased chylomicron levels and rebound hypertriglyceridemia [88, 89]. Blood purification therapies (plasmapheresis, high-volume hemofiltration, and double-filtration plasma apheresis) have been evaluated in two meta-analyses, both showing that TG reduction is faster with blood purification than with insulin with/without heparin. However, this is not associated with a reduction in organ dysfunction or mortality but with increased costs and complications, so its use is controversial [90–93].

Fibrates are highly effective at lowering triglyceride levels and are recommended by multiple medical societies as a first-line therapy for hypertriglyceridemia [94–96], which is why they are considered maintenance treatment after HTG-induced AP. Despite this, their effectiveness in preventing recurrent AP has not been confirmed by clinical trials. Other long-term strategies include omega-3 fatty acids [97–99], lifestyle modifications, and alcohol withdrawal [100, 101].

3.1.6 | Q6. How Should Severity Be Classified? How to Predict Severity Early in the Course of Disease?

3.1.6.1 | Statement and GRADE.

- The severity of AP should be assessed and classified based on the presence or absence of organ failure (OF) and the occurrence of local and/or systemic complications. *Strong recommendation, moderate quality evidence.*
- Both the Determinant-Based Classification (DBC) and the RAC effectively classify severity and are comparable.

However, RAC is recommended given its widespread use in both clinical practice and research. *Strong recommendation, moderate quality evidence.*

- The accuracy of the various factors and scores in the early prediction of severe AP is limited. The BISAP score and the presence of persistent SIRS are recommended for routine clinical use because of their simplicity and reasonable predictive utility. *Strong recommendation, low-quality evidence.*

3.1.6.2 | Remarks. Currently, there are two main classifications for assessing AP severity: the RAC and the DBC [4, 102]. In both systems, severity is determined by the presence of local or systemic complications, as well as transient (≤ 48 h) or persistent (> 48 h) OF involving the lungs, kidneys, and/or cardiovascular system. The DBC further distinguishes between sterile and infected pancreatic necrosis (IPN). The DBC categorizes AP severity as mild, moderate, severe, or critical, whereas the RAC stratifies severity as mild, moderately severe, or severe. Although both classifications are comparable in assessing severity, the DBC's severe categories may not always accurately reflect clinical outcomes [5, 103–105] (Table 2).

Clinical and laboratory parameters such as advanced age [5, 106, 107], sarcopenia, body-mass index > 30 [107–112], comorbidity [107], increased serum blood urea nitrogen > 20 mg/dL [113, 114], hematocrit > 44% [115–117], C-reactive protein (CRP) ≥ 190 mg/L [118–120], SIRS (particularly persistent SIRS > 48 h) [121, 122] and procalcitonin correlating with IPN [123, 124] demonstrated an association with higher risk of severe AP development. Other inflammatory markers (e.g., polymorphonuclear elastase [125], TNF-alpha, IL-6, and IL-8) showed predictive accuracy for severe AP in observational studies, but remain unavailable in most centers [125–129].

Numerous scoring systems, such as Ranson's criteria, Glasgow criteria, SIRS criteria, Acute Physiology and Chronic Health Evaluation II (APACHE II), Panc 3, Pancreatitis Outcome Prediction, BISAP [130], CT Severity Index, the revised Japanese Severity Score, and Harmless Acute Pancreatitis Score have been developed to predict severe AP by combining clinical, analytical, and radiological parameters. Typically, they are applied at admission (except for imaging-based scores, which require established local complications), while Ranson and Glasgow scores also rely on 48 h of data. Despite their widespread use, they have limited accuracy (70%–80%) with a high negative but low positive predictive value for severe AP [130–139]. The Pancreatitis Activity Scoring System, a promising tool, tracks clinical progression but has limited accuracy at a single time point [131, 132]. A recent systematic review and meta-analysis evaluating the most commonly used scores found that pretest probabilities of severe AP ranged 16.6%–25.3%, while posttest probabilities for positive/negative scores were: BISAP 47%/6%, APACHE II 43%/5%, Ranson 48%/5%, and SIRS 40%/12% [140]. These findings highlight the ongoing challenges in prognostic accuracy and underscore the need for new predictive models. Emerging scoring systems using artificial intelligence offer promising potential for improvement [141].

TABLE 2 | Severity classification in acute pancreatitis: revised atlanta classification versus determinant-based classification.

Aspect		Revised Atlanta Classification (2012) [4]	Determinant-based classification (2012) [102]
Severity categories		- Mild - Moderately severe - Severe	- Mild - Moderate - Severe - Critical
Basis of classification		- Presence and duration of OF - Presence of local or systemic complications	- Presence of three key determinants: 1. Presence and duration OF 2. Necrosis 3. IPN
Severity categories	Mild	- No OF - No local or systemic complications	- No OF - No necrosis - No IPN
	Moderately severe/ Moderate	- Transient OF (≤ 48 h) And/or - Local or systemic complications	- Sterile necrosis And/or - Transient OF
	Severe	- Persistent OF (> 48 h)	- Presence of either: 1. Persistent OF 2. IPN
	Critical	*Not defined in RAC*	- Both, persistent OF and IPN present

Abbreviations: IPN, infected pancreatic necrosis; OF, organ failure; RAC, revised atlanta classification.

Given the limitations of existing scores (suboptimal accuracy, complexity, or limited availability), clinical practice often favors simpler tools. Among these, BISAP and SIRS are widely used due to their straightforward application and reasonable predictive utility.

3.1.7 | Q7. Which Patients Should Be Admitted to an Intensive Care Unit?

3.1.7.1 | Statement and GRADE.

- **Intensive Care Unit (ICU) Admission:** Early ICU admission is advised for patients with OF unresponsive to initial resuscitation or in the presence of concomitant IPN with systemic compromise, given the markedly increased risk of mortality. Patients with persistent (> 48 h) single or multiple OF should also be managed in the ICU. *Strong recommendation, moderate-quality evidence.*
- **Intermediate Care Unit Admission:** Admission to an intermediate care unit is recommended for patients with predicted severe AP (BISAP ≥ 3 , persistent SIRS), or isolated OF (e.g., hypotension, respiratory failure, or acute renal failure) responsive to initial management without (peri)pancreatic infection. If it is unavailable, close monitoring is advised. Patients with early signs of intra-abdominal hypertension (IAH) should also be considered for intermediate care, as progression to abdominal compartment syndrome carries a high risk of mortality. *Strong recommendation, moderate-quality evidence.*

3.1.7.2 | Remarks. ICU admission should be guided by the need for organ support in patients at high risk of adverse outcomes. OF and IPN are the main determinants of morbidity and mortality in AP, each independently linked to mortality rates

approaching 30% [142]. When both are present, the risk of death increases substantially [5, 142].

Early mortality is primarily driven by persistent OF. Persistent dysfunction of respiratory, cardiovascular, or renal systems for > 48 h strongly indicates severe disease and typically warrants intensive care, irrespective of initial severity scores. Clinical judgment, based on the progression of organ dysfunction and treatment response, remains essential for determining the appropriate level of care.

Late mortality is more commonly linked to IPN. A systematic review and meta-analysis involving > 6900 patients reported significantly higher mortality in IPN (28%) than in sterile necrosis (13%), with an odds ratio of 3.30 (95% CI, 2.81–3.88) [143].

Finally, observational studies have identified IAH (see question 14) in critically ill patients as a predictor of shock, respiratory and renal failure, and increased mortality. This reinforces the need for close monitoring and potential escalation of care in patients with early signs of abdominal compartment syndrome [144].

3.1.8 | Q8. Fluid Resuscitation: What Type and Volume Rate?

3.1.8.1 | Statement and GRADE.

- Moderate fluid resuscitation, defined as an infusion rate of 1.5 mL/kg/h, is recommended. It should be preceded by an initial bolus of 10 mL/kg administered over 2 h in patients with signs of hypovolemia at admission. This bolus may be repeated during hospitalization if hypovolemia persists or appears. In the event of fluid overload, fluid volume must

be reduced or discontinued. *Strong recommendation, high-quality evidence.*

- Lactated Ringer's solution is recommended as the fluid of choice due to its apparent anti-inflammatory properties and improved AP outcomes. However, high-quality studies are needed to establish a robust recommendation. *Strong recommendation, moderate quality evidence.*

3.1.8.2 | Remarks. The WATERFALL trial, which randomized 249 patients with AP to aggressive (20 mL/kg bolus plus 3 mL/kg/h infusion) versus moderate fluid resuscitation (1.5 mL/kg/h infusion preceded by 10 mL/kg bolus only in patients with hypovolemia), demonstrated higher fluid overload with aggressive therapy (20.5% vs 6.3%; adjusted relative risk (RR) 2.85, 95% CI, 1.36 to 5.94; $p = 0.004$), without efficacy benefit [145]. Based on this, moderate fluid resuscitation is recommended [146–153]. Subsequent meta-analyses validated these findings [154–157].

Some RCTs comparing lactated Ringer's solution with normal saline have shown lower incidence of SIRS and CRP levels within 24–48 h (both surrogate variables) [158–162], fewer ICU admissions, and shorter hospital stays in the lactated Ringer's solution groups [163]. Recent meta-analyses also reported a lower incidence of local complications, moderately severe to severe AP, ICU admission, and mortality with lactated Ringer's solution [164–167]. In cell culture, it reduces macrophage inflammatory activation [160], which could explain its benefit. However, the heterogeneity and bias in current studies, mostly surrogate-based, underscore the need for well-designed multicenter RCTs with strong endpoints (e.g., severity) to consolidate these recommendations.

Hydroxyethyl starch, a colloid, is discouraged in AP due to increased adverse events and OF compared with lactated Ringer's solutions or normal saline [151].

3.1.9 | Q9. How to Manage Pain?

3.1.9.1 | Statements and GRADE.

- Pain management should follow a multimodal approach based on nonsteroidal anti-inflammatory drugs (NSAIDs) and/or opioids. The selection of analgesics should be guided by patient characteristics, comorbidities, pain intensity, and AP severity. *Strong recommendation, moderate quality evidence.*
- For patients with mild AP and/or low-intensity pain, treatment with NSAIDs and paracetamol (opioid-sparing) may suffice. Escalation to weak or strong opioids can be considered, if necessary, for adequate pain control. *Strong recommendation, moderate quality evidence.*
- For patients with moderate to severe pancreatitis and/or high-intensity pain, options could include bolus or continuous infusions of NSAIDs, strong opioids (alone or combined with NSAIDs), or epidural analgesia. This “Step-Down” approach should be continued with a gradual de-escalation of analgesic treatment, guided by effective pain

control and the patient's clinical progress. *Strong recommendation, moderate quality evidence.*

- NSAIDs should be carefully used or avoided in patients with acute or chronic renal failure. *Strong recommendation, low-quality evidence.*

3.1.9.2 | Remarks. Pain relief is a clinical priority in AP management, as it mitigates the stress response and improves patient well-being [168]. However, analgesia practices remain inconsistent across clinical settings, and systematic reviews of RCTs comparing different analgesics have shown a low overall evidence quality, failing to clearly favor any class or method [169–171]. As no internationally accepted, evidence-based analgesic algorithm exists for AP, most centers adopt a pragmatic step-up approach aligned with the World Health Organization analgesic ladder, although this has not been formally validated in AP. A more detailed United European Gastroenterology guideline on pain management in AP is currently under development and will address this topic in greater depth.

Pain severity assessment should consider patient characteristics and comorbidities when selecting an appropriate analgesic. For instance, NSAIDs require caution in patients with renal failure [172, 173]. Although clinical trials in AP have not demonstrated an increased risk of acute kidney injury or gastrointestinal bleeding, these studies may have been underpowered to detect such outcomes [169]. Two RCTs showed improved outcomes with COX-2 inhibitors, including fewer local complications and OF [174, 175], however, they should be used with caution in patients with known or suspected cardiovascular disease, and further studies are needed to confirm these findings.

In clinical practice, many patients ultimately require weak or strong opioids despite initiation with simple analgesics. A step-down strategy has been proposed by some experts, but the absence of robust studies prevents formal recommendations at this time [176].

Opioids remain the most prescribed analgesic for AP pain relief due to their potency, despite the heterogeneity of results from RCTs comparing them with NSAIDs [174, 177–181]. Furthermore, a recent meta-analysis has suggested comparable effectiveness and similar adverse event profiles between the two treatment types [182]. Combining different classes (paracetamol, NSAIDs, opioids) with distinct mechanisms allows effective pain relief with lower doses of each drug [183–186].

Growing evidence supports the use of epidural analgesia for pain management, offering superior pain control in the first 24 h and comparable effectiveness to opioids at 48 h [169]. Benefits may be associated with improved splanchnic perfusion and redistribution of blood flow to underperfused pancreatic areas, potentially enhancing outcomes [186–191]. However, a recent RCT has not consistently demonstrated benefits [192]. Given these potential advantages, epidural analgesia should be considered as an alternative or adjunct to intravenous analgesia, especially in patients requiring high opioid doses or at risk of opioid-related adverse events (e.g., respiratory failure, obesity), in the first 24 h [176].

There is no evidence supporting the use of parenteral local anesthetics (e.g., procaine) [193–195]. The usefulness of alternative therapies such as acupuncture remains unclear [196, 197]. Further research is needed to (A) optimize the use of opioids and non-opioids, alone or in combination, in patients with AP; B) determine the clinical indications and timing for epidural analgesia within a step-down analgesic approach.

3.1.10 | Q10. What is the Role of Antibiotic Therapy in the Management of Acute Pancreatitis?

3.1.10.1 | Statements and GRADE.

- Routine prophylactic antibiotic use is not recommended for necrotizing pancreatitis, as it does not significantly reduce pancreatic infection rates or mortality. *Strong recommendation, high-quality evidence.*
- Antibiotic treatment should be reserved for suspected or confirmed IPN, acute cholangitis, or other extrapancreatic infections. *Strong recommendation, high-quality evidence.*
- Employing procalcitonin as a biomarker could guide therapy, reducing unnecessary antibiotic use without compromising optimal outcomes. *Strong recommendation, moderate-quality evidence.*
- If required, antibiotics of choice are carbapenems, high-dose third-generation cephalosporins, and quinolones plus metronidazole. *Strong recommendation, high-quality evidence.*
- Antifungal prophylaxis is not advised; treatment is recommended only for highly suspected or confirmed fungal infection. *Strong recommendation, low-quality evidence.*

3.1.10.2 | Remarks. High-quality RCTs and meta-analyses over 2 decades consistently show prophylactic antibiotics do not significantly reduce IPN, surgical need, or mortality [198–208]. A recent meta-analysis of 21 trials involving 1383 patients found fewer overall infections (RR 0.60; 95% CI 0.49–0.74), mainly due to lower rates of sepsis (RR 0.43; 95% CI 0.25–0.73) and urinary infections (RR 0.46; 95% CI 0.25–0.86), but no significant decrease in IPN (RR 0.81; 95% CI 0.63–1.04) or mortality [200]. Therefore, prophylactic antibiotics in AP are discouraged because they have no impact on pancreatic outcomes and carry a risk of resistant strains.

Empiric antibiotics must be initiated in necrotizing pancreatitis with confirmed or strongly suspected infection. These recommendations should be applied within an antimicrobial stewardship framework, ensuring that antibiotic selection and duration are guided not only by suspected infection and pancreatic penetration but also by local resistance patterns and microbiological epidemiology. Common choices include carbapenems, high-dose third-generation cephalosporin, and quinolones plus metronidazole [203, 209]. Procalcitonin-guided therapy can minimize unnecessary use [210, 211]. In one RCT, 45% of patients in the procalcitonin-guided group received antibiotics when procalcitonin ≥ 1.0 ng/mL, compared with 63% in the standard care group, with an adjusted risk difference of -15.6% (95% CI -27.0 to -4.2 ; $p = 0.0071$). No significant

differences in hospital-acquired infections, secondary effects, or mortality were noted [211].

Patients with necrotizing AP are at increased risk of fungal infections, particularly with extended ICU stays, central venous catheters, parenteral nutrition, and prolonged broad-spectrum antibiotics [212, 213]. Invasive candidiasis occurs in up to 18% of ICU-treated severe AP [214] and 27% of cases treated for infected walled-off necrosis [215]. Nonetheless, prophylactic antifungal therapy is not advised, as no RCT has confirmed its efficacy. Antifungal treatment should be reserved for confirmed or highly suspected fungal infections.

3.1.11 | Q11. When Should Prophylaxis of Venous Thromboembolism Prophylaxis Be Given?

3.1.11.1 | Statement and GRADE.

- Pharmacological thromboprophylaxis is recommended for patients with predicted or established moderately severe to severe AP or those at high risk of thrombosis, provided they do not have an increased bleeding risk. Although specific studies in AP are lacking, this intervention has been shown to improve hospital outcomes in patients with limited mobility and acute inflammatory conditions. *Strong recommendation, low-quality evidence.*
- There is insufficient evidence to support thromboprophylaxis in patients with mild AP without high thrombosis risk. *Weak recommendation, low-quality evidence.*
- In patients who are actively bleeding or at high risk of bleeding, mechanical thromboprophylaxis (graduated compression stockings or intermittent pneumatic compression) may offer benefits over no intervention. However, pharmacological thromboprophylaxis should begin once the bleeding risk decreases. *Weak recommendation, low-quality evidence.*

3.1.11.2 | Remarks. Hospitalization for acute medical conditions increases the risk of venous thromboembolism [216]. Although AP-specific guidelines are lacking, available data indicate high rates of thromboembolic complications, particularly in necrotizing pancreatitis [217]. Risk assessment is challenging due to the heterogeneity of hospitalized medical patients. Numerous risk assessment models exist, each with distinct limitations. Among them, the Padua Prediction Score [218] effectively stratifies non-surgical inpatients into low- and high-venous thromboembolism risk groups.

Pharmacologic thromboprophylaxis using low-molecular-weight heparin, low-dose unfractionated heparin, or fondaparinux significantly reduces the incidence of symptomatic deep vein thrombosis and fatal pulmonary embolism in immobilized patients with acute inflammatory conditions, with minimal bleeding risk [219]. In studies involving patients with moderate to severe AP, heparin at prophylactic or therapeutic doses improves hospital outcomes and reduces local and systemic complications [220–223]. Two recent meta-analyses support these findings, showing a significant reduction in mortality and outcomes in the intervention group [224, 225].

Pharmacologic thromboprophylaxis is not advised in patients with active bleeding or high bleeding risk [226]. Major bleeding risk factors include active gastroduodenal ulcer, recent bleeding (3 months before admission), and platelet count $< 50 \times 10^9/L$ [226]. For these patients, indirect data from surgical populations suggest that graduated compression stockings or intermittent pneumatic compression may provide moderate effectiveness in preventing asymptomatic deep vein thrombosis and pulmonary embolism and are preferable to no prophylaxis [227, 228]. More high-quality AP-focused studies are needed to strengthen recommendations.

3.1.12 | Q12. How Should Nutritional Support Be Managed? When and How to Restart Oral Feeding?

3.1.12.1 | Statements and GRADE.

- Early oral feeding (within 24–48 h) is recommended for both mild and predicted severe AP if the patient feels able to eat. In mild cases, oral feeding may even be started immediately with a soft or solid diet. *Strong recommendation, high-quality evidence.*
- In patients unable to tolerate oral feeding 3–4 days after disease onset, enteral nutrition via nasogastric tube is preferred. The nasojejunal tube should be reserved for cases of difficult gastric emptying, proximal mechanical obstruction, or a high risk of aspiration. Parenteral nutrition should be reserved for cases in which oral and enteral nutrition are not feasible. *Strong recommendation, high-quality evidence.*

3.1.12.2 | Remarks. Traditionally, patients with AP were advised to fast for a few days for “pancreatic rest.” However, recent evidence shows that early feeding offers significant benefits. Six RCTs and two meta-analyses demonstrated that immediate refeeding in mild AP is safe, accelerates recovery, and does not increase gastrointestinal events [229–235]. Additionally, two other RCTs confirmed that a soft or solid diet is well tolerated and that there is no need to start with a liquid diet [236, 237]. Early feeding in these patients shortens hospital stay and reduces healthcare costs without raising complications [238].

For patients with moderately severe to severe AP, enteral nutrition within the first 3 days after disease onset is preferred over parenteral nutrition, which is associated with increased risk of infected pancreatic collections, organ failure, and mortality [235, 238–247]. A RCT by Bakker et al. found no benefit of early enteral tube feeding over on-demand enteral feeding (only in case of intolerance to oral feeding within 72 h), reducing tube placement in 67% of cases [248]. Therefore, enteral tube feeding is recommended only for patients unable to tolerate oral intake after 72 h. When required, both nasogastric or nasojejunal tubes may be used [249–255], with the nasogastric tube preferred if there is no gastric emptying obstruction, due to ease of placement and physiological advantage [252].

Seven meta-analyses suggest that immunonutritional support, such as supplementation with glutamine and omega-3 fatty acids, may improve clinical outcomes, particularly in severe AP

[256–262]. Conversely, probiotics are not recommended, as one RCT reported increased mortality with their use [263].

3.1.13 | Q13. What Are the Indications for Early Endoscopic Retrograde Cholangiopancreatography?

3.1.13.1 | Statements and GRADE.

- Urgent (≤ 24 h) ERCP is strongly recommended for patients with acute biliary pancreatitis and concurrent acute cholangitis. *Strong recommendation, high-quality evidence.*
- In patients with choledocholithiasis without cholangitis, ERCP may be delayed in the absence of acute cholangitis, as early ERCP is not associated with improved outcomes. *Weak recommendation, moderate-quality evidence.*

3.1.13.2 | Remarks. Initial studies suggested that early ERCP reduced complications in biliary AP [264–268], but limitations included heterogeneous populations (with or without cholangitis), non-uniform definitions of cholangitis, delayed ERCP timing, and inconsistent sphincterotomy. Studies excluding cholangitis showed no benefit of early ERCP [269–273].

A 2012 Cochrane meta-analysis [274] comprising 7 RCTs, including 2 with predicted severe biliary AP, found early ERCP did not reduce mortality or local/systemic adverse events compared to conservative treatment, regardless of severity. Subgroup analyses of patients with cholangitis revealed that early ERCP was associated with reduced mortality and adverse events. Based on this, urgent ERCP ≤ 24 h was recommended for biliary AP only in cases of cholangitis, and within 72 h for patients with ongoing biliary obstruction, whereas it was discouraged in the absence of cholangitis or biliary obstruction.

The recent APEC and APEC-2 multicenter RCTs [275, 276] demonstrated that early ERCP (≤ 24 h) in patients with predicted severe biliary AP with and without cholestasis, but without cholangitis, did not reduce mortality or major complications compared to conservative approach, defined as an ERCP performed only if cholestasis persisted or bile duct stones remained after recovery [275, 276]. This result was consistent even when ERCP was preceded by EUS-confirmed choledocholithiasis [277], supporting conservative management with delayed elective ERCP, even in patients with ongoing biliary obstruction.

3.1.14 | Q14. How to Diagnose and Manage Abdominal Compartment Syndrome?

3.1.14.1 | Statement and GRADE.

- IAH is defined as a persistent intra-abdominal pressure (IAP) > 12 mmHg, whereas abdominal compartment syndrome involves an IAP > 20 mmHg associated with a new onset OF. *Strong recommendation, moderate quality evidence.*
- IAP monitoring is recommended for all patients with AP requiring ICU admission. *Strong recommendation, moderate quality evidence.*

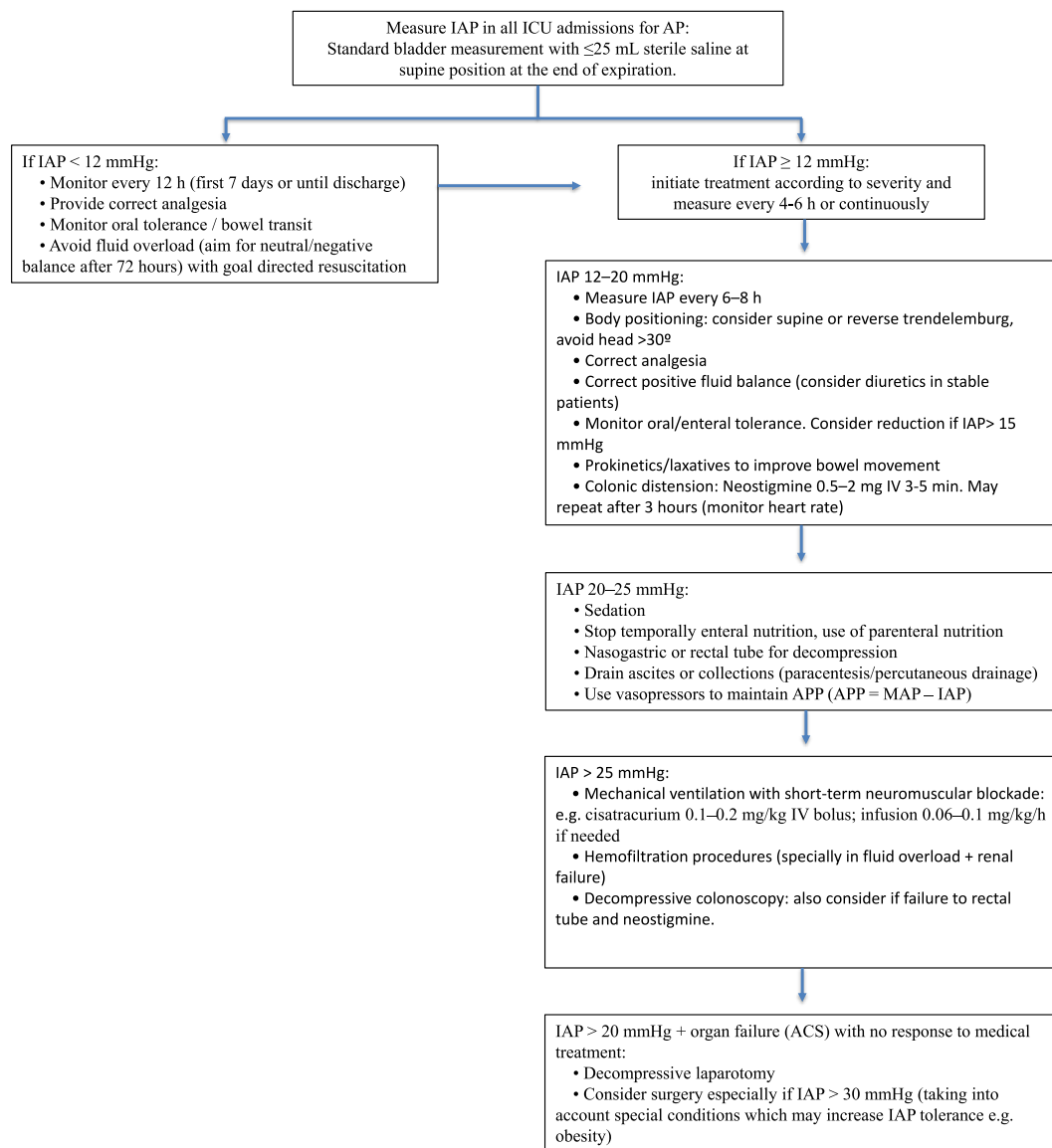


FIGURE 2 | Management of intra-abdominal hypertension (IAH). ACS, abdominal compartment syndrome; AP, acute pancreatitis; APP, abdominal perfusion pressure; IAP, intra-abdominal pressure; ICU, intensive care unit; IV, intravenous; MAP, mean arterial pressure.

- Medical management of IAH includes sedation, analgesia, neuromuscular blockade, supine positioning, vasoactive drugs, nasogastric suction, rectal tube, prokinetic/laxative agents, reduced or discontinued enteral nutrition, diuretics, and hemofiltration. *Strong recommendation, moderate quality evidence.*
- Percutaneous catheter drainage and paracentesis are preferred for fluid collections and ascites. *Strong recommendation, moderate quality evidence.*
- If medical or minimally invasive treatments fail and abdominal compartment syndrome develops, decompressive laparotomy is indicated. *Strong recommendation, moderate quality evidence* (Figure 2).

3.1.14.2 | Remarks. The 2013 World Society of the Abdominal Compartment Syndrome consensus criteria have

defined IAH and abdominal compartment syndrome over the last decade [278]. These conditions significantly contribute to increasing morbidity and mortality in AP, with elevated IAP causing pancreatic necrosis, intestinal ischemia, gut barrier dysfunction, and multiple OF [278, 279]. A systematic review of 226 patients with moderately severe to severe AP found prevalence rates of 66% for IAH and 38% for abdominal compartment syndrome, with 49% mortality in abdominal compartment syndrome [280].

High-quality studies on AP with IAH/abdominal compartment syndrome are scarce. The transvesical technique is commonly used to measure IAP [281]. Medical management of IAH follows a step-up approach; if there is no response, the next measures should be implemented. Initial measures include adequate sedation and analgesia, neuromuscular blockade (e.g., 0.15 mg/kg of cisatracurium [282], and supine position (with head-of-bed elevation < 20°) to improve abdominal compliance [278]. Vaso-

active agents help to maintain an abdominal perfusion pressure > 60 mmHg, while nasogastric suction and rectal tubes, prokinetics, laxatives, and reduced/discontinued enteral nutrition, reduce intraluminal contents [278]. An RCT showed that intramuscular neostigmine reduced IAP by ~20% by promoting peristalsis and defecation [283]. Diuretics and restrictive fluid resuscitation prevent volume overload [278].

Volume overload is a risk factor for IAH. Hemofiltration appears to induce volume depletion and the removal of inflammatory cytokines [284]. In a recent RCT of 74 severe AP patients, those with IAP > 20 mmHg treated with continuous veno-venous hemofiltration from one to seven days (vs conventional treatment) had negative fluid balance, shorter ventilation and ICU stay, and fewer operations at 28 days; no benefit was observed in patients with IAP < 20 mmHg [285].

Percutaneous drainage or paracentesis are other possible interventions. A retrospective case-control study of 206 AP patients showed lower mortality (3.7% vs. 8.2%), faster IAP reduction, and less OF with paracentesis [286]. A prospective cohort study of 105 AP patients found significant IAP reduction after percutaneous drainage (21.85 ± 4.53 mmHg to 12.5 ± 4.42 mmHg) in patients with IAH, with greater reduction linked to improved survival (63.3% vs. 36.7%, $p = 0.006$) [287] fewer complications (41.0% vs. 80.3%, $p < 0.001$), and mortality rates (18.9% vs. 52.5%, $p < 0.001$) compared to decompressive laparotomy in a retrospective study [288].

Percutaneous drainage is therefore a reasonable initial strategy, particularly when CT demonstrates large intra-abdominal fluid collections amenable to drainage [288]. Decompressive laparotomy, via midline xiphoid-pubic incision with vacuum-assisted closure is often reserved for abdominal compartment syndrome not responding to non-operative or percutaneous measures; however, when there is a clear temporal relationship between rising intra-abdominal pressure and progressive renal and/or respiratory failure, surgical decompression should be advocated and, in selected patients with rapidly progressive organ dysfunction early operative intervention may be indicated [278–280, 288, 289]. Although decompressive laparotomy rapidly reduces IAP, its effect on organ dysfunction is still uncertain, and the optimal timing or pressure threshold remains undefined [278–280, 288]. When indicated, surgical intervention seems to improve outcomes [289], while less invasive techniques, such as subcutaneous fasciotomy, require further study [288]. High-quality trials are needed to guide decompressive interventions.

3.1.15 | Q15. How to Diagnose and Manage Disconnected Pancreatic Duct Syndrome?

3.1.15.1 | Statements and GRADE.

- MRCP is recommended as the first-line diagnostic modality for suspected disconnected pancreatic duct syndrome (DPDS); secretin-enhanced MRCP is preferable, when available, due to its higher diagnostic sensitivity. *Weak recommendation, low-quality evidence.*

- In AP patients undergoing percutaneous drainage of fluid collections, measuring amylase in drained fluid is advised, given its high sensitivity for detecting DPDS. *Weak recommendation, low-quality evidence.*
- For suspected complete disruption of the main pancreatic duct associated with pancreatic necrosis, endoscopic transluminal drainage is preferred to transpapillary ERCP drainage, which adds no benefit, is technically demanding, and increases the risk of adverse events. *Weak recommendation, low-quality evidence.*
- Long-term placement of transluminal plastic stents is recommended for symptomatic (peri)pancreatic collections associated with DPDS. *Strong recommendation, low-quality evidence.*
- Before removing stents after endoscopic drainage of walled-off necrosis (WON), MRCP, preferably secretin-enhanced, is recommended to assess main duct integrity. *Weak recommendation, low-quality evidence.*
- Surgical timing in DPDS remains unclear; a step-up approach is generally preferred, with surgery reserved for refractory cases. *Weak recommendation, low-quality evidence.*

3.1.15.2 | Remarks. Acute necrotizing pancreatitis can rupture the pancreatic duct, causing pancreatic fluid leakage and collections. This complication occurs in ~25% of patients with necrotizing pancreatitis [290] and persistent leakage in 30%–50% of cases [291]. The diagnosis and management of DPDS are challenging, relying mainly on retrospective studies and complicated by the heterogeneity of clinical manifestations [291–293].

MRCP, preferably secretin-enhanced if available, is the recommended initial diagnostic test, with a pooled sensitivity of 83% and specificity of 100% according to a systematic review [294]. Secretin has a good safety profile and increases sensitivity by ~19% [295]. Timing is not standardized to exclude DPDS, but assessment is indicated if collections persist or before stent removal [293]. In patients undergoing percutaneous drainage, drained fluid amylase > 3 × serum levels showed 100% sensitivity and 50% specificity for DPDS [294].

Somatostatin analogs have no therapeutic role [296]. ERCP is useful for partial duct obstruction but is less effective for complete obstructions [297, 298]. EUS-guided drainage is the preferred method for symptomatic (peri)pancreatic collections associated with DPDS [293, 294, 299–301]. Evidence indicates that transpapillary drainage does not improve outcomes compared to transmural drainage in WON, and routine pancreatic duct stenting in combination with transluminal drainage is discouraged [302]. A systematic review reported a 92% success rate for endoscopic transluminal drainage of DPDS, with double pigtail plastic stents often left indefinitely [299]. A single-center RCT showed a lower recurrence rate with stents left in situ (0% vs. 38%), highlighting a higher recurrence risk after removal in DPDS [303]. Consequently, double-pigtail plastic stent placement is long-term recommended; if lumen-opposing metal stents (LAMS) are used initially, they should be replaced with a plastic stent within 4 weeks, [291, 304].

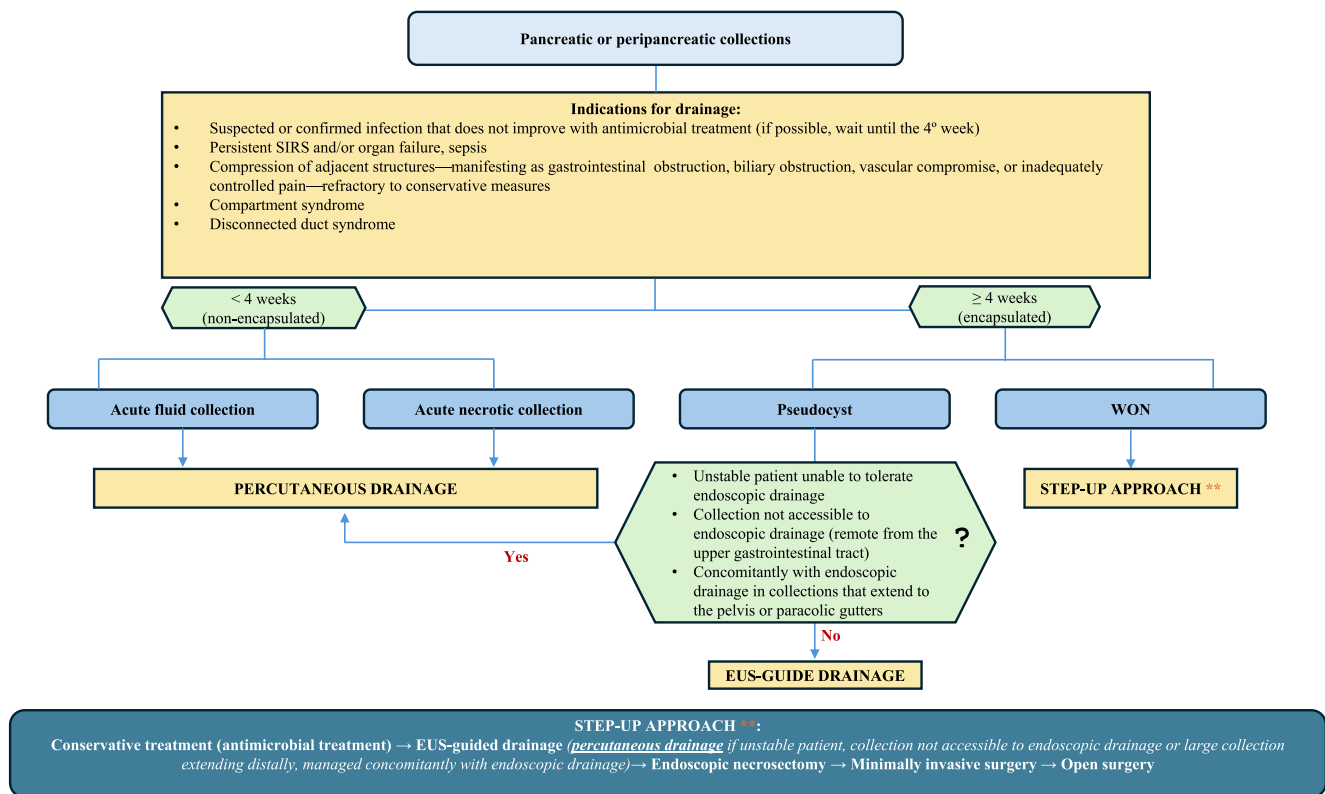


FIGURE 3 | Algorithm for diagnosis and management of sterile and infected pancreatic or peripancreatic collections. CECT: contrast enhanced computed tomography; EUS: endoscopic ultrasound; SIRS: systemic inflammatory response syndrome; WON: walled-off necrosis.

Surgery is reserved for refractory cases; no RCTs define optimal timing. A step-up approach is favored, reserving surgery for cases refractory to endoscopic treatment, with pooled success rates of 84% for cystojejunostomy and 80% for distal pancreatectomy [299]. In symptomatic DPDS with external fistulas, surgery remains the standard, although EUS-guided ductal access is emerging in expert centers [305]. Given surgical complexity and a postoperative morbidity approaching 50%, minimally invasive pancreatic endotherapy is increasingly preferred [292].

3.1.16 | Q16. How to Diagnose and Manage Sterile and Infected Pancreatic And/Or Peripancreatic Collections?

3.1.16.1 | Statement and GRADE.

- Contrast-enhanced CT is effective for diagnosing pancreatic and/or peripancreatic collections (PPPC). MRI can better characterize the contents (fluid or solid) when needed. *Weak recommendation, low-quality evidence.*
- Serum procalcitonin may help assess infection risk. *Strong recommendation, moderate quality evidence.*
- Broad-spectrum antibiotics should be reserved for suspected or confirmed infection; prophylaxis is not advised. *Strong recommendation, high-quality evidence.*
- Most PPPC resolve spontaneously. When intervention is warranted, delaying it by at least 4 weeks (≥ 4 weeks) is

preferable to minimize morbidity, reduce complication risk, and reduce the number of procedures. *Strong recommendation, high-quality evidence.*

- If early intervention (< 4 weeks) is unavoidable, percutaneous drainage is recommended; endoscopic drainage may be considered, preferably at third-level centers with experience in advanced endoscopy. *Strong recommendation, moderate quality evidence.*
- Indications for drainage are suspected or confirmed infection unresponsive to antibiotics, persistent SIRS or OF, sepsis, refractory abdominal pain, refractory gastrointestinal or biliary obstruction, vascular compression, abdominal compartment syndrome, or disconnected duct syndrome. *Strong recommendation, high-quality evidence.*
- Endoscopic drainage, when feasible, is preferred over percutaneous drainage. *Strong recommendation, high-quality evidence.*
- Double pigtail plastic stents (7-10 Fr) and metal stents, preferably LAMS, are equally effective for drainage. Endoscopic necrosectomy is only advised in the absence of clinical improvement with endoscopic drainage or if the patient's condition deteriorates. *Strong recommendation, high-quality evidence.*
- Minimally invasive surgical necrosectomy is recommended if percutaneous or endoscopic approaches fail, as it is preferable to open surgery. *Strong recommendation, high-quality evidence* (Figure 3).

3.1.16.2 | Remarks

3.1.16.2.1 | Diagnosis. Collections in AP are classified according to the RAC [4]. Acute collections, defined as those occurring within the first 4 weeks, include acute peripancreatic fluid collections associated with edematous pancreatitis and acute necrotic collections associated with necrotizing pancreatitis (pancreatic and/or peripancreatic fat necrosis). About 4 weeks after onset, a fibrous capsule-like inflammatory wall develops around the collection; such collections are referred to as pseudocysts (containing only liquid) and walled-off necrosis (WON) (containing liquid and necrotic debris), respectively. Contrast-enhanced CT is primary for diagnosis; MRI may provide additional insight, distinguishing between liquid and solid components [306]. Clinical worsening, no improvement, or gas within collections reliably indicate infection [306] and are sufficient to initiate specific treatments. Routine fine-needle aspiration for the diagnosis of infection is not recommended [307]. Additionally, serum procalcitonin levels may be useful for predicting infection risk [211, 308].

3.1.16.2.2 | Management (Figure 3). Most acute PPPC resolve spontaneously and do not require any intervention. Pseudocysts often regress; up to 40% of WON resolve conservatively, even when infected [309]. Broad-spectrum antibiotics (cephalosporins, carbapenems, quinolones plus metronidazole) should be used only with suspected/confirmed infection; prophylaxis is discouraged [203].

Drainage. Indications include suspected or confirmed infection unresponsive to antimicrobial therapy, persistent SIRS and/or OF, sepsis, persistent abdominal pain, refractory gastrointestinal or biliary obstruction, vascular compression, compartment syndrome, or DPDS [209]. The timing of interventions should be individualized and guided by clinical and imaging criteria, as there are currently no universally applicable guidelines. Delaying ≥ 4 weeks improves safety [309] by allowing encapsulation and liquefaction [310], reducing the risk of complications and even requiring fewer interventions [309]. Percutaneous drainage is recommended within the first 4 weeks for patients with IPN who are septic and unstable despite conservative management. Recent studies suggest that early endoscopic drainage (< 4 weeks) is feasible, and does not appear to increase overall adverse events or mortality, but the procedure carries greater technical risks and should therefore be restricted to expert centers [311–315]. Microbiological samples should be collected whenever drainage is performed to guide antibiotic therapy.

Endoscopic Drainage and Necrosectomy. The PENGUIN trial demonstrated that endoscopic drainage and necrosectomy are superior to open necrosectomy, reducing new-onset multiple OF and overall complications [316]. The TENSION trial, along with its long-term follow-up study, revealed that an endoscopic step-up approach, consisting of endoscopic drainage followed by endoscopic necrosectomy only if needed (refractory cases), offers shorter hospital stay and fewer pancreatic-cutaneous fistulas over the minimally invasive surgical approach, which involves percutaneous drainage followed by minimally invasive surgical necrosectomy if required [317, 318]. Additional studies have supported this recommendation [319, 320]. More recently, the ACCELERATE trial suggested that an endoscopic strategy, with

direct necrosectomy at the index drainage in patients with large (> 15 cm) WON, may further reduce major complications and hospital stay compared with the conventional step-up approach, although confirmation in larger multicenter studies is warranted to support this strategy [321]. Most endoscopic drainage procedures for PPPC adjacent to the stomach or duodenum are performed transmurally, either via a transgastric or transduodenal approach. EUS-guided access is preferred over conventional transmural drainage [322, 323]. Double pigtail plastic stents (7–10 Fr) and metal stents, particularly LAMS, are both recommended [324, 325]. LAMS with a diameter of 15–20 mm provide the advantage of improved drainage of necrotic material and facilitate endoscopic transluminal necrosectomy when needed. Additionally, placing one or more double pigtail plastic stents through the LAMS may help prevent complications such as stent migration, early occlusion by necrotic debris, and bleeding due to mucosal erosion [326].

Endoscopic necrosectomy is limited to refractory cases despite endoscopic drainage [324]. Although evidence is insufficient to support routine use, various strategies have been suggested to enhance drainage and minimize the need for necrosectomy, including the placement of a naso-cystic catheter for cavity irrigation with NS (typically 500–1000 mL/day) [316], antibiotic [327] or hydrogen peroxide lavage [328], and creating multiple transluminal fistulas, either endoscopically or in combination with percutaneous drainage. Some studies suggest PPIs may increase the number of procedures needed, as gastric acid promotes autodebridement of necrotic debris and prevents stent occlusion [329]. While early stent removal can lead to recurrent collections, prolonged use of LAMS has been associated with complications. A follow-up CT scan 2–4 weeks after drainage is generally recommended. If there is significant size reduction along with clinical resolution, the stent should be removed, ideally within 2–4 weeks for pseudocysts and 3–6 weeks for walled-off necrosis; if abundant necrosis persists requiring ongoing access for necrosectomy, the LAMS should be exchanged every 6 weeks or replaced with plastic stents [203, 209, 310–320, 322–325, 330].

Percutaneous Drainage. Percutaneous drainage is recommended in specific scenarios: need for drainage before encapsulation (< 3 –4 weeks from onset), unstable patient unfit for endoscopic or surgical drainage; collection inaccessible to endoscopic drainage; concomitant with endoscopic drainage in collections extending to the pelvis or paracolic gutters [324, 331]. In most published series and in the available randomized study, percutaneous drains were routinely flushed with saline at regular intervals (commonly every 8 h) to maintain catheter patency and reduce the risk of occlusion [332]. Streptokinase and hydrogen peroxide (3%) have been proposed as necrolytic agents to enhance drainage and potentially reduce the need for surgical necrosectomy in cases where saline irrigation alone is ineffective. However, evidence supporting their use is limited. A single randomized trial comparing streptokinase with hydrogen peroxide reported better outcomes and fewer complications with streptokinase; nevertheless, the current evidence remains insufficient to support a formal recommendation [333].

Surgical Necrosectomy. If percutaneous drainage or endoscopic approach fails, minimally invasive surgical necrosectomy is

recommended and preferred over open surgery. The PANTER trial demonstrated that it outperforms open necrosectomy, reducing new-onset multiple OF, hernias, and new-onset diabetes [334]. These benefits were sustained in long-term follow-up, in which death/major complications occurred in 44% of minimally invasive step-up patients versus 73% with open surgery ($p = 0.005$). Incisional hernias (23% vs. 53%, $p = 0.004$), pancreatic exocrine insufficiency (29% vs. 56%, $p = 0.03$), and endocrine insufficiency (40% vs. 64%, $p = 0.05$) were also significantly lower in the long term [335]. Open surgery should be limited to cases with extensive necrotic burden distributed across the entire abdominal cavity. The approach depends on institutional experience and collection location [324].

3.1.17 | Q17. How Should Peripancreatic Vein Thrombosis and Left Portal Hypertension Be Managed?

3.1.17.1 | Statements and GRADE.

- Evidence is insufficient to establish optimal management of splanchnic vein thrombosis in AP; therapeutic anticoagulation may be considered for acute portal vein thrombosis with multi-vessel involvement, or for progressive splenic vein thrombosis. *Weak recommendation, low-quality evidence.*
- Local inflammation likely triggers thrombosis; however, a thrombophilia evaluation is recommended after the acute thrombosis episode. *Weak recommendation, low-quality evidence.*
- Standard regimens use an initial course of low-molecular-weight heparin (LMWH), followed by oral anticoagulants for 3–6 months. Anticoagulation should be discontinued once the thrombus resolves or recanalization is not achieved, except in cases of confirmed thrombophilia, with case-by-case assessment due to limited efficacy data and potential complications. *Weak recommendation, low-quality evidence.*
- There is no evidence supporting beta-blockers or endoscopic therapy for primary or secondary prevention of bleeding in non-cirrhotic left-sided portal hypertension. Individualized endoscopic surveillance every 1–2 years appears reasonable for assessing variceal development and guiding tailored decisions. *Weak recommendation, low-quality evidence.*

3.1.17.2 | Remarks. The incidence of splanchnic vein thrombosis, including portal vein thrombosis, superior mesenteric vein thrombosis (which rarely occurs in isolation, typically representing progression from portal vein thrombosis or splenic vein thrombosis) and splenic vein thrombosis, is higher among patients with moderately severe to severe AP [336–343], mainly due to inflammation and venous stasis [339–345]. Thrombophilia can be present in a substantial proportion of AP patients but does not independently increase the risk of splanchnic vein thrombosis; however, it should be assessed to estimate recurrence risk and guide anticoagulation duration [346]. Additional risk factors include male sex, alcohol-related AP, smoking, IPN, and IAH [338–345].

Management is difficult given the scarcity of high-quality evidence. Some observational studies suggest that therapeutic anticoagulation may improve vessel recanalization rates without substantially increasing bleeding [347–352], but meta-analyses of retrospective studies show inconsistent results and no clear impact on varices, collaterals, cavernomatosis, or mortality compared with non-therapeutic approaches, likely due to study heterogeneity [352–356].

Anticoagulation is more clearly indicated in acute portal vein thrombosis, multi-vessel involvement, or progressive splenic vein thrombosis, understood as initial thrombosis limited to the splenic vein that extends over time to other splanchnic vessels, where anticoagulation appears to enhance recanalization [352–359]. Standard practice typically involves heparin or LMWH initially, followed by oral anticoagulants for 3–6 months [352–360].

Evidence on left-sided portal hypertension after AP is very limited. In this setting, beta-blockers and endoscopic interventions are not routinely recommended for primary or secondary variceal bleeding prevention [360]. In practice, individualized strategies with endoscopic surveillance every 1–2 years, as suggested in Baveno VII for isolated gastric varices type I, seem reasonable to assess varices and guide tailored prevention decisions [360]. High-quality studies are needed to improve management protocols for splanchnic vein thrombosis associated with AP.

3.1.18 | Q18. When Should Cholecystectomy Be Performed?

3.1.18.1 | Statement and GRADE.

- For patients with mild AP, laparoscopic cholecystectomy should be performed during the index hospitalization. *Strong recommendation, high-quality evidence.*
- For patients with moderate to severe acute pancreatitis, delaying cholecystectomy until 8 weeks post-discharge or until local complications resolve is recommended. *Weak recommendation, low-quality evidence.*

3.1.18.2 | Remarks. Evidence from RCTs strongly supports early laparoscopic cholecystectomy as the best strategy for mild AP. The PANC trial found that cholecystectomy within 24 h reduced ERCP need, time to surgery, and 30-day hospital stay [277]. Three RCTs showed that cholecystectomy within the first 48 h significantly decreased hospitalization time without increasing complications or conversions to open surgery and lowered biliary recurrences [361–363]. For laparoscopic cholecystectomy within 72 h of admission, Omar et al. reported fewer gallstone-related complications and shorter hospital stays [364], while Riquelme et al. also found no significant differences in ERCP need or postoperative complications [365]. The PONCHO trial demonstrated that same-admission cholecystectomy significantly reduced recurrent biliary events (5% vs. 17%, $p = 0.002$) [366], consistent with Jee et al. [367]. Facundo et al. noted that cholecystectomy on day 7 of admission did not lead to an increase in residual

choledocholithiasis or unnecessary ERCPs [368]. Notably, all RCTs incorporated intraoperative cholangiography or pre-cholecystectomy ERCP when choledocholithiasis was suspected or confirmed [277, 361–368]. Meta-analyses of RCTs and observational studies consistently confirm these findings [369–378]. Early cholecystectomy in mild AP is also cost-effective compared to delayed surgery, mainly through shorter stays and fewer complications [379, 380].

By contrast, in moderately severe to severe AP, particularly when PPPC are present, evidence on the timing of cholecystectomy is limited and mainly observational. Early cholecystectomy in these patients is associated with higher mortality, morbidity, infection rates [381], and postoperative complications [382] compared to delayed surgery. Delaying cholecystectomy allows for patient stabilization and resolution of inflammation, thereby reducing surgical risks and improving outcomes [383, 384]. A recent Dutch post hoc analysis of an RCT including 248 patients with necrotizing biliary AP demonstrated that cholecystectomy performed within 10 weeks of discharge significantly reduced the risk of recurrent biliary events, with the greatest reduction in recurrent pancreatitis observed when surgery was performed within 8 weeks. Surgical complication rates were not influenced by timing, and endoscopic sphincterotomy did not reduce recurrence risk [384].

Accordingly, in patients with PPPC, cholecystectomy should be delayed until collections resolve or, if absent, until 8 weeks after hospital discharge. [384]. When performed after clinical resolution of AP, the laparoscopic cholecystectomy approach is safe and associated with a low risk of surgical complications [383].

3.1.19 | Q19: When and How Should Choledocholithiasis Be Ruled out?

3.1.19.1 | Statement and GRADE.

- In mild or predicted severe biliary AP without cholangitis, but with persistent or progressive cholestasis or bile duct dilation, evaluation for choledocholithiasis may be deferred for up to 1 week if the patient is clinically stable. *Weak recommendation, low-quality evidence.*
- Patients with normalization of cholestasis and no bile duct dilation do not require further testing. *Weak recommendation, low-quality evidence.*
- In mild biliary AP with high suspicion of choledocholithiasis scheduled for early cholecystectomy, biliary exploration should be considered before surgery if any of the following ASGE criteria [385] are met:
 - I. Serum bilirubin > 70 µmol/L (4 mg/dL), or
 - II. Common bile duct > 6 mm and bilirubin 30–70 µmol/L (1.75–4 mg/dL), or
 - III. Signs of ascending cholangitis are present*Weak recommendation, moderate quality evidence.*
- MRCP and EUS offer high diagnostic accuracy for detecting choledocholithiasis in biliary AP and should be considered in cases of uncertainty, when indicated. *Strong recommendation, moderate quality evidence.*

3.1.19.2 | Remarks. Choledocholithiasis occurs in 20%–50% of biliary AP cases [386–390], but up to 80% resolve spontaneously as small stones (< 5 mm) pass into the duodenum. Thus, some studies suggest delaying diagnostic procedures for choledocholithiasis without cholangitis until after the first week [388] or clinical recovery [275, 276, 389], avoiding overdiagnosis and unnecessary interventions.

Predictive algorithms based on clinical factors (age, sex), laboratory tests (liver function abnormalities), and imaging findings (bile duct dilation) have been attempted to identify choledocholithiasis in patients without pancreatitis [385, 390–395]. However, in biliary AP their accuracy is limited [386–391], with significant variability and lack of validation in this setting [390–394, 396]. Moreover, inflammation and local complications of AP alter liver tests and imaging, weakening their diagnostic value [386].

The APEC and APEC-2 trials showed that early ERCP (≤ 24 h) for predicted severe biliary AP, with or without cholestasis but without cholangitis, did not reduce mortality or major complications compared with a conservative approach [275, 276], even when ERCP was preceded by EUS-confirmed choledocholithiasis [276]. In this context, the lack of observed benefit in early ERCP supports refraining from diagnostic procedures solely intended to identify choledocholithiasis early in the course of disease.

In patients with mild biliary AP scheduled for early cholecystectomy, preoperative bile duct evaluation is recommended when the suspicion of choledocholithiasis is high. Although clinical criteria vary across RCTs, the PONCHO trial [366] applied the ASGE criteria [385], which may represent a reasonable approach in this setting. According to these, preoperative evaluation is indicated if any of the following are present: serum bilirubin > 70 µmol/L (4 mg/dL), a common bile duct diameter > 6 mm with bilirubin 30–70 µmol/L (1.75–4 mg/dL), or clinical signs of ascending cholangitis [385]. In high-probability patients, MRCP or EUS should be used, reserving ERCP for confirmed stones [366]. Both EUS and MRCP outperform TUS and contrast-enhanced CT in detecting choledocholithiasis [397–399], and show accuracy comparable to ERCP [398–400]. Comparative studies generally report similar performance [401–403], though some suggest higher sensitivity and accuracy for EUS [55, 404, 405]. However, comparative research specifically focused on biliary AP remains limited in establishing recommendations favoring one modality.

3.1.20 | Q20. When and How Should Pancreatic Exocrine and Endocrine Insufficiency Be Assessed and Managed?

3.1.20.1 | Statement and GRADE. Current evidence is insufficient to define clear guidelines on timing and patient selection for pancreatic function testing after AP. However, specific scenarios warrant consideration:

- Pancreatic exocrine (PEI) and endocrine insufficiency assessment is recommended during follow-up for

necrotizing pancreatitis, alcohol-induced AP, RAP, or after necrosectomy. *Weak recommendation, low-quality evidence.*

- Post-discharge evaluation for endocrine insufficiency, using fasting glucose, glycated hemoglobin (HbA1c), and/or C-peptide, is also recommended in patients with pre-existing risk factors such as obesity, hyperlipidemia, or prediabetes. *Weak recommendation, low-quality evidence.*
- Fecal elastase is a suitable first-line screening test for PEI, given its accessibility and ease of use. *Weak recommendation, low-quality evidence.*
- Empirical PERT may be considered in patients with extensive necrotizing AP when resuming oral intake or those with maldigestion symptoms. *Weak recommendation, low-quality evidence.*
- Management of PEI typically involves PERT, following chronic pancreatitis dosing schemes. Treatment of endocrine insufficiency follows standard diabetes protocols, including oral antidiabetic agents and insulin, ideally within a multidisciplinary framework involving endocrinology. *Weak recommendation, low-quality evidence.*
- Follow-up for at-risk patients may include assessment of pancreatic function at 3, 6, and 12 months post-AP, and every 6–12 months thereafter if dysfunction persists. Monitoring must combine nutritional and diabetological laboratory tests with clinical assessment of maldigestion symptoms. Special attention should be given to endocrine insufficiency, as it may progress over time. *Weak recommendation, low-quality evidence.*

3.1.20.2 | Remarks. In AP, PEI occurs in 2.5%–34% of patients and endocrine insufficiency in 3.5%–37% [406–411], with higher rates when considering only patients with severe AP [412–417]. Evidence is limited to small observational studies with variable follow-up and methodological bias.

Some studies suggest that PEI may develop at any severity [418, 419], but is more common in AP with pancreatic necrosis [409, 410, 420, 421], RAP, alcoholic etiology [422–424] or after necrosectomy [318, 335, 336, 425–429]. It is usually transient, resolving within weeks or months [408, 421, 423]. Endocrine insufficiency is strongly associated with severe AP and pancreatic necrosis [414, 418, 430, 431], rarely occurs in mild cases, and is linked to obesity, hyperlipidemia, and prediabetes [432, 433]. Unlike PEI, its incidence seems to increase over time, particularly in the 4th–6th year after AP [408, 434]. Both PEI and diabetes often coexist, reflecting overlapping risk factors [412].

The diagnostic techniques used vary and lack validation in AP. For PEI, fecal elastase (preferred for its simplicity) and fecal fat measurement are the most commonly used tests, while direct duodenal testing is rarely applied. [416, 418, 422, 426]. For endocrine function, the oral glucose tolerance test, fasting blood glucose, HbA1c, fasting insulin, and/or C-peptide measurements are employed [407, 415, 430, 433]. No comparative studies on diagnostic techniques exist for AP.

Currently, no robust evidence guides the initiation of PERT in AP. However, empirical treatment may be started in severe

necrotizing disease when oral feeding resumes, or in patients presenting with maldigestive symptoms (steatorrhea, flatulence, digestive discomfort, etc.), and after confirmatory tests. In clinical practice, chronic pancreatitis regimens are adopted: 50,000 IU of enzymes per main meals (two capsules per meal: 2-2-2) and 25,000 IU (one capsule) with snacks [411, 435], with further adjustments based on clinical response. Diabetes management follows standard protocols with oral agents or insulin therapy, due to the lack of specific evidence in AP.

In the absence of high-quality evidence, the most recent European guidelines recommend a pragmatic follow-up for patients at risk of pancreatic dysfunction: exocrine and endocrine assessments at 3, 6, and 12 months after AP, and every 6–12 months thereafter if dysfunction persists [435]. Monitoring should combine laboratory evaluation of nutritional status (including fat-soluble vitamins, iron studies, vitamin B12, folate, calcium, magnesium, zinc, and selenium), diabetological markers (fasting glucose, HbA1c, lipid profile, and, when indicated, C-peptide), and clinical assessment of symptoms related to maldigestion (steatorrhea, diarrhea, bloating, weight loss) and endocrine dysfunction (polyuria, polydipsia, unintended weight loss) [435].

4 | Discussion

These iLATAM guidelines provide a comprehensive synthesis of current evidence for the management of acute pancreatitis (AP). However, across multiple sections, several recommendations remain supported by low-certainty evidence, reflecting persistent gaps in the literature. In some areas, strong recommendations were issued despite low certainty, because the panel judged that clinical necessity, consistent expert agreement, and a favorable balance of expected benefits over potential harms outweighed the limitations of the available trial data. This highlights the need for well-designed prospective studies to strengthen the evidence base. In addition, very few studies incorporate patient-reported outcome measures, such as the PAN-PROMISE symptom scale [168] which is a notable gap given the increasing emphasis on patient-centered care. Future research should extend beyond in-hospital management and short-term complications to address long-term morbidity and mortality [436], functional recovery, integration with primary care, and health-related quality of life after an AP episode. The development of structured post-discharge pathways and recovery-oriented protocols will be essential to meet the needs of this patient population. Although this guideline did not formally develop quality indicators or audit measures, several recommendations naturally map to measurable metrics. Future collaborative initiatives may therefore focus on defining context-appropriate quality indicators to support evaluation of adherence and outcomes across Ibero–Latin American healthcare systems.

Author Contributions

E. de-Madaria conceptualized and designed the study. J. Mira advised on methodological framework and contributed to defining the study steps and quality and safety evaluation criteria. K. Cárdenas-Jaén and E. de-Madaria oversaw the overall coordination and methodological processes. K. Cárdenas-Jaén, C. Mancilla, M. Bispo, P. Moutinho-Ribeiro, E.

Martínez-Moneo, and R. Mansilla coordinated the working teams. Each working team, comprising by one coordinator and four authors, conducted the systematic literature review, data extraction, and evidence synthesis for the assigned clinical questions, and developed recommendations following the GRADE approach. I. Carrillo configured the online voting platform for each clinical question and extracted the corresponding levels of agreement reached. All authors constituted the expert panel, which refined and voted on the recommendations. K. Cárdenas-Jaén and L. Guilbert drafted the final English manuscript. All authors critically revised and approved the final version.

Affiliations

¹Department of Gastroenterology, Dr. Balmis University General Hospital, Alicante, Spain | ²Alicante Institute for Health and Biomedical Research (ISABIAL), Alicante, Spain | ³Department of Gastroenterology, Cruces University Hospital, Barakaldo, Spain | ⁴Gastroenterology Section and Critical Care Unit, Clinical Hospital, University of Chile, Santiago, Chile | ⁵Department of Gastroenterology, Digestive Oncology Unit, Champalimaud Foundation, Lisbon, Portugal | ⁶Department of Gastroenterology and Hepatology, São João University Hospital Center, World Gastroenterology Organization (WGO) Porto Training Center, Porto, Portugal | ⁷Endoscopy Unit, Puerto Montt Hospital, San Sebastián University Patagonia Campus, Puerto Montt, Chile | ⁸Department of Gastroenterology, Unidade Local de Santo António (ULSSA), Porto, Portugal | ⁹Department of Gastroenterology and Hepatology, Ramon y Cajal University Hospital, Madrid, Spain | ¹⁰University of Alcalá, Ramon y Cajal Institute for Health Research (IRYCIS), Madrid, Spain | ¹¹Biomedical Research Center in Liver and Digestive Diseases (CIBERehd), Carlos III Health Institute, Madrid, Spain | ¹²Department of Digestive Medicine, Dr. Peset University Hospital, Valencia, Spain | ¹³University of Valencia, Valencia, Spain | ¹⁴Department of Gastroenterology, Senhora da Oliveira Hospital - Guimarães, Guimarães, Portugal | ¹⁵Department of Gastroenterology and Hepatology, Marqués de Valdecilla University Hospital, Santander, Spain | ¹⁶Clinical and Translational Research Group in Digestive Diseases, Valdecilla Research Institute (IDIVAL), Santander, Spain | ¹⁷Department of Gastroenterology, Biliary-Pancreatic Unit, Puerta de Hierro University Hospital, Madrid, Spain | ¹⁸Gastroenterology Unit, Edgardo Rebagliati Martins National Hospital, Lima, Peru | ¹⁹Peruvian University of Applied Sciences (UPC), Lima, Peru | ²⁰Gastroenterology Unit, Angloamerican Clinic, Lima, Peru | ²¹Department of Gastroenterology, Biliary-Pancreatic Unit, La Paz Hospital, Madrid, Spain | ²²Hepato-Biliary-Pancreatic and Transplant Surgery Department, Hospital Clinic of Barcelona, IDIBAPS, University of Barcelona, Barcelona, Spain | ²³Endoscopy Unit, Department of Gastroenterology, Cancer Institute of São Paulo, Hospital das Clínicas, Medical School of the University of São Paulo, CNPq Researcher, São Paulo, Brazil | ²⁴Endoscopy Unit, Bolivian-Japanese Institute of Gastroenterology, La Paz, Bolivia | ²⁵Hepato-Biliary-Pancreatic and Splenic Unit, General Surgery Department, São João University Medical Center, Porto, Portugal | ²⁶Department of Digestive Medicine, Clinical University Hospital of Valencia, Valencia, Spain | ²⁷Department of Internal Medicine/Gastroenterology and Endoscopy Service, School of Medicine and University Hospital "Dr. E. González", Autonomous University of Nuevo León, Monterrey, Mexico | ²⁸Department of General and Digestive Surgery, Dr. Balmis University General Hospital, Alicante, Spain | ²⁹Intensive Care Service, São Francisco Xavier Hospital, Lisbon, Portugal | ³⁰Department of Surgery, Hepato-Biliary-Pancreatic Surgery Section, San Roque Hospital, Córdoba, Argentina | ³¹Department of Surgery, Hepatobiliary and Pancreatic Surgery Section, Sanatorio Allende, Córdoba, Argentina | ³²Research Division, School of Medicine, National Autonomous University of Mexico, Mexico City, Mexico | ³³Department of Gastroenterology, National Institute of Medical Sciences and Nutrition Salvador Zubirán, Mexico City, Mexico | ³⁴Department of Digestive Diseases, Ourense University

Hospital Complex, Ourense, Spain | ³⁵Department of Gastroenterology, Bolivian-Japanese Institute of Gastroenterology, Cochabamba, Bolivia | ³⁶Gastroenterology Unit, San Ignacio University Hospital, Javeriana University, Bogotá, Colombia | ³⁷Pancreatic Diseases Section, Department of Clinical Gastroenterology, Hospital C.B. Udaondo, Buenos Aires, Argentina | ³⁸Academic Unit of Intensive Care Medicine, Hospital de Clínicas, School of Medicine, University of the Republic, Montevideo, Uruguay | ³⁹Gastroenterology Section, Department of Medicine, Clinical Hospital, University of Chile, Santiago, Chile | ⁴⁰Department of Health Psychology, Miguel Hernández University, Elche, Spain | ⁴¹Department of Gastroenterology, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile | ⁴²The National Pancreas Foundation, Bethesda, Maryland, USA | ⁴³Director, School of Medicine, Universidad Tecnológica del Perú (UTP), Lima, Peru | ⁴⁴Department of Gastroenterology, Local Health Unit of the Leiria Region, Leiria, Portugal | ⁴⁵Department of Gastroenterology, Central University Hospital of Asturias, Oviedo, Spain | ⁴⁶Department of Internal Medicine, Dr. Balmis University General Hospital, Alicante, Spain | ⁴⁷Department of Clinical Medicine, Faculty of Medicine, Miguel Hernández University, Elche, Spain

Acknowledgments

We would like to thank the Governing Boards of the participating associations for their support. Thanks to AEG for the funding (AEG grant from the Pancreas and Bile Duct Group 2022). These guidelines are dedicated to our Master and friend Guido Villagómez, from La Paz, Bolivia.

Funding

This project received financial support from the Spanish Association of Gastroenterology AEG, through a competitive research grant (AEG grant from the Pancreas and Bile Duct Group 2022).

Conflicts of Interest

Alberto Espino has received consulting fees from Olympus Latam Continuum Professional Education related to endoscopy (colonoscopy, ERCP, EUS). President of the Chilean Pancreas Club. Alejandro Piscoya is Vice-President of the Peruvian Society of Gastroenterology. Chair of the World Gastroenterology Organization (WGO) Guidelines Committee. President-elect of the Panamerican Gastroenterology Organization (OPGE). Ana García García de Paredes is recipient of a Río Hortega research grant from the Instituto de Salud Carlos III. Has received support for attending meetings from Viatrix, Casen, and Pentax. Honoraria from Elsevier. Antonio López-Serrano has received lecture honoraria from GlaxoSmithKline, S.A. and Sistemas Integrales de Medicina, S.A. Daniel de la Iglesia has received lecture honoraria from Viatrix and travel and meeting support from Viatrix. Emma Martínez-Moneo has received lecture honoraria and meeting attendance support from Viatrix. President of AESPANC and has been a member of the Executive Board of the Spanish Gastroenterology Association (AEG) as coordinator of the Pancreas section. Enrique de-Madaria has received research funding from Abbott, is chair of the adjudication committee in three studies by Arrowhead, has received travel grants from AbbVie, and has participated in educational events sponsored by Abbott and Viatrix. Past president of the Spanish Gastroenterology Association (AEG) and AESPANC. Independent councilor of the United European Gastroenterology and previous member of the Education committee. Eva Marín-Serrano has received travel and meeting support from Viatrix, Izasa, and Canon, and honoraria for lectures from Editorial Médica Panamericana and for teaching activities in the Master of Intestinal Permeability and the Ultrasound Course at Hospital La Paz. President of AEED and Secretary of FESUMB. Fauze Maluf-Filho is consultant for Boston Scientific, Cook Medical, and Medtronic. Isabel Pascual-Moreno has received travel and meeting support from Viatrix, and honoraria from the Spanish Gastroenterology Association (AEG) for a book chapter and

for lectures in a Master's program in inflammatory bowel disease (2021). Neftalí Jara Pérez-López has received travel and meeting support from Norgine. José Manuel Ramia is Chair of the Scientific Committee of EAHPBA, member of the Executive Board of SEOQ, member of the Executive Committee of EAHPBA, member of the Program Committee of the EAHPBA Lyon 2023 Congress, President of the Spanish Chapter of the American College of Surgeons. Karina Cárdenas-Jaén is Representative on the Executive board of the Asociación Española de Gastroenterología (AEG) as a member of the Pancreas Section. Lucas Granero has received payments for lectures and travel support from Abbott. Lucía Guilabert is recipient of a Río Hortega research grant from the Instituto de Salud Carlos III. Coordinator of YOUNPPIE (young group of the European Pancreatic Club (EPC), 2025). Member of the Education Committee of the EPC (2024). Has received travel and congress support from AbbVie, Janssen, Viatrix, Takeda, and Phaes Pharma. María Francisco González has received honoraria for lectures or expert activities, as well as travel and meeting support from Mylan. Has received lecture honoraria and travel support from Abbott, and travel and meeting support from Norgine. Sandra Basso has received lecture honoraria from Abbott and PTC Therapeutics. William Manzaneros Castro has received honoraria for lectures from Baxter International (Colombia) and Bioerix (Uruguay) and expert testimony fees from Baxter International (Colombia).

Data Availability Statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

References

1. A. Y. Xiao, M. L. Tan, L. M. Wu, et al., "Global Incidence and Mortality of Pancreatic Diseases: A Systematic Review, Meta-Analysis, and Meta-Regression of Population-Based Cohort Studies," *Lancet Gastroenterology & Hepatology* 1, no. 1 (2016): 45–55, [https://doi.org/10.1016/s2468-1253\(16\)30004-8](https://doi.org/10.1016/s2468-1253(16)30004-8).
2. J. P. Iannuzzi, J. A. King, J. H. Leong, et al., "Global Incidence of Acute Pancreatitis is Increasing Over Time: A Systematic Review and Meta-Analysis," *Gastroenterology* 162, no. 1 (2022): 122–134, <https://doi.org/10.1053/j.gastro.2021.09.043>.
3. A. F. Peery, C. C. Murphy, C. Anderson, et al., "Burden and Cost of Gastrointestinal, Liver, and Pancreatic Diseases in the United States: Update 2024," *Gastroenterology* 168, no. 5 (2025): 1000–1024, <https://doi.org/10.1053/j.gastro.2024.12.029>.
4. P. A. Banks, T. L. Bollen, C. Dervenis, et al., "Classification of Acute Pancreatitis–2012: Revision of the Atlanta Classification and Definitions by International Consensus," *Gut* 62, no. 1 (2013): 102–111, <https://doi.org/10.1136/gutjnl-2012-302779>.
5. H. Sternby, F. Bolado, H. J. Canaval-Zuleta, et al., "Determinants of Severity in Acute Pancreatitis: A Nation-Wide Multicenter Prospective Cohort Study," *Annals of Surgery* 270, no. 2 (2019): 348–355, <https://doi.org/10.1097/sla.0000000000002766>.
6. Beij A., Verdonk R., van Santvoort H. A.-O., de-Madaria E., "Voermans RA-OX. Acute Pancreatitis: An Update of Evidence-Based Management and Recent Trends in Treatment Strategies," (2050-6414 (Electronic)).
7. N. Lluís, H. Asbun, S. Basso, et al., "Survey on Initial Management of Acute Pancreatitis in Latin America," (0210–5705 (Print)).
8. Z. Berger, C. Mancilla, E. Tobar, et al., "Acute Pancreatitis in Chile: A Multicenter Study on Epidemiology, Etiology and Clinical Outcome: Retrospective Analysis of Clinical Files," (1424–3911 (Electronic)).
9. G. H. Guyatt, A. D. Oxman, G. E. Vist, et al., "GRADE: An Emerging Consensus on Rating Quality of Evidence and Strength of Recommendations," *BMJ* 336, no. 7650 (2008): 924–926, <https://doi.org/10.1136/bmj.39489.470347.ad>.
10. P. Alonso-Coello, H. J. Schünemann, J. Moher, et al., "GRADE Evidence to Decision (EtD) Frameworks: A Systematic and Transparent Approach to Making Well Informed Healthcare Choices. 1: Introduction," (1756–1833 (Electronic)).
11. M. C. Brouwers, M. E. Kho, G. P. Browman, et al., "AGREE II: Advancing Guideline Development, Reporting and Evaluation in Health Care," *Canadian Medical Association Journal* 182, no. 18 (2010): E839–E842, <https://doi.org/10.1503/cmaj.090449>.
12. J. Mayerle, M. Sendler, E. Hegyi, G. Beyer, M. M. Lerch, and M. Sahin-Toth, "Genetics, Cell Biology, and Pathophysiology of Pancreatitis," *Gastroenterology* 156, no. 7 (2019): 1951–1968.e1, <https://doi.org/10.1053/j.gastro.2018.11.081>.
13. L. Wen, T. A. Javed, D. Yimlamai, A. Mukherjee, X. Xiao, and S. Z. Husain, "Transient High Pressure in Pancreatic Ducts Promotes Inflammation and Alters Tight Junctions Via Calcineurin Signaling in Mice," *Gastroenterology* 155, no. 4 (2018): 1250–1263.e5, <https://doi.org/10.1053/j.gastro.2018.06.036>.
14. J. V. Gerasimenko, S. Peng, T. Tsugorka, and O. V. Gerasimenko, "Ca(2+) Signalling Underlying Pancreatitis," *Cell Calcium* 70 (2018): 95–101, <https://doi.org/10.1016/j.ceca.2017.05.010>.
15. P. Pallagi, T. Madacsy, A. Varga, and J. Maleth, "Intracellular Ca(2+) Signalling in the Pathogenesis of Acute Pancreatitis: Recent Advances and Translational Perspectives," *International Journal of Molecular Sciences* 21, no. 11 (2020): 4005, <https://doi.org/10.3390/ijms21114005>.
16. J. Maléth and P. Hegyi, "Ca2+ Toxicity and Mitochondrial Damage in Acute Pancreatitis: Translational Overview," *Philosophical Transactions of the Royal Society of London B Biological Sciences* 371, no. 1700 (2016): 20150425, <https://doi.org/10.1098/rstb.2015.0425>.
17. O. H. Petersen, J. V. Gerasimenko, O. V. Gerasimenko, O. Gryshchenko, and S. Peng, "The Roles of Calcium and ATP in the Physiology and Pathology of the Exocrine Pancreas," *Physiological Reviews* 101, no. 4 (2021): 1691–1744, <https://doi.org/10.1152/physrev.00003.2021>.
18. R. Mukherjee, O. A. Mareninova, I. V. Odinkova, et al., "Mechanism of Mitochondrial Permeability Transition Pore Induction and Damage in the Pancreas: Inhibition Prevents Acute Pancreatitis by Protecting Production of ATP," *Gut* 65, no. 8 (2016): 1333–1346, <https://doi.org/10.1136/gutjnl-2014-308553>.
19. A. Saluja, V. Dudeja, R. Dawra, and R. P. Sah, "Early Intra-Acinar Events in Pathogenesis of Pancreatitis," *Gastroenterology* 156, no. 7 (2019): 1979–1993, <https://doi.org/10.1053/j.gastro.2019.01.268>.
20. J. C. Hall and H. C. Crawford, "The Conspiracy of Autophagy, Stress and Inflammation in Acute Pancreatitis," *Current Opinion in Gastroenterology* 30, no. 5 (2014): 495–499, <https://doi.org/10.1097/mog.0000000000000097>.
21. A. S. Gukovskaya, I. Gukovsky, H. Algül, and A. Habtezion, "Autophagy, Inflammation, and Immune Dysfunction in the Pathogenesis of Pancreatitis," *Gastroenterology* 153, no. 5 (2017): 1212–1226, <https://doi.org/10.1053/j.gastro.2017.08.071>.
22. P. J. Lee and G. I. Papachristou, "New Insights Into Acute Pancreatitis," *Nature Reviews Gastroenterology & Hepatology* 16, no. 8 (2019): 479–496, <https://doi.org/10.1038/s41575-019-0158-2>.
23. R. Kang, M. T. Lotze, H. J. Zeh, T. R. Billiar, and D. Tang, "Cell Death and DAMPs in Acute Pancreatitis," *Molecular Medicine* 20, no. 1 (2014): 466–477, <https://doi.org/10.2119/molmed.2014.00117>.
24. P. K. Garg and V. P. Singh, "Organ Failure due to Systemic Injury in Acute Pancreatitis," *Gastroenterology* 156, no. 7 (2019): 2008–2023, <https://doi.org/10.1053/j.gastro.2018.12.041>.
25. R. J. Vissers, R. B. Abu-Laban, and D. F. McHugh, "Amylase and Lipase in the Emergency Department Evaluation of Acute Pancreatitis," *Journal of Emergency Medicine* 17, no. 6 (1999): 1027–1037, [https://doi.org/10.1016/s0736-4679\(99\)00136-5](https://doi.org/10.1016/s0736-4679(99)00136-5).

26. G. Rompianesi, A. Hann, O. Komolafe, S. P. Pereira, B. R. Davidson, and K. S. Gurusamy, "Serum Amylase and Lipase and Urinary Trypsinogen and Amylase for Diagnosis of Acute Pancreatitis," *Cochrane Database of Systematic Reviews* 4, no. 4 (2017): Cd012010, <https://doi.org/10.1002/14651858.CD012010.pub2>.
27. J. Hedstrom, V. Sainio, E. Kempainen, et al., "Urine Trypsinogen-2 as Marker of Acute Pancreatitis," *Clinical Chemistry* 42, no. 5 (1996): 685–690, <https://doi.org/10.1093/clinchem/42.5.685>.
28. K. Chang, W. Lu, K. Zhang, et al., "Rapid Urinary Trypsinogen-2 Test in the Early Diagnosis of Acute Pancreatitis: A Meta-Analysis," *Clinical Biochemistry* 45, no. 13–14 (2012): 1051–1056, <https://doi.org/10.1016/j.clinbiochem.2012.04.028>.
29. E. A. Kempainen, J. I. Hedstrom, P. A. Puolakkainen, et al., "Rapid Measurement of Urinary Trypsinogen-2 as a Screening Test for Acute Pancreatitis," *New England Journal of Medicine* 336, no. 25 (1997): 1788–1793, <https://doi.org/10.1056/nejm199706193362504>.
30. T. L. Bollen, H. C. van Santvoort, M. G. Besselink, W. H. van Es, H. G. Gooszen, and M. S. van Leeuwen, "Update on Acute Pancreatitis: Ultrasound, Computed Tomography, and Magnetic Resonance Imaging Features," *Seminars In Ultrasound CT and MR* 28, no. 5 (2007): 371–383, <https://doi.org/10.1053/j.sult.2007.06.002>.
31. S. S. Wang, X. Z. Lin, Y. T. Tsai, et al., "Clinical Significance of Ultrasonography, Computed Tomography, and Biochemical Tests in the Rapid Diagnosis of Gallstone-Related Pancreatitis: A Prospective Study," *Pancreas* 3, no. 2 (1988): 153–158, <https://doi.org/10.1097/00006676-198804000-00007>.
32. J. Ward, A. G. Chalmers, A. J. Guthrie, M. Larvin, and P. J. Robinson, "T2-Weighted and Dynamic Enhanced MRI in Acute Pancreatitis: Comparison With Contrast Enhanced CT," *Clinical Radiology* 52, no. 2 (1997): 109–114, [https://doi.org/10.1016/s0009-9260\(97\)80102-x](https://doi.org/10.1016/s0009-9260(97)80102-x).
33. R. Lecesne, P. Taourel, P. M. Bret, M. Atri, and C. Reinhold, "Acute Pancreatitis: Interobserver Agreement and Correlation of CT and MR Cholangiopancreatography With Outcome," *Radiology* 211, no. 3 (1999): 727–735, <https://doi.org/10.1148/radiology.211.3.r99jn08727>.
34. M. Arvanitakis, M. Delhay, V. De Maertelaere, et al., "Computed Tomography and Magnetic Resonance Imaging in the Assessment of Acute Pancreatitis," *Gastroenterology* 126, no. 3 (2004): 715–723, <https://doi.org/10.1053/j.gastro.2003.12.006>.
35. D. E. Morgan, T. H. Baron, J. K. Smith, M. L. Robbin, and P. J. Kenney, "Pancreatic Fluid Collections Prior to Intervention: Evaluation With MR Imaging Compared With CT and US," *Radiology* 203, no. 3 (1997): 773–778, <https://doi.org/10.1148/radiology.203.3.9169703>.
36. H. Sun, S. Jian, B. Peng, and J. Hou, "Comparison of Magnetic Resonance Imaging and Computed Tomography in the Diagnosis of Acute Pancreatitis: A Systematic Review and meta-analysis of Diagnostic Test Accuracy Studies," *Annals of Translational Medicine* 10, no. 7 (2022): 410, <https://doi.org/10.21037/atm-22-812>.
37. M. B. Zilio, T. F. Eyff, A. L. F. Azeredo-Da-Silva, V. P. Bersch, and A. B. Osvaldt, "A Systematic Review and Meta-Analysis of the Aetiology of Acute Pancreatitis," *HPB* 21, no. 3 (2019): 259–267, <https://doi.org/10.1016/j.hpb.2018.08.003>.
38. A. Adiamah, E. Psaltis, M. Crook, and D. N. Lobo, "A Systematic Review of the Epidemiology, Pathophysiology and Current Management of Hyperlipidaemic Pancreatitis," *Clinical Nutrition* 37, no. 6 Pt A (2018): 1810–1822, <https://doi.org/10.1016/j.clnu.2017.09.028>.
39. C. L. Liu, S. T. Fan, C. M. Lo, et al., "Clinico-Biochemical Prediction of Biliary Cause of Acute Pancreatitis in the Era of Endoscopic Ultrasonography," *Alimentary Pharmacology & Therapeutics* 22, no. 5 (2005): 423–431, <https://doi.org/10.1111/j.1365-2036.2005.02580.x>.
40. N. O. Zarnescu, R. Costea, E. C. Zarnescu Vasiliu, and S. Neagu, "Clinico-Biochemical Factors to Early Predict Biliary Etiology of Acute Pancreatitis: Age, Female Gender, and ALT," *Journal of Medicine and Life* 8, no. 4 (2015): 523–526, <https://pmc.ncbi.nlm.nih.gov/articles/PMC4656965/>.
41. S. Tenner, H. Dubner, and W. Steinberg, "Predicting Gallstone Pancreatitis With Laboratory Parameters: A Meta-Analysis," *American Journal of Gastroenterology* 89, no. 10 (1994): 1863–1866, <https://pubmed.ncbi.nlm.nih.gov/7942684/>.
42. U. Mathuram Thiagarajan, A. Ponnuswamy, and R. Thomas, "Predictivity of Biochemical Markers on Aetiology and Length of Hospitalisation in Acute Pancreatitis," *Cureus* 12, no. 12 (2020): e11989, <https://doi.org/10.7759/cureus.11989>.
43. B. Azevedo and D. J. Fagundes, "Differential Diagnosis Between Biliary and Nonbiliary Acute Pancreatitis: What is the Importance of Laboratory Tests?," *ABCD: Arquivos Brasileiros de Cirurgia Digestiva* 35 (2022): e1694, <https://doi.org/10.1590/0102-672020220002e1694>.
44. H. M. Irving, A. V. Samokhvalov, and J. Rehm, "Alcohol as a Risk Factor for Pancreatitis. A Systematic Review and Meta-Analysis," *Jop* 10, no. 4 (2009): 387–392, <https://pmc.ncbi.nlm.nih.gov/articles/PMC3299482/>.
45. R. A. Carr, B. J. Rejowski, G. A. Cote, H. A. Pitt, and N. J. Zyromski, "Systematic Review of Hypertriglyceridemia-Induced Acute Pancreatitis: A More Virulent Etiology?," *Pancreatology* 16, no. 4 (2016): 469–476, <https://doi.org/10.1016/j.pan.2016.02.011>.
46. M. Signoretti, F. Baccini, M. Piciocchi, et al., "Repeated Trans-abdominal Ultrasonography is a Simple and Accurate Strategy to Diagnose a Biliary Etiology of Acute Pancreatitis," *Pancreas* 43, no. 7 (2014): 1106–1110, <https://doi.org/10.1097/mpa.0000000000000164>.
47. N. D. Hallensleben, D. S. Umans, S. A. Bouwense, et al., "The Diagnostic Work-Up and Outcomes of 'Presumed' Idiopathic Acute Pancreatitis: A Post-hoc Analysis of a Multicentre Observational Cohort," *United European Gastroenterology Journal* 8, no. 3 (2020): 340–350, <https://doi.org/10.1177/2050640619890462>.
48. J. C. Ardengh, C. A. Malheiros, F. Rahal, V. Pereira, and A. J. Ganc, "Microlithiasis of the Gallbladder: Role of Endoscopic Ultrasonography in Patients With Idiopathic Acute Pancreatitis," *Revista da Associação Médica Brasileira* 56, no. 1 (2010): 27–31, <https://doi.org/10.1590/s0104-42302010000100011>.
49. J. L. Frossard, L. Sosa-Valencia, G. Amouyal, O. Marty, A. Hadengue, and P. Amouyal, "Usefulness of Endoscopic Ultrasonography in Patients With 'Idiopathic' Acute Pancreatitis," *American Journal of Medicine* 109, no. 3 (2000): 196–200, [https://doi.org/10.1016/s0002-9343\(00\)00478-2](https://doi.org/10.1016/s0002-9343(00)00478-2).
50. V. R. Mujica, J. S. Barkin, and V. L. Go, "Acute Pancreatitis Secondary to Pancreatic Carcinoma: Study Group Participants," *Pancreas* 21, no. 4 (2000): 329–332, <https://doi.org/10.1097/00006676-200011000-00001>.
51. S. A. Norton and D. Alderson, "Endoscopic Ultrasonography in the Evaluation of Idiopathic Acute Pancreatitis," *British Journal of Surgery* 87, no. 12 (2000): 1650–1655, <https://doi.org/10.1046/j.1365-2168.2000.01587.x>.
52. C. M. Wilcox, S. Varadarajulu, and M. Eloubeidi, "Role of Endoscopic Evaluation in Idiopathic Pancreatitis: A Systematic Review," *Gastrointestinal Endoscopy* 63, no. 7 (2006): 1037–1045, <https://doi.org/10.1016/j.gie.2006.02.024>.
53. A. Mariani, P. G. Arcidiacono, S. Curioni, A. Giussani, and P. A. Testoni, "Diagnostic Yield of ERCP and Secretin-Enhanced MRCP and EUS in Patients With Acute Recurrent Pancreatitis of Unknown Aetiology," *Digestive and Liver Disease* 41, no. 10 (2009): 753–758, <https://doi.org/10.1016/j.dld.2009.01.009>.
54. I. Smith, J. Ramesh, K. Mönkemüller, K. R. Kyanam Kabir Baig, K. Mönkemüller, and CM Wilcox, "Emerging Role of Endoscopic Ultrasound in the Diagnostic Evaluation of Idiopathic Pancreatitis," *American Journal of the Medical Sciences* 350, no. 3 (2015): 229–234, <https://doi.org/10.1097/maj.0000000000000541>.

55. J. Wan, Y. Ouyang, C. Yu, X. Yang, L. Xia, and N. Lu, "Comparison of EUS With MRCP in Idiopathic Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Gastrointestinal Endoscopy* 87, no. 5 (2018): 1180–1188.e9, <https://doi.org/10.1016/j.gie.2017.11.028>.
56. D. B. Kim, C. N. Paik, D. S. Song, et al., "The Role of Endoscopic Ultrasonography and Magnetic Resonance Cholangiopancreatography in Patients With Acute Pancreatitis After Negative Computed Tomography Findings of the Etiology," *Pancreas* 47, no. 9 (2018): 1165–1171, <https://doi.org/10.1097/mpa.0000000000001149>.
57. R. Pereira, G. Eslick, and M. Cox, "Endoscopic Ultrasound for Routine Assessment in Idiopathic Acute Pancreatitis," *Journal of Gastrointestinal Surgery* 23, no. 8 (2019): 1694–1700, <https://doi.org/10.1007/s11605-019-04272-3>.
58. F. Valverde-Lopez, E. J. Ortega-Suazo, C. M. Wilcox, M. C. Fernandez-Cano, J. G. Martinez-Cara, and E. Redondo-Cerezo, "Endoscopic Ultrasound as a Diagnostic and Predictive Tool in Idiopathic Acute Pancreatitis," *Annals of Gastroenterology* 33, no. 3 (2020): 305–312, <https://doi.org/10.20524/aog.2020.0464>.
59. J. J. Vila, F. J. J. Mendioroz, P. Yeaton, et al., "EUS is Superior to Secretin-Enhanced Cholangio-MRI to Establish the Etiology of Idiopathic Acute Pancreatitis," *Endoscopy International Open* 8, no. 10 (2020): E1441–E1447, <https://doi.org/10.1055/a-1233-1849>.
60. D. S. Umans, C. K. Rangkuti, C. J. Sperna Weiland, et al., "Endoscopic Ultrasonography Can Detect a Cause in the Majority of Patients With Idiopathic Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Endoscopy* 52, no. 11 (2020): 955–964, <https://doi.org/10.1055/a-1183-3370>.
61. S. Mazza, B. Elvo, C. B. Conti, et al., "Endoscopic Ultrasound Diagnostic Gain Over Computed Tomography and Magnetic Resonance Cholangiopancreatography in Defining Etiology of Idiopathic Acute Pancreatitis," *World Journal of Gastrointestinal Endoscopy* 14, no. 6 (2022): 376–386, <https://doi.org/10.4253/wjge.v14.i6.376>.
62. D. S. Umans, H. C. Timmerhuis, M. G. F. Anten, et al., "Prospective Multicentre Study of Indications for Surgery in Patients With Idiopathic Acute Pancreatitis Following Endoscopic Ultrasonography (PICUS)," *British Journal of Surgery* 110, no. 12 (2023): 1877–1882, <https://doi.org/10.1093/bjs/znad318>.
63. T. Khoury, A. Shahin, and W. Sbeit, "Exploring the Optimal Timing of Endoscopic Ultrasound Performance Post-Acute Idiopathic Pancreatitis," *Diagnostics* 12, no. 8 (2022): 1808, <https://doi.org/10.3390/diagnostics12081808>.
64. A. R. Ortega, R. Gomez-Rodriguez, M. Romero, S. Fernandez-Zapardiel, M. Cespedes Mdel, and J. M. Carrobes, "Prospective Comparison of Endoscopic Ultrasonography and Magnetic Resonance Cholangiopancreatography in the Etiological Diagnosis of "Idiopathic" Acute Pancreatitis," *Pancreas* 40, no. 2 (2011): 289–294, <https://doi.org/10.1097/mpa.0b013e318201654a>.
65. A. Thevenot, B. Bournet, P. Otal, G. Canevet, J. Moreau, and L. Buscail, "Endoscopic Ultrasound and Magnetic Resonance Cholangiopancreatography in Patients With Idiopathic Acute Pancreatitis," *Digestive Diseases and Sciences* 58, no. 8 (2013): 2361–2368, <https://doi.org/10.1007/s10620-013-2632-y>.
66. K. Sandrasegaran, B. Tahir, U. Barad, et al., "The Value of Secretin-Enhanced MRCP in Patients With Recurrent Acute Pancreatitis," *American Journal of Roentgenology* 208, no. 2 (2017): 315–321, <https://doi.org/10.2214/ajr.16.16566>.
67. T. Mitra, V. K. Dixit, D. P. Yadav, et al., "Idiopathic Acute Pancreatitis-A Myth or Reality? Role of Endoscopic Ultrasonography and Magnetic Resonance Cholangiopancreatography in Its Diagnosis," *Indian Journal of Gastroenterology* 40, no. 1 (2021): 22–29, <https://doi.org/10.1007/s12664-020-01125-9>.
68. A. H. Chowdhury, D. J. Humes, S. E. Pritchard, et al., "The Effects of Morphine-Neostigmine and Secretin Provocation on Pancreaticobiliary Morphology in Healthy Subjects: A Randomized, Double-Blind Crossover Study Using Serial MRCP," *World Journal of Surgery* 35, no. 9 (2011): 2102–2109, <https://doi.org/10.1007/s00268-011-1162-z>.
69. P. F. Toledo, G. Cardenas, Z. Berger, D. Simian, and F. Araya, "Neostigmine(R) Improves Pancreatic Duct Visualization in Magnetic Resonance Cholangiopancreatography and Could Be a Cheap Alternative for Secretin," *Turkish Journal of Gastroenterology* 33, no. 8 (2022): 704–709, <https://doi.org/10.5152/tjg.2022.21864>.
70. S. B. Yoon, S. H. Moon, J. H. Kim, T. J. Song, and M. H. Kim, "The Use of Immunohistochemistry for IgG4 in the Diagnosis of Autoimmune Pancreatitis: A Systematic Review and meta-analysis," *Pancreatology* 20, no. 8 (2020): 1611–1619, <https://doi.org/10.1016/j.pan.2020.10.028>.
71. T. Shimosegawa, S. T. Chari, L. Frulloni, et al., "International Consensus Diagnostic Criteria for Autoimmune Pancreatitis: Guidelines of the International Association of Pancreatology," *Pancreas* 40, no. 3 (2011): 352–358, <https://doi.org/10.1097/mpa.0b013e3182142fd2>.
72. J. A. Barkin, Z. Nemeth, A. K. Saluja, and J. S. Barkin, "Cannabis-Induced Acute Pancreatitis: A Systematic Review," *Pancreas* 46, no. 8 (2017): 1035–1038, <https://doi.org/10.1097/mpa.0000000000000873>.
73. A. Culetto, B. Bournet, A. Haennig, L. Alric, J. M. Peron, and L. Buscail, "Prospective Evaluation of the Aetiological Profile of Acute Pancreatitis in Young Adult Patients," *Digestive and Liver Disease* 47, no. 7 (2015): 584–589, <https://doi.org/10.1016/j.dld.2015.03.009>.
74. S. Munigala, F. Kanwal, H. Xian, J. F. Scherrer, and B. Agarwal, "Increased Risk of Pancreatic Adenocarcinoma After Acute Pancreatitis," *Clinical Gastroenterology and Hepatology* 12, no. 7 (2014): 1143–1150.e1, <https://doi.org/10.1016/j.cgh.2013.12.033>.
75. S. Werlin, F. M. Konikoff, Z. Halpern, et al., "Genetic and Electrophysiological Characteristics of Recurrent Acute Pancreatitis," *Journal of Pediatric Gastroenterology and Nutrition* 60, no. 5 (2015): 675–679, <https://doi.org/10.1097/mpg.0000000000000623>.
76. L. M. Cruz, J. Y. Kwon, S. P. Oman, et al., "Comparison of Idiopathic Recurrent Acute Pancreatitis [IRAP] and Recurrent Acute Pancreatitis With Genetic Mutations," *Digestive and Liver Disease* 53, no. 10 (2021): 1294–1300, <https://doi.org/10.1016/j.dld.2021.04.013>.
77. N. M. Guda, V. Muddana, D. C. Whitcomb, et al., "Recurrent Acute Pancreatitis: International State-of-the-Science Conference With Recommendations," *Pancreas* 47, no. 6 (2018): 653–666, <https://doi.org/10.1097/mpa.0000000000001053>.
78. G. Del Vecchio Blanco, C. Gesuale, M. Varanese, G. Monteleone, and O. A. Paoluzi, "Idiopathic Acute Pancreatitis: A Review on Etiology and Diagnostic Work-Up," *Clinical Journal of Gastroenterology* 12, no. 6 (2019): 511–524, <https://doi.org/10.1007/s12328-019-00987-7>.
79. J. Romagnuolo, N. Guda, M. Freeman, and V. Durkalski, "Preferred Designs, Outcomes, and Analysis Strategies for Treatment Trials in Idiopathic Recurrent Acute Pancreatitis," *Gastrointestinal Endoscopy* 68, no. 5 (2008): 966–974, <https://doi.org/10.1016/j.gie.2008.05.006>.
80. S. Kumar, C. Y. Ooi, S. Werlin, et al., "Risk Factors Associated With Pediatric Acute Recurrent and Chronic Pancreatitis: Lessons From INSPPIRE," *JAMA Pediatrics* 170, no. 6 (2016): 562–569, <https://doi.org/10.1001/jamapediatrics.2015.4955>.
81. N. Y. Jalaly, R. A. Moran, F. Fargahi, et al., "An Evaluation of Factors Associated With Pathogenic PRSS1, SPINK1, CTRF, And/OR CTRC Genetic Variants in Patients With Idiopathic Pancreatitis," *American Journal of Gastroenterology* 112, no. 8 (2017): 1320–1329, <https://doi.org/10.1038/ajg.2017.106>.
82. C. Lloret Linares, A. L. Pelletier, S. Czernichow, et al., "Acute Pancreatitis in a Cohort of 129 Patients Referred for Severe Hypertriglyceridemia," *Pancreas* 37, no. 1 (2008): 13–22, <https://doi.org/10.1097/mpa.0b013e31816074a1>.

83. S. Sandhu, A. Al-Sarraf, C. Taraboanta, J. Frohlich, and G. A. Francis, "Incidence of Pancreatitis, Secondary Causes, and Treatment of Patients Referred to a Specialty Lipid Clinic With Severe Hypertriglyceridemia: A Retrospective Cohort Study," *Lipids in Health and Disease* 10, no. 1 (2011): 157, <https://doi.org/10.1186/1476-511x-10-157>.
84. M. J. Murphy, X. Sheng, T. M. MacDonald, and L. Wei, "Hypertriglyceridemia and Acute Pancreatitis," *JAMA Internal Medicine* 173, no. 2 (2013): 162–164, <https://doi.org/10.1001/2013.jamainternmed.477>.
85. S. B. Pedersen, A. Langsted, and B. G. Nordestgaard, "Nonfasting Mild-to-Moderate Hypertriglyceridemia and Risk of Acute Pancreatitis," *JAMA Internal Medicine* 176, no. 12 (2016): 1834–1842, <https://doi.org/10.1001/jamainternmed.2016.6875>.
86. S. Dhindsa, A. Sharma, A. Al-Khazaali, et al., "Intravenous Insulin Versus Conservative Management in Hypertriglyceridemia-Associated Acute Pancreatitis," *Journal of the Endocrine Society* 4, no. 1 (2020): bvz019, <https://doi.org/10.1210/jendso/bvz019>.
87. V. P. Pulipati, A. Amblee, S. E. T. Yap, H. Shaka, B. Tahsin, and L. Fogelfeld, "Hypertriglyceridemia-Associated Acute Pancreatitis: Response to Continuous Insulin Infusion," *PLoS One* 16, no. 11 (2021): e0260495, <https://doi.org/10.1371/journal.pone.0260495>.
88. B. Nasstrom, G. Olivecrona, T. Olivecrona, and B. G. Stegmayr, "Lipoprotein Lipase During Continuous Heparin Infusion: Tissue Stores Become Partially Depleted," *Journal of Laboratory and Clinical Medicine* 138, no. 3 (2001): 206–213, <https://doi.org/10.1067/mlc.2001.117666>.
89. M. Weintraub, T. Rassin, S. Eisenberg, et al., "Continuous Intravenous Heparin Administration in Humans Causes a Decrease in Serum Lipolytic Activity and Accumulation of Chylomicrons in Circulation," *Journal of Lipid Research* 35, no. 2 (1994): 229–238, [https://doi.org/10.1016/s0022-2275\(20\)41211-8](https://doi.org/10.1016/s0022-2275(20)41211-8).
90. Y. Zhang, J. Lin, L. Wu, J. Lin, and Y. Liang, "Blood Purification for Hypertriglyceridemia-Induced Acute Pancreatitis: A Meta-Analysis," *Pancreas* 51, no. 5 (2022): 531–539, <https://doi.org/10.1097/mpa.0000000000002071>.
91. W. He, W. Cai, X. Yang, et al., "Insulin or Blood Purification Treatment for Hypertriglyceridaemia-Associated Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Pancreatology* 22, no. 7 (2022): 846–857, <https://doi.org/10.1016/j.pan.2022.07.013>.
92. L. H. Yan, X. H. Hu, R. X. Chen, et al., "Plasmapheresis Compared With Conventional Treatment for Hypertriglyceridemia-Induced Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Journal of Clinical Apheresis* 38, no. 1 (2023): 4–15, <https://doi.org/10.1002/jca.22018>.
93. S. Piplani, A. Jain, K. Singh, et al., "Efficacy and Adverse Effects of Insulin Versus Plasmapheresis in Patients With Hypertriglyceridemia-3-Induced Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Annals of Gastroenterology* 37, no. 1 (2024): 109–116, <https://doi.org/10.20524/aog.2023.0849>.
94. M. Kinoshita, K. Yokote, H. Arai, et al., "Japan Atherosclerosis Society (JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017," *Journal of Atherosclerosis and Thrombosis* 25, no. 9 (2018): 846–984, <https://doi.org/10.5551/jat.gl2017>.
95. F. Mach, C. Baigent, A. L. Catapano, et al., "2019 ESC/EAS Guidelines for the Management of Dyslipidaemias: Lipid Modification to Reduce Cardiovascular Risk," *European Heart Journal* 41, no. 1 (2020): 111–188, <https://doi.org/10.1093/eurheartj/ehz455>.
96. S. M. Grundy, N. J. Stone, A. L. Bailey, et al., "2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines," *Circulation* 139, no. 25 (2019): e1082–e1143, <https://doi.org/10.1161/cir.0000000000000625>.
97. M. Arca, C. Borghi, R. Pontremoli, et al., "Hypertriglyceridemia and omega-3 Fatty Acids: Their Often Overlooked Role in Cardiovascular Disease Prevention," *Nutrition, Metabolism, and Cardiovascular Diseases* 28, no. 3 (2018): 197–205, <https://doi.org/10.1016/j.numecd.2017.11.001>.
98. L. L. O'Mahoney, J. Matu, O. J. Price, et al., "Omega-3 Polyunsaturated Fatty Acids Favourably Modulate Cardiometabolic Biomarkers in Type 2 Diabetes: A Meta-Analysis and Meta-Regression of Randomized Controlled Trials," *Cardiovascular Diabetology* 17, no. 1 (2018): 98, <https://doi.org/10.1186/s12933-018-0740-x>.
99. M. Yokoyama, H. Origasa, M. Matsuzaki, et al., "Effects of Eicosapentaenoic Acid on Major Coronary Events in Hypercholesterolaemic Patients (JELIS): A Randomised Open-Label, Blinded Endpoint Analysis," *Lancet* 369, no. 9567 (2007): 1090–1098, [https://doi.org/10.1016/s0140-6736\(07\)60527-3](https://doi.org/10.1016/s0140-6736(07)60527-3).
100. P. Rawla, T. Sunkara, K. C. Thandra, and V. Gaduputi, "Hypertriglyceridemia-Induced Pancreatitis: Updated Review of Current Treatment and Preventive Strategies," *Clinical Journal of Gastroenterology* 11, no. 6 (2018): 441–448, <https://doi.org/10.1007/s12328-018-0881-1>.
101. V. Simha, "Management of Hypertriglyceridemia," *BMJ* 371 (2020): m3109, <https://doi.org/10.1136/bmj.m3109>.
102. E. P. Dellinger, C. E. Forsmark, P. Layer, et al., "Determinant-Based Classification of Acute Pancreatitis Severity: An International Multidisciplinary Consultation," *Annals of Surgery* 256, no. 6 (2012): 875–880, <https://doi.org/10.1097/sla.0b013e318256f778>.
103. Q. Guo, M. Li, Y. Chen, and W. Hu, "Determinant-Based Classification and Revision of the Atlanta Classification, Which One Should We Choose to Categorize Acute Pancreatitis?," *Pancreatology* 15, no. 4 (2015): 331–336, <https://doi.org/10.1016/j.pan.2015.05.467>.
104. J. H. Choi, M. H. Kim, D. Oh, et al., "Clinical Relevance of the Revised Atlanta Classification Focusing on Severity Stratification System," *Pancreatology* 14, no. 5 (2014): 324–329, <https://doi.org/10.1016/j.pan.2014.08.001>.
105. Y. Chen, L. Ke, Z. Tong, W. Li, and J. Li, "Association Between Severity and the Determinant-Based Classification, Atlanta 2012 and Atlanta 1992, in Acute Pancreatitis: A Clinical Retrospective Study," *Medicine (Baltimore)* 94, no. 13 (2015): e638, <https://doi.org/10.1097/md.0000000000000638>.
106. J. R. Carvalho, S. R. Fernandes, P. Santos, C. M. Moura, T. Antunes, and J. Velosa, "Acute Pancreatitis in the Elderly: A Cause for Increased Concern?," *European Journal of Gastroenterology and Hepatology* 30, no. 3 (2018): 337–341, <https://doi.org/10.1097/meg.0000000000001028>.
107. R. A. Moran, G. Garcia-Rayado, D. de la Iglesia-Garcia, et al., "Influence of Age, Body Mass Index and Comorbidity on Major Outcomes in Acute Pancreatitis, a Prospective Nation-Wide Multicentre Study," *United European Gastroenterology Journal* 6, no. 10 (2018): 1508–1518, <https://doi.org/10.1177/2050640618798155>.
108. J. Martinez, C. D. Johnson, J. Sanchez-Paya, E. de Madaria, G. Robles-Diaz, and M. Perez-Mateo, "Obesity is a Definitive Risk Factor of Severity and Mortality in Acute Pancreatitis: An Updated meta-analysis," *Pancreatology* 6, no. 3 (2006): 206–209, <https://doi.org/10.1159/000092104>.
109. S. Hong, B. Qiwen, J. Ying, A. Wei, and T. Chaoyang, "Body Mass Index and the Risk and Prognosis of Acute Pancreatitis: A Meta-Analysis," *European Journal of Gastroenterology and Hepatology* 23, no. 12 (2011): 1136–1143, <https://doi.org/10.1097/meg.0b013e318234b0e0e>.
110. D. Dobszai, P. Mátrai, Z. Gyöngyi, et al., "Body-Mass Index Correlates With Severity and Mortality in Acute Pancreatitis: A Meta-Analysis," *World Journal of Gastroenterology* 25, no. 6 (2019): 729–743, <https://doi.org/10.3748/wjg.v25.i6.729>.
111. R. Farquhar, S. Matthews, N. Baxter, et al., "Sarcopenia and Sarcopenic Obesity on Body Composition Analysis is a Significant Predictor of Mortality in Severe Acute Pancreatitis: A Longitudinal Observational

- Study," *World Journal of Surgery* 47, no. 11 (2023): 2825–2833, <https://doi.org/10.1007/s00268-023-07122-1>.
112. Y. Fei, K. Gao, J. Tu, W. Wang, G. Q. Zong, and W. Q. Li, "Predicting and Evaluation the Severity in Acute Pancreatitis Using a New Modeling Built on Body Mass Index and Intra-abdominal Pressure," *American Journal of Surgery* 216, no. 2 (2018): 304–309, <https://doi.org/10.1016/j.amjsurg.2017.04.017>.
 113. B. U. Wu, R. S. Johannes, X. Sun, D. L. Conwell, and P. A. Banks, "Early Changes in Blood Urea Nitrogen Predict Mortality in Acute Pancreatitis," *Gastroenterology* 137, no. 1 (2009): 129–135, <https://doi.org/10.1053/j.gastro.2009.03.056>.
 114. B. U. Wu, O. J. Bakker, G. I. Papachristou, et al., "Blood Urea Nitrogen in the Early Assessment of Acute Pancreatitis: An International Validation Study," *Archives of Internal Medicine* 171, no. 7 (2011): 669–676, <https://doi.org/10.1001/archinternmed.2011.126>.
 115. S. I. Gan and J. Romagnuolo, "Admission Hematocrit: A Simple, Useful and Early Predictor of Severe Pancreatitis," *Digestive Diseases and Sciences* 49, no. 11–12 (2004): 1946–1952, <https://doi.org/10.1007/s10620-004-9598-8>.
 116. J. D. Baillargeon, J. Orav, V. Ramagopal, S. M. Tenner, and P. A. Banks, "Hemoconcentration as an Early Risk Factor for Necrotizing Pancreatitis," *American Journal of Gastroenterology* 93, no. 11 (1998): 2130–2134, <https://doi.org/10.1111/j.1572-0241.1998.00608.x>.
 117. P. G. Lankisch, R. Mahlke, T. Blum, et al., "Hemoconcentration: An Early Marker of Severe And/Or Necrotizing Pancreatitis? A Critical Appraisal," *American Journal of Gastroenterology* 96, no. 7 (2001): 2081–2085, <https://doi.org/10.1111/j.1572-0241.2001.03966.x>.
 118. F. S. Cardoso, L. B. Ricardo, A. M. Oliveira, et al., "C-Reactive Protein Prognostic Accuracy in Acute Pancreatitis: Timing of Measurement and Cutoff Points," *European Journal of Gastroenterology and Hepatology* 25, no. 7 (2013): 784–789, <https://doi.org/10.1097/meg.0b013e32835fd3f0>.
 119. O. Komolafe, S. P. Pereira, B. R. Davidson, and K. S. Gurusamy, "Serum C-reactive Protein, Procalcitonin, and Lactate Dehydrogenase for the Diagnosis of Pancreatic Necrosis," *Cochrane Database of Systematic Reviews* 4, no. 4 (2017): Cd012645, <https://doi.org/10.1002/14651858.CD012645>.
 120. C. Lelubre, S. Anselin, K. Zouaoui Boudjeltia, P. Biston, and M. Piagnerelli, "Interpretation of C-Reactive Protein Concentrations in Critically Ill Patients," *BioMed Research International* 2013 (2013): 124021, <https://doi.org/10.1155/2013/124021>.
 121. R. Mofidi, M. D. Duff, S. J. Wigmore, K. K. Madhavan, O. J. Garden, and R. W. Parks, "Association Between Early Systemic Inflammatory Response, Severity of Multiorgan Dysfunction and Death in Acute Pancreatitis," *British Journal of Surgery* 93, no. 6 (2006): 738–744, <https://doi.org/10.1002/bjs.5290>.
 122. V. K. Singh, B. U. Wu, T. L. Bollen, et al., "Early Systemic Inflammatory Response Syndrome is Associated With Severe Acute Pancreatitis," *Clinical Gastroenterology and Hepatology* 7, no. 11 (2009): 1247–1251, <https://doi.org/10.1016/j.cgh.2009.08.012>.
 123. R. Mofidi, S. A. Suttie, P. V. Patil, S. Ogston, and R. W. Parks, "The Value of Procalcitonin at Predicting the Severity of Acute Pancreatitis and Development of Infected Pancreatic Necrosis: Systematic Review," *Surgery* 146, no. 1 (2009): 72–81, <https://doi.org/10.1016/j.surg.2009.02.013>.
 124. B. M. Rau, E. A. Kemppainen, A. A. Gumbs, et al., "Early Assessment of Pancreatic Infections and Overall Prognosis in Severe Acute Pancreatitis by Procalcitonin (PCT): A Prospective International Multicenter Study," *Annals of Surgery* 245, no. 5 (2007): 745–754, <https://doi.org/10.1097/01.sla.0000252443.22360.46>.
 125. G. I. Papachristou and D. C. Whitcomb, "Inflammatory Markers of Disease Severity in Acute Pancreatitis," *Clinics in Laboratory Medicine* 25, no. 1 (2005): 17–37, <https://doi.org/10.1016/j.cll.2004.12.003>.
 126. R. Pezzilli, P. Billi, R. Miniero, et al., "Serum Interleukin-6, Interleukin-8, and Beta 2-Microglobulin in Early Assessment of Severity of Acute Pancreatitis. Comparison With Serum C-Reactive Protein," *Digestive Diseases and Sciences* 40, no. 11 (1995): 2341–2348, <https://doi.org/10.1007/bf02063235>.
 127. E. Aoun, J. Chen, D. Reighard, F. C. Gleeson, D. C. Whitcomb, and G. I. Papachristou, "Diagnostic Accuracy of Interleukin-6 and Interleukin-8 in Predicting Severe Acute Pancreatitis: A Meta-Analysis," *Pancreatology* 9, no. 6 (2009): 777–785, <https://doi.org/10.1159/000214191>.
 128. N. Pooran, A. Indaram, P. Singh, and S. Bank, "Cytokines (IL-6, IL-8, TNF): Early and Reliable Predictors of Severe Acute Pancreatitis," *Journal of Clinical Gastroenterology* 37, no. 3 (2003): 263–266, <https://doi.org/10.1097/00004836-200309000-00013>.
 129. M. L. Malmstrom, M. B. Hansen, A. M. Andersen, et al., "Cytokines and Organ Failure in Acute Pancreatitis: Inflammatory Response in Acute Pancreatitis," *Pancreas* 41, no. 2 (2012): 271–277, <https://doi.org/10.1097/mpa.0b013e3182240552>.
 130. B. U. Wu, R. S. Johannes, X. Sun, Y. Tabak, D. L. Conwell, and P. A. Banks, "The Early Prediction of Mortality in Acute Pancreatitis: A Large Population-Based Study," *Gut* 57, no. 12 (2008): 1698–1703, <https://doi.org/10.1136/gut.2008.152702>.
 131. B. U. Wu, M. Batech, M. Quezada, et al., "Dynamic Measurement of Disease Activity in Acute Pancreatitis: The Pancreatitis Activity Scoring System," *American Journal of Gastroenterology* 112, no. 7 (2017): 1144–1152, <https://doi.org/10.1038/ajg.2017.114>.
 132. J. Buxbaum, M. Quezada, B. Chong, et al., "The Pancreatitis Activity Scoring System Predicts Clinical Outcomes in Acute Pancreatitis: Findings From a Prospective Cohort Study," *American Journal of Gastroenterology* 113, no. 5 (2018): 755–764, <https://doi.org/10.1038/s41395-018-0048-1>.
 133. R. Mounzer, C. J. Langmead, B. U. Wu, et al., "Comparison of Existing Clinical Scoring Systems to Predict Persistent Organ Failure in Patients With Acute Pancreatitis," *Gastroenterology* 142, no. 7 (2012): 1476–1482; quiz e15–6, <https://doi.org/10.1053/j.gastro.2012.03.005>.
 134. K. J. Lee, H. M. Kim, J. S. Choi, Y. J. Kim, Y. S. Kim, and J. H. Cho, "Comparison of Predictive Systems in Severe Acute Pancreatitis According to the Revised Atlanta Classification," *Pancreas* 45, no. 1 (2016): 46–50, <https://doi.org/10.1097/mpa.0000000000000433>.
 135. G. I. Papachristou, V. Muddana, D. Yadav, et al., "Comparison of BISAP, Ranson's, APACHE-II, and CTSI Scores in Predicting Organ Failure, Complications, and Mortality in Acute Pancreatitis," *American Journal of Gastroenterology* 105, no. 2 (2010): 435–441; quiz 42, <https://doi.org/10.1038/ajg.2009.622>.
 136. A. K. Khanna, S. Meher, S. Prakash, et al., "Comparison of Ranson, Glasgow, MOSS, SIRS, BISAP, APACHE-II, CTSI Scores, IL-6, CRP, and Procalcitonin in Predicting Severity, Organ Failure, Pancreatic Necrosis, and Mortality in Acute Pancreatitis," *HPB Surgery* 2013 (2013): 367581, <https://doi.org/10.1155/2013/367581>.
 137. J. H. Cho, T. N. Kim, H. H. Chung, and K. H. Kim, "Comparison of Scoring Systems in Predicting the Severity of Acute Pancreatitis," *World Journal of Gastroenterology* 21, no. 8 (2015): 2387–2394, <https://doi.org/10.3748/wjg.v21.i8.2387>.
 138. S. Chandra, A. Murali, R. Bansal, D. Agarwal, and A. Holm, "The Bedside Index for Severity in Acute Pancreatitis: A Systematic Review of Prospective Studies to Determine Predictive Performance," *Journal of Community Hospital Internal Medicine Perspectives* 7, no. 4 (2017): 208–213, <https://doi.org/10.1080/20009666.2017.1361292>.
 139. W. Gao, H. X. Yang, and C. E. Ma, "The Value of BISAP Score for Predicting Mortality and Severity in Acute Pancreatitis: A Systematic Review and Meta-Analysis," *PLoS One* 10, no. 6 (2015): e0130412, <https://doi.org/10.1371/journal.pone.0130412>.

140. G. Capurso, R. Ponz de Leon Pisani, G. Lauri, et al., "Clinical Usefulness of Scoring Systems to Predict Severe Acute Pancreatitis: A Systematic Review and Meta-Analysis With Pre and Post-Test Probability Assessment," *United European Gastroenterology Journal* 11, no. 9 (2023): 825–836, <https://doi.org/10.1002/ueg2.12464>.
141. B. Kui, J. Pinter, R. Molontay, et al., "EASY-APP: An Artificial Intelligence Model and Application for Early and Easy Prediction of Severity in Acute Pancreatitis," *Clinical and Translational Medicine* 12, no. 6 (2022): e842, <https://doi.org/10.1002/ctm2.842>.
142. M. S. Petrov, S. Shanbhag, M. Chakraborty, A. R. Phillips, and J. A. Windsor, "Organ Failure and Infection of Pancreatic Necrosis as Determinants of Mortality in Patients With Acute Pancreatitis," *Gastroenterology* 139, no. 3 (2010): 813–820, <https://doi.org/10.1053/j.gastro.2010.06.010>.
143. M. Werge, S. Novovic, P. N. Schmidt, and L. L. Gluud, "Infection Increases Mortality in Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis," *Pancreatology* 16, no. 5 (2016): 698–707, <https://doi.org/10.1016/j.pan.2016.07.004>.
144. P. Marcos-Neira, F. Bubia-Olaskoaga, S. Lopez-Cuenca, and L. Bordeje-Laguna, "Epidemiology of Acute Pancreatitis in Intensive Care Medicine Study G. Relationship Between Intra-abdominal Hypertension, Outcome and the Revised Atlanta and Determinant-Based Classifications in Acute Pancreatitis," *BJS Open* 1, no. 6 (2017): 175–181, <https://doi.org/10.1002/bjs5.29>.
145. E. de-Madaria, J. L. Buxbaum, P. Maisonneuve, et al., "Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis," *New England Journal of Medicine* 387, no. 11 (2022): 989–1000, <https://doi.org/10.1056/nejmoa220884>.
146. E. Q. Mao, Y. Q. Tang, J. Fei, et al., "Fluid Therapy for Severe Acute Pancreatitis in Acute Response Stage," *Chinese Medical Journal* 122, no. 2 (2009): 169–173, <https://doi.org/10.3760/cma.j.issn.0366-6999.2009.02.011>.
147. E. Q. Mao, J. Fei, Y. B. Peng, J. Huang, Y. Q. Tang, and S. D. Zhang, "Rapid Hemodilution is Associated With Increased Sepsis and Mortality Among Patients With Severe Acute Pancreatitis," *Chinese Medical Journal* 123, no. 13 (2010): 1639–1644, <https://doi.org/10.3760/cma.j.issn.0366-6999.2010.13.005>.
148. J. L. Buxbaum, M. Quezada, B. Da, et al., "Early Aggressive Hydration Hastens Clinical Improvement in Mild Acute Pancreatitis," *American Journal of Gastroenterology* 112, no. 5 (2017): 797–803, <https://doi.org/10.1038/ajg.2017.40>.
149. J. E. Cuellar-Monterrubio, R. Monreal-Robles, E. I. Gonzalez-Moreno, et al., "Nonaggressive Versus Aggressive Intravenous Fluid Therapy in Acute Pancreatitis With More than 24 Hours From Disease Onset: A Randomized Controlled Trial," *Pancreas* 49, no. 4 (2020): 579–583, <https://doi.org/10.1097/mpa.0000000000001528>.
150. A. Angsubhakorn, K. Tipchaichatta, and S. Chirapongsathorn, "Comparison of Aggressive Versus Standard Intravenous Hydration for Clinical Improvement Among Patients With Mild Acute Pancreatitis: A Randomized Controlled Trial," *Pancreatology* 21, no. 7 (2021): 1224–1230, <https://doi.org/10.1016/j.pan.2021.06.004>.
151. M. Di Martino, S. Van Laarhoven, B. Ielpo, et al., "Systematic Review and Meta-Analysis of Fluid Therapy Protocols in Acute Pancreatitis: Type, Rate and Route," *HPB* 23, no. 11 (2021): 1629–1638, <https://doi.org/10.1016/j.hpb.2021.06.426>.
152. F. Wu, D. She, Q. Ao, S. Zhang, and J. Li, "Aggressive Intravenous Hydration Protocol of Lactated Ringer's Solution Benefits Patients With Mild Acute Pancreatitis: A Meta-Analysis of 5 Randomized Controlled Trials," *Frontiers of Medicine* 9 (2022): 966824, <https://doi.org/10.3389/fmed.2022.966824>.
153. M. M. Gad and C. R. Simons-Linares, "Is Aggressive Intravenous Fluid Resuscitation Beneficial in Acute Pancreatitis? A Meta-Analysis of Randomized Control Trials and Cohort Studies," *World Journal of Gastroenterology* 26, no. 10 (2020): 1098–1106, <https://doi.org/10.3748/wjg.v26.i10.1098>.
154. X. W. Li, C. H. Wang, J. W. Dai, et al., "Comparison of Clinical Outcomes Between Aggressive and Non-Aggressive Intravenous Hydration for Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Critical Care* 27, no. 1 (2023): 122, <https://doi.org/10.1186/s13054-023-04401-0>.
155. X. Ding and B. Chen, "Effect of Aggressive Intravenous Fluid Resuscitation Versus Nonaggressive Fluid Resuscitation in the Treatment of Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Pancreas* 52, no. 2 (2023): e89–e100, <https://doi.org/10.1097/mpa.0000000000002230>.
156. K. He, L. Gao, Z. Yang, et al., "Aggressive Versus Controlled Fluid Resuscitation in Acute Pancreatitis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials," *Chinese Medical Journal* 136, no. 10 (2023): 1166–1173, <https://doi.org/10.1097/cm9.0000000000002684>.
157. A. Dawson, M. Karunakaran, Z. D. Sharma, S. Ullah, and S. G. Barreto, "Fluid Resuscitation in the Early Management of Acute Pancreatitis - Evidence From a Systematic Review and Meta-Analysis," *HPB* 25, no. 12 (2023): 1451–1465, <https://doi.org/10.1016/j.hpb.2023.08.013>.
158. B. U. Wu, J. Q. Hwang, T. H. Gardner, et al., "Lactated Ringer's Solution Reduces Systemic Inflammation Compared With Saline in Patients With Acute Pancreatitis," *Clinical Gastroenterology and Hepatology* 9, no. 8 (2011): 710–717.e1, <https://doi.org/10.1016/j.cgh.2011.04.026>.
159. S. Choosakul, K. Harinwan, S. Chirapongsathorn, et al., "Comparison of Normal Saline Versus Lactated Ringer's Solution for Fluid Resuscitation in Patients With Mild Acute Pancreatitis, A Randomized Controlled Trial," *Pancreatology* 18, no. 5 (2018): 507–512, <https://doi.org/10.1016/j.pan.2018.04.016>.
160. E. de-Madaria, I. Herrera-Marante, V. Gonzalez-Camacho, et al., "Fluid Resuscitation With Lactated Ringer's Solution Vs Normal Saline in Acute Pancreatitis: A Triple-Blind, Randomized, Controlled Trial," *United European Gastroenterology Journal* 6, no. 1 (2018): 63–72, <https://doi.org/10.1177/2050640617707864>.
161. S. Kayhan, B. Selcan Akyol, M. Ergul, and C. Baysan, "The Effect of Type of Fluid on Disease Severity in Acute Pancreatitis Treatment," *European Review for Medical and Pharmacological Sciences* 25, no. 23 (2021): 7460–7467, https://doi.org/10.26355/eurrev_202112_27443.
162. B. Karki, S. Thapa, D. Khadka, et al., "Intravenous Ringers Lactate Versus Normal Saline for Predominantly Mild Acute Pancreatitis in a Nepalese Tertiary Hospital," *PLoS One* 17, no. 1 (2022): e0263221, <https://doi.org/10.1371/journal.pone.0263221>.
163. A. Lee, C. Ko, C. Buitrago, et al., "Lactated Ringers vs Normal Saline Resuscitation for Mild Acute Pancreatitis: A Randomized Trial," *Gastroenterology* 160, no. 3 (2021): 955–957.e4, <https://doi.org/10.1053/j.gastro.2020.10.044>.
164. S. Zhou, C. Buitrago, A. Foong, et al., "Comprehensive Meta-Analysis of Randomized Controlled Trials of Lactated Ringer's Versus Normal Saline for Acute Pancreatitis," *Pancreatology* 21, no. 8 (2021): 1405–1410, <https://doi.org/10.1016/j.pan.2021.07.003>.
165. M. Aziz, Z. Ahmed, S. Weissman, et al., "Lactated Ringer's vs Normal Saline for Acute Pancreatitis: An Updated Systematic Review and meta-analysis," *Pancreatology* 21, no. 7 (2021): 1217–1223, <https://doi.org/10.1016/j.pan.2021.06.002>.
166. H. Chen, X. Lu, B. Xu, C. Meng, and D. Xie, "Lactated Ringer Solution is Superior to Normal Saline Solution in Managing Acute Pancreatitis: An Updated Meta-Analysis of Randomized Controlled Trials," *Journal of Clinical Gastroenterology* 56, no. 2 (2022): e114–e120, <https://doi.org/10.1097/mcg.0000000000001656>.

167. K. Ocskay, P. Mátrai, P. Hegyi, and A. Párnicsky, "Lactated Ringer's Solution Reduces Severity, Mortality, Systemic and Local Complications in Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Biomedicines* 11, no. 2 (2023): 321, <https://doi.org/10.3390/biomedicines11020321>.
168. E. de-Madaria, C. Sanchez-Marin, I. Carrillo, et al., "Design and Validation of a Patient-Reported Outcome Measure Scale in Acute Pancreatitis: The PAN-PROMISE Study," *Gut* 70, no. 1 (2021): 139–147, <https://doi.org/10.1136/gutjnl-2020-320729>.
169. N. Thavanesan, S. White, S. Lee, et al., "Analgesia in the Initial Management of Acute Pancreatitis: A Systematic Review and Meta-Analysis of Randomised Controlled Trials," *World Journal of Surgery* 46, no. 4 (2022): 878–890, <https://doi.org/10.1007/s00268-021-06420-w>.
170. W. Cai, F. Liu, Y. Wen, et al., "Pain Management in Acute Pancreatitis: A Systematic Review and Meta-Analysis of Randomised Controlled Trials," *Frontiers of Medicine* 8 (2021): 782151, <https://doi.org/10.3389/fmed.2021.782151>.
171. W. Meng, J. Yuan, C. Zhang, et al., "Parenteral Analgesics for Pain Relief in Acute Pancreatitis: A Systematic Review," *Pancreatology* 13, no. 3 (2013): 201–206, <https://doi.org/10.1016/j.pan.2013.02.003>.
172. P. Ungprasert, W. Cheungpasitporn, C. S. Crowson, and E. L. Matteson, "Individual Non-Steroidal Anti-Inflammatory Drugs and Risk of Acute Kidney Injury: A Systematic Review and Meta-Analysis of Observational Studies," *European Journal of Internal Medicine* 26, no. 4 (2015): 285–291, <https://doi.org/10.1016/j.ejim.2015.03.008>.
173. X. Zhang, P. T. Donnan, S. Bell, and B. Guthrie, "Non-Steroidal Anti-inflammatory Drug Induced Acute Kidney Injury in the Community Dwelling General Population and People With Chronic Kidney Disease: Systematic Review and Meta-Analysis," *BMC Nephrology* 18, no. 1 (2017): 256, <https://doi.org/10.1186/s12882-017-0673-8>.
174. Z. Huang, X. Ma, X. Jia, et al., "Prevention of Severe Acute Pancreatitis With Cyclooxygenase-2 Inhibitors: A Randomized Controlled Clinical Trial," *American Journal of Gastroenterology* 115, no. 3 (2020): 473–480, <https://doi.org/10.14309/ajg.0000000000000529>.
175. L. Huang, Z. Feng, W. Yang, et al., "Parecoxib Sequential With Imrecoxib for Occurrence and Remission of Severe Acute Pancreatitis: A Multicentre, Double-Blind, Randomised, Placebo-Controlled Trial," *Gut* 74, no. 9 (2025): 1467–1475, <https://doi.org/10.1136/gutjnl-2024-334038>.
176. S. Pandanaboyana, W. Huang, J. A. Windsor, and A. M. Drewes, "Update on Pain Management in Acute Pancreatitis," *Current Opinion in Gastroenterology* 38, no. 5 (2022): 487–494, <https://doi.org/10.1097/mog.0000000000000861>.
177. N. S. Kumar, G. Muktesh, T. Samra, et al., "Comparison of Efficacy of Diclofenac and Tramadol in Relieving Pain in Patients of Acute Pancreatitis: A Randomized Parallel Group Double Blind Active Controlled Pilot Study," *European Journal of Pain* 24, no. 3 (2020): 639–648, <https://doi.org/10.1002/ejp.1515>.
178. A. M. Peiro, J. Martinez, E. Martinez, et al., "Efficacy and Tolerance of Metamizole Versus Morphine for Acute Pancreatitis Pain," *Pancreatology* 8, no. 1 (2008): 25–29, <https://doi.org/10.1159/000114852>.
179. S. J. Mahapatra, S. Jain, S. Bopanna, et al., "Pentazocine, a Kappa-Opioid Agonist, is Better Than Diclofenac for Analgesia in Acute Pancreatitis: A Randomized Controlled Trial," *American Journal of Gastroenterology* 114, no. 5 (2019): 813–821, <https://doi.org/10.14309/ajg.0000000000000224>.
180. B. Gulen, A. Dur, M. Serinken, O. Karcioglu, and E. Sonmez, "Pain Treatment in Patients With Acute Pancreatitis: A Randomized Controlled Trial," *Turkish Journal of Gastroenterology* 27, no. 2 (2016): 192–196, <https://doi.org/10.5152/tjg.2015.150398>.
181. M. Saini, J. Samanta, A. Kumar, et al., "Buprenorphine Versus Diclofenac for Pain Relief in Acute Pancreatitis: A Double-Blinded Randomized Controlled Trial," *Clinical Gastroenterology and Hepatology* 22, no. 3 (2024): 532–541.e8, <https://doi.org/10.1016/j.cgh.2023.10.021>.
182. A. D. Nelson, N. S. Lugo-Fagundo, S. J. Mahapatra, et al., "A Systematic Review and Meta-Analysis of Opioids vs Nonopioids in Acute Pancreatitis," *Gastro Hep Advances* 1, no. 1 (2022): 83–92, <https://doi.org/10.1016/j.gastha.2021.09.006>.
183. A. A. Anekar, J. M. Hendrix, and M. Cascella. *WHO Analgesic Ladder*. (2025, Statpearls).
184. R. Chou, D. B. Gordon, O. A. de Leon-Casasola, et al., "Management of Postoperative Pain: A Clinical Practice Guideline From the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council," *Journal of Pain* 17, no. 2 (2016): 131–157, <https://doi.org/10.1016/j.jpain.2015.12.008>.
185. E. M. Helander, B. L. Menard, C. M. Harmon, et al., "Multimodal Analgesia, Current Concepts, and Acute Pain Considerations," *Current Pain and Headache Reports* 21, no. 1 (2017): 3, <https://doi.org/10.1007/s11916-017-0607-y>.
186. S. M. Sadowski, A. Andres, P. Morel, et al., "Epidural Anesthesia Improves Pancreatic Perfusion and Decreases the Severity of Acute Pancreatitis," *World Journal of Gastroenterology* 21, no. 43 (2015): 12448–12456, <https://doi.org/10.3748/wjg.v21.i43.12448>.
187. A. Tyagi, Y. R. Gupta, S. Das, G. Rai, and A. Gupta, "Effect of Segmental Thoracic Epidural Block on Pancreatitis-induced Organ Dysfunction: A Preliminary Study," *Indian Journal of Critical Care Medicine* 23, no. 2 (2019): 89–94, <https://doi.org/10.5005/jp-journals-10071-23123>.
188. Y. Sasabuchi, H. Yasunaga, H. Matsui, A. K. Lefor, K. Fushimi, and M. Sanui, "Epidural Analgesia is Infrequently Used in Patients With Acute Pancreatitis: A Retrospective Cohort Study," *Acta Gastro-Enterologica Belgica* 80, no. 3 (2017): 381–384, <https://www.ageb.be/ageb-journal/ageb-volume/ageb-article/273/>.
189. M. Jabaudon, N. Belhadj-Tahar, T. Rimmele, et al., "Thoracic Epidural Analgesia and Mortality in Acute Pancreatitis: A Multicenter Propensity Analysis," *Critical Care Medicine* 46, no. 3 (2018): e198–e205, <https://doi.org/10.1097/ccm.0000000000002874>.
190. M. Jabaudon, A. Genevri, S. Jaber, et al., "Thoracic Epidural Analgesia in Intensive Care Unit Patients With Acute Pancreatitis: The EPIPAN Multicenter Randomized Controlled Trial," *Critical Care* 27, no. 1 (2023): 213, <https://doi.org/10.1186/s13054-023-04502-w>.
191. Q. Wang, B. Fu, D. Su, and X. Fu, "Impact of Early Thoracic Epidural Analgesia in Patients With Severe Acute Pancreatitis," *European Journal of Clinical Investigation* 52, no. 6 (2022): e13740, <https://doi.org/10.1111/eci.13740>.
192. D. Al-Leswas, N. Baxter, W. B. Lim, et al., "The Safety and Efficacy of Epidural Anaesthesia in Acute Pancreatitis: A Systematic Review and Meta-Analysis," *HPB* 25, no. 2 (2023): 162–171, <https://doi.org/10.1016/j.hpb.2022.12.004>.
193. S. Kahl, S. Zimmermann, M. Pross, H. U. Schulz, U. Schmidt, and P. Malfertheiner, "Procaine Hydrochloride Fails to Relieve Pain in Patients With Acute Pancreatitis," *Digestion* 69, no. 1 (2004): 5–9, <https://doi.org/10.1159/000076541>.
194. R. Jakobs, M. U. Adamek, A. C. von Bubnoff, and J. F. Riemann, "Buprenorphine or Procaine for Pain Relief in Acute Pancreatitis: A Prospective Randomized Study," *Scandinavian Journal of Gastroenterology* 35, no. 12 (2000): 1319–1323, <https://doi.org/10.1080/003655200453692>.
195. B. Wilms, K. S. Meffert, and B. Schultes, "[Procaine Infusion for Pain Treatment of Acute Pancreatitis: A Randomized, Placebo-Controlled Double-Blind Trial]," *DMW - Deutsche Medizinische Wochenschrift* 135, no. 46 (2010): 2290–2295, <https://doi.org/10.1055/s-0030-1267512>.

196. K. Zhang, C. Gao, C. Li, et al., "Acupuncture for Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Pancreas* 48, no. 9 (2019): 1136–1147, <https://doi.org/10.1097/mpa.0000000000001399>.
197. F. Zhu, S. Yin, X. Zhu, et al., "Acupuncture for Relieving Abdominal Pain and Distension in Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Frontiers in Psychiatry* 12 (2021): 786401, <https://doi.org/10.3389/fpsy.2021.786401>.
198. E. P. Dellinger, J. M. Tellado, N. E. Soto, et al., "Early Antibiotic Treatment for Severe Acute Necrotizing Pancreatitis: A Randomized, Double-Blind, Placebo-Controlled Study," *Annals of Surgery* 245, no. 5 (2007): 674–683, <https://doi.org/10.1097/01.sla.0000250414.09255.84>.
199. A. Garcia-Barrasa, F. G. Borobia, R. Pallares, et al., "A Double-Blind, Placebo-Controlled Trial of Ciprofloxacin Prophylaxis in Patients With Acute Necrotizing Pancreatitis," *Journal of Gastrointestinal Surgery* 13, no. 4 (2009): 768–774, <https://doi.org/10.1007/s11605-008-0773-7>.
200. G. Poropat, K. Goričanec, A. Lacković, A. Kresović, A. Lončarić, and M. Marušić, "Systematic Review With Trial Sequential Analysis of Prophylactic Antibiotics for Acute Pancreatitis," *Antibiotics (Basel)* 11, no. 9 (2022): 1191, <https://doi.org/10.3390/antibiotics11091191>.
201. Y. Bai, J. Gao, D. W. Zou, and Z. S. Li, "Prophylactic Antibiotics Cannot Reduce Infected Pancreatic Necrosis and Mortality in Acute Necrotizing Pancreatitis: Evidence From a Meta-Analysis of Randomized Controlled Trials," *American Journal of Gastroenterology* 103, no. 1 (2008): 104–110, <https://doi.org/10.1111/j.1572-0241.2007.01575.x>.
202. T. Mazaki, Y. Ishii, and T. Takayama, "Meta-Analysis of Prophylactic Antibiotic Use in Acute Necrotizing Pancreatitis," *British Journal of Surgery* 93, no. 6 (2006): 674–684, <https://doi.org/10.1002/bjs.5389>.
203. E. Villatoro, M. Mulla, and M. Larvin, "Antibiotic Therapy for Prophylaxis Against Infection of Pancreatic Necrosis in Acute Pancreatitis," *Cochrane Database of Systematic Reviews* 2010, no. 5 (2010): Cd002941, <https://doi.org/10.1002/14651858.cd002941.pub3>.
204. N. Ding, Y. H. Sun, L. M. Wen, et al., "Assessment of Prophylactic Antibiotics Administration for Acute Pancreatitis: A Meta-Analysis of Randomized Controlled Trials," *Chinese Medical Journal* 133, no. 2 (2020): 212–220, <https://doi.org/10.1097/cm9.0000000000000603>.
205. R. Isenmann, M. Runzi, M. Kron, et al., "Prophylactic Antibiotic Treatment in Patients With Predicted Severe Acute Pancreatitis: A Placebo-Controlled, Double-Blind Trial," *Gastroenterology* 126, no. 4 (2004): 997–1004, <https://doi.org/10.1053/j.gastro.2003.12.050>.
206. G. Poropat, A. Radovan, M. Peric, et al., "Prevention of Infectious Complications in Acute Pancreatitis: Results of a Single-Center, Randomized, Controlled Trial," *Pancreas* 48, no. 8 (2019): 1056–1060, <https://doi.org/10.1097/mpa.0000000000001368>.
207. G. S. Xiong, S. M. Wu, and Z. H. Wang, "Role of Prophylactic Antibiotic Administration in Severe Acute Pancreatitis: A Meta-Analysis," *Medical Principles and Practice* 15, no. 2 (2006): 106–110, <https://doi.org/10.1159/000090913>.
208. E. Maravi-Poma, J. Gener, F. Alvarez-Lerma, et al., "Early Antibiotic Treatment (Prophylaxis) of Septic Complications in Severe Acute Necrotizing Pancreatitis: A Prospective, Randomized, Multicenter Study Comparing Two Regimens With Imipenem-Cilastatin," *Intensive Care Medicine* 29, no. 11 (2003): 1974–1980, <https://doi.org/10.1007/s00134-003-1956-z>.
209. M. Arvanitakis, J. M. Dumonceau, J. Albert, et al., "Endoscopic Management of Acute Necrotizing Pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Evidence-Based Multidisciplinary Guidelines," *Endoscopy* 50, no. 5 (2018): 524–546, <https://doi.org/10.1055/a-0588-5365>.
210. R. Qu, Y. Ji, Y. Ling, et al., "Procalcitonin is a Good Tool to Guide Duration of Antibiotic Therapy in Patients With Severe Acute Pancreatitis: A Randomized Prospective Single-Center Controlled Trial," *Saudi Medical Journal* 33, no. 4 (2012): 382–387, <https://pubmed.ncbi.nlm.nih.gov/22485232/>.
211. A. K. Siriwardena, S. Jegatheeswaran, J. M. Mason, P. Investigators, J. M. Mason, et al., "A Procalcitonin-Based Algorithm to Guide Antibiotic Use in Patients With Acute Pancreatitis (PROCAP): A Single-Centre, Patient-Blinded, Randomised Controlled Trial," *Lancet Gastroenterology & Hepatology* 7, no. 10 (2022): 913–921, [https://doi.org/10.1016/s2468-1253\(22\)00212-6](https://doi.org/10.1016/s2468-1253(22)00212-6).
212. R. R. Singh, W. Mitchell, Y. David, et al., "Pancreatic Fungal Infection in Patients With Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis," *Journal of Clinical Gastroenterology* 55, no. 3 (2021): 218–226, <https://doi.org/10.1097/mcg.0000000000001467>.
213. A. Ahmed, A. K. Baronia, A. Azim, et al., "External Validation of Risk Prediction Scores for Invasive Candidiasis in a Medical/Surgical Intensive Care Unit: An Observational Study," *Indian Journal of Critical Care Medicine* 21, no. 8 (2017): 514–520, https://doi.org/10.4103/ijccm.ijccm_33_17.
214. A. M. Hall, L. A. Poole, B. Renton, et al., "Prediction of Invasive Candidal Infection in Critically Ill Patients With Severe Acute Pancreatitis," *Critical Care* 17, no. 2 (2013): R49, <https://doi.org/10.1186/cc12569>.
215. N. Sahar, R. A. Kozarek, Z. S. Kanji, et al., "The Microbiology of Infected Pancreatic Necrosis in the Era of Minimally Invasive Therapy," *European Journal of Clinical Microbiology & Infectious Diseases* 37, no. 7 (2018): 1353–1359, <https://doi.org/10.1007/s10096-018-3259-x>.
216. J. A. Heit, M. D. Silverstein, D. N. Mohr, T. M. Petterson, W. M. O'Fallon, and L. J. Melton 3rd, "Risk Factors for Deep Vein Thrombosis and Pulmonary Embolism: A Population-Based Case-Control Study," *Archives of Internal Medicine* 160, no. 6 (2000): 809–815, <https://doi.org/10.1001/archinte.160.6.809>.
217. A. J. Robbins, E. Luszczek, M. D. Bellin, A. Benner, F. S. Alwan, and G. J. Beilman, "Thromboembolic Complications in the First Year After Acute Pancreatitis Diagnosis," *Pancreas* 50, no. 5 (2021): 751–755, <https://doi.org/10.1097/mpa.0000000000001827>.
218. S. Barbar, F. Noventa, V. Rossetto, et al., "A Risk Assessment Model for the Identification of Hospitalized Medical Patients at Risk for Venous Thromboembolism: The Padua Prediction Score," *Journal of Thrombosis and Haemostasis* 8, no. 11 (2010): 2450–2457, <https://doi.org/10.1111/j.1538-7836.2010.04044.x>.
219. S. R. Kahn, W. Lim, A. S. Dunn, et al., "Prevention of VTE in Nonsurgical Patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th Ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines," supplement, *Chest* 141, no. S2 (2012): e195S–e226S, <https://doi.org/10.1378/chest.11-2296>.
220. X. S. Lu, F. Qiu, Y. X. Li, J. Q. Li, Q. Q. Fan, and R. G. Zhou, "Effect of Lower-Molecular Weight Heparin in the Prevention of Pancreatic Encephalopathy in the Patient With Severe Acute Pancreatitis," *Pancreas* 39, no. 4 (2010): 516–519, <https://doi.org/10.1097/mpa.0b013e3181c3c954>.
221. J. D. Du, X. Zheng, Z. Q. Huang, et al., "Effects of Intensive Insulin Therapy Combined With Low Molecular Weight Heparin Anticoagulant Therapy on Severe Pancreatitis," *Experimental and Therapeutic Medicine* 8, no. 1 (2014): 141–146, <https://doi.org/10.3892/etm.2014.1694>.
222. B. Patil, L. N. Meena, D. C. Sharma, G. Agarwal, Y. Dadhich, and G. Gupta, "Impact of Low-Molecular-Weight Heparin in the Treatment of Moderately Severe and Severe Acute Pancreatitis; a Randomized, Single Blind, Phase 3 Control Trial," *International Journal of Surgery* 101 (2022): 106621, <https://doi.org/10.1016/j.ijsu.2022.106621>.
223. M. Tozlu, Y. Kayar, A. T. Ince, B. Baysal, and H. Senturk, "Low Molecular Weight Heparin Treatment of Acute Moderate and Severe Pancreatitis: A Randomized, Controlled, Open-Label Study," *Turkish Journal of Gastroenterology* 30, no. 1 (2019): 81–87, <https://doi.org/10.5152/tjg.2018.18583>.

224. C. Patoni, S. Bunduc, L. Frim, et al., "Low Molecular Weight Heparin Decreases Mortality and Major Complication Rates in Moderately Severe and Severe Acute Pancreatitis-A Systematic Review and Meta-Analysis," *Frontiers of Medicine* 10 (2023): 1241301, <https://doi.org/10.3389/fmed.2023.1241301>.
225. Q. Qiu, G. J. Li, L. Tang, et al., "The Efficacy of Low Molecular Weight Heparin in Severe Acute Pancreatitis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials," *Journal of Digestive Diseases* 20, no. 10 (2019): 512–522, <https://doi.org/10.1111/1751-2980.12815>.
226. H. Decousus, V. F. Tapson, J. F. Bergmann, et al., "Factors at Admission Associated With Bleeding Risk in Medical Patients: Findings From the IMPROVE Investigators," *Chest* 139, no. 1 (2011): 69–79, <https://doi.org/10.1378/chest.09-3081>.
227. C. T. Collaboration, M. Dennis, P. A. Sandercock, et al., "Effectiveness of Thigh-Length Graduated Compression Stockings to Reduce the Risk of Deep Vein Thrombosis After Stroke (CLOTS Trial 1): A Multicentre, Randomised Controlled Trial," *Lancet* 373, no. 9679 (2009): 1958–1965, [https://doi.org/10.1016/S0140-6736\(09\)60941-7](https://doi.org/10.1016/S0140-6736(09)60941-7).
228. R. W. Eppsteiner, J. J. Shin, J. Johnson, and R. M. van Dam, "Mechanical Compression Versus Subcutaneous Heparin Therapy in Postoperative and Posttrauma Patients: A Systematic Review and Meta-Analysis," *World Journal of Surgery* 34, no. 1 (2010): 10–19, <https://doi.org/10.1007/s00268-009-0284-z>.
229. G. E. Eckertwall, B. B. Tingstedt, P. E. Bergenzaun, and R. G. Andersson, "Immediate Oral Feeding in Patients With Mild Acute Pancreatitis is Safe and May Accelerate Recovery—A Randomized Clinical Study," *Clinical Nutrition* 26, no. 6 (2007): 758–763, <https://doi.org/10.1016/j.clnu.2007.04.007>.
230. M. Horibe, E. Iwasaki, A. Nakagawa, et al., "Efficacy and Safety of Immediate Oral Intake in Patients With Mild Acute Pancreatitis: A Randomized Controlled Trial," *Nutrition* 74 (2020): 110724, <https://doi.org/10.1016/j.nut.2020.110724>.
231. J. Li, G. J. Xue, Y. L. Liu, et al., "Early Oral Refeeding Wisdom in Patients With Mild Acute Pancreatitis," *Pancreas* 42, no. 1 (2013): 88–91, <https://doi.org/10.1097/mpa.0b013e3182575fb5>.
232. E. E. Lozada-Hernandez, O. Barron-Gonzalez, S. Vazquez-Romero, M. Cano-Rosas, and E. Apolinar-Jimenez, "Non-Inferiority Comparative Clinical Trial Between Early Oral REFEEDING and Usual Oral REFEEDING in Predicted Mild Acute Biliary Pancreatitis," *BMC Gastroenterology* 20, no. 1 (2020): 228, <https://doi.org/10.1186/s12876-020-01363-3>.
233. D. Qi, B. Yu, J. Huang, and M. Peng, "Meta-Analysis of Early Enteral Nutrition Provided Within 24 Hours of Admission on Clinical Outcomes in Acute Pancreatitis," *JPEN - Journal of Parenteral and Enteral Nutrition* 42, no. 7 (2018): 1139–1147, <https://doi.org/10.1002/jpen.1139>.
234. E. Ramirez-Maldonado, S. Lopez Gordo, E. M. Pueyo, et al., "Immediate Oral Refeeding in Patients With Mild and Moderate Acute Pancreatitis: A Multicenter, Randomized Controlled Trial (PADI Trial)," *Annals of Surgery* 274, no. 2 (2021): 255–263, <https://doi.org/10.1097/sla.0000000000004596>.
235. V. M. Vaughn, D. Shuster, M. A. M. Rogers, et al., "Early Versus Delayed Feeding in Patients With Acute Pancreatitis: A Systematic Review," *Annals of Internal Medicine* 166, no. 12 (2017): 883–892, <https://doi.org/10.7326/m16-2533>.
236. B. C. Jacobson, M. B. Vander Vliet, M. D. Hughes, R. Maurer, K. McManus, and P. A. Banks, "A Prospective, Randomized Trial of Clear Liquids Versus Low-Fat Solid Diet as the Initial Meal in Mild Acute Pancreatitis," *Clinical Gastroenterology and Hepatology* 5, no. 8 (2007): 946–951: quiz 886, <https://doi.org/10.1016/j.cgh.2007.04.012>.
237. J. Larino-Noia, B. Lindkvist, J. Iglesias-Garcia, S. Seijo-Rios, J. Iglesias-Canle, and J. E. Dominguez-Munoz, "Early And/Or Immediately Full Caloric Diet Versus Standard Refeeding in Mild Acute Pancreatitis: A Randomized Open-Label Trial," *Pancreatology* 14, no. 3 (2014): 167–173, <https://doi.org/10.1016/j.pan.2014.02.008>.
238. M. Al-Omran, Z. H. Albalawi, M. F. Tashkandi, and L. A. Al-Ansary, "Enteral Versus Parenteral Nutrition for Acute Pancreatitis," *Cochrane Database of Systematic Reviews* 2010, no. 1 (2010): Cd002837, <https://doi.org/10.1002/14651858.cd002837.pub2>.
239. M. S. Petrov, B. P. Loveday, R. D. Pylypchuk, K. McIlroy, A. R. Phillips, and J. A. Windsor, "Systematic Review and Meta-Analysis of Enteral Nutrition Formulations in Acute Pancreatitis," *British Journal of Surgery* 96, no. 11 (2009): 1243–1252, <https://doi.org/10.1002/bjs.6862>.
240. P. E. Marik and G. P. Zaloga, "Meta-Analysis of Parenteral Nutrition Versus Enteral Nutrition in Patients With Acute Pancreatitis," *BMJ* 328, no. 7453 (2004): 1407, <https://doi.org/10.1136/bmj.38118.593900.55>.
241. Y. Cao, Y. Xu, T. Lu, F. Gao, and Z. Mo, "Meta-Analysis of Enteral Nutrition Versus Total Parenteral Nutrition in Patients With Severe Acute Pancreatitis," *Annals of Nutrition & Metabolism* 53, no. 3–4 (2008): 268–275, <https://doi.org/10.1159/000189382>.
242. M. S. Petrov, H. C. van Santvoort, M. G. Besselink, G. J. van der Heijden, J. A. Windsor, and H. G. Gooszen, "Enteral Nutrition and the Risk of Mortality and Infectious Complications in Patients With Severe Acute Pancreatitis: A Meta-Analysis of Randomized Trials," *Archives of Surgery* 143, no. 11 (2008): 1111–1117, <https://doi.org/10.1001/archsurg.143.11.1111>.
243. P. H. Hsieh, H. Y. Su, C. Y. Lin, Y. N. Kang, and C. C. Chang, "Infection Rate Among Nutritional Therapies for Acute Pancreatitis: A Systematic Review With Network Meta-Analysis of Randomized Controlled Trials," *PLoS One* 14, no. 7 (2019): e0219151, <https://doi.org/10.1371/journal.pone.0219151>.
244. M. S. Petrov and K. Whelan, "Comparison of Complications Attributable to Enteral and Parenteral Nutrition in Predicted Severe Acute Pancreatitis: A Systematic Review and Meta-Analysis," *British Journal of Nutrition* 103, no. 9 (2010): 1287–1295, <https://doi.org/10.1017/S0007114510000887>.
245. M. Liu and C. Gao, "A Systematic Review and Meta-Analysis of the Effect of Total Parenteral Nutrition and Enteral Nutrition on the Prognosis of Patients With Acute Pancreatitis," *Annals of Palliative Medicine* 10, no. 10 (2021): 10779–10788, <https://doi.org/10.21037/apm-21-2469>.
246. J. Song, Y. Zhong, X. Lu, et al., "Enteral Nutrition Provided Within 48 Hours After Admission in Severe Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Medicine (Baltimore)* 97, no. 34 (2018): e11871, <https://doi.org/10.1097/md.00000000000011871>.
247. M. S. Petrov, M. V. Kukosh, and N. V. Emelyanov, "A Randomized Controlled Trial of Enteral Versus Parenteral Feeding in Patients With Predicted Severe Acute Pancreatitis Shows a Significant Reduction in Mortality and in Infected Pancreatic Complications With Total Enteral Nutrition," *Digestive Surgery* 23, no. 5–6 (2006): 336–344: discussion 44–5, <https://doi.org/10.1159/000097949>.
248. O. J. Bakker, S. van Brunschot, H. C. van Santvoort, et al., "Early Versus On-Demand Nasoenteric Tube Feeding in Acute Pancreatitis," *New England Journal of Medicine* 371, no. 21 (2014): 1983–1993, <https://doi.org/10.1056/nejmoa1404393>.
249. K. Jiang, X. Z. Chen, Q. Xia, W. F. Tang, and L. Wang, "Early Nasogastric Enteral Nutrition for Severe Acute Pancreatitis: A Systematic Review," *World Journal of Gastroenterology* 13, no. 39 (2007): 5253–5260, <https://doi.org/10.3748/wjg.v13.i39.5253>.
250. Y. S. Chang, H. Q. Fu, Y. M. Xiao, and J. C. Liu, "Nasogastric or Nasojejunal Feeding in Predicted Severe Acute Pancreatitis: A Meta-

- Analysis,” *Critical Care* 17, no. 3 (2013): R118, <https://doi.org/10.1186/cc12790>.
251. D. M. Nally, E. G. Kelly, M. Clarke, and P. Ridgway, “Nasogastric Nutrition is Efficacious in Severe Acute Pancreatitis: A Systematic Review and Meta-Analysis,” *British Journal of Nutrition* 112, no. 11 (2014): 1769–1778, <https://doi.org/10.1017/s0007114514002566>.
 252. F. C. Eatock, P. Chong, N. Menezes, et al., “A Randomized Study of Early Nasogastric Versus Nasojejunal Feeding in Severe Acute Pancreatitis,” *American Journal of Gastroenterology* 100, no. 2 (2005): 432–439, <https://doi.org/10.1111/j.1572-0241.2005.40587.x>.
 253. A. Kumar, N. Singh, S. Prakash, A. Saraya, and Y. K. Joshi, “Early Enteral Nutrition in Severe Acute Pancreatitis: A Prospective Randomized Controlled Trial Comparing Nasojejunal and Nasogastric Routes,” *Journal of Clinical Gastroenterology* 40, no. 5 (2006): 431–434, <https://doi.org/10.1097/00004836-200605000-00013>.
 254. N. Singh, B. Sharma, M. Sharma, et al., “Evaluation of Early Enteral Feeding Through Nasogastric and Nasojejunal Tube in Severe Acute Pancreatitis: A Noninferiority Randomized Controlled Trial,” *Pancreas* 41, no. 1 (2012): 153–159, <https://doi.org/10.1097/mpa.0b013e318221c4a8>.
 255. Y. Zhu, H. Yin, R. Zhang, X. Ye, and J. Wei, “Nasogastric Nutrition Versus Nasojejunal Nutrition in Patients With Severe Acute Pancreatitis: A Meta-Analysis of Randomized Controlled Trials,” *Gastroenterology Research and Practice* 2016 (2016): 6430632–6430638, <https://doi.org/10.1155/2016/6430632>.
 256. J. Zhou, Y. Xue, Y. Liu, X. K. Li, Z. H. Tong, and W. Q. Li, “The Effect of Immunonutrition in Patients With Acute Pancreatitis: A Systematic Review and Meta-Analysis,” *Journal of Human Nutrition and Dietetics* 34, no. 2 (2021): 429–439, <https://doi.org/10.1111/jhn.12816>.
 257. L. Yong, Q. P. Lu, S. H. Liu, and H. Fan, “Efficacy of Glutamine-Enriched Nutrition Support for Patients With Severe Acute Pancreatitis: A Meta-Analysis,” *JPEN - Journal of Parenteral and Enteral Nutrition* 40, no. 1 (2016): 83–94, <https://doi.org/10.1177/0148607115570391>.
 258. V. Asrani, W. K. Chang, Z. Dong, G. Hardy, J. A. Windsor, and M. S. Petrov, “Glutamine Supplementation in Acute Pancreatitis: A Meta-Analysis of Randomized Controlled Trials,” *Pancreatology* 13, no. 5 (2013): 468–474, <https://doi.org/10.1016/j.pan.2013.07.282>.
 259. X. Jiang, L. Y. Pei, W. X. Guo, X. Qi, and X. G. Lu, “Glutamine Supported Early Enteral Therapy for Severe Acute Pancreatitis: A Systematic Review and Meta-Analysis,” *Asia Pacific Journal of Clinical Nutrition* 29, no. 2 (2020): 253–261, [https://doi.org/10.6133/apjcn.202007_29\(2\).0007](https://doi.org/10.6133/apjcn.202007_29(2).0007).
 260. M. S. Petrov, V. A. Atduev, and V. E. Zagainov, “Advanced Enteral Therapy in Acute Pancreatitis: Is There a Room for Immunonutrition? A Meta-Analysis,” *International Journal of Surgery* 6, no. 2 (2008): 119–124, <https://doi.org/10.1016/j.ijsu.2008.01.003>.
 261. Q. C. Lei, X. Y. Wang, X. F. Xia, et al., “The Role of Omega-3 Fatty Acids in Acute Pancreatitis: A Meta-Analysis of Randomized Controlled Trials,” *Nutrients* 7, no. 4 (2015): 2261–2273, <https://doi.org/10.3390/nu7042261>.
 262. X. Tao, Y. Yang, S. Xu, and Q. Xiong, “Efficacy of Immune Nutrients in Severe Acute Pancreatitis: A Network Meta-Analysis,” *Medicine (Baltimore)* 102, no. 43 (2023): e35615, <https://doi.org/10.1097/md.00000000000035615>.
 263. M. G. Besselink, H. C. van Santvoort, E. Buskens, et al., “Probiotic Prophylaxis in Predicted Severe Acute Pancreatitis: A Randomised, Double-Blind, Placebo-Controlled Trial,” *Lancet* 371, no. 9613 (2008): 651–659, [https://doi.org/10.1016/s0140-6736\(08\)60207-x](https://doi.org/10.1016/s0140-6736(08)60207-x).
 264. J. P. Neoptolemos, D. L. Carr-Locke, N. J. London, I. A. Bailey, D. James, and D. P. Fossard, “Controlled Trial of Urgent Endoscopic Retrograde Cholangiopancreatography and Endoscopic Sphincterotomy Versus Conservative Treatment for Acute Pancreatitis Due to Gallstones,” *Lancet* 2, no. 8618 (1988): 979–983, [https://doi.org/10.1016/s0140-6736\(88\)90740-4](https://doi.org/10.1016/s0140-6736(88)90740-4).
 265. S. T. Fan, E. C. Lai, F. P. Mok, C. M. Lo, S. S. Zheng, and J. Wong, “Early Treatment of Acute Biliary Pancreatitis by Endoscopic Papillotomy,” *New England Journal of Medicine* 328, no. 4 (1993): 228–232, <https://doi.org/10.1056/nejm199301283280402>.
 266. V. K. Sharma and C. W. Howden, “Metaanalysis of Randomized Controlled Trials of Endoscopic Retrograde Cholangiography and Endoscopic Sphincterotomy for the Treatment of Acute Biliary Pancreatitis,” *American Journal of Gastroenterology* 94, no. 11 (1999): 3211–3214, <https://doi.org/10.1111/j.1572-0241.1999.01520.x>.
 267. J. M. Acosta, N. Katkhouda, K. A. Debian, S. G. Groshen, D. D. Tsao-Wei, and T. V. Berne, “Early Ductal Decompression Versus Conservative Management for Gallstone Pancreatitis With Ampullary Obstruction: A Prospective Randomized Clinical Trial,” *Annals of Surgery* 243, no. 1 (2006): 33–40, <https://doi.org/10.1097/01.sla.0000194086.22580.92>.
 268. L. M. A. Coutinho, W. M. Bernardo, R. S. Rocha, et al., “Early Endoscopic Retrograde Cholangiopancreatography Versus Conservative Treatment in Patients With Acute Biliary Pancreatitis: Systematic Review and Meta-Analysis of Randomized Controlled Trials,” *Pancreas* 47, no. 4 (2018): 444–453, <https://doi.org/10.1097/mpa.0000000000001032>.
 269. U. R. Folsch, R. Nitsche, R. Ludtke, R. A. Hilgers, and W. Creutzfeldt, “Early ERCP and Papillotomy Compared With Conservative Treatment for Acute Biliary Pancreatitis: The German Study Group on Acute Biliary Pancreatitis,” *New England Journal of Medicine* 336, no. 4 (1997): 237–242, <https://doi.org/10.1056/nejm199701233360401>.
 270. M. Q. Zhou, N. P. Li, and R. D. Lu, “Duodenoscopy in Treatment of Acute Gallstone Pancreatitis,” *Hepatobiliary and Pancreatic Diseases International* 1, no. 4 (2002): 608–610, <https://pubmed.ncbi.nlm.nih.gov/14607696/>.
 271. A. Oria, D. Cimmino, C. Ocampo, et al., “Early Endoscopic Intervention Versus Early Conservative Management in Patients With Acute Gallstone Pancreatitis and Biliopancreatic Obstruction: A Randomized Clinical Trial,” *Annals of Surgery* 245, no. 1 (2007): 10–17, https://journals.lww.com/annalsofsurgery/abstract/2007/01000/early_endoscopic_intervention_versus_early.3.aspx.
 272. P. Chen, B. Hu, C. Wang, Y. Kang, X. Jin, and C. Tang, “Pilot Study of Urgent Endoscopic Intervention Without Fluoroscopy on Patients With Severe Acute Biliary Pancreatitis in the Intensive Care Unit,” *Pancreas* 39, no. 3 (2010): 398–402, <https://doi.org/10.1097/mpa.0b013e3181bd6821>.
 273. M. C. Uy, M. L. Daez, P. P. Sy, V. P. Banez, W. Z. Espinosa, and M. C. Talingdan-Te, “Early ERCP in Acute Gallstone Pancreatitis Without Cholangitis: A Meta-Analysis,” *JOP: Journal of the Pancreas* 10, no. 3 (2009): 299–305, <https://pubmed.ncbi.nlm.nih.gov/19454823/>.
 274. F. Tse and Y. Yuan, “Early Routine Endoscopic Retrograde Cholangiopancreatography Strategy Versus Early Conservative Management Strategy in Acute Gallstone Pancreatitis,” *Cochrane Database of Systematic Reviews* 2012, no. 5 (2012): Cd009779, <https://doi.org/10.1002/14651858.cd009779.pub2>.
 275. N. J. Schepers, N. D. L. Hallensleben, M. G. Besselink, et al., “Urgent Endoscopic Retrograde Cholangiopancreatography With Sphincterotomy Versus Conservative Treatment in Predicted Severe Acute Gallstone Pancreatitis (APEC): A Multicentre Randomised Controlled Trial,” *Lancet* 396, no. 10245 (2020): 167–176, [https://doi.org/10.1016/s0140-6736\(20\)30539-0](https://doi.org/10.1016/s0140-6736(20)30539-0).
 276. N. D. Hallensleben, P. M. C. Stassen, N. J. Schepers, et al., “Patient Selection for Urgent Endoscopic Retrograde Cholangio-Pancreatography by Endoscopic Ultrasound in Predicted Severe Acute Biliary Pancreatitis (APEC-2): A Multicentre Prospective Study,” *Gut* 72, no. 8 (2023): 1534–1542, <https://doi.org/10.1136/gutjnl-2022-328258>.

277. K. M. Mueck, S. Wei, C. Pedroza, et al., "Gallstone Pancreatitis: Admission Versus Normal Cholecystectomy-A Randomized Trial (Gallstone PANC Trial)," *Annals of Surgery* 270, no. 3 (2019): 519–527, <https://doi.org/10.1097/sla.0000000000003424>.
278. A. W. Kirkpatrick, D. J. Roberts, J. De Waele, et al., "Intra-Abdominal Hypertension and the Abdominal Compartment Syndrome: Updated Consensus Definitions and Clinical Practice Guidelines From the World Society of the Abdominal Compartment Syndrome," *Intensive Care Medicine* 39, no. 7 (2013): 1190–1206, <https://doi.org/10.1007/s00134-013-2906-z>.
279. J. Jaipuria, V. Bhandari, A. S. Chawla, and M. Singh, "Intra-Abdominal Pressure: Time Ripe to Revise Management Guidelines of Acute Pancreatitis?," *World Journal of Gastrointestinal Pathophysiology* 7, no. 1 (2016): 186–198, <https://doi.org/10.4291/wjgp.v7.i1.186>.
280. S. van Brunschot, A. J. Schut, S. A. Bouwense, et al., "Abdominal Compartment Syndrome in Acute Pancreatitis: A Systematic Review," *Pancreas* 43, no. 5 (2014): 665–674, <https://doi.org/10.1097/mpa.000000000000108>.
281. A. A. Basu, "Low-Cost Technique for Measuring the Intra-abdominal Pressure in Non-Industrialised Countries," *Annals of the Royal College of Surgeons of England* 89, no. 4 (2007): 434–435, <https://doi.org/10.1308/rcsann.2007.89.4.434>.
282. I. De Laet, E. Hoste, E. Fau - Verholen, E. Verholen, J. J. Fau - De Waele, and J. J. De Waele, "The Effect of Neuromuscular Blockers in Patients With Intra-Abdominal Hypertension," (0342–4642 (Print)).
283. W. He, P. Chen, Y. Lei, et al., "Randomized Controlled Trial: Neostigmine for Intra-Abdominal Hypertension in Acute Pancreatitis," *Critical Care* 26, no. 1 (2022): 52, <https://doi.org/10.1186/s13054-022-03922-4>.
284. Y. Lin, S. He, J. Gong, et al., "Continuous Veno-Venous Hemofiltration for Severe Acute Pancreatitis," *Cochrane Database of Systematic Reviews* 10, no. 10 (2019): Cd012959, <https://doi.org/10.1002/14651858.CD012959.pub2>.
285. Y. Xie, Y. Yuan, W. Su, et al., "Effect of Continuous Hemofiltration on Severe Acute Pancreatitis With Different Intra-Abdominal Pressure: A Cohort Study," *Medicine* 100, no. 44 (2021): e27641, <https://doi.org/10.1097/md.00000000000027641>.
286. Y. Wen, W. Q. Zhuo, H. Y. Liang, et al., "Abdominal Paracentesis Drainage Improves Outcome of Acute Pancreatitis Complicated With Intra-Abdominal Hypertension in Early Phase," *American Journal of the Medical Sciences* 365, no. 1 (2023): 48–55, <https://doi.org/10.1016/j.amjms.2022.08.013>.
287. A. K. Singh, J. Samanta, S. Dawra, et al., "Reduction of Intra-Abdominal Pressure After Percutaneous Catheter Drainage of Pancreatic Fluid Collection Predicts Survival," (1424–3911 (Electronic)).
288. P. Nasa, G. Chanchalani, D. Juneja, and M. L. Malbrain, "Surgical Decompression for the Management of Abdominal Compartment Syndrome With Severe Acute Pancreatitis: A Narrative Review," *World Journal of Gastrointestinal Surgery* 15, no. 9 (2023): 1879–1891, <https://doi.org/10.4240/wjgs.v15.i9.1879>.
289. P. Mentula, P. Hienonen, E. Kempainen, P. Puolakkainen, and A. Leppaniemi, "Surgical Decompression for Abdominal Compartment Syndrome in Severe Acute Pancreatitis," *Archives of Surgery* 145, no. 8 (2010): 764–769, <https://doi.org/10.1001/archsurg.2010.132>.
290. H. C. Timmerhuis, S. M. van Dijk, R. A. Hollemans, et al., "Short-Term and Long-Term Outcomes of a Disruption and Disconnection of the Pancreatic Duct in Necrotizing Pancreatitis: A Multicenter Cohort Study in 896 Patients," *American Journal of Gastroenterology* 118, no. 5 (2023): 880–891, <https://doi.org/10.14309/ajg.0000000000002157>.
291. J. Y. Bang, C. M. Wilcox, U. Navaneethan, et al., "Impact of Disconnected Pancreatic Duct Syndrome on the Endoscopic Management of Pancreatic Fluid Collections," *Annals of Surgery* 267, no. 3 (2018): 561–568, <https://doi.org/10.1097/sla.0000000000002082>.
292. T. K. Maatman, A. M. Roch, K. A. Lewellen, et al., "Disconnected Pancreatic Duct Syndrome: Spectrum of Operative Management," *Journal of Surgical Research* 247 (2020): 297–303, <https://doi.org/10.1016/j.jss.2019.09.068>.
293. L. Boxhoorn, H. C. Timmerhuis, R. C. Verdonk, et al., "Diagnosis and Treatment of Pancreatic Duct Disruption or Disconnection: An International Expert Survey and Case Vignette Study," *HPB* 23, no. 8 (2021): 1201–1208, <https://doi.org/10.1016/j.hpb.2020.11.1148>.
294. H. C. Timmerhuis, S. M. van Dijk, R. C. Verdonk, et al., "Various Modalities Accurate in Diagnosing a Disrupted or Disconnected Pancreatic Duct in Acute Pancreatitis: A Systematic Review," *Digestive Diseases and Sciences* 66, no. 5 (2021): 1415–1424, <https://doi.org/10.1007/s10620-020-06413-0>.
295. S. Sherman, M. L. Freeman, P. R. Tarnasky, et al., "Administration of Secretin (RG1068) Increases the Sensitivity of Detection of Duct Abnormalities by Magnetic Resonance Cholangiopancreatography in Patients With Pancreatitis," *Gastroenterology* 147, no. 3 (2014): 646–654, <https://doi.org/10.1053/j.gastro.2014.05.035>.
296. S. L. Gans, H. L. van Westreenen, J. J. Kiewiet, E. A. Rauws, D. J. Gouma, and M. A. Boermeester, "Systematic Review and Meta-Analysis of Somatostatin Analogues for the Treatment of Pancreatic Fistula," *British Journal of Surgery* 99, no. 6 (2012): 754–760, <https://doi.org/10.1002/bjs.8709>.
297. R. Das, G. I. Papachristou, A. Slivka, et al., "Endotherapy is Effective for Pancreatic Ductal Disruption: A Dual Center Experience," *Pancreatology* 16, no. 2 (2016): 278–283, <https://doi.org/10.1016/j.pan.2015.12.176>.
298. J. W. Jang, M. H. Kim, D. Oh, et al., "Factors and Outcomes Associated With Pancreatic Duct Disruption in Patients With Acute Necrotizing Pancreatitis," *Pancreatology* 16, no. 6 (2016): 958–965, <https://doi.org/10.1016/j.pan.2016.09.009>.
299. S. M. van Dijk, H. C. Timmerhuis, R. C. Verdonk, et al., "Treatment of Disrupted and Disconnected Pancreatic Duct in Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis," *Pancreatology* 19, no. 7 (2019): 905–915, <https://doi.org/10.1016/j.pan.2019.08.006>.
300. T. Hamada, T. Iwashita, T. Saito, et al., "Disconnected Pancreatic Duct Syndrome and Outcomes of Endoscopic Ultrasound-Guided Treatment of Pancreatic Fluid Collections: Systematic Review and Meta-Analysis," *Digestive Endoscopy* 34, no. 4 (2022): 676–686, <https://doi.org/10.1111/den.14142>.
301. E. Chong, C. B. Ratnayake, S. Saikia, et al., "Endoscopic Transmural Drainage is Associated With Improved Outcomes in Disconnected Pancreatic Duct Syndrome: A Systematic Review and Meta-Analysis," *BMC Gastroenterology* 21, no. 1 (2021): 87, <https://doi.org/10.1186/s12876-021-01663-2>.
302. S. Amin, D. J. Yang, A. L. Lucas, S. Gonzalez, and C. J. DiMaio, "There is No Advantage to Transpapillary Pancreatic Duct Stenting for the Transmural Endoscopic Drainage of Pancreatic Fluid Collections: A Meta-Analysis," *Clinical Endoscopy* 50, no. 4 (2017): 388–394, <https://doi.org/10.5946/ce.2016.091>.
303. M. Arvanitakis, M. Delhay, M. A. Bali, et al., "Pancreatic-Fluid Collections: A Randomized Controlled Trial Regarding Stent Removal After Endoscopic Transmural Drainage," *Gastrointestinal Endoscopy* 65, no. 4 (2007): 609–619, <https://doi.org/10.1016/j.gie.2006.06.083>.
304. J. Y. Bang, C. Mel Wilcox, J. P. Arnoletti, and S. Varadarajulu, "Importance of Disconnected Pancreatic Duct Syndrome in Recurrence of Pancreatic Fluid Collections Initially Drained Using Lumen-Apposing Metal Stents," *Clinical Gastroenterology and Hepatology* 19, no. 6 (2021): 1275–1281.e2, <https://doi.org/10.1016/j.cgh.2020.07.022>.

305. S. Irani, M. Gluck, A. Ross, et al., "Resolving External Pancreatic Fistulas in Patients With Disconnected Pancreatic Duct Syndrome: Using Rendezvous Techniques to Avoid Surgery (With Video)," *Gastrointestinal Endoscopy* 76, no. 3 (2012): 586–593.e1–3, <https://doi.org/10.1016/j.gie.2012.05.006>.
306. A. Kamal, V. K. Singh, V. S. Akshintala, et al., "CT and MRI Assessment of Symptomatic Organized Pancreatic Fluid Collections and Pancreatic Duct Disruption: An Interreader Variability Study Using the Revised Atlanta Classification 2012," *Abdominal Imaging* 40, no. 6 (2015): 1608–1616, <https://doi.org/10.1007/s00261-014-0303-x>.
307. M. C. van Baal, T. L. Bollen, O. J. Bakker, et al., "The Role of Routine Fine-Needle Aspiration in the Diagnosis of Infected Necrotizing Pancreatitis," *Surgery* 155, no. 3 (2014): 442–448, <https://doi.org/10.1016/j.surg.2013.10.001>.
308. C. J. Yang, J. Chen, A. R. Phillips, J. A. Windsor, and M. S. Petrov, "Predictors of Severe and Critical Acute Pancreatitis: A Systematic Review," *Digestive and Liver Disease* 46, no. 5 (2014): 446–451, <https://doi.org/10.1016/j.dld.2014.01.158>.
309. L. Boxhoorn, S. M. van Dijk, J. van Grinsven, et al., "Immediate Versus Postponed Intervention for Infected Necrotizing Pancreatitis," *New England Journal of Medicine* 385, no. 15 (2021): 1372–1381, <https://doi.org/10.1056/nejmoa2100826>.
310. S. S. Rana, "An Overview of Walled-Off Pancreatic Necrosis for Clinicians," *Expert Review of Gastroenterology & Hepatology* 13, no. 4 (2019): 331–343, <https://doi.org/10.1080/17474124.2019.1574568>.
311. N. Oblizajek, N. Takahashi, S. Agayeva, et al., "Outcomes of Early Endoscopic Intervention for Pancreatic Necrotic Collections: A Matched Case-Control Study," *Gastrointestinal Endoscopy* 91, no. 6 (2020): 1303–1309, <https://doi.org/10.1016/j.gie.2020.01.017>.
312. S. S. Rana, R. Sharma, K. Kishore, L. Dhalaria, and R. Gupta, "Safety and Efficacy of Early (< 4 Weeks of Illness) Endoscopic Transmural Drainage of Post-acute Pancreatic Necrosis Predominantly Located in the Body of the Pancreas," *Journal of Gastrointestinal Surgery* 25, no. 9 (2021): 2328–2335, <https://doi.org/10.1007/s11605-021-04945-y>.
313. T. Chantarojanasiri, N. Yamamoto, Y. Nakai, et al., "Comparison of Early and Delayed EUS-Guided Drainage of Pancreatic Fluid Collection," *Endoscopy International Open* 6, no. 12 (2018): E1398–E1405, <https://doi.org/10.1055/a-0751-2698>.
314. G. Trikudanathan, P. Tawfik, S. K. Amateau, et al., "Early (< 4 Weeks) Versus Standard (>= 4 Weeks) Endoscopically Centered Step-Up Interventions for Necrotizing Pancreatitis," *American Journal of Gastroenterology* 113, no. 10 (2018): 1550–1558, <https://doi.org/10.1038/s41395-018-0232-3>.
315. D. Ramai, I. Enofe, S. S. Deliwala, et al., "Early (< 4 Weeks) Versus Standard (>= 4 Weeks) Endoscopic Drainage of Pancreatic Walled-off Fluid Collections: A Systematic Review and Meta-Analysis," *Gastrointestinal Endoscopy* 97, no. 3 (2023): 415–421.e5, <https://doi.org/10.1016/j.gie.2022.11.003>.
316. O. J. Bakker, H. C. van Santvoort, S. van Brunschot, et al., "Endoscopic Transgastric vs Surgical Necrosectomy for Infected Necrotizing Pancreatitis: A Randomized Trial," *JAMA* 307, no. 10 (2012): 1053–1061, <https://doi.org/10.1001/jama.2012.276>.
317. S. van Brunschot, J. van Grinsven, H. C. van Santvoort, et al., "Endoscopic or Surgical Step-Up Approach for Infected Necrotizing Pancreatitis: A Multicentre Randomised Trial," *Lancet* 391, no. 10115 (2018): 51–58, [https://doi.org/10.1016/s0140-6736\(17\)32404-2](https://doi.org/10.1016/s0140-6736(17)32404-2).
318. A. M. Onnekink, L. Boxhoorn, H. C. Timmerhuis, et al., "Endoscopic Versus Surgical Step-Up Approach for Infected Necrotizing Pancreatitis (Extension): Long-Term Follow-Up of a Randomized Trial," *Gastroenterology* 163, no. 3 (2022): 712–722.e14, <https://doi.org/10.1053/j.gastro.2022.05.015>.
319. C. M. Haney, K. F. Kowalewski, M. W. Schmidt, et al., "Endoscopic Versus Surgical Treatment for Infected Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis of Randomized Controlled Trials," *Surgical Endoscopy* 34, no. 6 (2020): 2429–2444, <https://doi.org/10.1007/s00464-020-07469-9>.
320. J. Y. Bang, C. M. Wilcox, J. P. Arnoletti, and S. Varadarajulu, "Superiority of Endoscopic Interventions Over Minimally Invasive Surgery for Infected Necrotizing Pancreatitis: Meta-Analysis of Randomized Trials," *Digestive Endoscopy* 32, no. 3 (2020): 298–308, <https://doi.org/10.1111/den.13470>.
321. G. A. Olsen, P. N. Schmidt, A. Hadi, et al., "Accelerated vs Step-Up Endoscopic Treatment for Pancreatic Walled-Off Necrosis: A Randomized Controlled Trial (ACCELERATE)," *Clinical Gastroenterology and Hepatology* (2025).
322. D. H. Park, S. S. Lee, S. H. Moon, et al., "Endoscopic Ultrasound-Guided Versus Conventional Transmural Drainage for Pancreatic Pseudocysts: A Prospective Randomized Trial," *Endoscopy* 41, no. 10 (2009): 842–848, <https://doi.org/10.1055/s-00029-1215133>.
323. S. Varadarajulu, J. D. Christein, A. Tamhane, E. R. Drelichman, and C. M. Wilcox, "Prospective Randomized Trial Comparing EUS and EGD for Transmural Drainage of Pancreatic Pseudocysts (With Videos)," *Gastrointestinal Endoscopy* 68, no. 6 (2008): 1102–1111, <https://doi.org/10.1016/j.gie.2008.04.028>.
324. T. H. Baron, C. J. DiMaio, A. Y. Wang, and K. A. Morgan, "American Gastroenterological Association Clinical Practice Update: Management of Pancreatic Necrosis," *Gastroenterology* 158, no. 1 (2020): 67–75.e1, <https://doi.org/10.1053/j.gastro.2019.07.064>.
325. L. Boxhoorn, R. C. Verdonk, M. G. Besselink, et al., "Comparison of Lumen-Apposing Metal Stents Versus Double-Pigtail Plastic Stents for Infected Necrotizing Pancreatitis," *Gut* 72, no. 1 (2023): 66–72, <https://doi.org/10.1136/gutjnl-2021-325632>.
326. P. Vanek, P. Falt, P. Vitek, et al., "EUS-Guided Transluminal Drainage Using Lumen-Apposing Metal Stents With or Without Coaxial Plastic Stents for Treatment of Walled-Off Necrotizing Pancreatitis: A Prospective Bicentric Randomized Controlled Trial," *Gastrointestinal Endoscopy* 97, no. 6 (2023): 1070–1080, <https://doi.org/10.1016/j.gie.2022.12.026>.
327. M. Werge, S. Novovic, S. Roug, et al., "Evaluation of Local Instillation of Antibiotics in Infected Walled-Off Pancreatic Necrosis," *Pancreatology* 18, no. 6 (2018): 642–646, <https://doi.org/10.1016/j.pan.2018.06.005>.
328. B. P. Mohan, D. Madhu, G. Toy, et al., "Hydrogen peroxide-assisted Endoscopic Necrosectomy of Pancreatic Walled-Off Necrosis: A Systematic Review and Meta-Analysis," *Gastrointestinal Endoscopy* 95, no. 6 (2022): 1060–1066.e7, <https://doi.org/10.1016/j.gie.2022.01.018>.
329. P. C. Powers, A. Siddiqui, R. Z. Sharaiha, et al., "Discontinuation of Proton Pump Inhibitor Use Reduces the Number of Endoscopic Procedures Required for Resolution of Walled-Off Pancreatic Necrosis," *Endoscopy Ultrasound* 8, no. 3 (2019): 194–198, https://doi.org/10.4103/eus.eus_59_18.
330. W. Ahmad, S. A. Fehmi, T. J. Savides, G. Anand, M. A. Chang, and W. T. Kwong, "Protocol of Early Lumen Apposing Metal Stent Removal for Pseudocysts and Walled off Necrosis Avoids Bleeding Complications," *Scandinavian Journal of Gastroenterology* 55, no. 2 (2020): 242–247, <https://doi.org/10.1080/00365521.2019.1710246>.
331. A. S. Ross, S. Irani, S. I. Gan, et al., "Dual-Modality Drainage of Infected and Symptomatic Walled-Off Pancreatic Necrosis: Long-Term Clinical Outcomes," *Gastrointestinal Endoscopy* 79, no. 6 (2014): 929–935, <https://doi.org/10.1016/j.gie.2013.10.014>.
332. M. C. van Baal, H. C. van Santvoort, and T. L. Fau - Bollen, et al., "Systematic Review of Percutaneous Catheter Drainage as Primary Treatment for Necrotizing Pancreatitis," (1365–2168 (Electronic)).

333. B. Mv, S. S. Fau - Rana, S. S. Rana, U. Gors, M. Kang, R. A.-O. Gupta, "Assessing the Efficacy and Outcomes Following Irrigation With Streptokinase Versus Hydrogen Peroxide in Necrotizing Pancreatitis: A Randomized Pilot Study," (1573–2568 (Electronic)).
334. H. C. van Santvoort, M. G. Besselink, O. J. Bakker, et al., "A Step-Up Approach or Open Necrosectomy for Necrotizing Pancreatitis," *New England Journal of Medicine* 362, no. 16 (2010): 1491–1502, <https://doi.org/10.1056/nejmoa0908821>.
335. R. A. Hollemans, O. J. Bakker, M. A. Boermeester, et al., "Superiority of Step-Up Approach vs Open Necrosectomy in Long-Term Follow-Up of Patients With Necrotizing Pancreatitis," *Gastroenterology* 156, no. 4 (2019): 1016–1026, <https://doi.org/10.1053/j.gastro.2018.10.045>.
336. J. Easler, V. Muddana, A. Furlan, et al., "Portosplenomesenteric Venous Thrombosis in Patients With Acute Pancreatitis is Associated With Pancreatic Necrosis and Usually Has a Benign Course," *Clinical Gastroenterology and Hepatology* 12, no. 5 (2014): 854–862, <https://doi.org/10.1016/j.cgh.2013.09.068>.
337. J. R. Butler, G. J. Eckert, N. J. Zyromski, M. J. Leonardi, K. D. Lillemo, and T. J. Howard, "Natural History of Pancreatitis-Induced Splenic Vein Thrombosis: A Systematic Review and Meta-Analysis of Its Incidence and Rate of Gastrointestinal Bleeding," *HPB* 13, no. 12 (2011): 839–845, <https://doi.org/10.1111/j.1477-2574.2011.00375.x>.
338. L. Nawacki, J. Matykievicz, E. Stochmal, and S. Gluszek, "Splanchnic Vein Thrombosis in Acute Pancreatitis and Its Consequences," *Clinical and Applied Thrombosis/Hemostasis* 27 (2021): 10760296211010260, <https://doi.org/10.1177/10760296211010260>.
339. L. Toque, A. Hamy, J. F. Hamel, et al., "Predictive Factors of Splanchnic Vein Thrombosis in Acute Pancreatitis: A 6-Year Single-Center Experience," *Journal of Digestive Diseases* 16, no. 12 (2015): 734–740, <https://doi.org/10.1111/1751-2980.12298>.
340. D. Oyon, C. Marra-Lopez, F. Bolado, et al., "Determinants and Impact of Splanchnic Vein Thrombosis in Acute Pancreatitis," *Digestive and Liver Disease* 55, no. 11 (2023): 1480–1486, <https://doi.org/10.1016/j.dld.2023.04.026>.
341. R. Garg, A. Mohammed, A. Singh, et al., "Mortality Trends, Outcomes, and Predictors of Portal Vein Thrombosis in Acute Pancreatitis Patients: A Propensity-Matched National Study," *Digestive Diseases and Sciences* 68, no. 6 (2023): 2674–2682, <https://doi.org/10.1007/s10620-023-07945-x>.
342. H. J. Gonzelez, S. J. Sahay, B. Samadi, B. R. Davidson, and S. H. Rahman, "Splanchnic Vein Thrombosis in Severe Acute Pancreatitis: A 2-Year, Single-Institution Experience," *HPB* 13, no. 12 (2011): 860–864, <https://doi.org/10.1111/j.1477-2574.2011.00392.x>.
343. A. M. Roch, T. K. Maatman, R. A. Carr, et al., "Venous Thromboembolism in Necrotizing Pancreatitis: An Underappreciated Risk," *Journal of Gastrointestinal Surgery* 23, no. 12 (2019): 2430–2438, <https://doi.org/10.1007/s11605-019-04124-0>.
344. J. Zhou, L. Ke, Z. Tong, et al., "Risk Factors and Outcome of Splanchnic Venous Thrombosis in Patients With Necrotizing Acute Pancreatitis," *Thrombosis Research* 135, no. 1 (2015): 68–72, <https://doi.org/10.1016/j.thromres.2014.10.021>.
345. J. Zhou, H. Zhang, W. Mao, et al., "Efficacy and Safety of Early Systemic Anticoagulation for Preventing Splanchnic Thrombosis in Acute Necrotizing Pancreatitis," *Pancreas* 49, no. 9 (2020): 1220–1224, <https://doi.org/10.1097/mpa.0000000000001661>.
346. S. U. Ahmed, S. S. Rana, J. Ahluwalia, et al., "Role of Thrombophilia in Splanchnic Venous Thrombosis in Acute Pancreatitis," *Annals of Gastroenterology* 31, no. 3 (2018): 371–378, <https://doi.org/10.20524/aog.2018.0242>.
347. T. M. Wilson, A. Daneshmand, S. Parys, and Y. Watanabe, "Splanchnic Vein Thrombosis in Acute Pancreatitis: A Review of Treatment Indications, Methods, and Outcomes in a Single Institution," *ANZ Journal of Surgery* 93, no. 10 (2023): 2487–2491, <https://doi.org/10.1111/ans.18442>.
348. W. Norton, G. Lazaraviciute, G. Ramsay, I. Kreis, I. Ahmed, and M. Bekheit, "Current Practice of Anticoagulant in the Treatment of Splanchnic Vein Thrombosis Secondary to Acute Pancreatitis," *Hepatobiliary and Pancreatic Diseases International* 19, no. 2 (2020): 116–121, <https://doi.org/10.1016/j.hbpd.2019.12.007>.
349. P. R. Junare, S. Udgirkar, S. Nair, et al., "Splanchnic Venous Thrombosis in Acute Pancreatitis: Does Anticoagulation Affect Outcome?," *Gastroenterology Research* 13, no. 1 (2020): 25–31, <https://doi.org/10.14740/gr1223>.
350. D. Pagliari, R. Cianci, M. G. Brizi, et al., "Anticoagulant Therapy in the Treatment of Splanchnic Vein Thrombosis Associated to Acute Pancreatitis: A 3-Year Single-Centre Experience," *Internal and Emergency Medicine* 15, no. 6 (2020): 1021–1029, <https://doi.org/10.1007/s11739-019-02271-5>.
351. I. Redman, P. Panahi, K. Bananis, and P. Drymoussis, "Therapeutic Anticoagulation in Patients With Acute Pancreatitis and Splanchnic Vein Thrombosis: A Best Evidence Topic," *Annals of Medicine and Surgery* 86, no. 1 (2024): 271–278, <https://doi.org/10.1097/ms9.0000000000001440>.
352. N. J. Sissingh, J. V. Groen, D. Koole, et al., "Therapeutic Anticoagulation for Splanchnic Vein Thrombosis in Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Pancreatology* 22, no. 2 (2022): 235–243, <https://doi.org/10.1016/j.pan.2021.12.008>.
353. Y. Yin, L. Wang, F. Gao, L. Liu, and X. Qi, "Anticoagulation Therapy for Splanchnic Vein Thrombosis Associated With Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Clinical and Applied Thrombosis/Hemostasis* 29 (2023): 10760296231188718, <https://doi.org/10.1177/10760296231188718>.
354. S. Chandan, A. Buddam, S. R. Khan, et al., "Use of Therapeutic Anticoagulation in Splanchnic Vein Thrombosis Associated With Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Annals of Gastroenterology* 34, no. 6 (2021): 862–871, <https://doi.org/10.20524/aog.2021.0661>.
355. W. Xu, X. Qi, J. Chen, C. Su, and X. Guo, "Prevalence of Splanchnic Vein Thrombosis in Pancreatitis: A Systematic Review and Meta-Analysis of Observational Studies," *Gastroenterology Research and Practice* 2015 (2015): 245460, <https://doi.org/10.1155/2015/245460>.
356. F. S. Anis, A. Adiamah, D. N. Lobo, and S. Sanyal, "Incidence and Treatment of Splanchnic Vein Thrombosis in Patients With Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Journal of Gastroenterology and Hepatology* 37, no. 3 (2022): 446–454, <https://doi.org/10.1111/jgh.15711>.
357. K. Thejasvin, S. J. Chan, C. Varghese, W. B. Lim, G. M. Cheemungtoo, N. Akter, et al., "A Selective Anticoagulation Policy for Splanchnic Vein Thrombosis in Acute Pancreatitis is Associated With Favourable Outcomes: Experience From a UK Tertiary Referral Centre," *HPB* 24, no. 11 (2022): 1937–1943, <https://doi.org/10.1016/j.hpb.2022.06.003>.
358. M. A. Ghazanfar, L. Ke, G. Ramsay, et al., "Management of Splanchnic Vein Thrombosis in Patients With Acute Pancreatitis: An International Survey of Current Practice," *Pancreas* 51, no. 9 (2022): 1211–1216, <https://doi.org/10.1097/mpa.0000000000002165>.
359. N. J. Sissingh, J. V. Groen, H. C. Timmerhuis, et al., "Therapeutic Anticoagulation for Splanchnic Vein Thrombosis in Acute Pancreatitis: A National Survey and Case-Vignette Study," *World Journal of Gastroenterology* 29, no. 21 (2023): 3328–3340, <https://doi.org/10.3748/wjg.v29.i21.3328>.
360. R. de Franchis, J. Bosch, G. Garcia-Tsao, et al., "Baveno VII - Renewing Consensus in Portal Hypertension," *Journal of Hepatology* 76, no. 4 (2022): 959–974, <https://doi.org/10.1016/j.jhep.2021.12.022>.

361. A. Aboulhian, T. Chan, A. Yaghoobian, et al., "Early Cholecystectomy Safely Decreases Hospital Stay in Patients With Mild Gallstone Pancreatitis: A Randomized Prospective Study," *Annals of Surgery* 251, no. 4 (2010): 615–619, <https://doi.org/10.1097/sla.0b013e3181c38f1f>.
362. R. Noel, U. Arnelo, L. Lundell, et al., "Index Versus Delayed Cholecystectomy in Mild Gallstone Pancreatitis: Results of a Randomized Controlled Trial," *HPB* 20, no. 10 (2018): 932–938, <https://doi.org/10.1016/j.hpb.2018.03.016>.
363. A. Davoodabadi, E. Beigmohammadi, H. Gilasi, A. Arj, and H. Taheri Nassaj, "Optimizing Cholecystectomy Time in Moderate Acute Biliary Pancreatitis: A Randomized Clinical Trial Study," *Heliyon* 6, no. 2 (2020): e03388, <https://doi.org/10.1016/j.heliyon.2020.e03388>.
364. M. A. M. N. Omar, "Acute Biliary Pancreatitis - Optimal Time for Cholecystectomy: A Prospective Randomized Study," *Clinics in Surgery* 3 (2018): 2151, <https://www.clinicsinsurgery.com/open-access/acute-biliary-pancreatitis-optimal-time-for-cholecystectomy-a-prospective-randomized-study-3578.pdf>.
365. F. Riquelme, B. Marinkovic, M. Salazar, et al., "Early Laparoscopic Cholecystectomy Reduces Hospital Stay in Mild Gallstone Pancreatitis: A Randomized Controlled Trial," *HPB* 22, no. 1 (2020): 26–33, <https://doi.org/10.1016/j.hpb.2019.05.013>.
366. D. W. da Costa, S. A. Bouwense, N. J. Schepers, et al., "Same-Admission Versus Interval Cholecystectomy for Mild Gallstone Pancreatitis (PONCHO): A Multicentre Randomised Controlled Trial," *Lancet* 386, no. 10000 (2015): 1261–1268, [https://doi.org/10.1016/s0140-6736\(15\)00274-3](https://doi.org/10.1016/s0140-6736(15)00274-3).
367. S. L. Jee, R. Jarmin, K. F. Lim, and K. Raman, "Outcomes of Early Versus Delayed Cholecystectomy in Patients With Mild to Moderate Acute Biliary Pancreatitis: A Randomized Prospective Study," *Asian Journal of Surgery* 41, no. 1 (2018): 47–54, <https://doi.org/10.1016/j.asjsur.2016.07.010>.
368. H. G. Facundo, R. R. Montoliu, D. R. C. Llanos, et al., "Cholecystectomy 7 Days Vs 4 Weeks After Mild Biliary Pancreatitis: Looking a Decrease the Incidence of Persistent Choledocholithiasis and ERCP: A Multicentric Randomized Clinical Trial," *International Journal of Surgery* 98 (2022): 106207, <https://doi.org/10.1016/j.ijsu.2021.106207>.
369. K. S. Gurusamy, C. Davidson, C. Gluud, and B. R. Davidson, "Early Versus Delayed Laparoscopic Cholecystectomy for People With Acute Cholecystitis," *Cochrane Database of Systematic Reviews*, no. 6 (2013): Cd005440, <https://doi.org/10.1002/14651858.CD005440.pub3>.
370. N. Moody, A. Adiamah, F. Yanni, and D. Gomez, "Meta-Analysis of Randomized Clinical Trials of Early Versus Delayed Cholecystectomy for Mild Gallstone Pancreatitis," *British Journal of Surgery* 106, no. 11 (2019): 1442–1451, <https://doi.org/10.1002/bjs.11221>.
371. W. Dai, Y. Zhao, G. L. Du, and R. P. Zhang, "Comparison of Early and Delayed Cholecystectomy for Biliary Pancreatitis: A Meta-Analysis," *Surgeon* 19, no. 5 (2021): 257–262, <https://doi.org/10.1016/j.surge.2020.06.012>.
372. X. Yuan, B. Xu, M. Wong, et al., "The Safety, Feasibility, and Cost-Effectiveness of Early Laparoscopic Cholecystectomy for Patients With Mild Acute Biliary Pancreatitis: A Meta-Analysis," *Surgeon* 19, no. 5 (2021): 287–296, <https://doi.org/10.1016/j.surge.2020.06.014>.
373. J. Prasanth, M. Prasad, S. J. Mahapatra, et al., "Early Versus Delayed Cholecystectomy for Acute Biliary Pancreatitis: A Systematic Review and Meta-Analysis," *World Journal of Surgery* 46, no. 6 (2022): 1359–1375, <https://doi.org/10.1007/s00268-022-06501-4>.
374. L. J. Randial Pérez, J. Fernando Parra, and G. Aldana Dimas, "[The Safety of Early Laparoscopic Cholecystectomy (< 48 Hours) for Patients With Mild Gallstone Pancreatitis: A Systematic Review of the Literature and Meta-Analysis]," *Cirugia Espanola* 92, no. 2 (2014): 107–113, <https://doi.org/10.1016/j.cireng.2013.01.009>.
375. F. P. Zhong, K. Wang, X. Q. Tan, J. Nie, W. F. Huang, and X. F. Wang, "The Optimal Timing of Laparoscopic Cholecystectomy in Patients With Mild Gallstone Pancreatitis: A Meta-Analysis," *Medicine* 98, no. 40 (2019): e17429, <https://doi.org/10.1097/md.00000000000017429>.
376. M. C. van Baal, M. G. Besselink, O. J. Bakker, et al., "Timing of Cholecystectomy After Mild Biliary Pancreatitis: A Systematic Review," *Annals of Surgery* 255, no. 5 (2012): 860–866, <https://doi.org/10.1097/sla.0b013e3182507646>.
377. Y. X. Lyu, Y. X. Cheng, H. F. Jin, X. Jin, B. Cheng, and D. Lu, "Same-Admission Versus Delayed Cholecystectomy for Mild Acute Biliary Pancreatitis: A Systematic Review and Meta-Analysis," *BMC Surgery* 18, no. 1 (2018): 111, <https://doi.org/10.1186/s12893-018-0445-9>.
378. D. J. Yang, H. M. Lu, Q. Guo, S. Lu, L. Zhang, and W. M. Hu, "Timing of Laparoscopic Cholecystectomy After Mild Biliary Pancreatitis: A Systematic Review and Meta-Analysis," *Journal of Laparoendoscopic & Advanced Surgical Techniques* 28, no. 4 (2018): 379–388, <https://doi.org/10.1089/lap.2017.0527>.
379. D. W. da Costa, L. M. Dijkstra, S. A. Bouwense, et al., "Cost-Effectiveness of Same-Admission Versus Interval Cholecystectomy After Mild Gallstone Pancreatitis in the PONCHO Trial," *British Journal of Surgery* 103, no. 12 (2016): 1695–1703, <https://doi.org/10.1002/bjs.10222>.
380. K. D. Isbell, S. Wei, S. M. Dodwad, et al., "Impact of Early Cholecystectomy on the Cost of Treating Mild Gallstone Pancreatitis: Gallstone PANC Trial," *Journal of the American College of Surgeons* 233, no. 4 (2021): 517–525.e1, <https://doi.org/10.1016/j.jamcollsurg.2021.06.023>.
381. M. Di Martino, B. Ielpo, F. Pata, et al., "Timing of Cholecystectomy After Moderate and Severe Acute Biliary Pancreatitis," *JAMA Surgery* 158, no. 10 (2023): e233660, <https://doi.org/10.1001/jamasurg.2023.3660>.
382. W. H. Nealon, J. Bawduniak, and E. M. Walser, "Appropriate Timing of Cholecystectomy in Patients Who Present With Moderate to Severe Gallstone-Associated Acute Pancreatitis With Peripancreatic Fluid Collections," *Annals of Surgery* 239, no. 6 (2004): 741–749: discussion 9–51, <https://doi.org/10.1097/01.sla.0000128688.97556.94>.
383. T. G. Ackermann, P. A. Cashin, M. Alwan, et al., "The Role of Laparoscopic Cholecystectomy After Severe And/Or Necrotic Pancreatitis in the Setting of Modern Minimally Invasive Management of Pancreatic Necrosis," *Pancreas* 49, no. 7 (2020): 935–940, <https://doi.org/10.1097/mpa.0000000000001601>.
384. N. D. Hallensleben, H. C. Timmerhuis, R. A. Hollemans, et al., "Optimal Timing of Cholecystectomy After Necrotising Biliary Pancreatitis," *Gut* 71, no. 5 (2022): 974–982, <https://doi.org/10.1136/gutjnl-2021-324239>.
385. C. ASOP, J. L. Buxbaum, S. M. Abbas Fehmi, et al., "ASGE Guideline on the Role of Endoscopy in the Evaluation and Management of Choledocholithiasis," *Gastrointestinal Endoscopy* 89, no. 6 (2019): 1075–1105.e15, <https://doi.org/10.1016/j.gie.2018.10.001>.
386. P. Videhult, G. Sandblom, C. Rudberg, and I. C. Rasmussen, "Are Liver Function Tests, Pancreatitis and Cholecystitis Predictors of Common Bile Duct Stones? Results of a Prospective, Population-Based, Cohort Study of 1171 Patients Undergoing Cholecystectomy," *HPB* 13, no. 8 (2011): 519–527, <https://doi.org/10.1111/j.1477-2574.2011.00317.x>.
387. A. Anderloni, M. Galeazzi, M. Ballare, et al., "Early Endoscopic Ultrasonography in Acute Biliary Pancreatitis: A Prospective Pilot Study," *World Journal of Gastroenterology* 21, no. 36 (2015): 10427–10434, <https://doi.org/10.3748/wjg.v21.i36.10427>.
388. F. Cavdar, M. Yildar, G. Tellioglu, M. Kara, M. Tilki, and M. I. Titiz, "Controversial Issues in Biliary Pancreatitis: When Should We Perform MRCP and ERCP?," *Pancreatology* 14, no. 5 (2014): 411–414, <https://doi.org/10.1016/j.pan.2014.08.002>.
389. P. C. do Amaral, E. A. Filho, J. E. Ettinger, et al., "Common Bile Duct Investigation in Patients With Mild Biliary Pancreatitis: When and How? A Prospective Analysis of 48 Patients," *Hepato-Gastroenterology* 54, no. 77 (2007): 1323–1325, <https://pubmed.ncbi.nlm.nih.gov/17708246/>.

390. M. E. Cohen, L. Slezak, C. K. Wells, D. K. Andersen, and M. Topazian, "Prediction of Bile Duct Stones and Complications in Gallstone Pancreatitis Using Early Laboratory Trends," *American Journal of Gastroenterology* 96, no. 12 (2001): 3305–3311, <https://doi.org/10.1111/j.1572-0241.2001.05330.x>.
391. H. C. van Santvoort, O. J. Bakker, M. G. Besselink, et al., "Prediction of Common Bile Duct Stones in the Earliest Stages of Acute Biliary Pancreatitis," *Endoscopy* 43, no. 1 (2011): 8–13, <https://doi.org/10.1055/s-0030-1255866>.
392. J. P. Neoptolemos, N. London, I. Bailey, et al., "The Role of Clinical and Biochemical Criteria and Endoscopic Retrograde Cholangiopancreatography in the Urgent Diagnosis of Common Bile Duct Stones in Acute Pancreatitis," *Surgery* 100, no. 4 (1986): 732–742, <https://pubmed.ncbi.nlm.nih.gov/2876528/>.
393. L. Chang, S. K. Lo, B. E. Stabile, R. J. Lewis, and C. de Virgilio, "Gallstone Pancreatitis: A Prospective Study on the Incidence of Cholangitis and Clinical Predictors of Retained Common Bile Duct Stones," *American Journal of Gastroenterology* 93, no. 4 (1998): 527–531, https://doi.org/10.1111/j.1572-0241.1998.159_b.x.
394. J. L. Sherman, E. W. Shi, N. E. Ranasinghe, M. T. Sivasankaran, J. G. Prigoff, and C. M. Divino, "Validation and Improvement of a Proposed Scoring System to Detect Retained Common Bile Duct Stones in Gallstone Pancreatitis," *Surgery* 157, no. 6 (2015): 1073–1079, <https://doi.org/10.1016/j.surg.2015.01.005>.
395. G. Manes, G. Paspatis, L. Aabakken, et al., "Endoscopic Management of Common Bile Duct Stones: European Society of Gastrointestinal Endoscopy (ESGE) Guideline," *Endoscopy* 51, no. 5 (2019): 472–491, <https://doi.org/10.1055/a-0862-0346>.
396. Z. P. Cerne, N. Sever, L. Strnisa, et al., "Performance of European and American Societies of Gastrointestinal Endoscopy Guidelines for Prediction of Choledocholithiasis in Patients With Acute Biliary Pancreatitis," *Medicina* 59, no. 12 (2023): 2176, <https://doi.org/10.3390/medicina59122176>.
397. C. L. Liu, C. M. Lo, J. K. Chan, et al., "Detection of Choledocholithiasis by EUS in Acute Pancreatitis: A Prospective Evaluation in 100 Consecutive Patients," *Gastrointestinal Endoscopy* 54, no. 3 (2001): 325–330, <https://doi.org/10.1067/mge.2001.117513>.
398. J. H. Moon, Y. D. Cho, S. W. Cha, et al., "The Detection of Bile Duct Stones in Suspected Biliary Pancreatitis: Comparison of MRCP, ERCP, and Intraductal US," *American Journal of Gastroenterology* 100, no. 5 (2005): 1051–1057, <https://doi.org/10.1111/j.1572-0241.2005.41057.x>.
399. S. De Lisi, G. Leandro, and E. Buscarini, "Endoscopic Ultrasonography Versus Endoscopic Retrograde Cholangiopancreatography in Acute Biliary Pancreatitis: A Systematic Review," *European Journal of Gastroenterology and Hepatology* 23, no. 5 (2011): 367–374, <https://doi.org/10.1097/meg.0b013e3283460129>.
400. S. L. Lee, H. K. Kim, H. H. Choi, et al., "Diagnostic Value of Magnetic Resonance Cholangiopancreatography to Detect Bile Duct Stones in Acute Biliary Pancreatitis," *Pancreatology* 18, no. 1 (2018): 22–28, <https://doi.org/10.1016/j.pan.2017.12.004>.
401. D. Verma, A. Kapadia, G. M. Eisen, and D. G. Adler, "EUS Vs MRCP for Detection of Choledocholithiasis," *Gastrointestinal Endoscopy* 64, no. 2 (2006): 248–254, <https://doi.org/10.1016/j.gie.2005.12.038>.
402. N. Jagtap, J. K. Kumar, R. Chavan, et al., "EUS Versus MRCP to Perform ERCP in Patients With Intermediate Likelihood of Choledocholithiasis: A Randomised Controlled Trial," *Gut* (2022), <https://doi.org/10.1136/gutjnl-2021-325080>.
403. E. Alper, S. Akay, Z. Buyrac, F. Aslan, I. Alper, and B. Unsal, "Endosonography and Magnetic Resonance Cholangiopancreatography Show Similar Efficacy in Selecting Patients for ERCP in mild-moderate Acute Biliary Pancreatitis," *Turkish Journal of Gastroenterology* 23, no. 5 (2012): 580–584, <https://doi.org/10.4318/tjg.2012.0537>.
404. Y. Meeralam, K. Al-Shammari, and M. Yaghoobi, "Diagnostic Accuracy of EUS Compared With MRCP in Detecting Choledocholithiasis: A Meta-Analysis of Diagnostic Test Accuracy in Head-to-Head Studies," *Gastrointestinal Endoscopy* 86, no. 6 (2017): 986–993, <https://doi.org/10.1016/j.gie.2017.06.009>.
405. M. Suzuki, Y. Sekino, K. Hosono, et al., "Endoscopic Ultrasound Versus Magnetic Resonance Cholangiopancreatography for the Diagnosis of Computed Tomography-Negative Common Bile Duct Stone: Prospective Randomized Controlled Trial," *Digestive Endoscopy* 34, no. 5 (2022): 1052–1059, <https://doi.org/10.1111/den.14193>.
406. L. Castoldi, P. De Rai, A. Zerbi, et al., "Long Term Outcome of Acute Pancreatitis in Italy: Results of a Multicentre Study," *Digestive and Liver Disease* 45, no. 10 (2013): 827–832, <https://doi.org/10.1016/j.dld.2013.03.012>.
407. T. Yasuda, T. Ueda, Y. Takeyama, et al., "Long-Term Outcome of Severe Acute Pancreatitis," *Journal of Hepato-Biliary-Pancreatic Surgery* 15, no. 4 (2008): 397–402, <https://doi.org/10.1007/s00534-007-1266-x>.
408. G. Uomo, F. Gallucci, E. Madrid, S. Miraglia, G. Manes, and P. G. Rabitti, "Pancreatic Functional Impairment Following Acute Necrotizing Pancreatitis: Long-term Outcome of a Non-Surgically Treated Series," *Digestive and Liver Disease* 42, no. 2 (2010): 149–152, <https://doi.org/10.1016/j.dld.2009.08.007>.
409. T. Symersky, B. van Hoorn, and A. A. Masclee, "The Outcome of a Long-Term Follow-Up of Pancreatic Function After Recovery From Acute Pancreatitis," *JOP: Journal of the Pancreas* 7, no. 5 (2006): 447–453, <https://pubmed.ncbi.nlm.nih.gov/16998241/>.
410. G. Garip, E. Sarandol, and E. Kaya, "Effects of Disease Severity and Necrosis on Pancreatic Dysfunction After Acute Pancreatitis," *World Journal of Gastroenterology* 19, no. 44 (2013): 8065–8070, <https://doi.org/10.3748/wjg.v19.i44.8065>.
411. S. Kahl, K. Schutte, B. Glasbrenner, et al., "The Effect of Oral Pancreatic Enzyme Supplementation on the Course and Outcome of Acute Pancreatitis: A Randomized, Double-Blind Parallel-Group Study," *JOP: Journal of the Pancreas* 15, no. 2 (2014): 165–174, <https://doi.org/10.6092/1590-8577/797>.
412. B. Boreham and B. J. Ammori, "A Prospective Evaluation of Pancreatic Exocrine Function in Patients With Acute Pancreatitis: Correlation With Extent of Necrosis and Pancreatic Endocrine Insufficiency," *Pancreatology* 3, no. 4 (2003): 303–308, <https://doi.org/10.1159/000071768>.
413. Y. Xu, D. Wu, Y. Zeng, and X. Wang, "Pancreatic Exocrine Function and Morphology Following an Episode of Acute Pancreatitis," *Pancreas* 41, no. 6 (2012): 922–927, <https://doi.org/10.1097/mpa.0b013e31823d7f2d>.
414. J. Tu, Y. Yang, J. Zhang, et al., "Effect of the Disease Severity on the Risk of Developing New-Onset Diabetes After Acute Pancreatitis," *Medicine* 97, no. 22 (2018): e10713, <https://doi.org/10.1097/md.00000000000010713>.
415. S. N. Duggan, D. B. O'Connor, A. Antanaitis, et al., "Metabolic Dysfunction and Diabetes Mellitus During Long-Term Follow-Up of Severe Acute Pancreatitis: A Case-Matched Study," *Pancreatology* 20, no. 5 (2020): 813–821, <https://doi.org/10.1016/j.pan.2020.03.016>.
416. R. Gupta, J. D. Wig, D. K. Bhasin, et al., "Severe Acute Pancreatitis: The Life After," *Journal of Gastrointestinal Surgery* 13, no. 7 (2009): 1328–1336, <https://doi.org/10.1007/s11605-009-0901-z>.
417. S. Appelros, S. Lindgren, and A. Borgstrom, "Short and Long Term Outcome of Severe Acute Pancreatitis," *European Journal of Surgery* 167, no. 4 (2001): 281–286, <https://doi.org/10.1080/110241501300091462>.
418. M. Vujasinovic, B. Tepes, J. Makuc, et al., "Pancreatic Exocrine Insufficiency, Diabetes Mellitus and Serum Nutritional Markers After Acute Pancreatitis," *World Journal of Gastroenterology* 20, no. 48 (2014): 18432–18438, <https://doi.org/10.3748/wjg.v20.i48.18432>.

419. B. Andersson, M. L. Pendse, and R. Andersson, "Pancreatic Function, Quality of Life and Costs at Long-Term Follow-Up After Acute Pancreatitis," *World Journal of Gastroenterology* 16, no. 39 (2010): 4944–4951, <https://doi.org/10.3748/wjg.v16.i39.4944>.
420. R. A. Hollemans, N. D. L. Hallensleben, D. J. Mager, et al., "Pancreatic Exocrine Insufficiency Following Acute Pancreatitis: Systematic Review and Study Level meta-analysis," *Pancreatology* 18, no. 3 (2018): 253–262, <https://doi.org/10.1016/j.pan.2018.02.009>.
421. W. Huang, D. de la Iglesia-García, I. Baston-Rey, et al., "Exocrine Pancreatic Insufficiency Following Acute Pancreatitis: Systematic Review and Meta-Analysis," *Digestive Diseases and Sciences* 64, no. 7 (2019): 1985–2005, <https://doi.org/10.1007/s10620-019-05568-9>.
422. M. Migliori, R. Pezzilli, P. Tomassetti, and L. Gullo, "Exocrine Pancreatic Function After Alcoholic or Biliary Acute Pancreatitis," *Pancreas* 28, no. 4 (2004): 359–363, <https://doi.org/10.1097/00006676-200405000-00001>.
423. H. Pelli, R. Lappalainen-Lehto, A. Piironen, S. Jarvinen, J. Sand, and I. Nordback, "Pancreatic Damage After the First Episode of Acute Alcoholic Pancreatitis and Its Association With the Later Recurrence Rate," *Pancreatology* 9, no. 3 (2009): 245–251, <https://doi.org/10.1159/000212089>.
424. J. Nikkola, J. Laukkanen, J. Lahtela, et al., "The long-term Prospective Follow-Up of Pancreatic Function After the First Episode of Acute Alcoholic Pancreatitis: Recurrence Predisposes One to Pancreatic Dysfunction and Pancreatogenic Diabetes," *Journal of Clinical Gastroenterology* 51, no. 2 (2017): 183–190, <https://doi.org/10.1097/mcg.0000000000000564>.
425. S. S. Rana, D. K. Bhasin, C. Rao, R. Sharma, and R. Gupta, "Comparative Evaluation of Structural and Functional Changes in Pancreas After Endoscopic and Surgical Management of Pancreatic Necrosis," *Annals of Gastroenterology* 27, no. 2 (2014): 162–166, <https://pmc.ncbi.nlm.nih.gov/articles/PMC3982632/>.
426. L. Sabater, E. Pareja, L. Aparisi, et al., "Pancreatic Function After Severe Acute Biliary Pancreatitis: The Role of Necrosectomy," *Pancreas* 28, no. 1 (2004): 65–68, <https://doi.org/10.1097/00006676-200401000-00010>.
427. P. Chandrasekaran, R. Gupta, S. Shenvi, et al., "Prospective Comparison of Long Term Outcomes in Patients With Severe Acute Pancreatitis Managed by Operative and Non Operative Measures," *Pancreatology* 15, no. 5 (2015): 478–484, <https://doi.org/10.1016/j.pan.2015.08.006>.
428. A. E. Phillips, K. Ooka, I. Pothoulakis, et al., "Assessment of Weight Loss and Gastrointestinal Symptoms Suggestive of Exocrine Pancreatic Dysfunction After Acute Pancreatitis," *Clinical and Translational Gastroenterology* 11, no. 12 (2020): e00283, <https://doi.org/10.14309/ctg.0000000000000283>.
429. M. Doepel, J. Eriksson, L. Halme, T. Kumpulainen, and K. Hockerstedt, "Good Long-Term Results in Patients Surviving Severe Acute Pancreatitis," *British Journal of Surgery* 80, no. 12 (1993): 1583–1586, <https://doi.org/10.1002/bjs.1800801229>.
430. J. Tu, J. Zhang, L. Ke, et al., "Endocrine and Exocrine Pancreatic Insufficiency After Acute Pancreatitis: Long-Term Follow-Up Study," *BMC Gastroenterology* 17, no. 1 (2017): 114, <https://doi.org/10.1186/s12876-017-0663-0>.
431. E. Malecka-Panas, A. Gasiorowska, A. Kropiwnicka, A. Zlobinska, and J. Drzewoski, "Endocrine Pancreatic Function in Patients After Acute Pancreatitis," *Hepato-Gastroenterology* 49, no. 48 (2002): 1707–1712, <https://pubmed.ncbi.nlm.nih.gov/12397772/>.
432. T. Man, R. Seicean, L. Lucaciu, A. Istrate, and A. Seicean, "Risk Factors for New-Onset Diabetes Mellitus Following Acute Pancreatitis: A Prospective Study," *European Review for Medical and Pharmacological Sciences* 26, no. 16 (2022): 5745–5754, https://doi.org/10.26355/eurev_202208_29511.
433. D. Wu, Y. Xu, Y. Zeng, and X. Wang, "Endocrine Pancreatic Function Changes After Acute Pancreatitis," *Pancreas* 40, no. 7 (2011): 1006–1011, <https://doi.org/10.1097/mpa.0b013e31821fde3f>.
434. S. L. Das, P. P. Singh, A. R. Phillips, R. Murphy, J. A. Windsor, and M. S. Petrov, "Newly Diagnosed Diabetes Mellitus After Acute Pancreatitis: A Systematic Review and Meta-Analysis," *Gut* 63, no. 5 (2014): 818–831, <https://doi.org/10.1136/gutjnl-2013-305062>.
435. J. E. Dominguez-Munoz, M. Vujasinovic, D. de la Iglesia, et al., "European Guidelines for the Diagnosis and Treatment of Pancreatic Exocrine Insufficiency: UEG, EPC, EDS, ESPEN, ESPGHAN, ESDO, and ESPCG Evidence-Based Recommendations," *United European Gastroenterology Journal* 13, no. 1 (2025): 125–172, <https://doi.org/10.1002/ueg2.12674>.
436. D. Czupáři, A. Váradi, N. Farkas, et al., "Detailed Characteristics of Post-Discharge Mortality in Acute Pancreatitis," (1528–0012 (Electronic))

Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Supporting Information S1: ueg270190-sup-0001-suppl-data.docx.

Supporting Information S2: ueg270190-sup-0002-suppl-data.pdf.

Supporting Information S3: ueg270190-sup-0003-suppl-data.pdf.