

# Efficacy and safety of endoscopic retrograde cholangiopancreatography for the treatment of acute biliary pancreatitis with or without cholangitis

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## Summary

**Objective:** To evaluate the result of endoscopic retrograde cholangiopancreatography (ERCP) for treatment of acute biliary pancreatitis (ABP) with or without cholangitis. **Subject and method:** A retrospective cohort study, 30 patients of ABP at Institute of Gastroenterology and Hepatology, 108 Military Central Hospital, from January 2019 to November 2021. **Result:** We divided the patients into 2 groups: 19 patients ABP with cholangitis, 11 patients without cholangitis. Mean age:  $60.7 \pm 17.9$  (26 - 92), male/female (1.5). The technical success rates were 94.7% and 100%, the clinical success rates were 100% and 90.9% of the two groups with and without cholangitis, respectively. The concomitant cholangitis was not associated with the timing of ERCP ( $p=0.192$ ), technical success rate ( $p=0.439$ ), and clinical success rate ( $p=0.367$ ). And the total length of hospital stay was not different between the two groups ( $7.7 \pm 3$  vs.  $7.7 \pm 4.1$  days,  $p=0.974$ ). No significant differences were found in the duration of hospital after ERCP or procedural-related complications, in patients with acute biliary pancreatitis, according to the concomitant disease (with vs without cholangitis). **Conclusion:** These findings support ERCP could be performed effectively and safely in acute biliary pancreatitis with or without cholangitis.

**Keywords:** Acute biliary pancreatitis, cholangitis, common bile duct stone, endoscopic retrograde cholangiopancreatography.

## 1. Background

Acute pancreatitis (AP) is among the most common gastrointestinal diagnosis for acute inpatient hospital admission. Worldwide, the incidence of AP ranges between 13 and 45 per 100,000 population. It is well known that alcohol and gallstone diseases are the primary causes, accounting for more than two-thirds of the cases of

AP [5, 7]. The acute biliary pancreatitis (ABP) event is an impaction of gallstones or sludge in the common bile duct and ampulla leading to increased pancreatic ductal pressure, pancreatic edema, inflammation, and possibly necrosis. Patients with ABP can develop cholangitis, organ failure, and other life-threatening complications. Endoscopic retrograde cholangiopancreatography (ERCP) with stone removing or stent placement could induce biliary decompression and impede progression into pancreatic necrosis [7]. But it is unclear whether ERCP is beneficial and safe for ABP patients with or without cholangitis. The aims of our study were to evaluate the result of ERCP for the treatment of acute biliary pancreatitis with or without cholangitis.

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## 2. Subject and method

### 2.1. Subject

We recruited 30 patients that were diagnosed with acute biliary pancreatitis and treated by ERCP at Institute of Gastroenterology and Hepatology, 108 Military Central Hospital, from January 2019 to November 2021. Exclusion criteria included acute pancreatitis due to other causes, absence of common bile duct (CBD) stone, a previous sphincterotomy or needle knife precut, or a history of chronic pancreatitis.

### 2.2. Method

In a retrospective cohort study, data were collected by using a standardized case record form in-hospital.

*Criteria:* Acute pancreatitis was defined as the presence of at least two of the following criteria: upper abdominal pain; serum amylase or lipase concentration more than three times the upper serum limit of normal; features of acute pancreatitis on imaging. The biliary cause was defined by either biliary sludge or gallstones on imaging, a dilated common bile duct on imaging ( $> 8\text{mm}$  in patients aged  $\leq 75$  years or  $> 10\text{mm}$  in patients aged  $> 75$  years), or an alanine aminotransferase (ALT) concentration of more than twice the upper limit of normal [5].

Cholangitis was defined based on the Tokyo Guidelines 2018 criteria including at least one item of both three groups: Systemic inflammation, cholestasis, and imaging of obstructed cause [6].

A biliary obstruction without cholangitis was defined as a biliary obstruction sign, such as a dilated CBD or jaundice, without any of the symptoms of cholangitis mentioned above [1].

The total length of the hospital stay was defined as the time between admission to and discharge, and the duration of hospitalization after ERCP was defined as the time between performing ERCP and discharge. ERCP-related complications were defined as following conditions: Gastrointestinal bleeding, duodenal perforation, cardiovascular complications such as myocardial infarction, cerebrovascular

accident, or shock; and post-ERCP pancreatitis diagnosed according to the signs and symptoms of pancreatitis with elevated pancreatic enzymes after ERCP.

The severity of pain was defined by the Visual Analogue Scale (VAS)

*ERCP procedure:* 30 patients were divided into two groups: with and without cholangitis. The ERCP procedures were performed by three experienced endoscopists who had at least 5 years of experience; each had previously performed  $> 1,000$  ERCP procedures. ERCPs were performed under conscious sedation with diazepam and pethidine, and monitoring was done by an anesthesiologist. All ERCPs were conducted under fluoroscopic guidance ERCP in acute biliary pancreatitis to diagnose and manage the obstruction using a large (4.2mm) accessory channel duodenoscope (JF-240, TJF 260V; Olympus Optical Co., Ltd., Tokyo, Japan). Cannulation of the common bile duct (CBD) was attempted with a conventional cannula (Contour ERCP cannula; Boston Scientific, Natick, MA, USA) with or without a guidewire, or with a pull-type sphincterotome (Clever-cut [Olympus Optical] or Autotome RX 44 [Boston Scientific]). A precut papillotomy was attempted when conventional cannulation methods failed. Collect the data of clinical, laboratory characteristics at hospital admission, result of ERCP treatment.

*Outcomes:* In both groups, the primary outcomes were total length of hospitalization and ERCP-related complications. The secondary outcomes included mortality, technical success rate, and clinical success rate. Technical success was defined as successful removal of stones or sludge from the bile duct. Clinical success was defined as normalization of the serum levels of pancreatic enzymes and relief of symptoms, such as abdominal pain.

*Statistical analysis:* SPSS software version 22.0. Chi-square or Student's t-test were performed. A two-sided p value of less than 0.05 was considered significant.

### 3. Result

**Table 1. Baseline characteristics**

	AP and concomitant biliary disease		p
	With cholangitis (n = 19)	Without cholangitis (n = 11)	
Male	13 (68.4)	6 (54.5)	0.696
Age, years (range)	58.8 ± 18.6	64.8 ± 14.7	0.37
Symptom on admission			
Abdominal pain (VAS)	7 ± 0.9	6.4 ± 1.6	0.242
Nausea/Vomitting	3 (15.8)	4 (36.4)	0.199
Jaundice	13 (68.4)	5 (45.5)	0.266
Fever	9 (47.4)	0	0.006
Leukocyte (G/l)	15.2 ± 5.8	7.1 ± 2.4	0.004
Amylase serum (U/l)	990.6 ± 691.2	614.8 ± 496.5	0.126
Lipase serum (U/l)	3819.8 ± 3721.7	1952.1 ± 1785.3	0.131
ALT (U/l)	290.9 ± 249	211.3 ± 226.4	0.391
Bilirubin serum (umol/l)	65.4 ± 58.9	47.2 ± 32.4	0.353

The mean age of 30 patients was 60.7 ± 17.9 years (min: 26, max: 92), male/female (1.5). Among 30 patients, 19 (63.3%) had acute biliary pancreatitis with concomitant cholangitis and 11 (36.7%) had ABP without concomitant cholangitis. The rate of fever and the level of leukocyte were higher in the concomitant cholangitis group than in the non-concomitant cholangitis group. No differences in any other baseline characteristics were observed between the groups.

**Table 2. Characteristics of ERCP procedures performed in patients**

	ABP with cholangitis (n = 19)	ABP without cholangitis (n = 11)	p
Timing of ERCP (day after admission)	3.2 ± 1.8	4.3 ± 2.3	0.192
Duration of ERCP procedure (min)	17 ± 0.2	16.8 ± 0.4	0.32
Technical success rate	18 (94.7)	11 (100.0)	0.439
Number of CBD stone	2.2 ± 1.9	1.8 ± 0.9	0.581
Dimension of CBD stone (mm)	9.8 ± 4.7	8.2 ± 3.3	0.323
Dimension of CBD dilation (mm)	12.5 ± 5.2	11.8 ± 3.9	0.721
Difficult cannulation	5 (26.3)	4 (36.4)	0.563
Precut	2 (10.5)	1 (9.1)	0.9
Stent placement in the pancreatic duct	2 (10.5)	1 (9.1)	0.9

The characteristics of ERCP performed in 30 patients are described in Table 2. The timing of ERCP of ABP with cholangitis and without cholangitis groups was 3.2 days and 4.2 days after admission, respectively. The duration of ERCP procedure of the two groups was 17 minutes and 16.8 minutes, respectively. The technical success rate was 94.7% (18/19) in the ABP with cholangitis group and 100% (11/11) in the ABP without cholangitis group. One patient had severe cholangitis that threatened biliary shock, then biliary stent placement without stone removal procedure was performed. However, no difference in technical success rate was detected between the two groups (p=0.439). The number and dimension of CBD stones, dimension of CBD dilation were higher in the concomitant cholangitis group than in the non-concomitant cholangitis group, but these differences were non-statistical significance. No differences in any other ERCP procedure

characteristics were observed between the groups. The reasons for technical difficulties of ERCP in both groups were mucosal edema or impacted stones, or anatomical difficulties during cannulation, for example, due to a diverticulum.

**Table 3. Clinical characteristics post-ERCP and hospitalization day**

	<b>ABP with cholangitis (n = 19)</b>	<b>ABP without cholangitis (n = 11)</b>	<b>p</b>
Clinical success rate	19 (100.0)	10 (90.9)	0.367
Duration of hospital after ERCP (days)	4.6 ± 3.4	3.4 ± 1.9	0.253
Total length of hospital stay (days)	7.7 ± 3	7.7 ± 4.1	0.974

Table 3 shows the clinical success rate and hospitalization duration. The clinical success rate was 100% (19/19) in the ABP with cholangitis group and 90.9% (10/11) in the ABP without cholangitis group. No significant difference was observed in the clinical success rate between the two groups ( $p=0.367$ ). One hundred percent in ABP with cholangitis group had not any complications. On the other hand, one patient of ABP without cholangitis group whose ERCP was performed on the third day after admission (early ERCP) had more severe pancreatitis with an elevation of the serum levels of pancreatic enzymes and progress of symptoms, such as abdominal pain and pleural effusion. This patient may have microcholedocholithiasis left in CBD because we performed neither sphincterotomy nor endoscopic balloon papillary large-balloon dilation. After conservative treatment in a few days, this patient was better and we did not perform another ERCP. The ABP with the concomitant cholangitis group tended to have a longer duration of hospitalization after ERCP compared with the non- concomitant cholangitis group (4.6 vs. 3.4 days,  $p=0.253$ ). The total length of hospital stay, which may be associated with cost, was not significantly different between the ABP with cholangitis group and the ABP without cholangitis group ( $7.7 \pm 3$  vs.  $7.7 \pm 4.1$  days,  $p=0.974$ ).

#### 4. Discussion

In the present study, we investigated the prediction of concomitant cholangitis with outcomes of ERCP treatment for acute biliary pancreatitis. Based on the results of this study,

concomitant cholangitis is not different from non-concomitant cholangitis in terms of complications or hospitalization duration. Furthermore, there were no differences in the technical or clinical success rates between the two groups.

The ESGE guideline published in 2018 [1] recommended urgent (less than 24 hours) ERCP and biliary drainage in patients with acute biliary pancreatitis combined with cholangitis. In the presence of cholangitis, urgent ERCP should be done only after hemodynamic stabilisation and relieved organ hypoperfusion with aggressive fluid replacement and antibiotic treatment within the first 24 hours. ERCP should be performed within 72 hours in patients with ongoing biliary obstruction that was defined as common bile duct stone and/or abnormal bilirubin and/or common bile duct dilation. This guideline also explained why ERCP should not be performed in a patient with severe pancreatitis without cholangitis: "A possible explanation why urgent ERCP with sphincterotomy within 24 hours did not show an advantage over conservative treatment could be that the opportunity to positively influence the disease course had already passed at the time of the ERCP, despite the fact that it was performed early. It is well known that most bile duct stones in patients with gallstone pancreatitis cause only temporary obstruction and pass spontaneously into the duodenum" [1]. It is the reason why some Western authors suggested waiting for 48 hours to implement an ERCP, as the impacted stone may fall down spontaneously and if the signs of obstruction persist after 48 hours, then the endoscopists should think about ERCP [7]. However, the prevalence of

choleliathisis in Eastern countries differed from that in Western countries. In the West, the majority of CBD stones are composed of cholesterol stones that originate from the gallbladder. On the other hand, in the East, because of a higher incidence of chronic biliary tree infection and infestation, the occurrence of pigment stones is much more common. This condition, which begins with inflammation in the bile ducts, is referred to as recurrent cholangitis [8]. It is the reason why common bile duct stones in Eastern patients should be removed instead of waiting for them to fall down spontaneously.

Several clinical trials have aimed to identify the necessity of ERCP for ABP patients with or without cholangitis, to reduce the rate of mortality and complications. Neoptolemos et al. [3] showed that patients with predicted severe acute pancreatitis had fewer complications if they underwent early ERCP (within 72 hours of admission; 24% vs. 61%,  $p=0.05$ ). Folsch et al. [2] reported that early ERCP was not beneficial in patients with ABP but without obstructive jaundice and cholangitis. On the other hand, Novikov A et al [4] reported that ERCP performed during in-patient admission for ABP without cholangitis was associated with decreased mortality, with best results occurring when intervention was performed between 3 and 9 days post-admission. Patients who had a shorter time to ERCP had a shorter length of stay when compared to those who had procedures later. This study supports ERCP in patients with acute biliary pancreatitis without cholangitis.

This study had several limitations. First, it used a nonrandomized, retrospective design. The optimal study design is a prospective, randomized control trial, not an observational study. However, we tried to exclude confounders related to the cause of acute biliary pancreatitis, such as the absence of stone in the common bile duct, or other factors that could cause pancreatitis, such as alcoholic or metabolic disorder diseases. Second, the present study had a small sample size. Table 3 shows that there was only one patient of ABP with the non-concomitant group had post-ERCP pancreatitis. Even if the proportion of complications in the two groups did not differ significantly, there was a possibility of a type II error

considering the small sample size. Because of the small number of patients per group, the study was underpowered to detect meaningful differences. It might indeed be that early ERCP in ABP with cholangitis group is associated with a lower complication rate compared to ABP without cholangitis group.

## 5. Conclusion

In conclusion, these findings support the notion that ERCP could be performed in acute biliary pancreatitis with or without cholangitis. ERCP is a highly effective and safe method of treatment for patients with acute pancreatitis due to common bile duct stones with or without cholangitis.

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