

# Comparison of one-stage endoscopic retrograde cholangiopancreatography and cholecystectomy versus two-stage endoscopic retrograde cholangiopancreatography and cholecystectomy for treatment of cholelithiasis with choledocholithiasis

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## Introduction

The optimal management of symptomatic or suspected common bile duct (CBD) stone continues to be controversial despite the fact that laparoscopic cholecystectomy (LC) has turned out to be the standard method for gallbladder removal and despite innovations in endoscopy and laparoscopic surgery.

## Aim

The aim of this study was to compare the two-stage intervention [endoscopic retrograde cholangiopancreatography (ERCP) under total intravenous anesthesia followed by interval LC] with the one-stage intervention (ERCP combined with LC) in terms of feasibility, safety, effectiveness, and hospital stay.

## Patients and methods

Eighty patients admitted to the Medical Research Institute, University of Alexandria, during the interval between January 2012 and January 2013, diagnosed as having cholelithiasis with choledocholithiasis proven by laboratory and radiological investigations (abdominal ultrasonography and/or MRCP), were studied prospectively, and they were classified into two equal groups: group A, in which a two-stage procedure was performed; and group B, in which a one-stage procedure was performed. Data were recorded, including patients' demographic, endoscopic, and operative details, success rate, postoperative complication (ERCP and LC), overall operative time, and length of hospital stay.

## Results

The operative time was significantly lower in the two-stage group (group A). There were no statistically significant differences between both groups as regards CBD stone retrieval, morbidity rates, or the mean hospital stay.

## Conclusion

Taking in consideration that our results showed no statistical difference between the two groups, there is still no gold standard of care for patients having chronic calculi cholecystitis and CBD stones. We prefer separating the two procedures in our routine practice.

## Keywords:

choledocholithiasis, cholelithiasis, endoscopic retrograde cholangiopancreatography, laparoscopic cholecystectomy

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## Introduction

Choledocholithiasis is a common surgical problem affecting about 3.5–10% of all patients with gallstone disease [1,2]. Traditional surgery in the form of open cholecystectomy and common bile exploration was the standard treatment for many years. However, in the past decades, traditional surgery has been replaced by minimal invasive surgery, especially after the advent of endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) [3]. Although laparoscopic cholecystectomy (LC) has turned out to

be the standard method for gallbladder removal, yet, there is still debate about the most effective and efficient method of clearing choledocholithiasis [3–5].

This has led to evolution of a range of therapeutic alternatives offered to patients, according to patient characteristics, stage of disease, or even physician

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experience and preference. These therapeutic modalities are as follows: (a) preoperative ERCP and ES followed by elective LC, (b) laparoscopic or open common bile duct (CBD) exploration with cholecystectomy, (c) intraoperative ERCP during LC 'rendezvous' technique [6], or (d) LC followed by ERCP and ES.

Preoperative ERCP and ES followed by LC is currently the most widely used procedure, yet not without a considerable percentage of complications [7] and prolonged hospital stay [8]. Endoscopic stone removal after LC (two-stage approach) had a failure rate of ~5%, where an additional procedure is mandatory to extract the CBD stone [9]. Intraoperative ERCP during LC requires specialized endoscopic devices and a longer operating time [10] and might be associated with excessive abdominal distension, which might hinder safe excision of gallbladder.

The aim of our study was to compare the one-stage intervention (ERCP combined with LC) versus the two-stage intervention (ERCP under total intravenous anesthesia-interval-LC) in terms of feasibility, safety, effectiveness, and hospital stay.

## Patients and methods

All patients gave their formal consent. The protocol was approved the ethical committee of the Medical Research Institute. The study was conducted on patients admitted to the Medical Research Institute, University of Alexandria, diagnosed as having cholelithiasis with choledocholithiasis proven by laboratory and radiological investigations (abdominal ultrasonography and/or MRCP) during the interval between January 2012 and January 2013.

Exclusion criteria for the study were as follows: patients presenting with acute pancreatitis or acute cholangitis, pregnancy, malignant pancreatic or biliary tumors, previous sphincterotomy, unfit for anesthesia and surgery, radiologically documented stones larger than 2 cm in horizontal diameter, and history of gastric bypass (e.g. gastrectomy or bariatric bypass surgery).

Eligible patients, 80 in number, were classified into two groups: two-stage and single-stage treatment groups.

All endoscopic procedures and endoscopies were performed by the same team (authors of the paper) who had good experience in both endoscopic and laparoscopic management of biliary stones (>1000 career ERCPs, with an ongoing workload of >200 ERCPs annually).

## Group A: two-stage group

The patients in this group were defined as having 'two-stage treatment', where preoperative ERCP and ES were performed with CBD stone extraction using a balloon or a basket. Patients with failed cannulation were scheduled for another trial after 1 week; in patients with incomplete stone extraction (residual stones), a plastic stent was inserted and patients were scheduled for another trial for stone extraction where lithotripsy or large balloon dilatation was performed. Patients were then scheduled to undergo LC within the next 3 days of the previous ERCP.

In all patients in this group, ERCP was performed under total intravenous anesthesia using a combination of propofol and ketamine with cardiopulmonary monitoring throughout the procedure by an anesthesiologist. All procedures were planned to be performed as an outpatient procedure where patients are discharged 2 h after complete recovery.

## Group B: intraoperative endoscopic retrograde cholangiopancreatography group

The patients in this group were defined as having 'single-stage treatment', where both ERCP and LC were performed in the same setting under general anesthesia. The patient was positioned in the prone position while performing ERCP and then turned to the supine position to have the cholecystectomy done.

All patients underwent continuous cardiopulmonary monitoring throughout the procedure by an anesthesiologist.

LC was performed with four-trocar technique by the same surgical team. Laparoscopic or open CBD exploration is added for LC in cases of failed cannulation or incomplete stone extraction.

Data were prospectively recorded, including patients' demographic, endoscopic, and operative details, success rate, postoperative complication (ERCP and LC), overall operative time, and length of hospital stay. These data were compiled using an SPSS computer program (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). All values were expressed as mean and range.

## Results

### Group A (staged management) outcome

This group included 40 patients, 11 male and 29 female, with a mean age of 53.1 years, ranging from

22 to 70 years Table 1. All patients had CBD dilatation based on ultrasound (US) examination, with a mean bilirubin level of 3.7 mg/dl. Nine patients had MRCP as their US examination showed biliary dilatation with normal laboratory level of bilirubin, and in all the nine patients MRCP showed floating CBD stones. Computed tomography (CT) examination was performed for three patients to exclude neoplasia.

ERCP was performed at the endoscopy unit with the patient under total intravenous anesthesia in prone position, with 97.5% cannulation success rate and complete stone extraction in 33 (82.5%) patients; one patient required stone crushing, another patient required large balloon dilatation, and 7.5% revealed no stones. In patients with failed cannulation, ERCP was repeated after 7 days and stone extraction was completed successfully. In three (7.5%) patients stone extraction was incomplete because of angulated stone in one patient and large stone in one patient, and because of bleeding from sphincterotomy with subsequent edema formation in the third patient, which prevented safe stone retrieval; a second ERCP was scheduled after 15 days, where stone extraction was performed in two patients and stone crushing was required in the third one (Table 2).

**Table 1 Demographic data of patients**

	One-stage	Two-stage
Number of patients	40	40
Age	52.1 (18–74)	53.1 (22–70)
Sex (male/female)	15/25	11/29
Total bilirubin (mg/dl)	4.2±2.3	3.7±1.9
Alkaline phosphatase	419±291	394±299
Ultrasound	40 (100)	40 (100)
CT	1 (2.5)	3 (7.5)
MRCP	6 (15)	9 (22.5)

Qualitative data were described using *n* (%). Normally quantitative data were expressed as mean±SD, whereas abnormally distributed data were expressed using median (minimum–maximum). CT, computed tomography; MRCP, magnetic resonance cholangiopancreatography.

**Table 2 Endoscopic retrograde cholangiopancreatography data**

	One-stage	Two-stage
No stones	3 (7.5)	3 (7.5)
Complete stone extraction	31 (77.5)	31 (77.5)
Incomplete stone extraction with stent insertion	4 (10)	3 (7.5) <sup>a</sup>
Failed cannulation	1 (2.5)	1 (2.5) <sup>b</sup>
Stone crushing or dilatation	1 (2.5)	2 (5)

Qualitative data were described using *n* (%). ERCP, endoscopic retrograde cholangiopancreatography. <sup>a</sup>ERCP was repeated after 2 weeks. <sup>b</sup>ERCP was repeated after 1 week.

Mean duration of ERCP was 27 min. Patients were discharged 2 h after the procedure with full instructions on possible complications. As long as they are not scheduled for another trial of ERCP, patients were scheduled to have a surgical procedure with a median time of 2 days (Table 3).

Cholecystectomy was completed laparoscopically in all patients with a mean operative duration of 43.5 min, which showed significantly shorter duration than the one-stage group. The mean duration for hospital stay was 3.33 days, which was insignificantly longer than the other group.

As regards complications, one patient developed acute post-ERCP pancreatitis, but it completely resolved with conservative medical treatment and LC was done after 6 weeks, and one patient developed cholangitis and it resolved with conservative medical treatment, and LC was performed after 6 weeks.

Readmission was required for four patients – after 7 days for one patient with failed cannulation and after 15 days for three patients with failed primary extraction of CBD stones.

#### Group B (one-stage) outcome

This group included 40 patients, 15 male and 25 female, with a mean age of 52.1 years, ranging from 18 to 74 years, Table 1. All patients had CBD dilatation based on US examination, with a mean bilirubin level of 4.2 mg/dl; MRCP was performed for six patients,

**Table 3 Duration of the procedure**

	One-stage	Two-stage	<i>P</i> value
Hospital stay	2.85±1.42	3.33±1.28	0.12
ERCP duration (min)	27.1±10.6	26.6±8.4	0.4
Cholecystectomy duration (min)	55.6±21.1	43.5±18.8	0.004 <sup>*</sup>

Normally quantitative data were expressed as mean±SD. ERCP, endoscopic retrograde cholangiopancreatography. <sup>\*</sup>Statistically significant at *P*≤0.05.

**Table 4 Operative details**

	One-stage ( <i>n</i> =40)	Two-stage ( <i>n</i> =40)
Laparoscopic cholecystectomy	34 (85)	40 (100)
Laparoscopic CBD exploration	1 (2.5)	0
Open CBD exploration with no T-tube	3 (7.5)	0
Open cholecystectomy	1 (2.5)	0
Open CBD exploration with T-tube	1 (2.5)	0

Qualitative data were described using *n* (%). CBD, common bile duct.

whereas CT examination was performed for one patient for similar reasons as in group A.

ERCP was performed in the operating theatre with the patient under general anesthesia in prone position, with 97.5% cannulation success rate and complete stone extraction in 32 (80%) patients; one patient required stone crushing and 7.5% revealed no stones, Table 2.

Mean duration of ERCP was 27 min, and the time interval until the start of surgical procedure was about 20 min; the mean duration of surgical operation was 55.6 min, which was significantly longer than group A ( $P=0.004$ ) (Table 3).

Cholecystectomy was completed laparoscopically in 34 patients, and it was converted to open cholecystectomy in one patient; open cholecystectomy and CBD exploration were done in four patients, with direct closure of CBD without T-tube insertion in three of them. Laparoscopic choledocotomy was performed in one patient, with direct closure and no T-tube insertion (Table 4).

The mean duration for hospital stay was 2.9 days.

As regards complications, two patients developed acute post-ERCP pancreatitis, which completely resolved under conservative medical treatment, and two patients developed cholangitis, which also resolved with conservative medical treatment.

Readmission was required for four patients after 30 days for removal of biliary stents, and they were discharged on the same day.

#### Group comparison

The mean hospital stay was insignificantly less in group B, whereas the operative time was significantly shorter in group A:  $P$  value less than 0.05. There were no statistically significant differences between both groups as regards CBD stone retrieval or morbidity rates.

#### Discussion

Before the era of LC, management for concomitant choledocholithiasis and cholelithiasis was carried out using open CBD exploration or ERCP, followed by open cholecystectomy and CBD exploration for failed stone extraction by ERCP. However, after LC became the standard management for cholelithiasis, there was much debate upon the best management for dealing with 8–20% of patients undergoing LC who have concomitant CBD stones. The management of CBD stones depends more on the technical skills and

experience of the endoscopic or surgical teams than on a clearly established and accepted consensus [10–15].

In our study, all patients were diagnosed as having choledocholithiasis based on ultrasonography, hyperbilirubinemia, and clinical jaundice. In case of nonmatching results or suspicion of neoplastic lesion, MRCP ( $n=15$ ) or CT ( $n=4$ ) was requested. Negative ERCP was encountered in 7.5% ( $n=6$ ), with a positive predictive value for US, MRCP, and CT of 93.4, 93.3, and 100% respectively. Varghese *et al.* [16] has shown a positive predictive value for US and MRCP of 89 and 97, respectively; similar results were obtained by Kats *et al.* [7], with a 97% positive predictive value for MRCP. Negative ERCP was attributed by the authors to be because of stone passing or because of the low specificity of US alone in detecting CBD stones.

The economic status in poor countries has forced medical service providers to change the admission policy toward decreasing costs by decreasing hospital stay and avoiding unnecessary expensive procedures [17]. This was proven to be efficient for high-frequency and low-risk surgical procedures such as cholecystectomy [18]. In our department, patients who have ERCP are discharged on the same day after 2 h of close observation, and instructions on possible complications and the contact information for rapid consultation are given. In our study, patients who were attributed to the two-stage group do have ERCP and discharge according to unit policy on the same day as long as there is no immediate postprocedure complications, and they have to be readmitted on the morning of the operation day and are discharged after full recovery from the cholecystectomy operation according to the discharge policy applied in the department. Applying this concept of unnecessary admission led to insignificantly shorter hospital stay in the single-stage group:  $P$  value more than 0.1.

The success rate for resolution of choledocholithiasis through ERCP with the same setting LC was 80%, which was not significantly different from the 82.5% success rate recorded in the two-stage group for the first trial ERCP. However, this ratio increased to 100% if we consider successful CBD clearance after repeated ERCP in failed cannulation patient and patients with incomplete stone extraction. These rates were similar to the rates reported by Wan *et al.* [19], who showed an 83% success rate in the first ERCP session with an overall success rate of 92%.

Incomplete stone extraction was 10% ( $n=4$ ) in the combined group and 7.5% ( $n=3$ ) in the two-stage



group; in all patients a plastic stent was inserted temporarily, ensuring biliary drainage until complete clearance of CBD. This was achieved in the two-stage group by repeating the ERCP procedure, and in the one-stage group through CBD exploration. Ramirez *et al.* [20] has shown an overall success rate of 95% after repeat ERCP, instead of 87%.

Cholecystectomy with CBD exploration was performed in five patients with successful CBD clearance: open procedure in four patients and laparoscopic in one patient. T-tube was inserted in only one patient who had failed cannulation; the biliary stent was removed later on after 1 month as an outpatient procedure. Direct CBD closure after open or laparoscopic exploration is also recommended by several authors [21–24].

The use of mechanical lithotripsy and large balloon dilatation has been proven to be safe and has increased the success rate of CBD clearance; however, it needs more prolonged procedure and more cost than the traditional method of CBD stone extraction using basket and balloon. Moreover, it might not be useful in stones larger than 2 cm. In this study, stones that are radiologically more than 2 cm were excluded from the study, and the mechanical lithotripsy and large balloon dilatation was used in one patient in the single-stage group and in four patients in the two-stage group.

The duration of cholecystectomy operation was significantly longer in the single-stage group, *P* value less than 0.004; this was attributed by the authors to be a result of intestinal inflation, which increased the time for safe trocar placement and meticulous dissection to avoid bowel injury.

## Conclusion

Taking into consideration that our results showed no statistical difference between the two groups as regards hospital stay, complications, or bile duct clearance, there is still no gold standard of care for patients having chronic calculous cholecystitis and CBD stones. We prefer the two-stage policy in our routine practice.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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