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Delayed endoscopic retrograde cholangiopancreatography: a game-changer for acute cholangitis patients in a resource-limited setting

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Abstract

Background: Acute cholangitis (AC) is a critical biliary infection caused by gallstones that can progress to systemic inflammation, sepsis, and organ failure. The 2018 Tokyo Guidelines advocate for early endoscopic retrograde cholangiopancreatography (ERCP) in moderate-to-severe AC, but its timing in resource-limited settings remains debated. In Vietnam, where healthcare resources may be limited, the timing of ERCP in patients with AC caused by gallstones has not been extensively studied.

Objectives: To compare outcomes of early ERCP (eERCP, ⩽48 h) versus delayed ERCP (dERCP, >48 h) in managing stone-induced AC.

Design: This was a retrospective cohort study analyzing outcomes of early versus dERCP in 708 patients with stone-induced AC. The study aimed to evaluate procedural efficacy, complications, and long-term outcomes, particularly in a resource-limited setting. Patients were stratified based on ERCP timing (⩽48 h for eERCP and >48 h for dERCP) to enable direct comparisons.

Methods: Data on demographics, clinical features, laboratory findings, and procedural outcomes were analyzed.

Results: The eERCP group exhibited higher rates of severe cholangitis and elevated inflammatory markers compared to the dERCP group. Intensive care unit admission rates were also higher in the eERCP group (3.1% vs 0.8%, $p = 0.02$). Perforation complications occurred more frequently in the dERCP group (1.2% vs 0%, $p = 0.01$), while stone treatment outcomes were comparable between the two groups. The eERCP group had a shorter hospital stay (6.5 vs 9.3 days, $p < 0.05$), although there were no significant differences in readmission or 1-year mortality rates. For patients with severe cholangitis, the treatment outcomes for stones, complications after intervention, and the 1-year mortality and readmission rates are similar between the two groups.

Conclusion: In resource-limited settings, dERCP following resuscitation provides outcomes comparable to eERCP, offering a viable alternative when resources are constrained.

Plain language summary

A viable strategy for treating common bile duct stones in resource-limited settings

Acute cholangitis (AC), a severe infection of the bile ducts often caused by gallstone obstructions, requires timely intervention to prevent complications. Endoscopic retrograde cholangiopancreatography (ERCP) is the gold-standard treatment to relieve obstruction and address infection. However, the optimal timing for ERCP, particularly in severe

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cases, remains debated. In Vietnam, resource constraints such as limited equipment and specialized staff can delay ERCP procedures. This study evaluated the impact of delayed ERCP on outcomes in AC patients caused by gallstones. The findings indicate that delayed ERCP, when preceded by antibiotics and supportive care to stabilize patients, is a safe and effective alternative in settings where early ERCP is not feasible. While early ERCP shortens hospital stays, it does not significantly improve long-term outcomes, including mortality and readmission rates. Thus, prioritizing patient stabilization before ERCP can help hospitals optimize resources without compromising care quality. This approach offers a practical and effective solution for managing AC in resource-limited settings, ensuring equitable treatment access and satisfactory patient outcomes. By adopting flexible treatment strategies, healthcare facilities can improve care delivery for patients with AC caused by gallstones, even in challenging environments.

Keywords: acute cholangitis, delayed ERCP, endoscopic retrograde cholangiopancreatography, time point of ERCP

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Introduction

Acute cholangitis (AC), caused mainly by gallstones, refers to a biliary system infection that arises due to the stagnation of bile flow.[1] Choledocholithiasis is the leading cause of obstruction, contributing to approximately half of all cases.[2] Therapeutic endoscopic retrograde cholangiopancreatography (ERCP) is considered the gold standard for biliary drainage among AC patients.[3] However, determining the most suitable timing for ERCP in cases of AC remains a subject of ongoing debate, and it may hinge on the severity of the cholangitis.

The 2018 Tokyo Guidelines (TG18) propose a classification system that stratifies patients into three severity grades: Grade I (mild), Grade II (moderate), and Grade III (severe) based on specific criteria indicating the severity of the condition.[3] For severe cholangitis, TG18 recommends performing ERCP as soon as possible once the patient is stable.[4] However, research examining the impact of ERCP timing on AC outcomes has yielded varied results. Several small retrospective studies conducted at single centers have suggested that performing early ERCP (eERCP; within 24–72 h of admission) is linked to lower in-hospital and 30-day mortality rates compared to late ERCP.[5–7] Moreover, an additional study in AC related to distal malignant biliary obstruction showed that urgent ERCP groups (⩽24 h after admission) had the lowest 30-day-mortality and 180-day-mortality, followed by eERCP groups (⩽48 h after admission) and delayed ERCP (dERCP) group (>48 h after admission).[8] Conversely, other studies have not identified a significant difference in mortality between early and late ERCP. The multicenter observational survey conducted by Kiriyama et al.[9] in Japan and Taiwan found no clear advantage in 30-day mortality for ERCP procedures performed within 24 or 48 h of admission compared to later techniques. Therefore, the influence of eERCP on outcomes may differ depending on the severity of the patient's condition.

In Vietnam, AC is a common medical emergency; however, the impact of early versus dERCP on outcomes in hospitalized cholangitis patients remains underexplored. At the 108 Military Central Hospital, one of the five largest hospitals in Vietnam, approximately 20 cases of stone-induced cholangitis are admitted daily. The question arises whether performing eERCP would provide significant benefits for Vietnamese AC patients while implementing ERCP for all hospitalized cases remains challenging due to limitations in equipment, facilities, and healthcare staff. In practice, many AC patients are initially treated with conservative management, including antibiotics, to control inflammation. Delayed ERCP is then performed, or patients are referred for surgery to remove stones in cases of large stones, concurrent intrahepatic stones, or failed ERCP. To address this issue, we conducted a retrospective analysis to evaluate the outcomes of eERCP

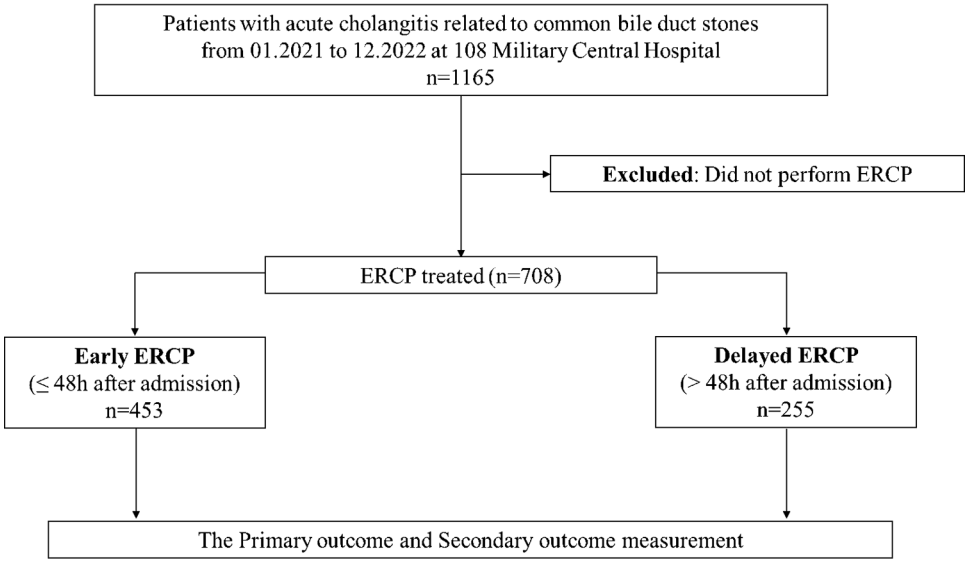

Figure 1. Flow diagram of the study.

(⩽48 h after admission) versus dERCP (>48 h after admission) in the treatment of AC. This study aims to provide scientific evidence regarding the optimal timing for ERCP in patients with stone-induced cholangitis in Vietnam.

Materials and methods

Study design and patient population

This retrospective observational study was conducted on patients diagnosed with choledocholithiasis-induced AC who underwent ERCP based on the national guideline[10] at the Institute of Gastroenterology and Hepatology, 108 Military Central Hospital, Vietnam, from January 2021 to December 2022. Recognized as one of Vietnam's five most prominent hospitals, the hospital manages complex biliary diseases, treating millions annually. At our center, ERCP has been the first line of treatment for patients with AC for the past two decades. Data were collected from hospital medical records, following strict inclusion and exclusion criteria. This point ensured a comprehensive representation of patients treated during this period. The study adhered to the 1975 Declaration of Helsinki and was approved by the Institutional Review Board (Approval No. 3761/HDDD). The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement, as recommended by the Equator network guidelines.[11] A STROBE checklist is included as Supplemental Material.

Inclusion criteria included radiographic or biochemical evidence of biliary obstruction and signs of systemic infection (fever, leukocytosis, bacteremia, and/or purulent bile drainage during ERCP). Exclusion criteria: AC patients who did not undergo ERCP due to successful conservative management, those with severe comorbidities contraindicating ERCP, those who underwent surgical stone removal, or those with complications such as bile leakage or abscess caused by stones, as well as patients under 18 years of age. Patients with incomplete medical records or loss of follow-up were excluded to ensure data reliability.

A total of 708 eligible patients were stratified into eERCP and dERCP groups based on timing. The study cohort was representative of diverse demographics and clinical presentations, enhancing generalizability. Detailed patient selection criteria ensured uniformity in diagnosis and treatment. A comprehensive patient selection flow diagram is provided in Figure 1, illustrating the inclusion, exclusion, and stratification process. This flow diagram, aligned with STROBE recommendations, details the steps taken to ensure transparency in patient recruitment and data analysis.

Patients receive care from a primary medical or surgical team, and those with digestive diseases

benefit from the involvement of the gastroenterology consultation team. All hospitalized patients were administered antibiotics, and the same gastroenterologists on staff, who were required to have conducted more than 200 procedures annually, performed ERCP. We use antibiotics following the local protocol or antibiotic susceptibility test result (if available). The most common antibiotic we use when a patient is newly admitted to the hospital and has not yet had an antibiotic susceptibility test result is a third- or fourth-generation Cephalosporin combined with a Quinolone or Aminoglycoside. The medical board of the Institute determines the indication for ERCP and the timing of the procedure. The criterion for assigning patients to eERCP (⩽48 h) or dERCP (>48 h) was based on their clinical stability and severity of cholangitis, also available personnel, and the ability to perform ERCP. Both moderate and severe cases could undergo dERCP depending on logistical and clinical factors, but severe cases were given priority for early intervention when clinically justified. All patients have thoroughly explained the process, and informed consent is obtained before performing ERCP. The hospital's professional council approved the surgical preliminary report before the procedure. Informed consent was obtained from all participants after a detailed explanation of the treatment. All patients were discussed by the hospital's multidisciplinary team and approved for ERCP treatment by the hospital directorate.

Data collection and definitions

Demographic information, such as age, gender, and comorbidities, was gathered. The treatment history of gallstone disease, including surgery, cholecystectomy, and prior ERCP procedures, was recorded. Clinical symptoms such as abdominal pain, jaundice, and fever were also documented. Laboratory results, including white blood cell count, platelet count, total bilirubin, albumin, aspartate transaminase, alanine transaminase, alkaline phosphatase, gamma-glutamyl transpeptidase, creatinine, and prothrombin time, were documented. Blood cultures were performed by collecting venous blood from both wrists, indicated when patients showed signs of sepsis such as high fever (>39°C), chills, or hypotension (systolic blood pressure <90 mmHg). Bile cultures were conducted using bile samples obtained immediately after access to the bile duct and collected with sterile instruments to prevent cross-contamination of bacteria.

Cholangitis was defined and graded according to the TG18.[4] Cholangitis is defined when at least one criterion A presents (including A1. Fever and/or shaking chills and A2. Laboratory data shows an inflammatory response), plus one criterion B (including B1. Jaundice and B2. Laboratory data has abnormal liver function tests), plus one criterion C (including C1. Imaging of Biliary dilatation and C2. Evidence of the etiology on imaging (stricture, stone, stent, etc.)). Suspected diagnosis is raised when there is one criterion A with one of criteria B or C.

Definition of time to ERCP. Time to ERCP was defined as the time from the department's administration to the commencement of ERCP. eERCP was defined as ERCP performed between ⩽48 h after admission, while ERCP performed after 48 h was defined as dERCP after entry.[8,12] The physicians and the medical board of the Institute decided when to perform ERCP based on the condition of the patients, including mild to severe cholangitis. The selection of emergency ERCP was conducted for patients experiencing clinical deterioration due to biliary sepsis, while ERCP was scheduled during regular office hours for patients with clinically stable cholangitis.

Missing data in this study were addressed using multiple imputation methods, ensuring robust statistical comparisons and minimizing the potential bias from incomplete records. In addition, cases with loss to follow-up were excluded from sensitivity analyses to validate the primary findings across different subgroups and inclusion criteria. In addition, there is a limitation in our study. Some patients were given antibiotics before the time of blood/bile culture, which could potentially impact the culture results by reducing the likelihood of identifying pathogens. Because blood culture is not performed routinely in patients with mild and intermittent fever. Or the patient has been given antibiotics from another hospital before coming to us.

Outcome assessment

The primary outcome measure was the mortality rate within 1 and 6 months. Secondary outcome measures included the rate of adverse events and admission to the intensive care unit (ICU), the

length of recovery after operation and hospital stays, and the readmission rate within 1 year. The post-ERCP complications included pancreatitis, hemorrhage, and perforation. Moreover, the recovery time after ERCP was calculated from when the patient underwent the procedure until discharge or when the patient stabilized and transitioned to the next phase of treatment.

Statistical analysis

Data were analyzed using SPSS version 25.0 (SPSS, Inc., Chicago, IL, USA). Continuous variables were reported as means and standard deviations, while categorical variables were expressed as counts and percentages. Comparisons between groups employed *t*-tests for continuous variables and Chi-square or Fisher's exact tests for categorical data. Multivariate logistic regression was conducted to identify independent predictors of mortality and complications, controlling for potential confounders such as age, comorbidities, and cholangitis severity. The survival analysis was calculated and reported by the Kaplan-Meier curve. Two-tailed *p*-values less than 0.05 were considered statistically significant.

Subgroup analyses examined outcome differences based on age groups, severity grades, and comorbid conditions. Missing data were addressed using multiple imputation methods to ensure robustness in statistical comparisons. Loss to follow-up was minimal (<5%) and addressed by excluding these cases from sensitivity analyses, which were performed to validate the primary findings across different patient subgroups and inclusion criteria.

Data collection was standardized across all included cases to address potential sources of bias and diagnostic criteria for outcomes were prespecified and uniformly applied. Efforts to minimize selection bias included applying strict inclusion and exclusion criteria and using a consecutive sampling approach.

Results

The baseline characteristics

The features at baseline according to three categories of patients are shown in Table 1. All groups were similar demographics, with a mean age of approximately 64 and over half male. There was no different ratio of symptoms of AC, such as abdominal pain and jaundice, among the groups at the admission. However, the inflammatory condition of patients increases over time due to the delay in ERCP, as reflected by the means WBC count of 11.5 G/L and Procalcitonin level of 19.2 g/L in the eERCP group versus 10.8 G/L and 6.1 g/L, respectively, in the dERCP (all $p < 0.05$). In the correspondent point, the higher proportion of severity cholangitis patients was in the eERCP group (19.6%) than in the dERCP group (15.7%), although the differences were insignificant. On the other hand, other factors of AC patients, such as comorbid diseases and histological treatments, were all the same among all groups of patients.

Regarding the group of patients with severe cholangitis, in our study, 16 patients required admission to the ICU, including 14 who underwent eERCP and 2 who underwent dERCP. This group of patients was elderly (Mean ± SD (min−max): 76.56 ± 8.76 years (62–93)), predominantly male (12/16 = 75%), and mainly without a history of biliary surgery or ERCP for stone removal. All these patients presented with severe biliary infections, septic shock, and multiple organ failure, and 2 out of 16 had respiratory failure. The patients were admitted to the ICU and initially treated with supportive care and medical management until clinical stabilization, particularly regarding hemodynamics. ERCP was performed after stabilization. Typically, intensive resuscitation combined with continuous plasma exchange led to clinical improvement within 24 h, allowing eERCP to be performed in 14 out of 16 patients. For the two patients who underwent dERCP, ERCP was delayed for over 72 h due to severe septic shock, multiple organ failure, and a more extended resuscitation period. One of these patients experienced a duodenal perforation during stone removal, requiring multiple clips to close the perforation. This patient was returned to the ICU for aggressive management of systemic infection and post-intervention resuscitation. In addition, there were 39 patients in the eERCP group and 15 patients in the dERCP group who met the diagnostic criteria for acute pancreatitis before ERCP.

Endoscopic techniques

The results of the ERCP intervention are demonstrated in Table 2.

Table 1. Cohort characteristics at the baseline ($n = 708$).

Characteristic	Early ERCP	Delay ERCP	*p* Value
	***n* = 453**	***n* = 255**	
Age (years), mean ± SD	63.9 ± 18.1	64.6 ± 15.3	0.9
Male, *n* (%)	232 (51.2%)	140 (54.9%)	0.3
Abdominal pain, *n* (%)	403 (89%)	222 (87.1%)	0.4
Jaundice, *n* (%)	253 (55.8%)	127 (49.8%)	0.1
WBC (G/L), mean ± SD	11.5 ± 6.5	10.8 ± 5.4	**0.03**
Neutrophil (G/L), mean ± SD	9.2 ± 6.5	8.6 ± 5.4	0.06
Platelet (U/L), mean ± SD	235.6 ± 103.9	258.7 ± 109.7	**0.03**
AST (U/L), mean ± SD	170.5 ± 230.9	185.2 ± 300	0.5
ALT (U/L), mean ± SD	178.1 ± 205.4	200.1 ± 228.2	0.8
GGT (U/L), mean ± SD	520.3 ± 469.2	556.4 ± 493.5	0.6
Total bilirubin (μmol/L), mean ± SD	63.78 ± 59.8	74.5 ± 82.9	0.9
Direct bilirubin (μmol/L), mean ± SD	38.6 ± 37.8	44.9 ± 51.7	0.9
Procalcitonin (ng/mL), mean ± SD	19.2 ± 36.6	6.1 ± 9.5	**0.02**
TOKYO severity, *n* (%)			
Mild and moderate	364 (80.4%)	215 (84.3%)	0.2
Severe	89 (19.6%)	40 (15.7%)	
Combines comorbid, *n* (%)			
Cardiovascular disease	132 (29.1%)	77 (30.2%)	0.8
Diabetes mellitus	61 (13.5%)	34 (13.3%)	0.9
Others	22 (4.9%)	20 (7.8%)	0.1
Previous abdominal surgery, *n* (%)	86 (19%)	40 (15.7%)	0.2
Previous cholecystectomy, *n* (%)	86 (19%)	38 (14.9%)	0.3
Previous ERCP, *n* (%)	99 (21.9%)	42 (16.5%)	0.2

ALT, alanine transaminase; AST, aspartate transaminase; ERCP, endoscopic retrograde cholangiopancreatography; GGT, gamma-glutamyl transpeptidase; SD, standard deviation; WBC, white cell count.

Our evaluation of bile duct imaging revealed that patients in the early intervention group had significantly larger bile ducts (mean diameter: 14.7 mm) than those in the late-intervention group (mean diameter: 10.1 mm; $p = 0.008$). Consistent with this finding, the stones in the bile ducts of the early intervention group were also more giant (mean diameter: 11.9 mm) compared to those in the late-intervention group (mean diameter: 10.1 mm; $p = 0.004$).

Cannulation success rates exceeded 96% in all patients. While both eERCP and dERCP groups achieved high success rates, eERCP demonstrated

Table 2. Endoscopic techniques measurement among two groups.

	Early ERCP	Delay ERCP	*p* Value
	n = 453	*n* = 255	
Diameter of CBD (mm), mean ± SD	14.7 ± 5.9	13.4 ± 5	**0.008**
Size of stone (mm), mean ± SD	11.9 ± 7.3	10.1 ± 6.6	**0.004**
Cannulation success rate, *n* (%)	446 (98.5%)	245 (96.1%)	**0.04**
Difficult biliary cannulation or impacted Oddi's sphincter stone, *n* (%)	107 (23.6%)	75 (29.4%)	0.09
Precut sphincterotomy, *n* (%)	30 (6.6%)	29 (11.4%)	**0.03**
ERCP procedure, *n* (%)			
Remove all stones, *n* (%)	292 (65.5%)	168 (68.6%)	0.4
Remove a part of the stones, *n* (%)	72 (16.1%)	32 (13.1%)	0.3
Placing a biliary plastic stent, *n* (%)	151 (33.9%)	61 (24.9%)	**0.01**

CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography.

a statistically significant higher success rate (98.5% vs 96.1%; $p < 0.05$). However, eERCP required a significantly lower rate of precut sphincterotomy (6.6% vs 11.4%; $p < 0.05$).

Complete stone retrieval was achieved in approximately 65% of cases, with partial stone removal in 15% of cases across all groups. That means about 20% of patients were only placed stents without trying to remove the stones in the first intervention. No significant differences were found in stone retrieval rates between groups. However, the placement rate of plastic biliary stents was significantly higher in the eERCP group (33.9%) compared to the dERCP group (24.9%; $p = 0.01$).

Regarding the characteristics of the number of CBD stones, 86/453 patients had negative cholangiography in the eERCP group, and 60/255 patients had negative cholangiography in the dERCP group. There were 223/453 patients with one stone in the eERCP group and 131/255 patients in the dERCP group. 144/453 patients had multiple stones in the eERCP group, and 64/255 patients had multiple stones in the dERCP group.

Operative outcome

The treatment outcomes of ERCP are presented in Table 3.

The mean delay times for ERCP intervention in the two groups were 26.7 and 92.5 h, respectively, for eERCP and dERCP.

Our findings indicated disparities in mortality rates between the early and delayed intervention groups. Although the early group experienced two deaths attributed to heart failure and pneumonia, the delayed group exhibited a progressive rise in mortality over time. Conversely, readmission rates declined across all groups. However, these differences were not statistically significant ($p > 0.05$).

Patients in the eERCP group required intensive care more frequently (3.1%) compared to the dERCP group (0.8%; $p = 0.02$). Post-ERCP recovery time seemed prolonged in the early intervention group, although this finding did not reach statistical significance ($p = 0.06$). In contrast, hospitalization duration was significantly longer for the delayed intervention group (9.3 vs 6.5 days; $p < 0.001$).

The overall complication rate following ERCP was consistent across all groups at approximately 15%. Rates of acute pancreatitis and bleeding complications were comparable. However, perforation complications were more prevalent in the dERCP group (1.2%) compared to other groups ($p = 0.01$).

Table 3. Operative outcomes.

	Early ERCP	Delay ERCP	*p* Value
	***n* = 453**	***n* = 255**	
Time from admission to ERCP (hours)	26.7	92.5	**<0.0001**
ICU hospitalization, *n* (%)	14 (3.1%)	2 (0.8%)	**0.02**
Duration of recovery after intervention, mean ± SD (days)	4.3 ± 3.3	4.2 ± 3.5	0.06
Duration of hospitalization, mean ± SD (days)	6.5 ± 4.7	9.3 ± 5.1	**<0.0001**
Post-ERCP complications, *n* (%)	64 (14.1%)	40 (15.7%)	0.8
ERCP-related pancreatitis, *n* (%)	59 (13%)	35 (13.7%)	0.9
Bleeding, *n* (%)	5 (1.1%)	2 (0.8%)	0.9
Perforation, *n* (%)	0 (0%)	3 (1.2%)	**0.01**
1-Month mortality, *n* (%)	2 (0.4%)	0 (0%)	0.9
6-Month mortality, *n* (%)	16 (3.5%)	14 (5.5%)	0.4
12-Month mortality, *n* (%)	30 (6.6%)	23 (9%)	0.3
6-Month readmission, *n* (%)	48 (10.6%)	19 (7.5%)	0.4
12-Month readmission, *n* (%)	64 (14.1%)	32 (12.5%)	0.3

ERCP, endoscopic retrograde cholangiopancreatography; ICU, intensive care unit.

The eERCP group exhibited a significantly higher rate of positive bacterial cultures in bile (21.9%) compared to the dERCP group (10.6%; $p = 0.0003$, Figure 2). Moreover, the early intervention group had a significantly higher rate of septicemia (13.9%) compared to the dERCP group (7.5%; $p = 0.01$).

Outcome of AC severity patients

The ERCP treatment and outcomes of AC severity cases are presented in Table 4.

At the time of hospital admission, clinical characteristics such as age, gender, liver enzyme levels, and biliary obstruction markers were similar between the two groups. Additionally, the rate of bloodstream infections did not differ significantly between the groups. However, the incidence of septic shock was considerably higher in the early intervention group compared to the delayed intervention group (52.8% vs 30%, $p = 0.03$).

ERCP outcomes were comparable in successful cannulation and complete stone removal, but plastic biliary stent placement was higher in the eERCP group (58.4% vs 37.5%, $p = 0.04$). Complication rates, 1-year mortality, and 1-year readmission rates showed no significant differences (Figure 3 and Table 4).

Discussion

AC caused by bile duct stones is an acute inflammatory condition that can progress severely, causing multiorgan damage and a high risk of mortality if not treated promptly.[1,2] ERCP is currently the primary technique to relieve biliary obstructions and treat stones.[3] For inflammatory conditions of the biliary tract caused by malignant factors, performing ERCP as early as possible leads to better recovery outcomes and reduces the 30-day mortality risk for patients.[8] However, when it comes to acute biliary tract inflammation due to stones, there is no consensus among studies regarding when ERCP should be performed: early (⩽48 h)

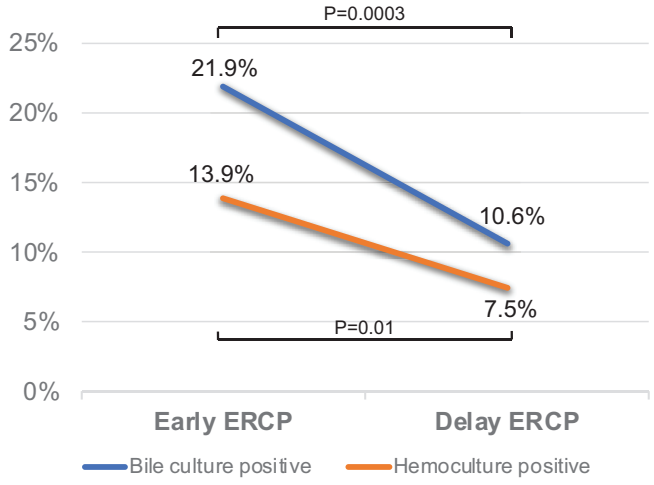

Figure 2. Positive cultures related to ERCP timing.
ERCP, endoscopic retrograde cholangiopancreatography.

or delayed (>48 h). Some studies supported performing eERCP because of the benefit of patient outcomes,[6,13] while others found no difference in 30-day and mortality risk.[9,14]

In Vietnam, the performance of ERCP for treating biliary tract inflammation due to stones follows the recommendations of the Tokyo Guidelines and the guidelines of the Ministry of Health.[3,10] While most studies have promoted eERCP for patients with acute biliary tract inflammation,[5,6,12,13] the current availability of equipment and specialized endoscopic interventionalists in Vietnam may not meet the immediate demand for all ERCPs upon hospital admission. Despite severe biliary tract inflammation, many patients may not be able to undergo ERCP immediately upon admission and may require stabilization of their condition first. As a result, the timing of ERCP for patients depends on the assessment of the physician and the medical board based on their experiences. Currently, there are no studies or guidelines in Vietnam recommending the optimal timing for performing ERCP in patients. Moreover, the question of whether dERCP after initial antibiotic therapy worsens patient outcomes, increases mortality, or raises the risk of hospital readmission remains unanswered. Therefore, we conducted this study to retrospectively evaluate the ERCP practices at our hospital—one of the five largest hospitals in Vietnam—and to compare and analyze differences in hospitalization duration and ultimate outcomes between the eERCP and dERCP groups. The aim is to provide preliminary scientific evidence on the optimal timing for ERCP in Vietnam.

At admission, the inflammatory markers were elevated in the eERCP group compared to the dERCP group (the differences were statistically significant, with $p < 0.05$, Table 1). Consequently, the rate of patients with severe cholangitis in the eERCP group (19.6%) appeared to be higher than in the dERCP group (15.7%). Thus, more patients in the anterior group require intensive care (3.1% vs 0.8%, corresponding to eERCP and dERCP). In addition, the rate of acute pancreatitis in the eERCP group was also higher than that in the dERCP group. These findings align with reports from other authors, such as Park et al.[8] Therefore, our study's indication for eERCP prioritized patients with severe cholangitis.[3,4] This treatment approach is consistent with other reports, advocating for selecting patients for eERCP.[8,15]

Average ERCP delay times were 26.7 and 92.5 h for the two groups, respectively, as defined by our classification criteria (see section "Materials and Methods" and Figure 1). While the early intervention group exhibited a higher 1-month mortality rate (0.4% vs 0%), this difference was not statistically significant. This disparity is attributed to a higher proportion of critically ill patients requiring intensive care in the early intervention group (3.1% vs 0.8%, $p = 0.02$). These patients succumbed to progressive cardiac events and

Table 4. Clinical characteristics and outcomes of patients with acute cholangitis severity based on the ERCP timing after hospital admission.

	Early ERCP	Delay ERCP	*p* Value
	n = 89	*n* = 40	
Age (years), mean ± SD	70.7 ± 16.1	67.7 ± 14.0	0.2
Male, *n* (%)	47 (52.8%)	23 (57.5%)	0.8
WBC (G/L), mean ± SD	15.1 ± 8.9	11.8 ± 6.1	0.1
AST (U/L), mean ± SD	169.6 ± 216.5	144.0 ± 144.1	0.6
ALT (U/L), mean ± SD	166.5 ± 183.1	175.8 ± 187.4	0.9
GGT (U/L), mean ± SD	459.9 ± 397.4	466 ± 428.3	0.9
Total bilirubin (μmol/L), mean ± SD	80.0 ± 68.1	132.8 ± 121.4	0.06
Septic shock, *n* (%)	47 (52.8%)	12 (30%)	**0.03**
Septicemia, *n* (%)	30 (33.7%)	8 (20%)	0.2
ICU hospitalization, *n* (%)	12 (13.5%)	1 (2.5%)	0.1
Cannulation success rate, *n* (%)	86 (96.6%)	37 (92.5%)	0.5
Difficult biliary cannulation or impacted Oddi's sphincter stone, *n* (%)	16 (18%)	11 (27.5%)	0.3
Remove all stones in ERCP, *n* (%)	68 (76.4%)	28 (70%)	0.5
Placing a biliary plastic stent in ERCP, *n* (%)	52 (58.4%)	15 (37.5%)	**0.04**
Post-ERCP-related pancreatitis, *n* (%)	5 (5.6%)	4 (10%)	0.6
Post-ERCP related to bleeding, *n* (%)	2 (2.2%)	1 (2.5%)	0.5
Duration of recovery after intervention, mean ± SD (days)	5.4 ± 4.8	4.3 ± 2.7	0.2
Duration of hospitalization, mean ± SD (days)	7.4 ± 5.6	9.5 ± 3.8	**0.0004**
1-Month mortality, *n* (%)	2 (2.2%)	0 (0%)	0.8
6-Month mortality, *n* (%)	9 (10.1%)	4 (10%)	0.8
12-Month mortality, *n* (%)	12 (13.5%)	8 (20%)	0.5
6-Month readmission, *n* (%)	11 (12.4%)	2 (5%)	0.3
12-Month readmission, *n* (%)	15 (16.9%)	6 (15%)	0.9

ALT, alanine transaminase; AST, aspartate transaminase; ERCP, endoscopic retrograde cholangiopancreatography; GGT, gamma-glutamyl transpeptidase; ICU, intensive care unit; SD, standard deviation; WBC, white cell count.

pneumonia. Conversely, the 6-month mortality rate was elevated in the delayed intervention group (3.5% in eERCP, 5.5% in dERCP). Late mortality was primarily linked to the progression of underlying chronic conditions, such as heart failure, chronic kidney disease, and liver cirrhosis. Our findings suggest that delaying ERCP might be a risk factor accelerating the silent progression

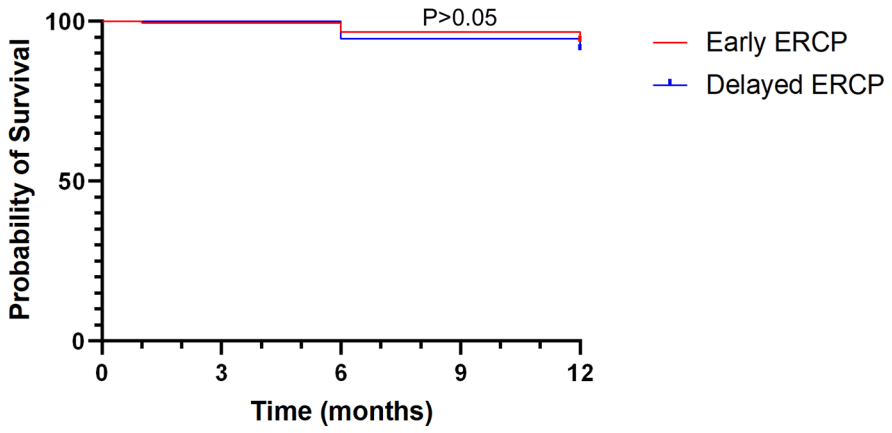

Figure 3. The survival of acute cholangitis patients who underwent either early ERCP or delayed ERCP, calculated by the Kaplan-Meier test.
ERCP, endoscopic retrograde cholangiopancreatography.

of chronic diseases. These results align with those of Park et al.,[8] who observed increasing 1- and 6-month mortality rates with dERCP, particularly between the eERCP and dERCP groups.

Moreover, these mortality rates were associated with the levels of biliary inflammation.[8] Similarly, in the Mulki et al.[13] study, patients undergoing ERCP within 1 day of hospital admission had a significantly reduced risk of in-hospital mortality and 30-day mortality compared to those undergoing dERCP. Consistent with this trend, patients undergoing early intervention in our study exhibited higher hospital readmission rates at 6 and 12 months compared to the late-intervention group. The reason behind this might be the significantly higher stent placement rate in the early intervention group compared to the late-intervention group (33.9% vs 24.9%, corresponding to eERCP vs dERCP, $p=0.01$, Table 2). Stents were placed due to the risk of retained stones or prophylaxis against recurrent biliary obstruction caused by gallstones falling into the bile duct. Therefore, these patients needed late readmission to remove the bile duct stent and undergo further stages of treatment. Our results further support findings from other authors, indicating that patients undergoing early intervention are more likely to require bile duct stent placement.[13,15]

The Tokyo Guidelines recommend urgent or eERCP for patients with moderate-to-severe cholangitis.[3] In our research, the earlier ERCP group had a significantly greater proportion of patients with severe cholangitis compared to the later ERCP group (Table 1). While this could contribute to the extended recovery time, this difference did not reach statistical significance (Table 3). Notably, the hospitalization duration for the early intervention group was significantly shorter than that of the delayed intervention group (6.5 vs 9.3 days, $p<0.0001$). These findings align with numerous reports in the literature, indicating that eERCP shortens the patient's hospital stay.[5,13,15,16] On the other hand, treatment outcomes for stone removal and post-ERCP complications were similar between the two groups (Tables 2 and 3). In addition, 1-year mortality and 1-year readmission rates showed no significant differences between the groups (Table 3). These findings suggest that delaying ERCP may not negatively impact stone treatment outcomes or increase the risk of adverse events for patients, and aligns with the results reported by Jagtap et al.[17]

Severe AC should be managed with urgent or eERCP, as recommended by the Tokyo Guidelines and numerous international studies.[3,4,13,18] However, in our study, approximately one-third of patients (40/129) underwent dERCP (beyond 48 h) due to limited availability of medical equipment and the patient's conditions being unsuitable for early intervention. These patients received intensive care, antibiotics, stabilization of comorbidities, and dERCP. Our analysis revealed that both groups had similar clinical and laboratory characteristics of severe cholangitis at admission. However, septic shock was more prevalent in the eERCP group (52.8% vs 30%, eERCP vs dERCP, $p=0.03$). Regarding ERCP outcomes, the success

rates for stone removal were comparable between the groups, although plastic biliary stent placement was more frequent in the eERCP group. This aligns with treatment recommendations emphasizing early biliary drainage in such patients. Finally, post-ERCP complications and adverse events within 1 year, including mortality and readmission rates, showed no statistically significant differences between the groups.

Therefore, performing eERCP for patients with cholangitis due to stones may reduce the risk of complications after the procedure, and decrease hospitalization time. However, dERCP did not worsen stone treatment outcomes or increase adverse events such as 1-year mortality and readmission rates, even in patients with severe cholangitis (Figure 3). Therefore, in settings with limited equipment, facilities, and personnel to perform eERCP for all patients, intensive resuscitation, antibiotic therapy, and stabilization of comorbidities followed by dERCP may be a viable alternative.

Approximately 50% of patients in both groups had a single stone. The rate of negative cholangiography was higher in the dERCP group than in the eERCP group (23.5% vs 19.0%). This result raises the question of whether dERCP is associated with spontaneous stone passage rates. We need further analysis of the stone size and whether patients were given antispasmodic drugs (e.g., Buscopan) before the intervention.

The findings of this retrospective study should be interpreted with caution due to several limitations. These include incomplete data, particularly regarding intervention time, blood/bile culture timing, and the lack of a standardized protocol for patient selection. In addition, the single-center design limits the generalizability of the results. To address these limitations, future prospective studies with rigorous methodology are required to confirm these findings and provide more definitive evidence.

Conclusion

This study provides novel insights into the ongoing debate surrounding the optimal timing of ERCP in AC caused by bile duct stones. In resource-limited settings, intensive resuscitation, antibiotic therapy, and stabilization of comorbidities, followed by dERCP, represent a feasible alternative strategy.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Institutional Review Board of 108 Military Central Hospital (Approval No. 3761/HDDD). Written informed consent was obtained from all participants or their legal guardians.

Consent for publication

Not applicable, as no identifiable patient data or images were included.

Author contributions

Nguyen Thi Hue: Data curation; Formal analysis; Writing – original draft.

Nguyen Thi Huyen Trang: Formal analysis; Software.

Nguyen Anh Tuan: Validation; Writing – review & editing.

Pham Minh Ngoc Quang: Formal analysis; Software.

Mai Thu Hoai: Data curation; Formal analysis; Software.

Mai Thanh Binh: Design; Study concept; Validation; Writing – review & editing.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to the Vietnam military hospital's privacy policy. However, they are available from the corresponding author upon reasonable request.

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Supplemental material

Supplemental material for this article is available online.

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Appendix

Abbreviations

AC	acute cholangitis
ALT	alanine transaminase
AST	aspartate transaminase
dERCP	delayed endoscopic retrograde cholangiopancreatography
eERCP	early endoscopic retrograde cholangiopancreatography
ERCP	endoscopic retrograde cholangiopancreatography
GGT	gamma-glutamyl transpeptidase
ICU	intensive care unit