

# Early Versus Delayed Laparoscopic Cholecystectomy after Endoscopic Retrograde Cholangio-Pancreatography (ERCP) Removal of Choledocholithiasis: An Evidence-based Case Report

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## ABSTRACT

**Aim:** To determine the preferred method of treatment in patients with choledocholithiasis after endoscopic retrograde cholangiopancreatography (ERCP) by evaluating efficacy of early laparoscopic cholecystectomy compared to delayed laparoscopic cholecystectomy.

**Method:** Literature searching was carried out on two databases, PubMed and Cochrane, according to the inclusion and exclusion criteria. Two randomized clinical trial (RCT) studies were appraised critically for validity, importance, and applicability.

**Results:** Early laparoscopic cholecystectomy after ERCP shows lower outcomes in incidence of recurrent choledocholithiasis, acute cholecystitis, duration of hospitalization, and treatment costs ( $p < 0.05$ ). Meanwhile, there was no significant difference ( $p > 0.05$ ) between the two groups regarding the incidence of biliary adhesions, bleeding during cholecystectomy, and laboratory parameters such as total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma glutamyl transferase (GGT).

**Conclusion:** Early cholecystectomy, within three days after ERCP, is recommended for the treatment of choledocholithiasis after ERCP removal.

**Keywords:** early cholecystectomy, delayed cholecystectomy, ERCP, choledocholithiasis

## ABSTRAK

**Tujuan:** menentukan metode tatalaksana pada pasien dengan koledokolitiasis pasca ERCP, apakah kolesistektomi segera dibandingkan dengan kolesistektomi elektif memberikan efikasi lebih baik.

**Metode:** Penelusuran artikel penelitian dilakukan pada dua database yaitu Pubmed dan Cochrane sesuai kriteria inklusi dan kriteria eksklusi yang ditetapkan. Dua artikel digunakan menggunakan metode randomized clinical trial (RCT) ditelaah kritis terhadap validitas, importance, dan applicability.

**Hasil:** Kolesistektomi segera pasca ERCP menunjukkan insiden koledokolitiasis berulang, kolesistitis akut, durasi perawatan, serta biaya kesehatan yang lebih rendah ( $p < 0,05$ ). Sementara itu, tidak terdapat perbedaan bermakna ( $p > 0,05$ ) antara kedua kelompok terkait insiden adhesi bilier, perdarahan saat kolesistektomi, dan parameter laboratorium seperti bilirubin total, enzim aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma glutamyl transferase (GGT).

**Simpulan:** Kolesistektomi segera, dalam kurun waktu tiga hari pasca ERCP, lebih disarankan digunakan sebagai tatalaksana koledokolitiasis.

**Kata kunci:** kolesistektomi segera, kolesistektomi elektif, ERCP, koledokolitiasis

## INTRODUCTION

Choledocholithiasis, known as gallstones in common bile duct, accounts for about 1% to 15% of patients with cholelithiasis. Risk factors include women, obesity, metabolic syndrome, and fatty liver.<sup>1</sup> Etiology of choledocholithiasis is the formation of stones from the common bile duct or rocks from the vesica fellea that come out and then settle in the common bile duct.<sup>1</sup> Choledocholithiasis needs proper treatment because it can cause complications such as jaundice, recurrent abdominal pain, infections such as cholecystitis, and even sepsis.<sup>1</sup> Treatment modality is endoscopic retrograde cholangiopancreatography (ERCP) which aims to extract clogged up bile in the duct.<sup>2</sup> Then the following action is cholecystectomy so that the gallstones do not form again.<sup>1,2</sup>

The issue of when to perform cholecystectomy after ERCP is a matter of debate.<sup>1,2</sup> Opinions differ as to whether cholecystectomy is performed immediately after ERCP, known as early cholecystectomy, or electively after ERCP, known as delayed cholecystectomy. This review discusses which method is more effective, whether early cholecystectomy or delayed cholecystectomy after ERCP removal procedure of choledocholithiasis.

## CLINICAL QUESTION

A 50-year-old male patient was admitted to the hospital, sent from the gastroenterology clinic for ERCP with suspicion of choledocholithiasis with the chief complaint of recurrent right upper abdominal pain one month before hospital admission accompanied by jaundice. ERCP examination revealed the presence of gallstones in the common bile duct, and extraction of these stones was performed. This patient's action plan is cholecystectomy, considered immediately or early in hospitalization or can be done delayed, postponed, and scheduled later from the polyclinic. Is early cholecystectomy better than

delayed cholecystectomy after the ERCP procedure in patients with choledocholithiasis?

## METHOD

Literature searching was carried out in two databases, PubMed and Cochrane, using the keywords listed in Table 1. The keywords used were choledocholithiasis, immediate cholecystectomy, elective cholecystectomy, and ERCP. The inclusion criteria were included: clinical trial study design or meta-analysis, English, and human research subjects. Meanwhile, the exclusion criteria were research subjects outside the substance of this paper, such as acute pancreatitis and stones in the pancreas. After applying these criteria, a screening of duplicate articles found in the two databases was carried out, and a search for available journal articles in the form of full articles resulted in two pieces. These two articles will then be critically reviewed for validity, research results, and application using the *Center for Evidence-Based Medicine guidelines* of the University of Oxford. Exclusion criteria using in this report include: acute pancreatitis, stone in pancreas and unreported time of cholecystectomy. These criteria are used because: (1) acute pancreatitis and stone in pancreas is not suitable if we compared to this patient in this report, and (2) timing of cholecystectomy is crucial because determining when to do because the aim of this report is to elaborate the timing cholecystectomy, after the procedure ERCP.

## RESULTS

Two studies were included for critical appraisal. The articles correspond to the clinical question and the inclusion criteria used. One article written by Nakeeb et al (2016) conducted a double-blind randomized clinical trial. Another article written by Muhammedoglu B and Kale IT (2020) conducted a single-blind randomized clinical trial.

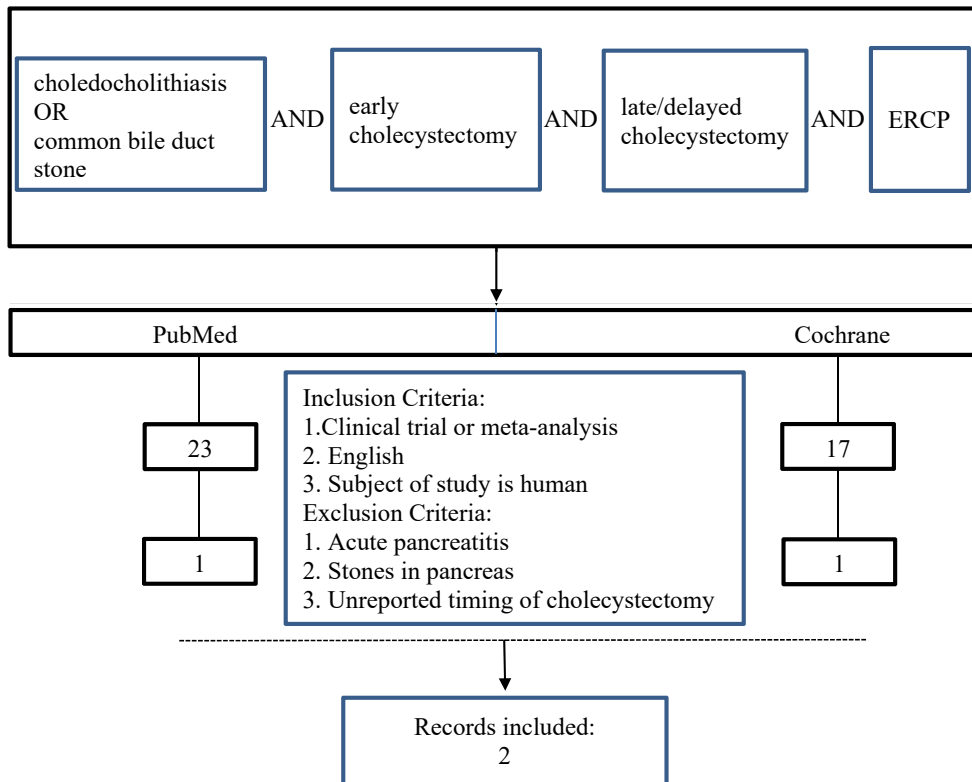


Figure 1. Literature search flowchart

Table 1. Literature search strategy

Database	Keywords	Hits	Included
PubMed	(((Choledocholithiasis[Title/Abstract] OR common bile duct stone[Title/Abstract] OR CBD stone[Title/Abstract]) AND ((early cholecystectomy)[Title/Abstract])) AND ((late cholecystectomy[Title/Abstract] OR delayed cholecystectomy)[Title/Abstract])) AND (ERCP[Title/Abstract])	23	1
Cochrane	"choledocholithiasis" and "early cholecystectomy" and "late cholecystectomy" and "ERCP"	17	1

Critical appraisal of the two articles shown in Table 2. The critical appraisal includes aspects of validity, importance, and applicability of each article. The rating of evidence resulting from this paper is level II.<sup>3</sup> The clinical trial used in this paper assessed the efficacy of immediate cholecystectomy compared with elective cholecystectomy in cases of choledocholithiasis following ERCP procedures.

Result of critical appraisal from two articles consistently demonstrated that laparoscopic cholecystectomy performed immediately after ERCP was more effective. These efficacy include the higher incidence of recurrent choledocholithiasis and acute cholecystitis in the delayed cholecystectomy group. However, the incidence, such as biliary adherence, bleeding during surgery, was not significantly different between the two groups. Early cholecystectomy has shown other positive effects, such as shorter duration of hospitalization and lower healthcare cost.

## DISCUSSION

Both of the included research articles are randomized, blinded clinical trial.<sup>4,5</sup> The first article used a double-blind randomized clinical trial and the second article used a single-blind randomized clinical trial.<sup>4</sup> Both articles provide interventional laparoscopic cholecystectomy in populations who have undergone ERCP for indications of choledocholithiasis.<sup>5</sup> The difference in the intervention is the duration of time, divided into two, namely early cholecystectomy, performed within three days after ERCP, and delayed cholecystectomy, completed within 4 weeks to 6 weeks after ERCP.<sup>4,5</sup> According to EASL guideline (2016), the preferred option is ERCP which is done before the procedure of laparoscopic cholecystectomy. The reasoning is lower incidence of ERCP-related pancreatitis, shorter length of hospital stay, and lower healthcare cost.<sup>6</sup>

Table 2. Critical appraisal

	Indicators	Nakeeb et al (2016)	Muhammedoglu B dan Kale IT (2020)
Validity	a) Was the assignment of patients to treatments randomized?	Yes	Yes
	b) Were the groups similar at the start of the trial?	Yes	Yes
	c) Aside from the allocated treatment, were groups treated equally?	Yes	Yes
	d) Were all patients who entered the trial accounted for? And were they analyzed in the groups to which they were randomized?	Yes	Yes
	e) Were measures objective or where the patients and clinicians kept "blind" to which treatment was being received?	Yes	No
Importance (results)		There was no significant difference ( $p > 0.05$ ) with outcomes such as adhesions of the gallbladder and biliary tract to surrounding structures, bleeding during laparoscopic cholecystectomy, injury to common bile ducts. In the delayed cholecystectomy group, there was a significant difference in the incidence of recurrent choledocholithiasis, acute cholecystitis, and pancreatitis ( $p = 0.03$ ).	There was no significant difference between liver enzymes (AST, ALT), total bilirubin, and GGT between immediate cholecystectomy and elective cholecystectomy. There is a significant difference in the duration of treatment and health costs. ( $p < 0,05$ ).
Applicability	a) Is my patient so different to those in the study that the results cannot apply?	Yes	Yes
	b) Is the treatment feasible in my setting?	Yes	Yes
	c) Will the potential benefits of treatment outweigh the potential harms of treatment for my patient?	Yes	Yes

Critical appraisal on validity aspects of the two included studies are generally fine and meet the proper validity criteria.<sup>4,5</sup> The research subjects involved in the study were randomized using simple random sampling. They had similar demographic characteristics in the two treatment groups before the laparoscopic cholecystectomy intervention, including gender, age, leukocytes, total bilirubin value, and liver function. The limitation in the second journal is the randomization allocation of the subject is known by the researcher so that it does not make it "blind." The number of *lost to follow-up* in these two articles did not exist. All participating research subjects, 110 subjects in the first article and 117 subjects in the second article, were analyzed.<sup>4,5</sup>

The outcomes assessed in the two groups consisted of clinical aspects (recurrent choledocholithiasis, acute cholecystitis, biliary adhesions, bleeding during cholecystectomy), laboratory aspects (total bilirubin, AST, ALT enzymes, and gamma GT), and social aspects (duration of hospitalization and cost of treatment). In the group treated with early cholecystectomy, within three days after ERCP, the incidence of recurrent choledocholithiasis, acute cholecystitis, duration of hospitalization, and health costs were lower ( $p < 0.05$ ).<sup>4,5</sup> Meanwhile, there was no

significant difference ( $p > 0.05$ ) between the two groups regarding the incidence of biliary adhesions, bleeding during cholecystectomy, and laboratory parameters such as total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma glutamyl transferase (GGT).<sup>4,5</sup>

The mechanism that explains, it is that cholecystectomy is performed delayed within 4 weeks to 6 weeks after ERCP provides more time for re-formation of the stones.<sup>7</sup> The inflammatory process continues so that choledocholithiasis and cholelithiasis are likely to recur. If the obstruction occurs again, there is a possibility of infection such as acute cholecystitis. This explanation shows that urgency of immediately to remove the gallbladder after ERCP for stone extraction is necessary so that stones do not re-form and the subsequent inflammatory cascade can be prevented.<sup>7,8</sup>

The results of these two articles can be applied to these patients because they are clinically appropriate for patients with choledocholithiasis who have recently undergone ERCP.<sup>9</sup> This immediate cholecystectomy method of management can be applied in the sense that after ERCP is performed, the patient is referred to digestive surgery for laparoscopic cholecystectomy.<sup>10</sup> This method provides more excellent benefits, such as avoiding the risk of recurrent choledocholithiasis and

acute cholecystitis. In addition, it has other positive impacts, shorter duration of hospitalization, and lower treatment costs.

## CONCLUSION

Early laparoscopic cholecystectomy is suggested in cases of choledocholithiasis after the ERCP procedure because of lower healthcare cost. The recommendation for the patient is to consult a digestive surgeon to perform a laparoscopic cholecystectomy within three days after the ERCP procedure.

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