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Correlation Between ERCP Implementation Time and Outcomes of Patients with Acute Cholangitis Due to Choledocholithiasis

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Abstract

Acute cholangitis is a serious condition, and timely ERCP is essential for effective management. This prospective cohort study was conducted at Dr. Hasan Sadikin Hospital in Bandung, Indonesia, from June 2023 to April 2024, to evaluate the feasibility of performing ERCP beyond 48 hours in the presence of various limitations. The study included patients with acute cholangitis caused by common bile duct stones. The ERCP timing was categorized into three groups: less than 48 hours, 48-72 hours, and more than 72 hours. Outcomes measured were hospital stay duration, ICU admission, and 30-day mortality. Of these patients, 52.8% underwent ERCP at 48-72 hours, 27.8% after 72 hours, and 19.4% before 48 hours. The median hospital stay was 7.5 days (IQR 3-15). ICU admissions occurred only in patients receiving ERCP after 72 hours (30.0%), a significantly higher rate compared to the other groups (p=0.014). A strong correlation was found between delayed ERCP and longer hospital stays (r=0.711, p<0.01), as well as ICU admission (r=0.405, p=0.014), though no significant correlation with mortality was observed (r=-0.021, p=0.905).

Keywords: Acute cholangitis, biliary drainage, choledocholithiasis, duration of surgery, endoscopic retrograde cholangiopancreatography

Introduction

Acute cholangitis, also known as ascending cholangitis, is a serious illness that affects the entire body. It presents with a set of symptoms including fever, jaundice, and abdominal discomfort (known as Charcot's triad). This condition can be life-threatening, with a historically documented fatality rate of over 50%.[1] Acute cholangitis, also known as angiocholitis, is a highly infectious condition that affects the bile and bile ducts. The discovery of this ailment can be attributed to Jean Martin Charcot (1825–1893) in 1877.[2] Two choledocholithiasis is believed to be the cause in 28-70% of cases of acute cholangitis. The symptoms of this condition include abdominal pain, jaundice, fever, and hepatomegaly.[3]

Studies indicate that the occurrence of acute cholangitis varies between 0.3% and 1.6%, with approximately 12.3% of cases being classified as severe cholangitis.[4] Four Research conducted in the United States revealed that choledocholithiasis is present in approximately 10% to 15% of the Caucasian population in the country. Among patients with choledocholithiasis who present to the emergency room, around 6% to 9% receive a diagnosis of acute cholangitis. The study reported that there were no notable gender disparities, and the majority of participants were between the ages of 50 and 60. Acute cholangitis affects around 200,000 individuals annually in the United States.[5] There is a lack of available data on the occurrence of acute cholangitis in Indonesia or specifically in the region of West Java.

The management of acute cholangitis, as outlined in several studies and the 2018 Tokyo Guidelines, necessitates prompt intervention to address the two primary issues: infection and obstruction of the biliary path. Regarding infection, prompt treatment is administered, specifically by fluid resuscitation and antibiotics.

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Elevated intraductal pressure hinders the release of antibiotics from the biliary path, necessitating the use of biliary drainage to address this form of obstruction. The Tokyo Guidelines 2018 suggest that immediate biliary draining should be performed for cases of moderate and severe cholangitis. Biliary drainage is indicated in cases of mild acute cholangitis only when there is no response to antibiotic treatment.[6]

Endoscopic retrograde cholangiopancreatography (ERCP) is a specialized operation that uses an endoscope to diagnose and treat abnormalities of the pancreatic and biliary systems. This process was created as a diagnostic method in the late 1960s and early 1970s. The inaugural biliary sphincterotomy took place in 1974, and since then, ERCP has had swift advancement as a therapeutic intervention for the biliary tract. ERCP is a superior alternative to PTBD (percutaneous biliary drainage) due to its lower invasiveness, enhanced safety, ability to be performed at the patient's bedside, effectiveness in removing bile duct stones, independence from the need for coagulopathy correction, and the option to avoid radiation exposure if required (such as in pregnant patients). ERCP has a better success rate compared to PTBD. Percutaneous transhepatic biliary drainage (PTBD) is typically carried out in individuals who do not respond to initial endoscopic retrograde cholangiopancreatography (ERCP) or if there is aberrant anatomy caused by past surgical interventions.[7]

The ERCP surgery commences by inserting the duodenoscope through the oral cavity. The duodenoscope subsequently traverses the pylorus of the stomach and enters the duodenal bulb. The wire-guided procedure is advised to be performed under fluoroscopy, with the wire being inserted into either the bile duct or pancreatic duct prior to injecting contrast. The European Society of Gastrointestinal Endoscopy (ESGE) advises the utilization of 5-Fr stents, which are shorter in size, instead of 3-Fr stents, for individuals at high risk. Stents that are kept in place should be taken out within a maximum of 10 days after they are inserted.[8]

According to the 2018 Tokyo guidelines, a quick implementation of ERCP is associated with improved patient outcomes. The optimal timeframe for implementing ERCP in individuals with acute cholangitis remains a topic of active debate. Nevertheless, the consensus among the majority of experts is that biliary decompression should be carried out within a 48-hour timeframe. Retrospective studies examining the most favorable timing for ERCP and early drainage (within 24-48 hours of cholangitis onset) have shown a decrease in the occurrence of organ failure, shorter hospital stays, and lower mortality rates compared to delayed drainage. The majority of patients experienced benefits from receiving immediate drainage within 24 hours.[6] A meta-analysis study yielded consistent results when ERCP was conducted within a 48-hour timeframe.[9] A study conducted by Khamaysi and Taha in Turkey demonstrated that doing ERCP within 12 hours can significantly decrease the death rate at day 30.[10] The current European recommendations also advise performing ERCP within 12 hours for patients experiencing septic shock.[11] Hou et al's findings diverged from previous studies, as they concluded that the timing of ERCP implementation had no impact on adverse events or the success of ERCP procedures.[12]

At Dr. Hasan Sadikin General Hospital (RSHS), ERCP has become a routine procedure for managing cholangitis, guided by TG18 recommendations. However, challenges remain, including limited ERCP-trained staff and equipment availability, making procedures within 24 hours unfeasible. In this context, there is a lack of local data assessing the impact of ERCP timing on patient outcomes in Indonesia. Costs related to the ERCP procedure might be covered by private or governmental insurance, such as National Health Insurance (BPJS), which aids in the treatment process. The implementation of the ERCP procedure at RSHS faces the challenge of a limited number of nurses having the expertise and skills required to assist during the surgery.. Therefore, this study aims to evaluate the relationship between ERCP timing—specifically procedures performed within 48 to 72 hours—and clinical outcomes in patients with acute cholangitis at Dr. Hasan Sadikin General Hospital, Bandung.

Methods

This prospective cohort study was conducted from June 2023 to April 2024 at Dr. Hasan Sadikin General Hospital, Bandung. The study population consisted of patients diagnosed with acute cholangitis at RSUP Dr. Hasan Sadikin between June 2023 and April 2024. The study included patients who met the following criteria: (1) age >18 years, (2) diagnosis of Choledocholithiasis with Acute Cholangitis, and (3) underwent

ERCP. The exclusion criteria for this study are as follows: (1) Patient refusal to provide informed consent to participate as a research subject, and (2) Patient history of malignancy. The exclusion criteria for this trial were: (1) The patient was compelled to leave the study or declined to have ERCP during the designated period. Sampling was performed using a total sampling method. The samples utilized by researchers included only of cases of Choledocholithiasis complicated by acute cholangitis at Dr. Hasan Sadikin Bandung. Data were analyzed using Microsoft Excel 2027 and SPSS version 25.0. Descriptive analysis will provide a detailed account of the specific attributes of every patient. The data will be displayed as frequency (n) and percentage (%) for categorical variables, and as average and standard deviation for continuous variables. Patients will be categorized based on the timing of ERCP implementation into three groups: those who receive ERCP within 48 hours, those who receive it between 48 and 72 hours, and those who receive it beyond 72 hours. Subsequently, a bivariate analysis was conducted. Bivariate analysis is a statistical analysis conducted to examine the correlation between two variables. This study employed bivariate analysis using the chi-square test to examine the link between the timing of ERCP implementation and the outcome of patients with acute cholangitis. Ethical approval was obtained from the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital (No. 1B.02.01/X.6.5/152/2023).

Results

This prospective cohort study was conducted at Dr. Hasan Sadikin General Hospital, Bandung, from June 2023 to April 2024, involving patients with choledocholithiasis and acute cholangitis. A total of 36 patients met the inclusion criteria and were included in the analysis. Data collected included demographic characteristics, history of cholangitis, severity of cholangitis (Tokyo Guidelines), ERCP timing, and laboratory findings. Patient characteristics are shown in Table 1.

The mean age of participants was 45.36±15.02 years. Most were female (58.3%). All patients had a history of cholangitis. Based on Tokyo Guidelines 2018,55.6% had Grade I cholangitis, 36.1% Grade II, and 8.3% Grade III When considering the timing of ERCP, it is observed that the majority of patients, specifically 52.8%, underwent the surgery between 48–72 hours of diagnosis. This was followed by 27.8% of patients who had the treatment more than 72 hours after diagnosis, and 19.4% of patients who had it within less than 48 hours.

The clinical characteristics of the research subjects were assessed using the timing of the ERCP operation, specifically the implementation method within several time frames: less than 48 hours, 48-72 hours, and more than 72 hours after the diagnosis was made. This information is presented in Table 2. Based on this investigation, numerous inferences can be inferred. The research revealed that there was no statistically significant variation in the average age among the various ERCP timing groups. This indicates that age does not play a decisive role in the selection of ERCP timing. Regarding gender, there was no notable disparity in the distribution of male or female patients across the three groups. This demonstrates that the timing of ERCP does not have an impact on the gender distribution of individuals who undergo the surgery. Based on the results obtained from 3 patients diagnosed with grade 3 cholangitis, it was found that 2 patients (10.5%) underwent ERCP within 48-72 hours, 1 patient (10.0%) underwent ERCP after 72 hours, and no patient underwent ERCP within 48 hours. According to the 2018 Tokyo

Table 1 Subject Characteristics

Variable	Total (n=36)
Age (year)	45.36±15.02
Sex (%)	
Male	15 (41.7%)
Female	21 (58.3%)
Grade of Cholangitis (%)	
Grade 1	20 (55.6%)
Grade 2	13 (36.1%)
Grade 3	3 (8.3%)
ERCP Implementation Time (%)	
<48 hours	7 (19.4%)
48–72 hours	19 (52.8%)
>72 hours	10 (27.8%)

Note: Categorical data is typically provided in terms of numbers or frequencies, as well as percentages. On the other hand, numerical data is usually presented using measures such as mean, median, standard deviation, and range. ERCP=Endoscopic Retrograde Cholangiopancreatography.; SGOT=serum glutamic oxaloacetic transaminase;

Table 2 Comparison of Characteristics Across ERCP Timing Groups

Variable	<48 hours (n=7)	48-72 hours (n=19)	>72 hours (n=10)	p-value
Age (year)	48.43±14.60	44.95±16.03	44,00±14.54	0.832
Sex (%)				0.992
Male	3 (42.9%)	8 (42.1%)	4 (40.0%)	
Female	4 (57.1%)	11 (57.9%)	6 (60.0%)	
History of cholangitis (%)				1.000
Yes	7 (100%)	19 (100%)	10 (100%)	
No	-	-	-	
Grade of cholangitis (%)				0.329
Grade 1	5 (71.4%)	12 (63.2%)	3 (30.0%)	
Grade 2	2 (28.6%)	5 (26.3%)	6 (60.0%)	
Grade 3	-	2 (10.5%)	1 (10.0%)	

Guideline, the recommended treatment for grade 3 cholangitis is urgent biliary drainage, which necessitates ERCP to be performed within 24 hours. However, at RSUP Dr. Hasan Sadikin, the timing of ERCP differs from the guideline. Due to limited human resources, it is now not possible to do ERCP within 24 hours. Additionally, the prompt execution of ERCP at grade 3 is hindered by the Anesthesia department's evaluation of anesthesia risks, since the patient's condition is more unstable at this stage. In general, there were no notable variations in clinical characteristics between the three groups categorized by the date of ERCP. These findings indicate that the three groups have similar patient features, allowing for the analysis to progress to the next stage.

Table 3 provides a description of the results obtained from the research participants, categorized according to the timing of the ERCP surgery. Various inferences can be derived from this table. In this study, the patients had a median length of stay of 7.5 days, with an interquartile range of 3-15 days. The length of stay varied significantly between the groups of patients who had ERCP operations more than 72 hours and less than 48 hours after diagnosis (15.5 [IQR 14–25.5] vs. 3 [IQR 2–3] days; p<0.01) (Figure

Table 3 Outcomes Based on ERCP Timing Group

Variable	Total (n=36)	<48 hours (n=7)	48-72 hours (n=19)	>72 hours (n=10)	p-value
Length of stay (days)	7.5 (3–15)	3 (2–3)	7 (3–11)	15.5 (14–25.5)	<0.01*
Grade I	4 (3–9.75)	3 (3–3)	4 (2.75–7.25)	15 (15–21)	0.453
Grade II	11 (9–16)	3 (2.25–2.75)	9 (9–11)	16 (15.25–22.75)	0.018*
Grade III	10 (8.5–25)	–	24 (7–40)	10 (N/A)	1.00
ICU admission (%)	3 (8.3%)	–	–	3 (30.0%)	0.014*
Grade I	1 (5.0%)	–	–	1 (33.3%)	0.051
Grade II	2 (15.4%)	–	–	2 (33.3%)	0.252
Grade III	–	–	–	–	
Mortality (%)	1 (2.8%)	–	1 (5.3%)	–	0.631
Grade I	–	–	–	–	
Grade II	–	–	–	–	
Grade III	1 (33.3%)	–	1 (50.0%)	–	0.386

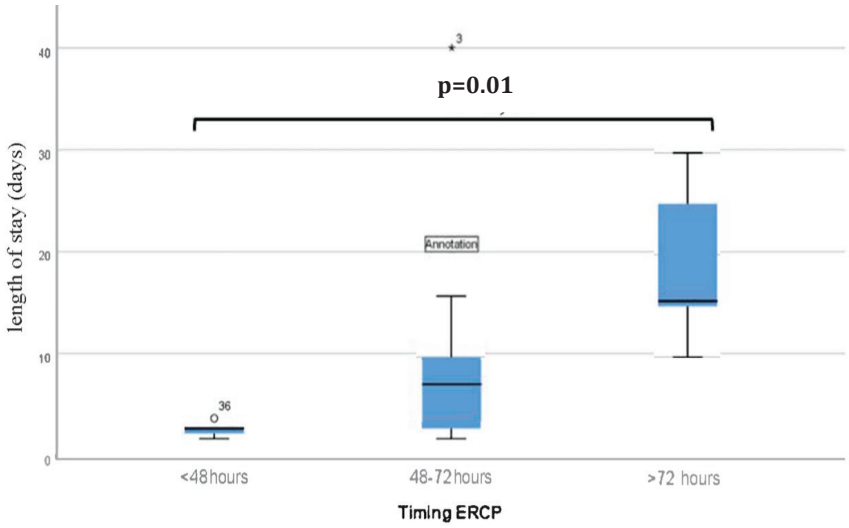

Figure 1 Comparison of Length of Stay by ERCP Timing Group

1). Out of the patients who underwent the ERCP surgery, 3 individuals (8.3% of the total) were hospitalized to the Intensive Care Unit (ICU). 30.0% of these patients were part of the ERCP timing group that exceeded 72 hours, which was substantially more than the ERCP timing groups that were less than 48 hours and between 48 and 72 hours (P=0.014). One patient, accounting for 2.8% of the total, died following the ERCP operation in this study. The patients included in the ERCP timing group of 48-72 hours accounted for 5.3% of the total. Nevertheless, the analytical findings indicated that there were no substantial disparities among the three groups (p=0.631).

This study further categorized each outcome based on the Grade of cholangitis. Patients with cholangitis Grade I had a median stay of 4 days with interquartile range of 3-9.75 days. Patients with cholangitis grade II had a median stay of 11 days (IQR: 9-16) and patients with cholangitis Grade III had a median stay of 10 days (IQR: 8.5-25). Interestingly, in patients with grade II cholangitis, the timing of ERCP was significantly associated with the duration of hospital stay (p=0.018). Patients with grade I cholangitis had a 5% rate of ICU admission, which was one patient admitted after ERCP procedure within >72 hours. While patients with grade II cholangitis had a 15.4% rate of ICU admission in which two of them are admitted into the ICU after ERCP procedure within >72 hours. However, both of them are not statistically significant (p=0.051 and p=0.252, respectively). Ultimately, performing ERCP more than 72 hours after diagnosis is associated with a longer hospital stay and a higher rate of intensive care unit (ICU) admission compared to procedures performed within 72 hours.

The analysis aims to establish the correlation between an independent variable, specifically the timing of ERCP, and a dependent variable, which encompasses the length of stay, ICU admission, and mortality. Based on the statistical analysis using the Spearman correlation test, numerous conclusions can be derived in accordance with Table 4. The link between the ERCP timing variable and length of stay was shown to be statistically significant, with a P value of <0.01. The correlation coefficient (r) is

Table 4 Correlation between ERCP Timing and Outcomes

Variable	Correlation Coefficient (r)	p-value
Length of Stay (days)	0.711	<0.01*
ICU Admission	0.405	0.014*
Mortality	-0.021	0.905

Note: Spearman's correlation test. *p<0.05 indicates statistical significance

0.711, indicating a strong positive association. Between the temporal variable of ERCP and ICU admission, the correlation had a p-value of 0.014, indicating a statistically significant link. The correlation coefficient (r) of 0.405 suggests a positive association with moderate strength. The association between the temporal variable of ERCP and death was assessed, yielding a P value of 0.905. This result indicates that there is no significant or statistically meaningful correlation between the two variables. The correlation coefficient (r) obtained is -0.021, indicating a weak negative connection that can be disregarded due to its minor strength.

In summary, delayed ERCP implementation beyond 72 hours was significantly associated with prolonged hospitalization and higher ICU admission rates. However, no significant association was observed between ERCP timing and mortality, likely due to the low number of events. These findings suggest timely ERCP may improve short-term outcomes in acute cholangitis patients.

Discussion

Acute cholangitis is a severe infection of the bile and bile ducts that is life-threatening. It is characterized by the presence of fever, jaundice, and stomach discomfort, which together are known as Charcot's triad. The death rate for this condition can exceed 50%.[2] Choledocholithiasis has been found to be present in 28-70% of cases.[3] Acute cholangitis is a condition characterized by inflammation of the bile ducts.

According to the Tokyo Guidelines 2018 early biliary drainage through ERCP is a recommended approach to manage the infection and relieve obstruction. However, there remains debate regarding the optimal timing of ERCP. The recommendations also advise that performing ERCP at an earlier stage will result in a more favorable outcome for the patient.[13,14] However, there is still ongoing disagreement regarding the optimal timing for performing ERCP in individuals with acute cholangitis.

This research is the first in Indonesia to evaluate the relationship between ERCP timing and clinical outcomes in patients with acute cholangitis secondary to choledocholithiasis. Findings indicate that delayed ERCP (>72 hours) is significantly associated with prolonged hospital stay and increased ICU admission. The study cohort predominantly consisted of females (58.3%), with a mean age of 45.36 ± 15.02 years.

Similarly, Similarly, Lee et al. reported 55% female patients with a mean age of 59 ± 19 years, with no significant differences between early and delayed ERCP groups.[15] In line with previous studies conducted by Parikh et al., Patel et al., and Mulki et al., who also reported that females constituted more than 50% of patients across all ERCP timing groups.[16-18] On et al. also observed a higher proportion of females (55.8%) in their study.[19] When assessing the severity of cholangitis based on the Tokyo Guideline classification, grade 1 was the most common grade in our study cohort, accounting for 5.6% of patients. There was no significant difference observed between the ERCP timing groups in terms of the distribution of cholangitis grades. Similarly, On et al. reported that 51.3% of their patients were categorized as having mild acute cholangitis, while 32.6% had moderate grade and 16.1% had severe grade. Furthermore, there was no discernible variation in the duration of ERCP (endoscopic retrograde cholangiopancreatography) among patients with acute cholangitis caused by choledocholithiasis, regardless of the severity classification.[19]

Grade 1 cholangitis is defined by the lack of distinct features seen in grades 2 and 3 cholangitis. Grade 2 cholangitis can be diagnosed based on the presence of fever, a white blood cell counts higher than 12,000 cells/mm^3 or lower than 4000 cells/mm3, bilirubin levels over 5 mg/dL, low albumin levels, or advanced age. Within this study sample, 13 patients (36.1%) were categorized as grade 2. Three of our patients (8.3%) were diagnosed with grade 3 cholangitis, characterized by the presence of end-organ destruction. Assessing the gravity of cholangitis is crucial as it will aid in determining the subsequent therapeutic approach. For moderate and severe cases of illness, it is imperative to promptly perform biliary drainage. Meanwhile, patients with moderate acute cholangitis typically only require antibiotic therapy. Biliary drainage will be explored if the patient does not show improvement with antibiotic therapy. Most patients with acute cholangitis caused by choledocholithiasis will often respond to initial conservative therapy, especially those with mild instances. Nevertheless, approximately 15% of these patients may potentially undergo deterioration to the extent of sepsis, a condition linked to significant morbidity and mortality. Thus, it is crucial for patients to undergo regular reassessment using the most up-to-date Tokyo Guideline criteria. This assessment should be conducted immediately after the diagnosis, within 24 hours of the diagnosis, and within the

24-to-48-hour timeframe. This will allow for timely identification of patients who were initially diagnosed with mild cholangitis but later meet the criteria for moderate or severe cholangitis, thus requiring treatment. Timely biliary decompression and avoiding unnecessary delays in doing ERCP can help prevent complications.[2]

Patients who received the ERCP surgery more than 72 hours after diagnosis had a substantially longer hospital stay compared to those who received the treatment within 48 hours (15.5 [IQR 14–25.5] vs. 3 [IQR 2–3] days; p<0.01). The correlation analysis revealed a statistically significant and high positive connection (r=0.711; P<0.01) between the timing of ERCP and the length of stay. Furthermore, we measured a subgroup analysis based on cholangitis severity. It was found that in patients with grade II cholangitis, the timing of ERCP was significantly correlated with the duration of hospital stay (p = 0.018). This finding indicated that prompt intervention may be particularly effective in this population. This trend was not evident in grade I or III, likely due to variations in baseline severity or a small sample size. These results are consistent with multiple findings from prior research. In a retrospective study, Khashab et al. found that when ERCP procedures were delayed by more than 72 hours after admission, it led to longer hospital stays (odds ratio [OR] = 19.8; P = 0.008) and higher inpatient costs (OR=11.3; P = 0.03).[20] Another study by Navaneethan et al. also showed that when the time from arrival to ERCP exceeded 72 hours, it resulted in a 70% increase in the average length of hospital stay (P < 0.01).[21] In a retrospective assessment conducted by Chak et al, individuals with cholangitis who received Early ERCP (within 24 hours of hospital admission) had a considerably shorter hospital stay compared to those who underwent delayed ERCP (median 4 vs 7 days; P<0.005).[22] In Zhu et al.'s report, it was found that a delay of 1 day in the Biliary draining treatment results in an increase of 1.49 days in the length of hospital stay (p<0.0001). There was a significant correlation between delayed biliary drainage (>48 hours) and a longer stay in the intensive care unit (ICU) (p=0.0096).[23]

In the study conducted by Patel et al., a variation in the duration of hospitalization was observed. Patients who underwent ERCP within 24 hours had a hospital stay of 7 days, while those who had the procedure between 24-48 hours stayed for 6 days, and those who had it after 48 hours stayed for 14 days.[17] A similar trend was observed in another study conducted in Thailand, where ERCP performed within 48 hours was associated with a higher median length of hospital stay. The duration of hospitalization was significantly shorter in the group with a 6-day average compared to the group with an 11-day average (p < 0.01).[24] In a study conducted by Parikh et al. comprising 107,253 patients, the group that received ERCP after 48 hours had the longest hospital stay and incurred the highest costs compared to other groups (p<0.01).[16] A study conducted by Aboelsoud et al. found that patients who underwent ERCP within 24 hours had shorter hospital stays (7.71 vs. 13.57 days, p=0.01) and ICU stays (3.25 vs. 4.95 days, p=0.040).[6] Another study by Mulki et al. showed that the mean length of stay was longer in the group that underwent ERCP after 48 hours compared to the group that underwent early ERCP (6.9 days vs. 4.5 days, p<0.01).[18]

Lyu et al. conducted a systematic review and meta-analysis involving 7 observational studies with a total of 88,562 patients with acute cholangitis. The study found that performing ERCP within 24 or 48 hours after admission was linked to a shorter hospital stay (p<0.01).[13] Another meta-analysis by Iqbal et al. involving 9 observational studies and a total of 7,534 patients also showed that patients who underwent ERCP within 48 hours had a significantly lower length of stay, with a mean difference of 5.56 days (95% CI: 1.59–9.53).[9] The longer hospital stay in patients with delayed ERCP can be attributed to the time spent managing the underlying decompensated condition.[17] These findings emphasize that decisive treatment not only improves patient outcomes, but also reduces the expenditures associated with hospitalization for cholangitis.[18]

In this study, the group of patients who underwent ERCP after 72 hours had the greatest rate of admission to the intensive care unit compared to the other groups (30% vs. 0% vs. 0%; p=0.014). The correlation analysis revealed a statistically significant moderate positive association (r=0.405, p=0.014) between the date of ERCP and the likelihood of being admitted to the ICU. Khashab et al. discovered in their prior study that delays of 72 hours in ERCP were linked to worse clinical outcomes, including the need for ICU admission.[20] The prolongation of hospitalization and transfer to the intensive care unit (ICU) may also be linked to a heightened likelihood of enduring organ dysfunction in patients. who had a delayed endoscopic retrograde cholangiopancreatography (ERCP) procedure. In retrospective research conducted

by Lee et al., delayed endoscopic retrograde cholangiopancreatography (ERCP) was defined as ERCP performed at least 48 hours after hospitalization. The researchers discovered that the delay in ERCP was linked to a higher occurrence of persistent organ failure more than 48 hours after admission. Persistent organ failure was defined as a ≥1.5-fold increase in creatinine levels from baseline to ≥1.5 mg/dL, or the need for dialysis, mechanical ventilation, and/or vasopressors to treat hypotension. The odds ratio for this association was 3.1, with a 95% confidence interval of 1.4–7.0. Furthermore, the study revealed that for every 1-day delay in ERCP, there was a 17% higher risk of persistent organ failure (95% CI: 5-29%). Another study conducted by Boender et al., which included 95 patients with acute cholangitis caused by choledocholithiasis, also demonstrated that a delay in ERCP (>3 days) was linked to a greater likelihood of complications and morbidity.[38]

Cholangitis, being a systemic condition, often leads to the occurrence of persistent organ failure and multiorgan failure.[15] Increased pressure in the bile ducts can lead to the breakdown of tight connections between liver cells, allowing germs to enter the bloodstream and cause sepsis.[20] Research has demonstrated that performing biliary decompression can effectively decrease the occurrence of cholangiovenous reflux, leading to a subsequent reduction in levels of bile and serum endotoxins. This process of decompression can also enhance the elimination of IgA and antibiotics via bile excretion. In theory, implementing early biliary drainage could enhance organ function and reduce hospitalization duration.(6) However, our study did not consider persistent organ failure as one of the variables examined. Therefore, we cannot definitively determine its possible impact as a confounding factor in the study's conclusions.

The study found that the in-hospital death rate was 2.8% among patients who underwent ERCP between 48 and 72 hours. The analytical results indicated that there were no statistically significant differences seen among the three ERCP timing groups (P=0.631). Similarly, in the examination of correlation, there was no statistically significant association seen between the two values (r=-0.021; P=0.905). Similarly, a multi-center observational research undertaken by Kiriyama et al. in Japan and Taiwan found that performing ERCP within 24 or 48 hours following hospital admission did not result in better 30-day death rates compared to performing ERCP at a later time.[22] Zhu et al. discovered that there was no notable rise in in-hospital mortality (OR=1.03; 95% CI 0.93–1.13) or 30-day mortality (OR=1.01; 95% CI 0.87–1.14) when patients with severe acute cholangitis underwent delayed biliary drainage.[23] A study conducted by Patel et al. found that the timing of ERCP did not have an impact on mortality, regardless of the severity of the cholangitis.[17] In another study by Aboelsoud et al., there was a slight decrease in in-hospital mortality in the group that underwent ERCP within 24-48 hours, but this difference was not statistically significant (OR = 0.47; 95% CI: 0.17–1.29; p = 0.146).[6] Similar results were reported by Khamaysi and Taha, with a 30-day mortality rate of 15% in the group that underwent ERCP within 12 hours and 21%.[10] Inamdar et al. found no significant difference in hospital mortality between patients treated on weekdays and those treated on weekends. However, it was observed that a higher number of patients treated on weekdays underwent ERCP within 48 hours compared to patients treated on weekends in this study. The weekend mortality rate was 70% compared to 65.4%, with a p-value of less than 0.01.[11] In another study by Athigakunagorn et al., there was no significant difference in overall mortality rate between the group who received early ERCP (<48 hours) and the group that received delayed ERCP.[24]

These data align with our own, providing support for the concept that promptly conducted biliary drainage may not be linked to reduced mortality. Indeed, it is believed that impulsive actions can heighten the risk of anesthesia and trigger temporary bacteremia, which may result in clinical deterioration.[23] In a study conducted by Huang et al., it was discovered that the group of patients who underwent ERCP within 24 hours had a notably higher rate of admissions to the intensive care unit (ICU). The difference in percentages was statistically significant, with a substantially greater rate of 11.2% compared to 4% (p=0.01).[23] Therefore, it may not be crucial for patients with severe acute cholangitis to undergo biliary decompression as early as possible. Instead, it can be safely performed after administering antibiotics, ensuring adequate resuscitation, and stabilizing organ function within 24 hours.[23] According to Jang et al., urgent ERCP (≤24 hours) can be considered for patients with grade 1 or 2 acute cholangitis as it can reduce the duration of hospitalization.[24] However, due to the limited number of patients with severe cholangitis, our study did not conduct an analysis stratified by the severity of the condition. Therefore, we cannot draw a

conclusion based on this.

Nevertheless, multiple prior research have discovered advantages in relation to mortality when ERCP implementation time is expedited. According to Navaneethan et al., they found that a door to ERCP time longer than 72 hours was independently linked with a higher 30-day mortality rate (OR=3.36; 95%CI: 1.12-10.20). Another study, which included 166 patients with Acute cholangitis, demonstrated that performing early ERCP (within 24 hours) resulted in a significant reduction in death within 30 days. The odds ratio (OR) was 0.23, with a 95% confidence interval (CI) of 0.05-0.95, and a p-value of 0.04.[25] In a comprehensive study conducted by Parikh et al., they examined a large database of patients with acute cholangitis caused by choledocholithiasis. The study found that the highest risk of in-hospital mortality was observed in patients who did not undergo ERCP. The second highest risk was seen in patients who underwent ERCP after 48 hours (P<0.01).[16] Furthermore, a comprehensive analysis conducted by Seo et al. discovered that performing ERCP more than 72 hours after admission was linked to a higher death rate (odds ratio 1.80; P<0.01). The same result was found in the study conducted by Lyu et al.[25] A meta-analysis has found that performing ERCP within 48 hours of hospital admission is associated with lower in-hospital and 30-day mortality rates (p<0.01 and p=0.03) compared to performing ERCP more than 48 hours after admission.[13] Another meta-analysis by Iqbal et al. has also shown that patients who undergo emergency ERCP within 48 hours have a reduced risk of organ failure (OR 0.69; 95% CI: 0.33–1.46) and 30-day mortality (OR 0.39; 95% CI: 0.14–1.08).[9] Therefore, the findings of this study cannot be directly concluded. In addition, due to the limited size of this study sample, particularly in the group that underwent ERCP within 48 hours, and with just 1 patient experiencing mortality as the outcome, the statistical power is diminished.

Prior research has demonstrated that timely identification of cholangitis and increased utilization of biliary drainage can effectively decrease the overall mortality rate linked to acute cholangitis.[13] Several prior guidelines have also specified the precise timing of endoscopic biliary drainage for individuals with acute cholangitis. Current guidelines provide varied recommendations on ERCP timing. The European Society of Gastrointestinal Endoscopy recommends performing ERCP within 12 to 72 hours based on severity, while the Tokyo Guidelines 2018 define urgent ERCP as within 24 hours and early ERCP as 24-48 hours post-admission.[12] In practice, early ERCP within 24 hours remains difficult to implement at Dr. Hasan Sadikin General Hospital Bandung due to staffing limitations.

This study has limitations, including its non-randomized observational design, small sample size, single-center setting, and short follow-up duration confined to in-hospital mortality. The inability to control for confounding variables further restricts generalizability. Future research should employ larger, multicenter cohorts and examine long-term outcomes of ERCP timing.

In conclusion, delayed ERCP beyond 72 hours is significantly associated with prolonged hospitalization and increased ICU admission, suggesting that earlier ERCP may yield better outcomes. No significant association was found between ERCP timing and in-hospital mortality; however, this should be noted since our study has limited sample sizes. Furthermore, multi-center studies with larger sample sizes are required to support these findings and analyze the effects of ERCP timing on various severity grades of cholangitis.

References

1. Sulzer JK, Ocuin LM. Cholangitis: causes, diagnosis, and management. Surg Clin North Am. 2019;99(2):175–84. doi:10.1016/j.suc.2018.11.002
2. Sokal A, Sauvanet A, Fantin B, de Lastours V. Acute cholangitis: Diagnosis and management. J Visc Surg. 2019;156(6):515–25. doi:10.1016/j.jviscsurg.2019.05.007
3. Yusoff AR, Anuar QZDK, Khalid S, Mokhtar S. Acute cholangitis secondary to a clogged biliary stent: a review on the cause of clogging and the appropriate time of replacement. Case Rep Gastroenterol. 2022;16(1):55–61. doi:10.1159/000521942
4. Christeven R, Frandy F, Andersen A. Acute cholangitis: an update in management based on severity assessment. Indones J Gastroenterol Hepatol Dig Endosc. 2020;19(3):170–7.
5. Ahmed M. Acute cholangitis - an update. World J Gastrointest Pathophysiol. 2018;9(1):1–7. doi:10.4291/wjgp.v9.i1.1
6. Aboelsoud M, Siddique O, Morales A, Seol Y, Al-Qadi M. Early biliary drainage is associated with favourable outcomes in critically-ill patients with acute cholangitis.

Prz Gastroenterol. 2018;13(1):16–21. doi:10.5114/pg.2018.74557
7. Dumonceau JM, Kapral C, Aabakken L, Papanikolaou IS, Tringali A, Vanbiervliet G, et al. ERCP-related adverse events: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2020;52(2):127–49. doi:10.1055/a-1075-4080
8. Meseeha M, Attia M. Endoscopic Retrograde Cholangiopancreatography. In: StatPearls. Treasure Island (FL): StatPearls Publishing; August 8, 2023.
9. Iqbal U, Khara HS, Hu Y, Khan MA, Ovalle A, Siddique O, et al. Emergent versus urgent ERCP in acute cholangitis: a systematic review and meta-analysis. Gastrointest Endosc. 2020;91(4):753–60.e4. doi:10.1016/j.gie.2019.09.040
10. Khamaysi I, Taha R. ERCP for severe acute cholangitis: The earlier, the better. Turkish J Gastroenterol. 2020;31(1):78–9. doi:10.5152/tjg.2020.19103
11. Manes G, Paspatis G, Aabakken L, Anderloni A, Arvanitakis M, Ah-Soune P, et al. Endoscopic management of common bile duct stones: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2019;51(5):472–91. doi:10.1055/a-0862-0346
12. Hou LA, Laine L, Motamedi N, Sahakian A, Lane C, Buxbaum J. Optimal timing of endoscopic retrograde cholangiopancreatography in acute cholangitis. J Clin Gastroenterol. 2017;51(6):534–8. doi:10.1097/MCG.0000000000000763
13. Lyu Y, Wang B, Ye S, Cheng Y. Impact of the timing of endoscopic retrograde cholangiopancreatography for the treatment of acute cholangitis: a meta-analysis and systematic review. Surg Laparosc Endosc Percutaneous Tech. 2022;32(6):764–9. doi:10.1097/SLE.0000000000001110
14. Kiriyama S, Kozaka K, Takada T, Strasberg SM, Pitt HA, Gabata T, et al. Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). J Hepatobiliary Pancreat Sci. 2018;25(1):17–30. doi:10.1002/jhbp.512
15. Lee F, Ohanian E, Rheem J, Laine L, Che K, Kim JJ. Delayed endoscopic retrograde cholangiopancreatography is associated with persistent organ failure in hospitalised patients with acute cholangitis. Aliment Pharmacol Ther. 2015;42(2):212–20. doi:10.1111/apt.13253
16. Parikh MP, Wadhwa V, Thota PN, Lopez R, Sanaka MR. Outcomes associated with timing of ERCP in acute cholangitis secondary to choledocholithiasis. J Clin Gastroenterol. 2018;52(10):e97–102. doi:10.1097/MCG.0000000000000982
17. Harish Patel V. Acute cholangitis: does the timing of ERCP alter outcomes?. JOP J Pancreas. 2016;17(5):504–9.
18. Mulki R, Shah R, Qayed E. Early vs late endoscopic retrograde cholangiopancreatography in patients with acute cholangitis: A nationwide analysis. World J Gastrointest Endosc. 2019;11(1):41–53. doi:10.4253/wjge.v11.i1.41
19. On W, Watters C, Dwyer L, Hood S, Saleem R, Sturgess R, et al. P55 Timing of ERCP and outcomes in patients with acute gallstone cholangitis graded by severity. Gut. 2021;70(Suppl 1):A69.1–A69. doi: 10.1136/gutjnl-2020-bsgcampus.130
20. Khashab MA, Tariq A, Tariq U, Kim K, Ponor L, Lennon AM, et al. Delayed and unsuccessful endoscopic retrograde cholangiopancreatography are associated with worse outcomes in patients with acute cholangitis. Clin Gastroenterol Hepatol. 2012;10(10):1157–61. doi:10.1016/j.cgh.2012.03.029
21. Navaneethan U. Factors predicting adverse short-term outcomes in patients with acute cholangitis undergoing ERCP: A single center experience. World J Gastrointest Endosc. 2014;6(3):74. doi:10.4253/wjge.v6.i3.74
22. Kohga A, Suzuki K, Okumura T, Yamashita K, Isogaki J, Kawabe A, Kimura T. Does preoperative MRCP imaging predict risk for conversion to subtotal cholecystectomy in patients with acute cholecystitis?. Surgical Endoscopy. 2021;35:6717–23. doi:10.1007/s00464-020-08175-2
23. Zhu Y, Tu J, Zhao Y, Jing J, Dong Z, Pan W. Association of timing of biliary drainage with clinical outcomes in severe acute cholangitis: A retrospective cohort study. Int J Gen Med. 2021;14:2953–63. doi:10.2147/IJGM.S315306
24. Athigakunagorn J, Rujitanon P, Jaseanchiun W, Kasetsuwan P. Does the timing of ERCP affect to the outcomes of acute cholangitis?. J Assoc Gen Surg Thail. 2021;2564(2):43–53.
25. Boender J, Nix GA, de Ridder MA, Dees J, Schütte HE, van Buuren HR, et al. Endoscopic sphincterotomy and biliary drainage in patients with cholangitis due to common bile duct stones. Am J Gastroenterol. 1995;90(2):233–8.