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Colangiopancreatografia Retrógrada Endoscópica em Emergência Médica

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Resumo

Introdução: O tratamento agudo das doenças biliopancreáticas no serviço de urgência continua a ser um pilar fundamental da gastroenterologia moderna. Embora a colangiopancreatografia retrógrada endoscópica (CPRE) esteja estabelecida como a modalidade terapêutica de referência para a descompressão biliar, a sua aplicação ideal no contexto agudo continua a ser um motivo de debate. As principais questões envolvem o tempo de intervenção, o seu papel específico na pancreatite aguda biliar e a gestão dos riscos associados ao procedimento. Apesar da literatura existente, é necessária uma síntese atualizada com evidência de alto nível para definir com precisão a "janela terapêutica" ideal para a CPRE neste contexto. Assim, o objetivo desta revisão é identificar as indicações, bem como a eficácia e a segurança, da CPRE emergente no tratamento de doentes que apresentam colangite aguda ou pancreatite biliar aguda.

Métodos: Seguindo as mais recentes *Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines,* esta revisão sistemática (PROSPERO: CRD420261278934) sintetizou a evidência publicada entre 2020 e 2025 para avaliar o momento ideal para a realização da CPRE no tratamento das doenças biliopancreáticas agudas. A pesquisa foi realizada nas bases de dados *PubMed, Scopus* e *Web of Science*. O estudo deu prioridade a evidências de alto nível para comparar a intervenção urgente com a intervenção tardia em diferentes graus de gravidade da doença. Os resultados da eficácia incluíram a mortalidade intra-hospitalar e aos 30 dias, a duração do internamento hospitalar, a admissão na unidade de cuidados intensivos e readmissão aos 30 dias, enquanto a segurança foi avaliada através do registo das complicações locais e sistémicas. Dois revisores independentes realizaram a seleção dos estudos e a extração de dados, tendo a qualidade metodológica dos estudos incluídos sido avaliada através da ferramenta ROBINS-I.

Resultados: Foram incluídos um total de 12 estudos publicados entre 2020 e 2025. No caso da colangite aguda de grau III, foi identificada uma janela terapêutica crítica de 48 horas, atrasos para além deste limiar estiveram associados a uma mortalidade significativamente mais elevada ($p = 0,017$) e a um aumento acentuado na utilização de recursos de saúde, incluindo um aumento médio de 5,56 dias na permanência na unidade de cuidados intensivos ($p = 0,0096$) . Além disso, verificou-se que a bacteremia modulava significativamente a relação entre o tempo de intervenção e a mortalidade ($p = 0,010$), sugerindo uma janela mais restrita para doentes com infeções sistémicas. Em contrapartida, para a colangite aguda não grave e a pancreatite biliar aguda, a intervenção precoce (< 24–48h) não alterou a mortalidade ou o curso clínico da doença. No entanto, serviu como um preditor robusto e consistente de internamentos hospitalares mais curtos em quase todas as coortes, incluindo procedimentos "muito urgentes" (≤ 3h), que facilitaram significativamente a alta mais precoce em comparação com abordagens urgentes ou eletivas ($p < 0,01$). As complicações

locais foram, no geral, independentes do momento da intervenção, embora os procedimentos após as 48h estivessem associados a taxas mais elevadas de perfuração biliar (p = 0,01).

Conclusão: O impacto clínico do momento da realização da CPRE é determinado pela gravidade da doença. Embora um intervalo de 48 horas seja essencial para reduzir a mortalidade e a sobrecarga sobre os cuidados intensivos em casos graves, os benefícios da intervenção precoce em quadros não graves são principalmente de natureza logística e económica, impulsionados pela melhoria da eficiência hospitalar. Os protocolos hospitalares devem dar prioridade à drenagem no prazo de 48 horas para doentes de grau III e aqueles com bacteremia, enquanto uma abordagem de "estabilização em primeiro lugar" continua a ser segura para casos não graves. São necessários futuros ensaios clínicos multicêntricos randomizados para validar estas janelas terapêuticas.

Abstract

Introduction: The management of acute biliopancreatic diseases in the emergency department remains a cornerstone in modern gastroenterology. While endoscopic retrograde cholangiopancreatography (ERCP) has established itself as the gold-standard therapeutic modality for biliary decompression, its optimal application in the acute setting remains a subject of debate. Key controversies involve intervention timing, its specific role in acute biliary pancreatitis and the management of procedure-related risks. Despite existing literature, an updated synthesis of high-level evidence is required to precisely define the optimal “therapeutic windows” for ERCP. The aim of this review is to identify the indications, as well as the efficacy and safety, of emergency ERCP in the treatment of patients presenting with acute cholangitis or acute biliary pancreatitis.

Methods: Following the latest Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, this systematic review (PROSPERO: CRD420261278934) synthesized evidence from 2020 to 2025 to evaluate optimal ERCP timing in acute biliopancreatic diseases. A comprehensive search was conducted across PubMed, Scopus and Web of Science. The study prioritized high-level evidence to compare urgent versus delayed intervention across varying disease severities. Primary efficacy outcomes included in-hospital and 30-day mortality, length of hospital stay, intensive care unit admission and 30-day readmission, while safety was assessed through local and systemic complications. Two independent reviewers performed study selection and data extraction, with methodological quality of the included studies evaluated using the ROBINS-I tool.

Results: A total of 12 studies published between 2020 and 2025 were included. For grade III acute cholangitis, a critical 48-hour therapeutic window was identified, delays beyond this threshold were associated with significantly higher mortality ($p = 0.017$) and a profound escalation in healthcare resource utilization, including an average 5.56-day increase in ICU stay ($p = 0.0096$). Furthermore, bacteremia was found to significantly modulate the relationship between intervention timing and mortality ($p = 0.010$), suggesting a narrower window for patients with systemic infections. In contrast, for non-severe cholangitis and acute biliary pancreatitis, early intervention (< 24–48h) did not consistently alter mortality or the clinical course of the disease. However, it served as a robust and consistent predictor of shorter hospital stays across almost all cohorts, including "very urgent" procedures (≤ 3h) which significantly facilitated earlier discharge compared to urgent or elective approaches ($p < 0.01$). Local complications were generally independent of timing, although procedures beyond 48h were linked to higher rates of biliary perforation ($p = 0.01$).

Conclusions: The clinical impact of ERCP timing is dictated by disease severity. While a 48-hour window is essential to reduce mortality and critical care burden in severe cases, the benefits of early

intervention in non-severe presentations are primarily logistical and economic, driven by improved hospital throughput. Hospital protocols should prioritize drainage within 48 hours for grade III patients and those with bacteremia, while a "stabilization-first" approach remains safe for non-severe cases. Future multicenter randomized trials are required to validate these therapeutic windows.

Abbreviations list

AC - Acute Cholangitis

AGA - American Gastroenterological Association

AP - Acute Pancreatitis

ASA - American Society of Anesthesiologists

CECT - Contrast-Enhanced Computed Tomography

ERCP - Endoscopic Retrograde Cholangiopancreatography

EUS - Endoscopic Ultrasound

HR - Hazard Ratio

ICU - Intensive Care Unit

IHM - In-Hospital Mortality

LHS - Length of Hospital Stay

MeSH - Medical Subject Headings do Index Medicus

MRCP - Magnetic Resonance Cholangiopancreatography

PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PSM - Propensity Score Matching

RAC - Revised Atlanta Classification

ROBINS-I - Risk of Bias In Non-Randomized Studies - of Interventions

TG18 - Tokyo Guidelines 2018

WSES - World Society of Emergency Surgery

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Introduction

Initially introduced in 1968, Endoscopic Retrograde Cholangiopancreatography (ERCP) has undergone a significant paradigm shift: originally a diagnostic innovation, it has now evolved into an almost exclusively therapeutic modality following the advent of non-invasive diagnostic techniques such as magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS). Today, ERCP is the gold standard for therapeutic interventions in the management of biliopancreatic diseases. [1, 2]

The majority of these disorders are susceptible to curative or palliative endoscopic treatment with ERCP. In acute presentation of these diseases the timing of ERCP is crucial, since procedures performed too early or too late are equally risky. However, besides the risks inherent to the technique, ERCP is a technically challenging procedure with potentially serious complications, even in expert hands. [2] Hence the importance of defining an optimal time and appropriate indications for using it carefully.

The endoscopic retrograde cholangiopancreatography procedure

ERCP is performed in both inpatient and ambulatory settings, depending on the patient's clinical status. The choice of anesthesia is tailored to the procedure's complexity and patient risk factors, ranging from conscious sedation (utilizing rapid-acting opioids and benzodiazepines) to deep sedation with propofol — often administered via monitored anesthesia care without intubation — or general anesthesia. While the prone position is the standard for optimizing ductal opacification and cannulation, alternative positioning (e.g., supine or lateral decubitus) may be required in cases of morbid obesity, altered surgical anatomy or open abdominal wounds. [3, 4]

The procedure involves advancing a side-viewing duodenoscope to the descending duodenum to visualize the major duodenal papilla. Precise inspection of the ampullary morphology provides essential diagnostic clues for various biliary and pancreatic pathologies. Selective cannulation of the biliary tree is typically achieved using a sphincterotome — a specialized catheter equipped with a cutting wire — often pre-loaded with a flexible guidewire to facilitate entry into the desired duct. Once selective access is confirmed, radiopaque contrast medium is injected under fluoroscopic guidance to obtain a high-definition cholangiogram. This step is the cornerstone of the intervention, as it enables the clinician to visualize the biliary lumen, identify filling defects (such as choledocholithiasis), and map anatomical variations. In biliary nomenclature, "proximal" refers to the segment closest to the hepatic parenchyma, while "distal" indicates the portion toward the ampulla. The extrahepatic biliary tree typically comprises the common bile duct, which bifurcates

at the hepatic hilum into the right and left main hepatic ducts. However, clinicians must account for significant anatomical diversity at the hilar confluence to ensure safe and effective therapeutic outcomes. [3, 5]

Indications for endoscopic retrograde cholangiopancreatography

Acute cholangitis

Definition and epidemiology of acute cholangitis

Acute cholangitis (AC), first described by Charcot in 1877, associated with abdominal pain, fever and jaundice, is an inflammatory condition that is caused by a bacterial infection of the bile duct. Current literature indicates a mortality rate ranging from 20% to 30% for this condition. [6]

Pathogenesis and etiology of acute cholangitis

Under physiological conditions, bile is a sterile substance possessing innate bacteriostatic properties. The integrity of the biliary system is maintained by the mechanical barrier of the sphincter of Oddi, which exerts a basal pressure of 10-15 mmHg to prevent the ascending migration of intestinal pathogens and portal bacteremia. [7]

The pathogenesis of acute cholangitis is primarily driven by the combination of biliary obstruction and bacterial contamination. When the biliary tract is obstructed, the subsequent rise in endoluminal pressure disrupts normal bile flow and facilitates cholangiovenous and cholangiolymphatic reflux. This process allows pathogens and endotoxins to enter the systemic circulation, often resulting in a rapidly progressive and life-threatening infection. While choledocholithiasis is the most prevalent etiological factor, various other pathologies can obstruct the extrahepatic biliary tree and trigger this condition. These include malignant obstructions such as pancreatic cancer, ampullary carcinoma, or metastatic disease, as well as mechanical and infectious causes including biliary stent occlusion, Mirizzi syndrome, Lemmel syndrome, parasitic infections, and AIDS-related cholangiopathy. In its most severe clinical manifestations, acute cholangitis is characterized by systemic sepsis and rapid physiological deterioration. [7, 8]

Diagnosis and classification of acute cholangitis

AC may present with the Charcot's triad, which is the manifestation of biliary obstruction with upper abdominal pain (which may radiate to the back or to the right shoulder), [8] fever and jaundice. The condition may progress rapidly to Reynolds' pentad, which consists of Charcot's triad with confusion and hypotension. [9] The presence of this triad strongly suggests the presence of acute

cholangitis. However, due to the low sensitivity, it is not valid for use as diagnostic criteria for acute cholangitis. [10]

The Tokyo Guidelines 2018 (TG18), [11] divide the diagnosis of acute cholangitis into 3 grades: grade I (mild), grade II (moderate) and grade III (severe).

Mild acute cholangitis is defined as cholangitis that does not meet the TG18 severity assessment criteria for moderate or severe cholangitis.

Moderate acute cholangitis is cholangitis that is not severe but requires early biliary drainage. In the TG18 severity assessment criteria, moderate cholangitis is assessed if at least two of the following five criteria are met: WBC ≥ 12,000 or < 4,000, temperature ≥ 39°C, age ≥ 75 years, total bilirubin ≥ 5 mg/dL, or albumin < (lower limit of normal value x 0.73 g/dL).

Severe acute cholangitis is cholangitis with sepsis-induced organ damage. In the TG18 severity assessment criteria, severe cholangitis is assessed if any one of the following criteria is met: cardiovascular dysfunction (requiring the use of dopamine ≥ 5 μg/kg per minute or noradrenaline), neurological dysfunction (disturbance of consciousness), respiratory dysfunction (PaO_2/FiO_2 ratio < 300), renal dysfunction (oliguria or serum creatinine > 2.0 mg/dL), hepatic dysfunction (PT-INR > 1.5), or coagulation disorder (platelet count < $10^4/\mu L$).

Management of acute cholangitis

According to TG18, biliary drainage by ERCP is recommended regardless of disease severity, except for mild cases that can be managed, at least initially, with conservative treatment alone. [11]

In fact, most patients respond to aggressive medical management with intravenous fluids and antibiotic therapy. However, about 20% to 30% fail to respond to medical management alone, [7] which leads to a high risk of progression to sepsis. [12] Biliary drainage is considered to be a critical step in the treatment of AC and ERCP has become the gold standard method of biliary drainage in these patients. [6]

The Tokyo guidelines [11] describe that in most cases of grade I AC, initial treatment including antibiotics is sufficient. However, biliary drainage should be considered if a patient does not respond to it. Endoscopic sphincterotomy and subsequent choledocholithotomy may be performed at the same time as biliary drainage.

In grade II, early endoscopic or percutaneous transhepatic biliary drainage is indicated. If the underlying etiology requires treatment, this should be provided after the patient's general condition has improved and, again, endoscopic sphincterotomy and subsequent choledocholithotomy may be performed with biliary drainage.

In cases of Grade III AC, as the patient's condition may deteriorate promptly, needing appropriate respiratory/circulatory management, endoscopic or percutaneous transhepatic biliary drainage should be performed as soon as possible once the patient has been stabilized through initial medical therapy.

In case of severe acute cholangitis, ERCP with biliary sphincterotomy becomes a life-saving therapeutic procedure and should be performed as soon as possible. Otherwise, in case of non-severe acute cholangitis, conservative management with antibiotic therapy for 24h should be attempted before ERCP, which can be delayed for 48-72h. [7] In case of therapy failure, ERCP should be performed in these patients as soon as possible, or within 24h. [2]

Acute pancreatitis

Definition and epidemiology of acute pancreatitis

Acute pancreatitis (AP) is among the most common gastrointestinal diagnoses for acute inpatient hospital admission. It is an inflammatory condition of the exocrine pancreas with a global rising incidence at a rate of 2% to 5% annually, with rates ranging from 3.4 to 110 cases per 100,000 individuals. [13] It is increasing worldwide in part because of increased rates of obesity and gallstones. [14]

Etiology and pathogenesis of acute pancreatitis

Acute pancreatitis is a frequent inflammatory condition affecting the exocrine pancreas, marked by the premature activation and leakage of digestive enzymes. This leads to local pancreatic damage and triggers an inflammatory response, which can result in systemic inflammatory response syndrome. [13]

The different etiologies include gallstones, alcohol abuse, autoimmune pancreatitis, smoking, hypertriglyceridemia, pancreas divisum, obesity, drugs, hypercalcemia, and pancreatitis post-ERCP, although some cases may be multifactorial. [15]

Gallstone disease is the most common cause of acute pancreatitis, and while most cases are self-limiting with a benign course, approximately 25% of patients develop severe pancreatitis associated with multi-organ failure, local complications of the pancreas (necrosis, abscess, or pseudocyst), or both. Mortality is approximately 4% to 7% for all cases, and 20% to 30% for severe cases. [16]

In gallstone pancreatitis, the initiating event is impaction of gallstone stones or sludge in the common bile duct and ampulla, which causes reflux of bile and duodenal content into the pancreatic duct, increased pressure in the pancreatic duct, or both. This in turn leads to unregulated activation

of pancreatic enzymes and pancreatic auto-digestion, which triggers a local pancreatic damage and an inflammatory response. Patients with gallstone pancreatitis can develop cholangitis, organ failure and other life-threatening complications. [13, 14, 16]

Diagnosis of acute pancreatitis

According to the Revised Atlanta Classification (RAC) 2012 [17], the diagnosis of acute pancreatitis requires two of the following three features: abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back); serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal; and characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging or transabdominal ultrasonography.

If abdominal pain suggests strongly that acute pancreatitis is present, but the serum amylase and/or lipase activity is less than three times the upper limit of normal, as may be the case with delayed presentation, imaging will be required to confirm the diagnosis. If the diagnosis of acute pancreatitis is established by abdominal pain and by increases in the serum pancreatic enzyme activities, the imaging resources are not usually required for diagnosis in the emergency room or on admission to the hospital. [17]

Relying exclusively on two of these criteria can miss approximately 25% of AP diagnoses and could result in misdiagnosis in about 10% of patients. Initial evaluations should take into account the patient's medical history, other symptoms, identifying past episodes of AP and associated risk factors, such as gallstone disease, alcohol consumption, family history of pancreatitis, recent infections, trauma, insect bites, and new medications. [13]

Additional symptoms may include nausea, vomiting, tachycardia, and low to moderate fever. Jaundice can occur if the common bile duct is obstructed due to gallstones or pancreatic edema. In severe cases, shock may develop. Physical exams often show abdominal distension and decreased bowel sounds. [13]

While amylase has traditionally been used, lipase is more sensitive and specific for confirming AP. Amylase typically normalizes within 3-5 days, whereas lipase may take 8-14 days. Elevated serum levels of amylase and lipase support a clinical suspicion of AP, although amylase also derives from the salivary glands, with only about 40% coming from the pancreas. Other conditions, such as bowel obstruction, infarction, cholecystitis, or perforated ulcers, can also cause elevated amylase and lipase levels. The lipase/amylase ratio may help determine whether alcohol is the cause of AP. [13]

Classification of acute pancreatitis

The RAC 2012 [17], is the most widely utilized classification system for AP, distinguishing between interstitial edematous pancreatitis and necrotizing pancreatitis, three severity levels and an early and a late phase. [13]

The two most important markers of severity in acute pancreatitis are organ failure (particularly multisystem organ failure) and pancreatic necrosis. CECT is the best available test to distinguish interstitial from necrotizing pancreatitis, particularly after 2-3 days of disease. Mortality of sustained multisystem organ failure in association with necrotizing pancreatitis is generally > 36%. [17, 18]

The early phase (typically the first week) is driven by the host's systemic inflammatory response to pancreatic injury. During this stage, severity is defined by the presence and duration of organ failure: transient if resolved within 48 hours, or persistent if it exceeds this timeframe. While local complications may emerge, they are not the primary determinants of severity in this phase, as morphologic changes often do not correlate with the degree of organ dysfunction. [13, 17]

The late phase is characterized by prolonged systemic inflammation or the development of local complications, occurring only in moderately severe or severe AP. In this stage, management is guided by a combination of clinical criteria - primarily persistent organ failure - and morphologic characteristics identified through imaging. Accurate differentiation of these complications is essential, as they directly dictate therapeutic interventions. [13, 17]

According to the RAC [17], the severity of AP is categorized into three levels based on the duration of organ dysfunction and the presence of complications - mild AP, characterized by the absence of both organ failure and local or systemic complications. It is associated with a swift recovery and negligible mortality; moderately severe AP, identified by the presence of local/systemic complications or transient organ failure, which resolves within 48 hours; and severe AP, defined by persistent organ failure exceeding 48 hours. This stage carries the highest risk of mortality and often requires intensive multidisciplinary care. [15, 17]

Management of acute pancreatitis

In general, pancreatitis caused by gallstones can be managed with two treatment strategies.

The initial management of biliary pancreatitis follows a conservative-first strategy, prioritizing aggressive intravenous fluid resuscitation to mitigate the risks of hypovolemia and subsequent organ failure. This clinical stabilization is complemented by nothing by mouth, optimized analgesia, and, when indicated, antibiotic therapy. Following hemodynamic resuscitation, the necessity and timing of ERCP are dictated by the patient's clinical evolution. Immediate

endoscopic intervention is mandatory in the presence of concomitant acute cholangitis or signs of persistent biliary obstruction. Conversely, if the patient demonstrates progressive clinical and biochemical improvement, suggesting spontaneous stone passage, ERCP is not routinely required, thereby avoiding potential procedural complications. [2, 16]

The second strategy involves the early use of ERCP (within 72 hours of admission) in addition to conservative medical management routinely in all patients. [2] However, a meta-analysis by *Tse & Yuan* found that routine ERCP in biliary AP is not beneficial. [16]

Most of the times EUS or MRCP can be used first to identify common bile duct stones and determine the need for ERCP in clinically ambiguous situations. [18]

Many studies including a multicenter randomized controlled trial by *Schepers et al*. in 2020, showed that in patients with severe acute biliary pancreatitis without cholangitis, urgent ERCP with sphincterotomy did not decrease complications or mortality compared with conservative treatment. In patients with associated cholangitis, early ERCP showed the opposite decreasing mortality and complications, helping reducing local complications in cases of pancreatitis with biliary obstruction. [14, 19, 20]

Timing of endoscopic retrograde cholangiopancreatography

In acute biliopancreatic disease, the timing of ERCP is crucial, as procedures performed too early or too late may be equally harmful. [2]

Acute cholangitis

In acute cholangitis, there are multiple discrepancies according to the optimal time of performing ERCP. Several retrospective studies have shown that ERCP performed within 24 to 72 hours of admission is associated with lower in-hospital mortality (IHM), length of hospital stay (LHS) and 30-day mortality, whereas others did not show a difference in the mortality associated with early or late ERCP. [6]

Tokyo guidelines from 2018, recommend early ERCP for patients with AC, but the optimal timing of this early ERCP has not yet been determined. According to them, ERCP should be performed within 24h. In TG18, “urgent” referred to a procedure on the day of admission and “early” referred to a procedure on the day following admission. [6, 10, 21]

If following the European Society of Digestive Endoscopy guidelines biliary drainage should be performed as soon as possible and within 12 h in patients with septic shock. ESGE recommends the following timing for biliary drainage, preferably endoscopic, in severe AC, as soon as possible and within 12 hours for patients with septic shock, in moderate AC, within 48 – 72 hours and in mild cases of AC, an elective approach. [22]

Using a large nationally representative database, *Mulki et al.* found an association between early ERCP (< 48h) 50% lower mortality rate and up to 66% lower 30-day readmission rate, a decreased hospital length of stay and costs. They recommend performing ERCP within 48h in patients presenting with acute cholangitis regardless of disease severity. [23]

The first review and meta-analysis on evaluating the impact of timing of ERCP on patient outcomes in AC by *Iqbal et al.* revealed that performing emergent ERCP within 48 hours in patients with moderate to severe acute cholangitis was associated with lower IHM, 30-day mortality, LHS and organ failure. [7] Later, a meta-analysis by *Lyu et al.* in 2022, agreed that ERCP performed within 48 hours has advantages in IHM, 30-day mortality and LHS over ERCP performed later. In addition, they showed that ERCP performed within 24 hours was associated with lower IHM and LHS. [6] The meta-analysis of observational studies, performed by *Du et al.*, showed that the performance of earlier ERCP, even those urgently performed < 24 hours from presentation, was associated with a 20%-50% reduction in mortality. Additionally, ERCP performed < 24 hours compared with > 24 hours resulted in an approximately 3-day reduction in hospital stay. [12]

In addition to the optimal time frame for performing ERCP, if it is less than 48 hours, the question remains whether the patient is admitted at the weekend, when professional teams are reduced and often unable to perform the procedure in an urgent context, if that is the case.

Several studies have shown a “weekend effect” for many acute conditions, where patients admitted on weekends have worse clinical outcomes, attributed to the shortage of weekend staffing, which may result in delay of care. [24] The weekend effect is a medical phenomenon that is increasingly being described in the literature. [25]

Most of the time, patients admitted on the weekend requiring ERCP for biliary disorders often have their ERCP delayed until the weekday. This occurs as staffing for ERCP generally requires an endoscopist trained in ERCP, a technician familiar with ERCP equipment, a nurse familiar with ERCP, an interventional endoscopy room equipped with fluoroscopy and in many instances, anesthesia services. However, the majority of the patients with moderate or severe AC often require first stabilization with intravenous fluids and antibiotics, before the urgent ERCP, so it is unclear whether these patients admitted on the weekend have these procedures delayed vs. weekday admissions. [24, 25] The Parikh’s study showed that performing ERCP on weekends results in reduction in LHS. [24] A retrospective review by *Banta et al.* concluded that ERCP performed on weekends was associated with significantly more postoperative complications and intensive care unit (ICU) admissions compared to ERCP performed on weekdays. [26]

In 2023, *Mukai et al.* introduce a critical nuance regarding procedural safety and resource management. They argue that for non-severe cases, it may be safer to defer the procedure to a standby schedule during normal working hours to ensure the presence of a full expert team. [27]

However, they also emphasize that in moderate cases, failing to intervene within 24 hours—or delaying drainage when conservative treatment fails in mild cases—leads to a significant increase in medical costs, ICU admissions, and persistent organ failure. [27, 28]

Fundamentally, we return to the initial question of the ideal time for performing ERCP not being well established.

Acute pancreatitis

In AP, there has been much debate as to which management strategy is better, especially in severe episodes of pancreatitis. In the absence of cholangitis, the role and timing of ERCP in AP are still under debate. Since biliary stones often pass spontaneously, immediate intervention may result in unwarranted procedures. ERCP within 48-72 h has been suggested in the setting of severe acute pancreatitis (as defined by the Revised Atlanta Classification) [17] that shows persistent or worsening signs of biliary tract obstruction. Otherwise, if signs of biliary obstruction improve or finally regress, a more conservative approach should be performed by a EUS evaluation or MRCP within 24-48 h to avoid inappropriate ERCP. [2, 16]

World Society of Emergency Surgery (WSES) guidelines suggest biliary decompression within 24 hours for pancreatitis patients with suspected cholangitis to improve survival outcomes. [13, 29]

However, the American Gastroenterological Association (AGA) suggests a more conservative approach. The AGA prioritizes initial clinical stabilization, with early oral feeding as tolerated rather than keeping the patient in a *nil per os* status, and observation, recommending that ERCP should be reserved for cases of persistent common bile duct obstruction within a 72-hour window. They concluded that urgent ERCP had no impact on critical outcomes, such as mortality and organ failure. [13, 19] In patients with acute biliary pancreatitis and no cholangitis, the AGA suggests against the routine use of urgent ERCP. [19]

Besides the inconsistencies many guidelines [18, 19, 30] agree in two aspects: early ERCP is not indicated in patients with predicted mild gallstone pancreatitis and co-existing cholangitis and biliary obstruction is an indication for urgent ERCP. However, these guidelines differ in their recommendations in the early use of ERCP in severe gallstone pancreatitis. Tse & Yuan analysis did not find significant improvement for clinically important outcomes including mortality, and local or systemic complications of pancreatitis with the early routine ERCP strategy compared to the early conservative management strategy with selective use of ERCP in mild or severe pancreatitis. They agree that assuming risks associated with ERCP, early conservative management with selective use of ERCP should be considered for unselected patients with acute gallstone pancreatitis regardless

of the severity of pancreatitis. Timing of ERCP (urgent < 24 hours versus early < 72 hours) should therefore depend on the level of suspicion, the condition of the patient and response to initial conservative management. [16]

More recently, in 2025, the International Association of Pancreatology revised their guidelines, where is advised that patients with acute biliary pancreatitis with AC should be approached with an early ERCP/ES (within 24–72 hours). In patients with acute biliary pancreatitis without cholangitis, elective ERCP/ES is indicated when a common bile duct stone is identified on imaging such as EUS or MRCP. Otherwise in acute settings (within 72h) it is not indicated. [30]

Complications of endoscopic retrograde cholangiopancreatography

The most frequent complications of performing ERCP include: acute pancreatitis, infections like cholangitis or cholecystitis, hemorrhagic events and perforation. Therefore, it is clinically useful to define the situations that require urgent endoscopic treatment in acute biliopancreatic diseases. [2]

Acute pancreatitis is the most common ERCP-associated adverse event, being the cause of 1-2% pancreatitis episodes. The overall incidence (3.5%) and mortality (0.11%) of post-ERCP pancreatitis continue to increase, despite the mandatory approach to minimizing this complication. [31] Multiple attempts at bile duct cannulation, unintended pancreatic duct cannulation and prolonged procedures increase the risk of post-ERCP pancreatitis. The risk factors for post-ERCP pancreatitis can be patient-related or procedure-related, including young women with small bile ducts, a sphincter of Oddi dysfunction, history of pancreatitis or non-chronic pancreatitis [15, 32] and pre-cut sphincterotomy, pancreatic duct injection, 5 or more cannulations, pancreatic sphincterotomy, papillary balloon dilation and endoscopic papillectomy. [31]

ESGE recommends routine rectal administration of 100 mg of diclofenac or indomethacin immediately before ERCP in all patients without contraindications to nonsteroidal anti-inflammatory drug administration. [33]

Security and safety profile of endoscopic retrograde cholangiopancreatography

In comparison to surgical biliary decompression, endoscopic retrograde cholangiography directed biliary decompression is associated with lower morbidity and mortality, regardless of severity. [34]

The contraindications ERCP generally align with those of systemic endoscopy. The procedure is discouraged when the findings are unlikely to alter clinical management or improve patient outcomes or when the procedural risks disproportionately outweigh the potential benefits.

Furthermore, ERCP should not be performed if informed consent or patient cooperation is unattainable for elective cases, or if safe administration of sedation or anesthesia is unfeasible. For example, interventions with a high risk of hemorrhage, such as biliary sphincterotomy are typically contraindicated in patients receiving therapeutic anticoagulation or antiplatelet therapy. In such scenarios, the risk of bleeding must be meticulously weighed against the necessity of the intervention, and alternative, lower-risk endoscopic techniques may be considered. Finally, institutional factors serve as relative contraindications for high-complexity cases. The absence of specialized endoscopic expertise, necessary equipment, or robust multidisciplinary support from surgical and radiological teams can significantly compromise procedural safety and should be carefully evaluated prior to intervention. [3]

Rationale of the thesis

The management of acute biliopancreatic diseases in the emergency department represents one of the most complex decision-making challenges in modern gastroenterology. While ERCP has established itself as the definitive therapeutic modality for biliary decompression, its optimal application in the acute setting remains fraught with controversy.

The primary tension lies in the "timing of intervention". For acute cholangitis, while the Tokyo Guidelines 2018 provide a framework for severity-based drainage, emerging data regarding the "weekend effect" and the safety of overnight procedures suggest that institutional logistics often conflict with clinical ideals. [26, 27] Furthermore, in the context of acute biliary pancreatitis, a significant paradigm shift is underway. International guidelines from the WSES and AGA present diverging recommendations on whether urgent ERCP (< 24h) offers any mortality benefit over a conservative-first approach in the absence of cholangitis. [13, 19, 29]

Additionally, the inherent risks of the procedure — most notably post-ERCP pancreatitis — necessitate a rigorous selection process to avoid unnecessary interventions, particularly when spontaneous stone passage is common. [16, 31] Despite the abundance of primary studies, the lack of a unified global protocol for ERCP in the emergency room creates significant variability in patient outcomes.

Therefore, this systematic review was conducted following the latest Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [35], justified by the need to synthesize the most recent high-level evidence to clarify the definitive “therapeutic windows” for ERCP in varying severities of acute cholangitis and acute pancreatitis. It further aims to provide an evidence-based consensus that balances the life-saving potential of emergency biliary drainage against the risk of iatrogenic complications, addressing the critical need for hospital policies that mitigate differential outcomes based on provider availability and admission timing. [26]

Objectives

The aim of this review is to identify the indications, as well as the efficacy and safety, of emergency ERCP in the treatment of patients presenting with acute cholangitis or acute biliary pancreatitis, by comparing the outcomes reported in the existing scientific literature, such as, in-hospital mortality, 30-day mortality, length of hospital stay, admission to the intensive care unit, 30-day readmission and local and systemic complications.

Systematic Review- Endoscopic Retrograde Cholangiopancreatography in Emergency Medicine

Methods

This systematic review was written in accordance with the most recent PRISMA guidelines [35] and is registered in PROSPERO database under the following code CRD420261278934.

Eligibility criteria

This revision included randomized clinical trials, cohort studies and case series, either retrospective or prospective, published between 2020 and 2025, written in English, about the approach of ERCP in adult patients (men/women) with acute cholangitis or acute biliary pancreatitis, addressing at least one of the selected outcomes: regarding efficacy — in-hospital mortality, 30-day mortality, length of hospital stay, admission to intensive care unit, 30-day readmissions — or safety — documented local and systemic complications.

Exclusion criteria included studies written in other languages than English and other forms of scientific literature (reviews, meta-analysis, single case reports, textbooks chapters, letters to the editor, guidelines). Studies regarding other treatment approaches, as well as those that did not address the interest outcomes of this systematic review or conducted in paediatric or animal populations were also excluded.

Information sources

The articles were retrieved from three electronic databases: PubMed (Medline), Scopus (Elsevier) and Web of Science (Clarivate Analytics), accessed on September 5th, 2025.

Search Strategy

The search was carried out according to the following search query: ("Cholangitis"[*Mesh*] OR “cholangitis” OR "acute cholangitis" OR "Pancreatitis"[*Mesh*] OR “pancreatitis” OR "Choledocholithiasis"[*Mesh*] OR “choledocholithiasis” OR "biliary tract infection") AND ("Cholangiopancreatography, Endoscopic Retrograde"[*Mesh*] OR "endoscopic retrograde cholangiopancreatography" OR ERCP OR CPRE) NOT "complete primary repair of exstrophy" AND (("early" OR "urgent" OR "delayed" OR "Time Factors"[*Mesh*]).

On all search platforms, the results were refined to show only articles published between 2020 and 2025 and written in English, in accordance with the previously mentioned eligibility criteria.

Selection process

The results of the searches above mentioned were exported to a systematic literature review app (Rayyan®) where they were screened for any duplicates. Subsequently, the reports were blindly shortlisted by two separate investigators — Carolina Miranda and João Pedro Paulo (MD) — according to their title and abstract. Finally, a full-text screening of the remaining articles was undertaken to assess if they met the inclusion criteria. The disagreements between screeners were settled by a third investigator — Paulo Salgueiro (MD, PhD).

Data collection process

Data extraction was performed using a standardized data extraction form developed in Microsoft Excel®, designed according to the Cochrane Handbook for Systematic Reviews of Interventions guidelines. To ensure the reliability and comprehensiveness of the process, the form was pilot-tested on three randomly selected studies. This pilot phase allowed for the refinement of data categories, ensuring that all variables — specifically those regarding ERCP timing and post-procedural complications — were captured consistently by both reviewers.

We collected the following data from each included study: author and year of publication, study design, study period, overall number of patients, baseline characteristics of all included patients (age – mean or median; sex – male/female; classification of AC or AP according to the TG18 and RAC, respectively; acute cholangitis or acute pancreatitis etiology), applied intervention characteristics (timing of the ERCP) and evaluated outcomes.

In cases of missing or ambiguous data, the study was analysed based on available information and the limitation was noted. Regarding “timing” variables, due to heterogeneity in the literature, interventions were categorized into: “Urgent” (< 24h), “Early” (24-48h) and “Delayed” (> 48h) to facilitate comparative analysis. All outcomes, particularly safety events, were extracted as reported by the original authors.

Data items (outcomes)

Regarding efficacy outcomes we considered in-hospital mortality, 30-day mortality, length of hospital stay, admission to intensive care unit and 30-day readmissions. As for safety outcomes, we analysed the documented local (such as perforation, bleeding, acute pancreatitis, peripancreatic

collections, splanchnic venous thrombosis) and systemic complications (such as new-onset organ failure and septicemia).

Study risk of bias assessment

The methodological quality of the included studies was evaluated by a specialized tool: the Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) [36], as the final articles were all non-randomized designs.

The ROBINS-I tool evaluates seven key domains: bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes and bias in selection of the reported result. After considering these domains, a final judgment was reached for each study, classifying them as “Low”, “Moderate”, “Serious”, “Critical”, or “No information” (in cases where data were insufficient to apply the tool).

To ensure reliability, the assessment was performed by one investigator and subsequently verified by a second researcher.

Effect measures and synthesis methods

The studies were firstly categorized into three primary groups based on the timing of procedure: “Urgent” (< 24h), “Early” (24-48h) and “Delayed” (> 48h), regarding the AC [11] or the AP [17] classification. Within these groups, data from each study were initially described individually, in a table format (Table I, II, III and IV). Subsequently, in instances where multiple studies examined the same outcome, a descriptive comparative analysis was conducted. Differences with a p-value < 0.05 were considered statistically significant. A Hazard Ratio (HR) < 1 suggested a decreased risk of discharge, which in turn implied a longer LHS. No meta-analysis was conducted due to the heterogeneity of outcome measurements.

Results

A total of 10473 records were initially identified across PubMed (n = 484), Scopus (n = 9419) and Web of Science (n = 570). Of these, 9586 remained after duplicate removal. Initially screening based on title and abstract led to the exclusion of 9561 articles and the remaining 25 were sought for retrieval. Five of these articles lacked full-text availability, so a full text analysis was conducted on the remaining 20. Six were eliminated as not evaluating the interest outcomes and two eliminated as not including the interest population.

The flowchart illustrating the process of study selection (Figure 1) is provided in appendix.

Study characteristics and risk of bias

Tables I to IV in the appendix delineate the characteristics of the included studies. All of the studies were single-center retrospective cohort studies.

Figure 2 presents the results of risk of bias evaluation.

Acute cholangitis

Eight of the studies included only patients with acute cholangitis in their sample. The diagnostic criteria for acute cholangitis were defined by the 2018 Tokyo Guidelines [21]. The majority of them (*Lyu et al.* [37], *Huang et al.* [40], *Chantarojanasiri et al*. [38], *Fridgeirsson et al.* [39] and *Hue et al.* [45]) included patients with acute cholangitis across all severity levels (grade I - mild, grade II - moderate, and grade III - severe). Two studies (*Zhu et al*. [40] and *Hedjoudje et al.* [44]) focused specifically on patients with severe acute cholangitis (grade III). *Sugiura et al.* [41] restricted its inclusion criteria to patients with non-severe acute cholangitis (grades I and II).

The underlying etiology of the biliary obstruction prompting ERCP also varied slightly among the articles. The studies conducted by *Lyu et al.* [38], *Hedjoudje et al*. [44] and *Hue et al.* [45] restricted the indication for ERCP exclusively to patients with acute cholangitis secondary to choledocholithiasis. The studies by *Zhu et al*. [40], *Huang et al.* [40], *Chantarojanasiri et al.* [39], *Sugiura et al*. [42] and *Fridgeirsson et al.* [39] included patients whose indication for ERCP were due to both benign causes (stones or inflammatory strictures) and malignant conditions, as well as the dysfunction or occlusion of previously placed biliary stents.

The timing of the procedure was defined differently across the studies. Three of these studies divided the participants into the same three groups “Urgent” (< 24h), “Early” (24-48h) and “Delayed” (> 48h) as those defined for this review. These were the studies conducted by *Zhu et al.* [40], *Lyu et al.* [37] and *Huang et al.* [42]

The study by *Chantarojanasiri et al.* [38] evaluated other time divisions beyond the 48h: < 24h, 24-48h, 48-72h, 72h-7 days and > 7 days.

Sugiura et al. [41] used two shorter intervals in addition to the “Urgent” (< 24h) timing: ≤ 3h, 3-24h and > 24h. Two articles set the cutoff at 24 hours (*Fridgeirsson et al.* [39], *Hedjoudje et al.* [43]) and the last one at 48h (*Hue et al.* [44]).

Hedjoudje et al. [43] used a propensity score matching (PSM) analysis at a 1:1 ratio, where 77 patients were assigned to the urgent ERCP group (≤ 24h) and 77 to the non-urgent ERCP group (>24h). It was aimed to minimize potential confounding and selection biases.

Acute pancreatitis

Regarding the four articles with populations presenting with acute biliary pancreatitis, in the first three articles (*Lyu et al.* [45], *Muangkaew et al.* [46] and *Comoglu et al.* [47]) the indication for ERCP was the simultaneous presence of acute biliary pancreatitis accompanied by acute cholangitis, in accordance with the TG18. [21] Acute biliary pancreatitis was defined and classified in accordance with the 2012 Revised Atlanta Classification [17]. Only *Muangkaew et al.* [46] study defined the allocation to the early ERCP cohort (≤ 72h), that was determined by the presence of cholangitis with organ failure, high-grade fever refractory to antibiotics for 24 hours, or a total bilirubin level > 4 mg/dL. Outside of these parameters, patients were preferentially managed with a delayed (> 72h) endoscopic approach.

Conversely, *Kaur et al.* [48] excluded all the acute cholangitis patients and included only the ones presenting evidence of cholestasis or biliary obstruction, characterized by the clinical and laboratory probability of choledocholithiasis. The majority of patients (63.9%) were classified as "high risk" due to the direct visualization of common bile duct stones on imaging modalities, total bilirubin levels > 4 mg/dL, or the combination of a dilated common bile duct with a bilirubin level between 1.8 and 4 mg/dL.

In terms of timing of the ERCP, two of the four studies collected divided the population into ≤ 72h and > 72h (*Lyu et al.* [45], *Muangkaew et al.* [46]) and the other two into ≤ 24h and 24-72h (*Comoglu et al.* [47], *Kaur et al.* [48]).

To minimize the effect of confounding factors and reduce selection bias, *Comoglu et al.* [47] also performed a PSM analysis. Using PSM analysis at a 1:1 ratio, 55 patients were assigned to the urgent ERCP group (≤ 24h) and 55 to the non-urgent ERCP group (24-72h). After matching, there were no significant differences between the groups in terms of comorbidities, other baseline characteristics the distribution of severity of the cholangitis or the severity scores for pancreatitis.

Results of individual studies

The outcomes evaluated in each study are presented in the Tables III and IV and specified in Tables V to VII.

Mortality: in-hospital mortality and 30-day mortality

The mortality outcomes were obtained by dividing the participants into several groups based on the timing of the intervention. Within this division, they were further categorised according to the severity of their acute cholangitis with or without acute biliary pancreatitis.

Firstly, it will be mentioned the findings presented in the three studies conducted by *Zhu et al.* [40], *Lyu et al.* [37] and *Huang et al.* [42], which divided the participants into "urgent" (< 24h), "early" (24-48h) and "delayed" (> 48h) ERCP timing.

Regarding only severe cases of AC, *Zhu et al.* [40] reported an overall IHM and 30-day mortality rates of 13.2% and 14.2%, respectively. Although numerical increases in mortality were noted with the delayed group (11.1% for < 24h vs. 15.4% for 24-48h vs. 19.0% for > 48h, for IHM and 13.8% for < 24h vs. 7.7% for 24-48h vs. 19.0% for > 48h, for 30-day mortality), multivariable logistic regression showed no statistically significant association between ERCP timing and in-hospital (OR = 1.03; 95% CI 0.93–1.13; p = 0.93279) or 30-day mortality (OR = 1.01; 95% CI 0.87–1.14; p = 0.9461). However, interaction analysis identified that bacteremia significantly modulated this relationship (p = 0.010), suggesting that the urgency of the procedure may be more critical in patients with confirmed bloodstream infections. For patients without bacteremia, delayed intervention timing appeared to be more correlated to 30-day mortality as a risk factor (OR = 1.26; 95% CI 0.24–1.53, p = 0.010).

Consistent with these findings, *Lyu et al.* [37] found no advantage of urgent or early ERCP over delayed intervention regarding mortality (p = 0.82), however there was no IHM and only one fatality recorded within the first 30 days.

Similarly, *Huang et al.* [42] found no statistical difference only evaluating 30-day mortality when using a 24-hour threshold (p = 0.356). However, when applying a 48-hour cutoff, mortality was significantly lower in the ≤ 48h group vs. the > 48h group (0% vs. 1.9%, p = 0.017), a benefit that persisted when analysing only the grade III AC patients (0% vs. 6.1%, p = 0.039). In this cohort, 30-day mortality was also significantly associated with malignant biliary obstruction (p = 0.013), organ dysfunction (hepatic, respiratory, neurological, or cardiovascular, all p < 0.02) and every one-day delay in ERCP (p = 0.003).

Chantarojanasiri et al. [38], the one that evaluated the timing of ERCP before and beyond the 7 days, identified a significant correlation between shorter waiting times and higher 30-day mortality specifically in mild AC (p = 0.05). While no significant effect was seen in the broader cohort, including the three timing groups defined for this review, this study also looked for mortality many days after (48-72h vs. 72h-7 days vs. > 7days), and observed only a trend toward lower overall mortality when ERCP was performed within 7 days (p = 0.07) vs. > 7 days. When studying possible association factors, mortality rates were significantly higher in cases of severe cholangitis (OR = 14.47; 95% CI, 3.10–67.55, p < 0.001) and malignant biliary obstruction (OR = 8.61; 95% CI, 2.43–30.52, p < 0.001), other factors, including age (p = 0.99), ASA (American Society of Anesthesiologists) status (p = 0.7) and total bilirubin (p = 0.2), did not show statistically significant associations.

The two studies that divide their participants into ≤ 24h vs. > 24h groups reach different conclusions.

Fridgeirsson et al. [39] reported that 30-day mortality was comparable between ≤ 24h and >24h intervention groups (p = 0.4), suggesting that procedural latency may not be the primary driver of death in unselected populations. In contrast, *Hedjoudje et al.* [43] utilizing a propensity score-matched analysis to minimize baseline imbalances, found a huge increase in mortality for patients waiting more than 24 hours. Their data showed that > 24h ERCP was associated with a nearly quadruple increase in 30-day mortality (45.5% vs. 13.0%, p < 0.001) and a similarly impact at one year (59.7% vs. 15.6%, p < 0.001).

Hue et al. [44] defined their groups into ≤ 48h vs. > 48h ERCP groups and through this they observed a numerically higher 30-day mortality in the ≤ 48h intervention group (0.4% vs. 0%, p = 0.16), but no statistically important conclusion.

Muangkaew et al. [46], found no significant differences in terms of mortality (3.0% vs. 0, p = 0.35) between the two groups studied (≤ 72h ERCP vs. > 72h ERCP).

Comoglu et al. [47] studied ≤ 24h ERCP vs. 24-72h ERCP, finding comparable results among the groups before and after PSM matching (p = 0.758 and p = 0.161, respectively).

The studies of *Sugiura et al.* [41] and *Lyu et al.* [45] in 2022, had as outcome IHM, but had no fatalities and therefore no conclusions were reached.

Length of Hospital Stay

The impact of ERCP timing on the length of hospital stay was a consistent finding across most included studies, with earlier intervention generally correlating with reduced hospitalization.

Regarding severe acute cholangitis, *Zhu et al.* [40] reported a median LHS of 2.65 days, noting a substantial prolongation when biliary drainage was delayed beyond 24 hours (+11.86 days, 95% CI 5.14–18.59; p = 0.0008) and 48 hours (+20.91 days, 95% CI 13.82–28.00; p < 0.0001).

Consistent with this, *Hedjoudje et al*. [43], using PSM analysis also in a severe acute cholangitis population, found a significantly shorter LHS in the ≤ 24h group (9.22 vs. 11.88 days, p = 0.042), while *Kaur et al.* [48] also reported a significant reduction for the same threshold (p ≤ 0.01).

Huang et al. [42] observed significantly shorter stays for both ≤ 24h (6.0 vs. 7.0 days, p = 0.018) and ≤ 48h (6.0 vs. 8.0 days, p < 0.001) groups. This benefit was maintained in all severity grades, except for grade III. Similarly, *Hue et al.* [44] reported a shorter LHS for intervention within 48 hours (6.5 vs. 9.3 days, p < 0.001). *Lyu et al.* [37] in 2023 demonstrated a shorter stay for urgent and early groups compared to delayed (> 48h) intervention (13.93 vs. 8.82 vs. 14.20 days, p = 0.02), though this benefit was notably restricted to non-severe cases. For *Fridgeirsson et al*. [39] patients who underwent ERCP within 24 hours also experienced a significantly shorter hospitalization compared to those with a later intervention (4.0 vs. 6.0 days, p = 0.004). Notably, this reduction in stay occurred

despite the fact that the early intervention group had a higher prevalence of severe acute cholangitis.

Regarding the 72-hour threshold, results were heterogeneous. *Muangkaew et al.* [46] reported a shorter total LHS for the ≤ 72h group (6.3 vs. 9.8 days, P=0.002), while *Lyu et al.* [45] in 2022 found no significant difference in total stay (p = 0.13), but a shorter post-ERCP stay in the delayed group (6.59 vs. 10.94 days, p = 0.00).

In a study where the timing for ERCP was defined as "very urgent" (≤ 3h), "urgent" (3-24h) and "early" (> 24h), *Sugiura et al.* [41] found through a multivariate analysis that very urgent ERCP was associated with a significantly shorter LHS than urgent and elective ERCP (HR, 0.71, p = 0.04 and HR, 0.47, p < 0.01, respectively).

Chantarojanasiri et al. [38] demonstrated that shorter waiting times for ERCP were associated with a significant reduction in the length of hospital stay across all severity levels, particularly when the procedure was performed within 7 days for overall population (p < 0.05) and regarding only mild acute cholangitis (p < 0.05).

In contrast, *Comoglu et al.* [47] found no significant differences in LHS both before and after propensity score matching (p = 0.556 and p = 0.201, respectively).

Finally, several studies identified independent predictors for prolonged LHS. *Sugiura et al.* [41] found that age ≥ 75 years, concomitant acute pancreatitis, serum albumin ≤ 2.8 g/dL and requiring multiple ERCP procedures were significantly associated with longer stays (HRs < 1, p < 0.05). For *Zhu et al.* [40], the reduction in LHS driven by early ERCP was modulated by the patients' comorbidity burden (p = 0.002) and the severity of cholestasis (bilirubin levels) (p = 0.005), suggesting that more complex patients benefit even more from early intervention.

Admission to intensive care unit

The utilization of intensive care unit resources varied significantly across studies, often reflecting the clinical prioritization of more severe cases.

Regarding ICU admission rates, *Huang et al.* [42] reported that patients undergoing ERCP within 24 hours had significantly higher admission rates compared to those with delayed procedures (11.2% vs. 4.0%, p = 0.001). This trend persisted within 24h only restricting the population to grade III AC (9.0% vs. 2.6%, p = 0.002) and when comparing ≤ 48h vs. > 48h also in this specific population (22.2% vs. 10.2%, p = 0.031).

Similarly, *Hue et al.* [44] found that ICU admission was more frequent in the early intervention group (≤ 48h) than in the delayed (> 48h) group (3.1% vs. 0.8%, p = 0.02).

In contrast, *Fridgeirsson et al.* [39] (where 12% of the total cohort was admitted to the ICU), *Comoglu et al.* [47] (p = 0.680 post-matching) and *Kaur et al.* [48] found no statistically significant difference in ICU requirements based on procedural timing.

Regarding the length of ICU stay, *Zhu et al.* [40] demonstrated that in severe AC, every day of delay in ERCP was associated with a significant increase of 0.47 days in the duration of ICU stay (95% CI 0.23–0.71; p = 0.0002). While no significant difference was observed using a 24-hour threshold (p = 0.0997), delays of 48 hours or longer resulted in a profound prolongation of ICU stay, with an average increase of 5.56 days (95% CI 1.43–9.68; p = 0.0096). This impact was notably influenced by patient age (p = 0.005), but remained consistent regardless of bilirubin levels or comorbidity scores.

30-day readmissions

The incidence of unplanned 30-day readmission following ERCP was evaluated in several studies with contrasting results.

Lyu et al. [37] (2023) (p = 0.14), *Sugiura et al.* [41] (p = 0.30) and *Huang et al.* [42] (p = 0.757 and p = 0.999, for 24 and 48h cutoffs) found no significant difference in readmission rates regardless of the intervention timing.

In contrast, *Kaur et al.* [48] reported that performing ERCP within the first 24 hours significantly reduced the risk of 30-day readmission compared to the 24–72h cohort (5.2% vs. 16.9%, p = 0.0186).

Conversely, *Chantarojanasiri et al.* [38] observed a paradoxical association, where ERCP performed within 7 days was linked to higher 30-day rehospitalization rates ($p < 0.05$), particularly in mild cases.

Local and systemic complications

Across the included studies, the incidence and nature of complications varied significantly depending on the timing of the intervention.

Regarding ERCP-related and local complications, in the 2023 study by *Lyu et al.* [37], the timing of biliary drainage was not found to be a significant predictor of complications in acute cholangitis (p = 0.19).

Notably, these findings align with the authors' parallel investigation [45] into acute biliary pancreatitis, which revealed that delaying ERCP beyond 72 hours did not increase the risk of local complications compared to earlier intervention. Which was also consistent with *Muangkaew et al.* [46] acute biliary pancreatitis population study, that reported comparable rates of ERCP-related complications (7.5% vs. 10.7%, p = 0.60), for equal cutoff of 72h.

Similarly, *Sugiura et al.* [41], using three different groups for timing the ERCP (≤3h, 3-24h and >24h), reach the same conclusion: the local complications related to the ERCP procedure were not significantly different (p = 0.66) among the three groups.

Specific local complications, however, showed occasional associations with delayed procedures. In the study by *Hue et al.* [44], while the overall complication rate remained constant at approximately 15%, biliary perforation was significantly more prevalent in the > 48h group compared to the early intervention group (1.2% vs. 0%, p = 0.01).

In cases of acute biliary pancreatitis, *Comoglu et al.* [47] initially observed more frequent local pancreatic complications in the 24–72h group (29.2% vs. 14.5%, p = 0.037), however, this difference was not maintained after propensity score matching (p = 0.449).

Regarding systemic complications, the evidence was also heterogeneous. *Hedjoudje et al.* [43] reported that ERCP performed after 24 hours in patients with AC was associated with a significantly higher rate of respiratory adverse events (54.5% vs. 27.8%, p = 0.002 after PSM), although no increased risk of persistent kidney failure was observed. In contrast, *Hue et al.* [44] found that the incidence of septicemia and septic shock was significantly higher in the early (≤ 48h) intervention group (13.9% vs. 7.5%, p = 0.01; and 52.8% vs. 30%, p = 0.03, respectively).

Finally, other studies demonstrated non-significant trends in systemic outcomes. *Comoglu et al.* [47] found no significant differences both before and after matching (p = 0.550 and p = 0.067, respectively). *Kaur et al.* [48] noted lower rates of systemic complications in the ≤ 24h group compared to the 24–72h group (3.9% vs. 9.0%), though this did not reach statistical significance (p = 0.188). Overall, no consistent association was found between ERCP timing and systemic complications across the broader cohort.

Individual Factors

Two studies showed some individual factors among the population that might interfered with the delayed of the procedure. *Hedjoudje et al.* [43] found several factors that were significantly associated with > 24h ERCP: cardiac arrythmias (OR = 2.37, 95% CI 1.10–5.26, p = 0.030), liver disease (OR = 7.42, 95% CI 1.87–38.27, p = 0.007), creatinine value at baseline (OR = 1.41, 95% CI 1.06–1.92, p = 0.022) and white blood cell count (OR = 0.94, 95% CI 0.90–0.99, p = 0.023).

For *Muangkaew et al.* [46] the low total bilirubin level 4 mg/dL (OR = 0.37, 95% CI 0.14–0.97, p = 0.04) and patients taking antiplatelet or anticoagulant (OR = 2.54, 95% CI 1.01–7.29, p = 0.03) were independent factors for delayed ERCP. Regarding this, ERCP was more likely to be delayed in patients who took aspirin which might be from the endoscopist's hesitation and concerns regarding the bleeding. Also, there were significantly fewer patients with end stage renal disease in the ≤ 72h

ERCP group (0/67, 0%) compared with the > 72h group (3/28, 10.7%) (p = 0.006). Moreover, these patients had a higher rate of delayed ERCP due to difficulties in preparing and stabilizing them for ERCP under general anesthesia.

Results of synthesis

Mortality: in-hospital mortality and 30-day mortality

The analysis of mortality across the included studies revealed heterogeneous results depending on disease severity and intervention thresholds.

Overall in-hospital and 30-day mortality

Zhu et al. [40] (IHM, OR = 1.03; 95% CI 0.93–1.13; p = 0.9327 or 30-day mortality, OR = 1.01; 95% CI 0.87–1.14; p = 0.9461*), Lyu et al.* [37] (2023) (p = 0.82), *Huang et al.* [42] (p = 0.356 for ≤ 24h), *Fridgeirsson et al.* [39] (p = 0.4), *Hue et al.* [44] (p = 0.16), *Muangkaew et al.* [46] (p = 0.35) and *Comoglu et al.* [47] (p = 0.758 and p = 0.161, before and after matching respectively) found no statistically significant difference in mortality between the timing of the intervention. However, when applying a 48-hour cutoff, *Huang et al.* [42] found mortality was significantly lower in the ≤ 48h group (p = 0.017).

Hue et al. [44] found no statistically significant correlation between mortality and the timing of ERCP, however, observed a numerically higher 30-day mortality in the ≤ 48h intervention group (0.4% vs. 0%, p = 0.16) likely explained by the significantly higher proportion of critically ill patients requiring ICU admission in ≤ 48h ERCP group (3.1% vs. 0.8%, p = 0.02).

Chantarojanasiri et al. [38] observed only a trend toward lower overall mortality when ERCP was performed within 7 days (p = 0.07), finding no overall significance, a finding they attributed to selection bias, where attending physicians prioritized the most critical and comorbid patients for urgent intervention.

In contrast, *Hedjoudje et al.* [43] reported a quadruple increase in mortality for the > 24h group compared to the ≤ 24h group at both 30 days (p < 0.001) and 1 year (p < 0.001), after propensity score matching.

Impact of severity on mortality

The benefit of early intervention appears most pronounced in patients with severe AC (grade III). *Huang et al.* [42] demonstrated that while a 24-hour cutoff was non-significant, a 48-hour threshold was associated with significantly lower 30-day mortality, particularly in grade III cases (p = 0.039). However, the population was drawn from an endoscopy database, in which patients who died prior to the procedure were excluded, potentially leading to an underestimation of 30-day

mortality. *Chantarojanasiri et al.* [38] also agreed that the mortality rate was significantly higher in those with severe cholangitis (OR, 14.47; 95% CI, 3.10 – 67.55, p < 0.001).

Conversely, *Zhu et al.* [40], whose population consisted entirely of patients with severe acute cholangitis, found no direct association between timing and mortality in grade III patients (p = 0.93).

One study [38] found a significantly association between < 7 days ERCP and higher 30-day mortality in the mild AC population (p = 0.05), this could be justified by the prioritization of terminal cancer patients for urgent ERCP, incurring a selection bias.

Independent factors predictors of mortality

Beyond the timing of the ERCP, several independent factors were significantly associated with increased mortality across the literature: malignant biliary obstruction (*Huang et al.* [42], p = 0.013; *Chantarojanasiri et al.* [38], OR = 8.61; 95% CI, 2.43–30.52, p < 0.001), organ dysfunction, whether hepatic, respiratory, neurological, or cardiovascular (Huang et al. [42], p < 0.02) and bacteremia (*Zhu et al.* [40], OR = 1.26; 95% CI 0.24–1.53, p = 0.010), suggesting that for the subgroup of patients with systemic bloodstream infections, the window for intervention may be much narrower and the benefits of early drainage more vital.

Length of hospital stay

The impact of ERCP timing on the length of hospital stay was a consistent finding across the majority of the included studies, with earlier intervention generally correlating with a significant reduction in total hospitalization time.

ERCP in the first 24 or 48 hours

Evidence strongly suggests that biliary drainage within the first 24 to 48 hours is a primary driver for reducing LHS.

Significant reductions in LHS for the ≤ 24h threshold were confirmed by *Hedjoudje et al.* [43] (9.22 vs. 11.88 days, p = 0.042), *Fridgeirsson et al.* [39] (4 vs. 6 days, p = 0.004) and Kaur et al. [48] (p ≤ 0.01). Similarly, intervention within 48 hours was associated with shorter stays in *Huang et al.* [42] (6 vs. 8 days, p < 0.001) and *Hue et al.* [44] (6.5 vs. 9.3 days, p < 0.001).

Further restricting the timing, *Sugiura et al.* [41] found that "very urgent" ERCP (≤ 3h) was superior to both urgent (3–24h) and elective (> 24h) approaches (HR, 0.71, p = 0.04 and HR, 0.47, p < 0.01, respectively).

Heterogeneity at the 72-hour mark and long-term waiting

Results regarding the 72-hour cutoff were less consistent.

Muangkaew et al. [46] observed a shorter LHS for the ≤ 72h group (6.3 vs. 9.8 days, p = 0.002). However, *Comoglu et al.* [47] found no significant differences in LHS either before or after propensity

score matching (p = 0.201). *Lyu et al.* [45] in 2022 found no difference in total stay (p = 0.13), though post-ERCP stay was paradoxically shorter in the delayed group.

Chantarojanasiri et al. [38] identified that even within a 7-day window, shorter waiting times significantly reduced LHS, particularly in mild AC (p < 0.05).

According to the severity of AC

Zhu et al. [40] with an exclusive population of grade III AC reported a substantial prolongation of stay when ERCP was delayed beyond 24 hours (+11.86 days, P=0.0008) and 48 hours (+20.91 days, p < 0.001).

Conversely, *Lyu et al.* [37] in 2023 and *Huang et al.* [42] noted that the reduction in LHS was primarily restricted to or more evident in non-severe cases.

Independent predictors of prolonged stay

Several factors were identified as independent drivers for longer hospitalization regardless of timing, including age ≥ 75 years, concomitant acute pancreatitis, low serum albumin (≤ 2.8 g/dL), the need for multiple ERCP procedures (HRs < 1, p < 0.05), comorbidity burden (p = 0.002) and the severity of cholestasis (bilirubin levels) (p = 0.005). [40, 41]

Admission to intensive care unit

The analysis of ICU resource utilization across the included studies demonstrated significant heterogeneity, often reflecting clinical prioritization based on disease severity.

ICU admission rates were paradoxically higher in early intervention groups across several cohorts (*Huang et al.* [42], ≤ 24h, p = 0.001; *Hue et al.* [44], ≤ 48h, p = 0.02), a finding that likely reflects selection bias where critically ill patients (grade III AC) are prioritized for urgent drainage.

When restricting the population for grade III AC, for *Huang et al.* [42] the ICU admission rates were higher in early intervention groups (≤ 24h, p = 0.002 and ≤ 48h, p = 0,031, when comparing with > 24h an > 48h, respectively).

Conversely, other studies (*Fridgeirsson et al.* [39], *Kaur et al.* [48], *Comoglu et al.* [47]) found no significant correlation between ERCP timing and the requirement for ICU care.

While admission rates were often tied to initial severity, the duration of ICU stay was significantly impacted by procedural delays in specific high-risk cohorts.

In patients with severe AC, *Zhu et al.* [40] demonstrated that each day of delay in performing ERCP resulted in a significant increase of 0.47 days in the duration of ICU stay (95% CI 0.23–0.71; p = 0.0002). Notably, while a 24-hour threshold was not significant (p = 0.0997), delays exceeding 48 hours led to a substantial prolongation of ICU stay, with an average increase of 5.56 days (95% CI 1.43–9.68; p = 0.0096).

The prolongation of ICU stay identified by *Zhu et al.* [40] was significantly influenced by patient age, though it remained independent of bilirubin levels or baseline comorbidity scores.

30-day readmissions

The impact of ERCP timing on unplanned 30-day readmission rates was evaluated across several studies, yielding divergent results that suggest an influence of both procedural timing and patient selection.

The majority of the analysed cohorts found that the timing of biliary drainage did not significantly alter the risk of early rehospitalization: *Lyu et al.* [37] in 2023 (p = 0.14), *Sugiura et al.* [41] (p = 0.30) and *Huang et al.* [42], which demonstrated that neither a 24-hour (p = 0.757) nor a 48-hour threshold (p = 0.999) was associated with readmission risk.

In contrast to the neutral findings above, specific clinical settings demonstrated a benefit for very early intervention. *Kaur et al.* [48] reported that performing ERCP within the first 24 hours significantly reduced the 30-day readmission rate compared to the 24–72h cohort (p = 0.0186), suggesting a potential long-term benefit of prompt biliary clearance in certain populations.

One study by *Chantarojanasiri et al.* [38] reported a contradictory trend, highlighting the importance of baseline patient characteristics, where it was observed that ERCP performed within a 7-day window was linked to higher 30-day rehospitalization rates ($p < 0.05$), particularly in mild cases. The authors attributed this finding to selection bias, noting that high-risk patients with pancreatobiliary malignancies were prioritized for earlier intervention, subsequently requiring more frequent medical attention post-discharge. Readmission within 30 days may not be the best indicator of the success of ERCP in cancer or palliative care patients, as their underlying condition is more likely to dictate readmission than the effectiveness of biliary drainage itself.

Local and systemic complications

The analysis of complications across the included studies reveals a distinction between adverse events directly related to the ERCP procedure (local) and broader systemic inflammatory responses.

ERCP-related and local complications

The incidence of procedural and local complications was generally independent of intervention timing across several clinical contexts.

Regarding the AC population, *Lyu et al.* [37] (p = 0.19) and *Sugiura et al.* [41] (p = 0.66) found no significant differences in ERCP-related complications, regardless of whether thresholds of 24 hours or even 3 hours were applied.

Multiple studies while studying populations with acute biliary pancreatitis reported that delaying ERCP beyond 72 hours did not increase the risk of local complications, with consistent findings between *Lyu et al.* [45], *Muangkaew et al.* [46], *Kaur et al.* [48] and *Comoglu et al.* [47], whatever the cut-off point may be. Notably, *Comoglu et al.* [47] initially observed a higher rate of local pancreatic complications in the 24-72h group ($p = 0.037$), but this difference was not maintained after propensity score matching ($p = 0.449$).

Most studies agree that delaying ERCP does not drastically increase procedural-specific risks (e.g., post-ERCP pancreatitis or bleeding). A significant exception was noted by *Hue et al.* [44], where biliary perforation was more prevalent in the delayed (> 48h) group compared to earlier intervention.

Systemic complications and organ failure

The relationship between ERCP timing and systemic outcomes was characterized by significant heterogeneity.

Hedjoudje et al. [43] reported that performing ERCP after 24 hours in AC patients was associated with a significantly higher rate of respiratory adverse events, although no significant impact was observed regarding persistent kidney failure.

In contrast, *Hue et al.* [44] found significantly higher rates of septicemia and septic shock in the ≤ 48h intervention group, a finding likely attributed to the higher baseline severity of patients prioritized for urgent drainage.

Kaur et al. [48] observed numerically lower systemic complications in the ≤ 24h group compared to the 24–72h group, but this did not reach statistical significance ($p = 0.188$). Similarly, *Comoglu et al.* [47] found no significant differences in systemic outcomes post-matching ($p = 0.067$).

Systemic complications appear more closely linked to the patient's initial clinical state (severe acute cholangitis or severe acute biliary pancreatitis) than to the timing of the procedure itself, except for respiratory failure in specific high-risk cohorts.

Discussion

The management of acute biliopancreatic diseases in the emergency department represents a significant challenge, requiring a balance between prompt biliary decompression and clinical stabilization. [2] This systematic review demonstrates that while ERCP is a definitive therapy, its optimal timing is heavily influenced by disease severity and specific clinical indicators rather than a universal "urgent" mandate for all patients.

Regarding mortality, the evidence remains heterogeneous. In the previous literature, as mentioned in the introduction section, a nationwide analysis by *Mulki et al.* [23] and a *Iqbal et al.* [7] meta-analysis found an association between < 48 h ERCP and a decrease of the mortality rate, especially in moderate to severe acute cholangitis patients (in Iqbal's review). Later, a meta-analysis by *Lyu et al.* [6] in 2022, agreed with this and, in addition, showed that ERCP performed within 24 hours was also associated with lower in-hospital mortality. The meta-analysis of observational studies, performed by *Du et al.* [12], served to reinforce this idea with a 20%-50% reduction in mortality, in < 24h ERCP groups.

Considering mortality, while the Tokyo Guidelines 2018 [21] recommend urgent drainage for severe cases, several cohorts (*Zhu et al.* [40], *Lyu et al.* [37], *Huang et al.*[40]) found no statistically significant survival advantage for intervention within 24 hours in unselected severe populations. However, a critical window of 48 hours was identified by *Huang et al.* [40], where mortality was significantly lower in the ≤ 48h group compared to the > 48h group for the overall population and specially when restricting to grade III cases. Despite the severity of the acute cholangitis, most of the studies found no statistical correlation between timing of ERCP and mortality. Which, in patients with acute biliary pancreatitis, is consistent with what the literature states. [16, 19] However, *Hedjoudje et al.* [43] reported a quadruple increase in mortality in AC for the > 24h group, after PSM, which may reinforce the view that urgent ERCP is beneficial in terms of mortality.

Furthermore, the presence of bacteremia acts as a vital modulator; for patients with systemic bloodstream infections, the therapeutic window may be much narrower, making prompt drainage essential for survival. [40] Other independent factors were significantly associated with increased mortality as malignant biliary obstruction [38, 42] and previous organ dysfunction. [42]

The most consistent finding across the literature was the impact on length of hospital stay. *Mulki et al.* [23], *Iqbal et al.* [7] and *Lyu et al.* [6], aside from the a lower mortality, found a decreased in the hospital length of stay when performing emergent ERCP within 48 hours. *Lyu et al.* [6] and *Du et al.* [12] found that the same was seen for a 24h threshold.

Therefore, in this review, early intervention (specifically within 24-48 hours) was a robust predictor of shorter hospitalization across nearly all severity grades. This suggests that even when

urgent ERCP does not alter the clinical course of the disease itself, it provides substantial logistical and economic benefits by improving hospital throughput and reducing healthcare costs associated with prolonged stays. Interestingly, as noted by *Sugiura et al.* [41], very urgent procedures (≤ 3h) may actually require a higher total number of ERCPs due to lower rates of single-stage stone removal in the acute phase, often requiring temporary discontinuation of antiplatelet or anticoagulation therapy. However, the timing of the initial ERCP remains a more significant driver of early discharge than the total number of procedures performed.

The evidence becomes more heterogeneous when the waiting period extends to 72 hours, in acute biliary pancreatitis population. While *Muangkaew et al.* [46] observed a shorter LHS for the ≤ 72h group, other studies, such as *Comoglu et al.* [47] and *Lyu et al.* [45], found no significant differences in total stay for this threshold.

These data support the role of early ERCP as a critical optimizer of hospital resources. Independent predictors such as age ≥ 75 years, comorbidities, low albumin levels, and the severity of cholestasis (bilirubin levels) contribute to longer hospitalizations, [40, 41] but early intervention serves to mitigate this logistical burden, thereby reducing costs and improving hospital throughput.

The utilization of ICU resources reveals a significant divergence between admission rates and the actual duration of stay. A recurring theme in this review is the selection bias observed in several cohorts, where ICU admission rates were paradoxically higher in early intervention groups. [42, 44]

This phenomenon likely reflects clinical prioritization, where patients presenting with grade III AC or higher baseline severity are fast-tracked for urgent drainage. However, the impact of procedural delay becomes evident when examining the length of ICU stay. In severe AC, procedural latency serves as a direct driver of prolonged critical care. Notably, while a 24-hour threshold may not always show significance, delays exceeding 48 hours resulted in a substantial prolongation of stay - averaging over five additional days. [40] This suggests that while early stabilization is vital, delaying the definitive procedure beyond 48 hours incurs a heavy logistical and clinical burden that is independent of initial bilirubin levels or comorbidity scores.

The data on 30-day readmissions further underscore the influence of patient selection on perceived outcomes. While the majority of studies showed that ERCP timing does not significantly alter rehospitalization risks, [37, 41, 42] the contradictory findings by *Chantarojanasiri et al.* [38] are particularly instructive. Their observation of higher readmission rates in early groups was attributed to the prioritization of high-risk patients with pancreatobiliary malignancies. This indicates that in cancer or palliative care populations, underlying disease severity, rather than the timing or success of the biliary drainage, is the primary determinant of readmission. Conversely, in more stable

populations, early intervention (< 24h) may offer long-term logistical benefits by significantly reducing readmission rates. [48]

A critical finding for clinical practice is that ERCP-related local complications (such as post-ERCP pancreatitis or bleeding) appear generally independent of intervention timing. This supports the safety of performing urgent ERCP even in unstable patients. A notable exception is the increased risk of biliary perforation reported with delayed procedures (> 48h), suggesting that prolonged biliary obstruction may compromise ductal integrity. [44]

In contrast, systemic complications are more closely linked to the patient's initial clinical state (septic shock or organ dysfunction) than to the procedure itself. The higher rates of septicemia and shock observed in early cohorts [44] are consistent with the prioritization of the most critically ill patients. Nevertheless, delayed intervention is not without systemic risk, as evidenced by higher respiratory adverse events in patients waiting over 24 hours, [43] likely due to the prolonged inflammatory response associated with unresolved biliary sepsis.

It is critical to emphasize that acute biliary pancreatitis is only an indication for emergent ERCP when acute cholangitis coexists, making this the real reason for urgent action. Patients who present with concomitant acute cholangitis and acute biliary pancreatitis constitute a unique and highly vulnerable population; current evidence suggests that this specific subgroup benefits from accelerated endoscopic decompression, which should arguably be performed earlier, independent of the baseline severity of the cholangitis itself. [10, 19, 29] This aligns with the dichotomy between the findings of *Kaur et al*. [48], who argue that early ERCP in biliary pancreatitis without cholangitis offers purely logistical benefits and the data from *Comoglu et al*. [47], which highlight the dynamic complexity and urgent clinical needs of patients with both overlapping pathologies.

Several limitations within the included studies must be addressed. The fact that all the studies were retrospective cohort studies, introduces potential selection bias, particularly in patients with cardiovascular or respiratory dysfunction that were more likely to undergo ERCP earlier. [42] All of the studies were single-center studies, many of them with a relatively small sample size, especially in the urgent and early groups, what may limit the generalizability of these conclusions. Also, studies relying on endoscopy or administrative databases might underestimate mortality by excluding patients who died prior to the procedure. [42]

The lack of standardized definitions for "urgent" (ranging from ≤ 3h to < 48h) and the inclusion of varying etiologies (benign vs. malignant) limit the ability to generalize a single optimal timeframe. As high-risk patients with pancreatobiliary malignancies were associated with higher mortality and prioritized for earlier intervention, subsequently requiring more frequent medical attention post-discharge. [38, 42]

Several authors [39, 42] reported higher mortality or ICU admission rates in early groups. This is likely a "severity paradox" where attending physicians prioritized the most critical and comorbid patients for urgent intervention, potentially masking the statistical benefits of urgency.

There are also some diagnostic challenges, as noted by *Lyu et al.* [45], in identify specific diagnostic criteria for acute cholangitis within the context of acute biliary pancreatitis, as systemic inflammation markers may be elevated by the pancreatitis itself.

While this review followed a rigorous protocol, certain limitations were inherent. Due to the high heterogeneity in outcome measurements and intervention timings, a quantitative synthesis was not feasible, limiting the analysis to a descriptive comparative synthesis. All included articles were observational, which increases the risk of unmeasured confounding factors despite the use of multivariate analysis and propensity score matching in some studies. [40, 41, 43, 47]

Conclusion

The management of acute biliopancreatic diseases in the emergency setting remains a complex challenge, balancing life-saving interventions with institutional logistical constraints. This systematic review synthesizes high-level evidence from 2020 to 2025 to clarify the therapeutic windows for ERCP in acute cholangitis and acute pancreatitis.

The findings suggest that the clinical impact of ERCP timing is heavily dictated by disease severity. For grade III acute cholangitis, a definitive therapeutic window of 48 hours appears critical. Delays beyond this threshold are associated with significantly higher mortality rates and a profound escalation in critical care utilization, including an increase in the ICU stay. Furthermore, the presence of bacteremia serves as a vital clinical modulator, narrowing the window for safe intervention and making prompt drainage essential for survival.

In contrast, for non-severe acute cholangitis and acute pancreatitis, the benefits of early ERCP (< 24h or < 48h) are primarily logistical and economic rather than clinical. While early intervention in these groups does not consistently alter the systemic inflammatory course or mortality, it is a robust and consistent predictor of shorter hospital stays. This reduction in LHS offers substantial benefits for hospital throughput and resource management.

Regarding safety, ERCP-related local complications were found to be generally independent of timing, supporting the procedural safety of urgent intervention even in unstable patients. However, a "severity paradox" often complicates the data, where the most critical patients are fast-tracked for drainage, leading to higher observed mortality and ICU admission rates in early intervention groups.

To summarize, hospital policies should prioritize biliary drainage within 48 hours for grade III AC and patients with systemic infections. For non-severe cases, a "stabilization-first" approach within the first 24 hours is safe and feasible, potentially mitigating the "weekend effect" and logistical strain on overnight emergency teams. Notably, acute pancreatitis alone is not an indication for ERCP unless concomitant acute cholangitis is present. However, patients presenting with both conditions represent a distinct, high-risk population that benefits from very early biliary clearance, potentially regardless of the initial cholangitis severity. Early ERCP should be recognized as a key tool for improving hospital efficiency, even when mortality benefits are not statistically evident.

Future studies should prioritize multicenter randomized controlled trials to definitively establish the benefits of urgent intervention (< 12-24h) versus early intervention (< 48h), specifically in cohorts stratified by TG18 severity criteria. Additionally, further investigation into the cost-effectiveness of maintaining 24/7 ERCP availability versus the observed reductions in LHS is warranted to guide global emergency gastroenterology protocols.

Appendix

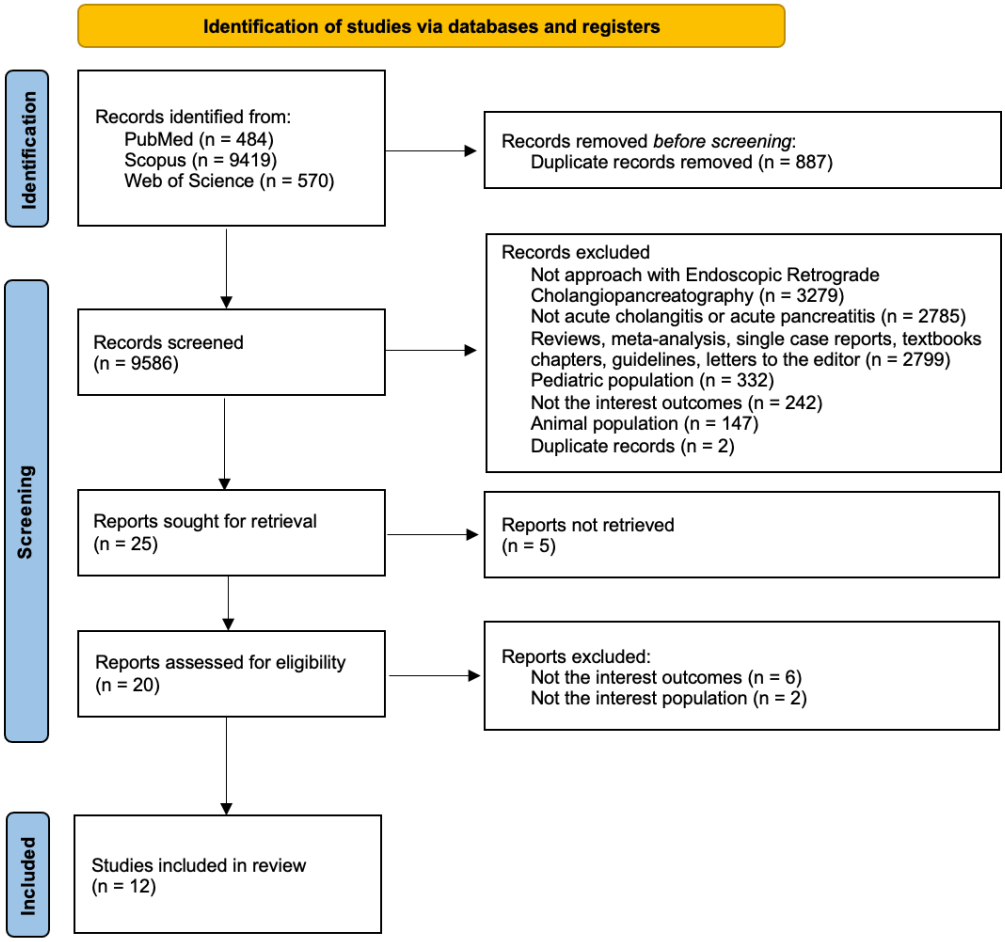

Figure 1 Flowchart of the study selection

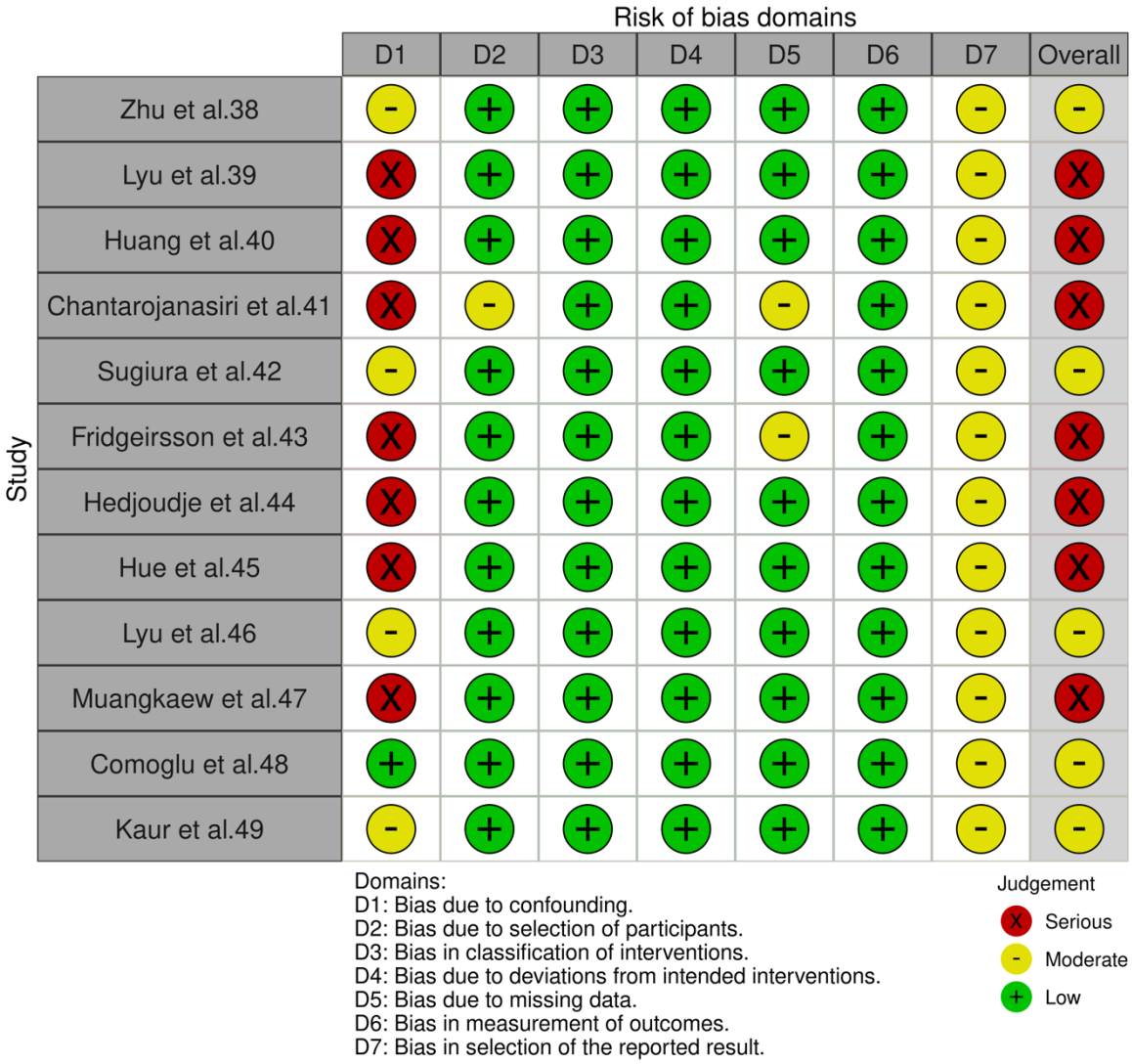

Figure 2 Risk of bias using ROBINS-I tool

Table I Included studies' design and baseline characteristics regarding all participant

Title	Number of participants					Baseline characteristics (regarding all participants)								
	Author, publication year	Study design, study period	Total	with AC	with AP	Age	Sex		AC grade TG18 [11]			AP grade RAC [17]			AC/AP etiology
							Female	Male	I	II	III	Mild	Mod. Severe	Severe	
Association of timing of biliary drainage with clinical outcomes in severe acute cholangitis: a retrospective cohort study	*Zhu, 2021*	Single-center retrospective cohort study, 2001-2012	106	106	-	Median, 75y	46%	54%	0	0	106		NA		84.9% benign etiology and 15.1% malignant etiology
Early is not superior to late endoscopic intervention for acute cholangitis	*Lyu, 2023*	Single-center retrospective cohort study, June 2016 to May 2021	121	121	-	Mean ± SD <24h group: 65.9y ± 16.9 24-48h group: 69.6y ± 17.5 >48h group: 70.0y ± 14.1	<24h group: 46.7% 24-48h group: 47.4% >48h group: 41.4%	<24h group: 53.3% 24-48h group: 52.6% >48h group: 58.6%	78	29	14		NA		121 choledocholithiasis
Timing of endoscopic retrograde cholangiopancreatography in the treatment of acute cholangitis of different severity	*Huang, 2022*	Single-center retrospective cohort study, 2016-2017	2121	683	-	Median, 66y	43%	57%	334	179	170		NA		508 choledocholithiasis; 70 malignant obstruction; 61 Stent dysfunction; 31 benign strictures; 13 others
Effect of delayed endoscopic retrograde cholangiopancreatography after diagnosis of acute cholangitis; a real-life experience	*Chantarojanasiri, 2024*	Single-center retrospective cohort study, May 2018 to April 2021	300	300	-	Mean± SD 61.36y ± 18.08	50%	50%	174	103	23		NA		179 choledocholithiasis; 59 benign strictures; 62 malignant obstructions
Very urgent endoscopic retrograde cholangiopancreatography is associated with early discharge in patients with non-severe acute cholangitis	*Sugiura, 2022*	Single-center retrospective cohort study, April 2011 to June 2020	291	291	-	Median ≤3h group: 74y 3-24h group: 77y >24h group: 75y	≤3h group: 46.8% 3-24h group: 42.9% >24h group: 35.4%	≤3h group: 53.2% 3-24h group: 57.1% >24h group: 64.6%	137	106	0		NA		217 choledocholithiasis; 46 stent occlusion; 28 others
Incidence and outcomes in patients with acute cholangitis: a population-based study	*Fridgeirsson, 2023*	Single-center retrospective cohort study, 2010-2021	2616	240	-	Median, 74y	45%	55%	72	116	52		NA		180 choledocholithiasis; 9 benign strictures; 46 malignant obstructions
Outcomes and predictors of delayed endoscopic biliary drainage for severe acute cholangitis due to choledocholithiasis in an intensive care unit	*Hedjoudje, 2023*	Single-center retrospective cohort study with propensity score matching analysis, 2001-2012	136	136	-	Mean, 79.5y	61%	39%	0	0	136		NA		136 choledocholithiasis

AC: acute cholangitis; AP: acute pancreatitis; Mod. Severe: Moderately Severe; NA: Not applicable; RAC: Revised Atlanta Classification; TG18: Tokyo Guidelines 2018

Table II Included studies' design and baseline characteristics regarding all participant (continuation)

Title	Number of participants					Baseline characteristics (regarding all participants)								
	Author, publication year	Study design, study period	Total	with AC	with AP	Age	Sex		AC grade TG18 [11]			AP grade RAC [17]			AC/AP etiology
							Female	Male	I	II	III	Mild	Mod. Severe	Severe	
Delayed endoscopic retrograde cholangiopancreatography a game-changer for acute cholangitis patients in a resource-limited setting	*Hue, 2025*	Single-center retrospective cohort study, January 2021 to December 2022	708	708	-	Mean ± SD ≤48h group: 63.9y ± 18.1 >48h group: 64.6y ± 15.3	≤48h group: 48.8% >48h group: 45.1%	≤48h group: 51.2% >48h group: 54.9%	I and II: 579		129		NA		708 choledocholithiasis
Outcomes of delayed versus early endoscopic intervention for acute biliary pancreatitis with non-severe acute cholangitis	*Lyu, 2022*	Single-center retrospective cohort study, January 2016 to December 2021	164	164	164	Mean ± SD ≤72h group: 62.5y ± 14.4 >72h group: 64.9y ± 16.0	51%	49%	123	41	0		NR		164 acute biliary pancreatitis
Outcomes of delayed endoscopic retrograde cholangiopancreatography in patients with acute biliary pancreatitis with cholangitis	*Muangkaew, 2020*	Single-center retrospective cohort study, May 2012 to April 2018	95	95	95	Mean ± SD ≤72h group: 67.7y ± 16.3 >72h group: 66.3 ± 16.2	≤72h group: 52.5% >72h group: 60.7%	≤72h group: 47.8% >72h group: 39.3%		NR		74	12	9	95 acute biliary pancreatitis
Effect of urgent ERCP on clinical outcomes in acute cholangitis with concurrent acute gallstone pancreatitis: a propensity score matching analysis	*Comoglu, 2025*	Single-center retrospective cohort study with propensity score matching analysis, March 2019 to February 2024	144	144	144	Mean, 66.3y	47%	53%	56	49	39	94	34	16	144 acute biliary pancreatitis
Utility of urgent endoscopic retrograde cholangiopancreatography in patients with predicted mild acute pancreatitis and cholestasis	*Kaur, 2023*	Single-center retrospective cohort study, January 2018 to December 2021	960	62	166	Median, 65y	45,8%	54,2%		NR		144	22	0	166 acute biliary pancreatitis

AC: acute cholangitis; AP: acute pancreatitis; Mod. Severe: Moderately Severe NA: Not applicable; NR: Not reported; RAC: Revised Atlanta Classification; TG18: Tokyo Guidelines 2018

Table III Included studies' details of intervention and outcomes assessed

Title	Timing of ERCP (number of participants according to TG18 AC classification)															Outcomes
	<24h			24-48h			>48h									
	I	II	III	I	II	III	I	II	III							
Association of timing of biliary drainage with clinical outcomes in severe acute cholangitis: a retrospective cohort study	-	-	72	-	-	85	-	-	87							The primary outcomes were IHM and 30-day mortality. The secondary outcomes were the LHS and admission to the ICU.
Early is not superior to late endoscopic intervention for Acute Cholangitis	8	3	4	13	4	2	57	22	8							The primary outcomes were technical success and mortality (IHM and 30-day mortality). The secondary outcomes were post-ERCP complications, LHS, duration of antibiotic therapy, 30-day readmission and ICU stay.
Timing of endoscopic retrograde cholangiopancreatography in the treatment of acute cholangitis of different severity	56	39	39	98	49	33	180	91	98							The primary outcome was 30-day mortality. Secondary outcomes were admission to the ICU, LHS and 30-day readmission rate.
	<24h			24-48h			>48h			72h-7d			>7d			
	I	II	III	I	II	III	I	II	III	I	II	III	I	II	III	
Effect of delayed endoscopic retrograde cholangiopancreatography after diagnosis of acute cholangitis; a real-life experience	16	11	6	14	16	9	19	18	3	43	37	3	82	21	2	The outcomes were 30-day mortality, 30-day readmission and LHS.
	≤3h			3-24h			>24h									
	I	II	III	I	II	III	I	II	III							
Very urgent endoscopic retrograde cholangiopancreatography is associated with early discharge in patients with non-severe acute cholangitis	27	20	-	110	86	-	36	12	-							The primary outcome was LHS. The secondary outcomes were IHM, ICU admission, 30-day readmission, number of ERCP procedures and post-ERCP complications.
	≤24h			>24h												
	I	II	III	I	II	III										
Incidence and outcomes in patients with acute cholangitis: a population-based study	16	26	19	56	90	33										The outcomes were LHS, ICU admission and 30-day mortality.
Outcomes and predictors of delayed endoscopic biliary drainage for severe acute cholangitis due to choledocholithiasis in an intensive care unit	-	-	85 (77) [a]	-	-	51 (77) [a]										The primary outcome was 30-day mortality. Secondary outcomes included LHS, admission to the ICU and onset or persistent organ failure.

AC: acute cholangitis; ERCP: Endoscopic Retrograde Cholangiopancreatography; ICU - Intensive Care Unit; IHM: In-Hospital Mortality; LHS: Length of Hospital Stay; TG18: Tokyo Guidelines 2018

Table IV Included studies' details of intervention and outcomes assessed (continuation)

Title	Timing of ERCP (number of participants according to TG18 AC classification)						Outcomes
	≤48h			>48h			
	I	II	III	I	II	III	
Delayed endoscopic retrograde cholangiopancreatography a game-changer for acute cholangitis patients in a resource-limited setting	I and II: 364		89	I and II: 215		40	The primary outcome was the mortality rate within 1 and 6 months. Secondary outcome were post-ERCP complications, ICU admission, the length of recovery after operation, LHS, readmission rate within 1 year.
	≤72h			>72h			
	I	II	III	I	II	III	
Outcomes of delayed versus early endoscopic intervention for acute biliary pancreatitis with non-severe acute cholangitis	52	18	-	71	23	-	The primary outcomes were the technical success rate and ERCP-related complications. The secondary outcomes were LHS and patient cost.
	Timing of ERCP (number of participants according to RAC AP classification)						
	≤72h			>72h			
	Mild	Moderately severe	Severe	Mild	Moderately severe	Severe	
Outcomes of delayed endoscopic retrograde cholangiopancreatography in patients with acute biliary pancreatitis with cholangitis	52	9	7	23	3	2	The outcomes were IHM, disease-related complications, ERCP-related complications, LHS and rate of complete stone removal.
	≤24h			24-72h			
	Mild	Moderately severe	Severe	Mild	Moderately severe	Severe	
Effect of urgent ERCP on clinical outcomes in acute cholangitis with concurrent acute gallstone pancreatitis: a propensity score matching analysis	43 (40) [a]	12 (11) [a]	7 (4) [a]	51 (37) [a]	22 (9) [a]	9 (9) [a]	The primary outcomes were IHM, LHS, ERCP-related complications, late localized or systemic complications of pancreatitis. Secondary outcomes were ICU admission, length of ICU stay and inotrope requirement.
Utility of urgent endoscopic retrograde cholangiopancreatography in patients with predicted mild acute pancreatitis and cholestasis	69	8	-	75	14	-	The primary outcome was the development of moderately severe or severe pancreatitis during the index hospitalization. Secondary outcomes were the technical success of biliary cannulation and stone clearance, the development of local or systemic complications, LHS, ICU admission and ERCP-related complications.

AC: acute cholangitis; AP: acute pancreatitis; ERCP: Endoscopic Retrograde Cholangiopancreatography; ICU - Intensive Care Unit; IHM: In-Hospital Mortality; LHS: Length of Hospital Stay; RAC: Revised Atlanta Classification; TG18: Tokyo Guidelines 2018; [a]: after propensity score matching

Table V Clinical outcomes: mortality measured in terms of in-hospital mortality and 30-day mortality

	In-hospital mortality (%)			30-day mortality (%)		
	<24h	**24-48h**	**>48h**	**<24h**	**24-48h**	**>48h**
Zhu et al. [40]	11.1[b]	15.4[b]	19.0[b]	13.8[b]	7.7[b]	19.0[b]
Lyu et al. [37]	0	0	0	0	0	0
Huang et al. [42]	NE	NE	NE	0	0	1.9
Chantarojanasiri et al. [38]	NE	NE	NE	6.1	5.1	4.8
	≤3h	**3-24h**	**>24h**	**≤3h**	**3-24h**	**>24h**
Sugiura et al. [41]	0	0	0	NE	NE	NE
	≤24h		**>24h**	**≤24h**		**>24h**
Fridgeirsson et al. [39]	NE		NE	4.9		2.8
Hedjoudje et al. [43]	NE		NE	13.0[a]		45.5[a]
	≤48h		**>48h**	**≤48h**		**>48h**
Hue et al. [44]	NE		NE	0.4		0
	≤72h		**>72h**	**≤72h**		**>72h**
Lyu et al. [45]	0		0	NE		NE
Muangkaew et al. [46]	3.0		0	NE		NE
	≤24h		**24-72h**	**≤24h**		**24-72h**
Comoglu et al. [47]	6.5	3.6[a]	8.5 12.7[a]	NE		NE

[a]: after propensity score matching [b]: regarding only grade III acute cholangitis patients

Table VI Clinical outcomes: lengh of hospital stay, 30-day readmission and Intensive care unit admission

	Lengh of hospital stay (median)				30-day readmission (%)				Intensive care unit admission (%)			
	<24h	**24-48h**	**>48h**		**<24h**	**24-48h**	**>48h**		**<24h**	**24-48h**	**>48h**	
Zhu et al. [40]	2.65	2.65+11.86	2.65+20.91		NE	NE	NE		NE	NE	NE	
Lyu et al. [37]	13.93	8.82	14.20		13.3	1.4	2.3		0	0	2.3	
Chantarojanasiri et al. [38]	6.0	5.0	6.0		9.1	NR	9.2		NE	NE	NE	
	≤24h	**>24h**	**≤48h**	**>48h**	**≤24h**	**>24h**	**≤48h**	**>48h**	**≤24h**	**>24h**	**≤48h**	**>48h**
Huang et al. [42]	6.0	7.0	6.0	8.0	11.9	12.9	12.7	12.7	11.2	4.0	7.0	4.07
	≤3h	**3-24h**	**>24h**		**≤3h**	**3-24h**	**>24h**		**≤3h**	**3-24h**	**>24h**	
Sugiura et al. [41]	12.0	14.0	15.0		6.4	2.6	2.1		0	0	0	
	≤24h	**>24h**			**≤24h**	**>24h**			**≤24h**	**>24h**		
Fridgeirsson et al. [39]	4.0	6.0			NE	NE			16	10		
Hedjoudje et al. [43]	9.22[1a]	11.88[1a]			NE	NE			NE	NE		
	≤48h	**>48h**			**≤48h**	**>48h**			**≤48h**	**>48h**		
Hue et al. [44]	6.5 ± 4.7[2]	9.3 ± 5.1[2]			NE	NE			3.1	0.8		
	≤72h	**>72h**			**≤72h**	**>72h**			**≤72h**	**>72h**		
Lyu et al. [45]	12.76 ± 9.33[2]	13.48 ± 4.53[2]			NE	NE			NE	NE		
Muangkaew et al. [46]	6.3 ± 4.4[2]	9.8 ± 6.1[2]			NE	NE			NE	NE		
	≤24h	**24-72h**			**≤24h**	**24-72h**			**≤24h**	**24-72h**		
Comoglu et al. [47]	8[a]	10[a]			NE	NE			29.1[a]	32.7[a]		
Kaur et al. [48]	3	3			5.2%	16.9%			3.9	6.7		

NR: Not Reported; NE: Not evaluated; [a]: after propensity score matching

[1]: Expressed as mean

[2]: Expressed as mean ± SD

Table VII Clinical outcomes: local and systemic complications

	Local complications, n (%)				Systemic complications, n (%)			
	<24h	**24-48h**	**>48h**		**<24h**	**24-48h**	**>48h**	
Lyu et al. [37]	1 (6.7) cholangitis 1 (6.7) cholecystitis	1 (5.3) pancreatitis 1 (5.3) bleeding 1 (5.3) cholangitis	3 (3.5) pancreatitis 1 (1.2) cholangitis 2 (2.3) cholecystitis		NE	NE	NE	
	≤3h	**3-24h**	**>24h**		**≤3h**	**3-24h**	**>24h**	
Sugiura et al. [41]	3 (6.4) pancreatitis 1 (2.1) cholecystitis	11(5.6) pancreatitis	2 (4.2) pancreatitis		NE	NE	NE	
	≤24h		**>24h**		**≤24h**		**>24h**	
Hedjoudje et al. [43]	NE		NE		5 (6.5) persistent kidney failure [a] 20 (27.8) respiratory failure [a]		4 (5.2) persistent kidney failure [a] 42 (54.5) respiratory failure [a]	
	≤48h		**>48h**		**≤48h**		**>48h**	
Hue et al. [44]	59 (13) pancreatitis 5 (1.1) bleeding		35 (13.7) pancreatitis 2 (0.8) bleeding 3 (1.2) perfuration		13.9% septicemia		7.5% septicemia	
	≤72h		**>72h**		**≤72h**		**>72h**	
Lyu et al. [45]	4 (5.71) pancreatitis 1 (1.43) bleeding 1 (1.43) cholangitis		7 (7.45) pancreatitis 1 (1.06) cholangitis 1 (1.06) cholecystitis		NE		NE	
Muangkaew et al. [46]	2 (3.0) bleeding 2 (3.0) cholecystitis 1 (1.5) cholangitis		2 (7.1) cholecystitis 1 (3.6) pancreatitis		NE		NE	
	≤24h		**24-72h**		**≤24h**		**24-72h**	
Comoglu et al. [47]	7 (11.3) Acute peripancreatic fluid collection 2 (3.2) Walled-off necrosis 1 (1.6) Splanchnic venous thrombosis	6 (10.9) Acute peripancreatic fluid collection [a] 2 (3.6) Walled-off necrosis [a] 1 (1.8) Splanchnic venous thrombosis [a]	20 (24.4) Acute peripancreatic fluid collection 1 (1.2) Acute necrotic collection 1 (1.2) Walled-off necrosis 2 (2.4) Pseudocyst 1 (1.2) Splanchnic venous thrombosis	8 (14.5) Acute peripancreatic fluid collection [a] 1 (1.8) Acute necrotic collection [a] 1 (1.8) Walled-off necrosis [a] 1 (1.8) Pseudocyst [a] 1 (1.8) Splanchnic venous thrombosis[a]	5 (8.1)	3 (5.5) [a]	9 (11)	9 (16.4) [a]
Kaur et al. [48]	6.5%		5.6%		4.0%		9.0%	

NE: Not evaluated; [a]: after propensity score matching

Other information

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