# Endoscopic retrograde cholangiopancreatography plus laparoscopic cholecystectomy versus laparoscopic common bile duct exploration and cholecystectomy for cholecysto-choledocholithiasis – The same operator: a multicenter randomized controlled trial

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**Background**
Laparoscopic cholecystectomy (LC) plus either intraoperative endoscopic retrograde cholangiopancreatography (intraERCP) or laparoscopic common bile duct exploration (LCBDE) are one-stage, minimally invasive procedures to treat cholecysto-choledocholithiasis. This study aimed to compare the safety, efficacy, and surgical outcomes of the LC-intraERCP and LC-LCBDE for patients with cholecysto-choledocholithiasis. Both authors completely performed both procedures.
**Patients and methods**
This multicenter randomized controlled trial included 218 patients with cholecysto-choledocholithiasis randomized to LC-intraERCP ($n=109$) and LC-LCBDE ($n=109$) treatment groups between February 2019 and October 2022. The primary outcome was a technical success, while conversion to open surgery, operative time, morbidity, mortality, length of hospital stay, and cost were considered secondary outcomes.
**Results**
Both groups had no significant differences in success (94.5% for LC-intraERCP and 87.2% for LC-LCBDE) and morbidity rate. The conversion to open surgery, the mean operative time, the length of hospital stay, and the cost were significantly lower in the LC-intraERCP. There was no mortality in either group.
**Conclusion**
LC-intraERCP is safer and more effective than LC-LCBDE for treating cholecysto-choledocholithiasis. Moreover, it is associated with reduced hospital stay and cost.

**Keywords:**
common bile duct stones, intraoperative endoscopic retrograde cholangiopancreatography, laparoscopic common bile duct exploration, one-stage

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## Introduction

Common bile duct stones (CBDS), which occur in 4–20% of patients with symptomatic gallstones [1,2], can cause severe biliary colic, jaundice, cholangitis, and pancreatitis [2]. Therefore, to avoid these severe complications, the European Society for Gastrointestinal Endoscopy has recommended removing all CBDS if the patient can tolerate surgical treatment [3]. Laparoscopic cholecystectomy (LC) has become the treatment of choice for gallstones [2]. However, the optimal management of CBDS is still debatable [1,4]. Currently, there are two minimally invasive treatment procedures available. The first is the two-stage procedure, which includes the sequential laparo-endoscopic treatments, which include LC plus preoperative endoscopic retrograde cholangiopancreatography (LC-preERCP) or LC plus postoperative ERCP (LC-postERCP) [4,5]. The second is a one-stage procedure that includes totally laparoscopic treatment (LC plus laparoscopic common bile duct exploration, LC-LCBDE) and simultaneous laparo-endoscopic treatment (LC plus intraoperative ERCP, LC-intraERCP) [4,5].

LC-preERCP is the standard and preferred treatment method worldwide for cholecysto-choledocholithiasis [6,7]. However, it has some drawbacks, as it is a two-stage technique requiring two hospital admissions, which increases medical expenses [8]. Cost-effectiveness is one of the most serious challenges in healthcare, and there is no doubt that reducing hospital length of stay is one of the most efficient strategies for reducing costs [1].

Recently, many studies compared the one- and two-stage techniques and concluded that one-stage procedures are more efficacious, safer, and associated with a shorter hospital stay and reduced healthcare costs [9–11]. As a result, LC-intra-ERCP and LC-LCBDE have been suggested as effective alternatives and gained more popularity in recent years [5]; however, most previous studies and the latest consensus guidelines have collectively failed to demonstrate the superiority of one technique over the other [12,13].

This study aimed to compare the safety, efficacy, and surgical outcomes of two minimally invasive one-stage procedures using laparoscopy (LCBDE) and endoscopy (ERCP) to determine the best treatment approach for patients undergoing LC with choledocholithiasis.

## Patients and methods

### Study design

This is a multicenter, open-label, randomized clinical trial (RCT) with parallel groups. Group 1 was the LC-intraERCP, and Group 2 was the LC-LCBDE. Ethics committee approval for the study was obtained from all centers. This trial was carried out under the Declaration of Helsinki, and the results were reported under the Consolidated Standards of Reporting Trials (CONSORT) guidelines [14]. This trial was registered retrospectively in the ClinicalTrials.gov database. Written informed consent was obtained from all patients before study participation.

### Study participants

This study included all consecutive patients who presented with cholecysto-choledocholithiasis between February 2019 and October 2022 at two tertiary centers in Upper Egypt. The inclusion criteria were patients diagnosed with cholecysto-choledocholithiasis with American Society of Anesthesiologists (ASA) scores of I-III and aged 20–70 years. Patients with severe cholangitis, severe pancreatitis, Mirizzi syndrome, hepatobiliary malignancy, perforated gallbladder, biliary peritonitis, intrahepatic stones, pregnancy, previous ERCP, or contraindications to ERCP or laparoscopic surgery were excluded.

### Sample size calculation and randomization

We calculated the sample size (*https://clincalc.com/Stats/Sample Size.aspxhttps://clincalc.com/Stats/Sample Size.aspx*) based on an estimated success rate of 87% in ERCP and 69% in LCBDE [15], with a power of 90% and a reliability of 0.05. It was calculated that 105 patients were needed for each group. Nurses who weren't involved in the study randomly assigned patients to the LC-intraERCP or LC-LCBDE groups by opening a sealed opaque envelope during surgery after IOC and confirmation of choledocholithiasis. The envelopes were prepared at a 1:1 ratio, carefully jumbled, and placed in an opaque box. Blinding was not performed (Fig. 1).

### Preoperative assessment

All patients were evaluated clinically (history of biliary colic, cholangitis, pancreatitis, or jaundice), laboratory (elevated levels of bilirubin or alkaline phosphatase), and radiologically (abdominal ultrasonography showing possible CBDS or dilated CBD >7 mm) for parameters suggesting CBDS. All suspected patients underwent magnetic resonance cholangiopancreatography (MRCP) for confirmation. Computed tomography (CT) was done in selected cases. Expert radiologists reported on all radiological investigations.

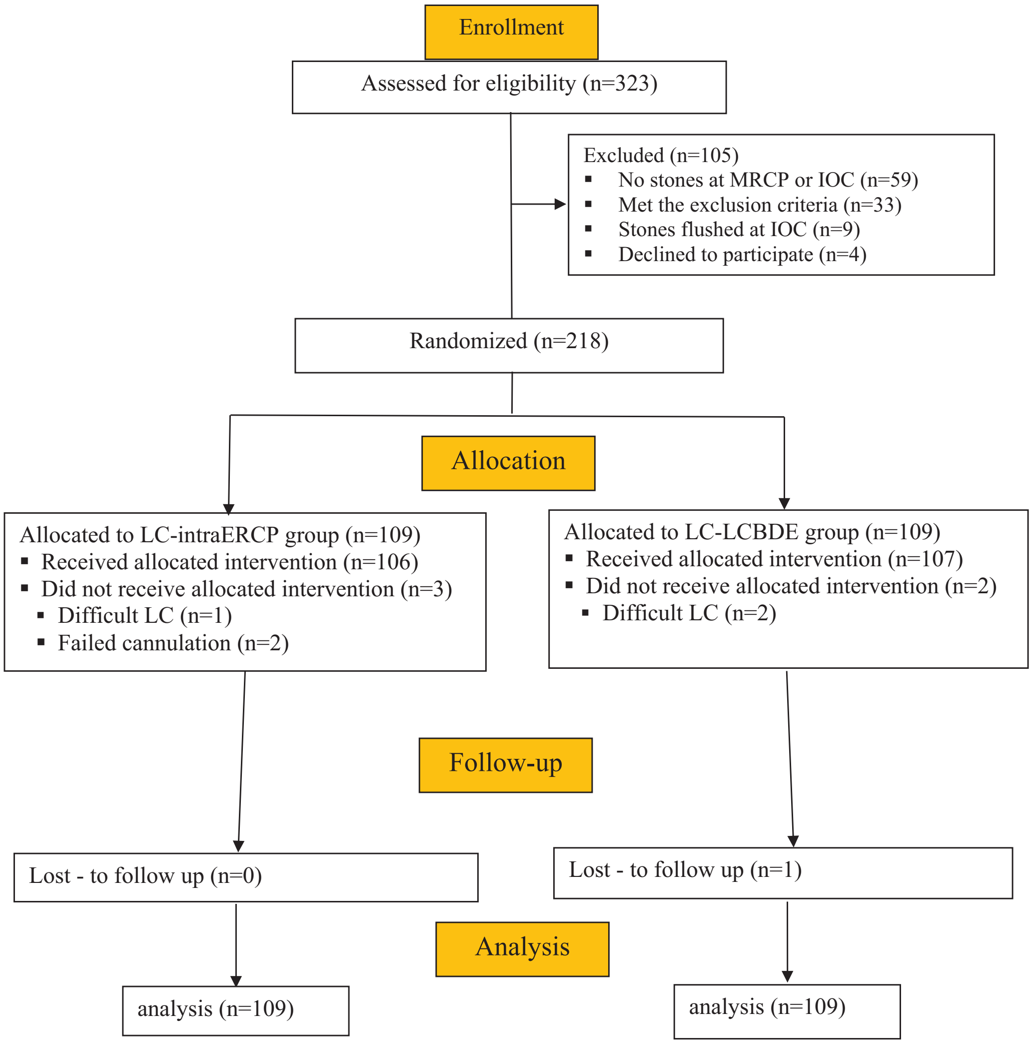
### Operative procedure

Two consultant surgeons with at least 10 years of experience in LC, LCBDE, and ERCP performed all procedures. We initially inserted three ports, adding a fourth or fifth port accordingly. We started with the dissection of Calot's triangle, identification, clipping, and cutting of the cystic artery. Then, we clipped the cystic duct higher near the gallbladder, and a small incision was made to insert the cholangio-catheter (ERCP cannula) through the right midclavicular port for performing an IOC. If the IOC revealed small CBDS suitable for flushing, a saline flush with intravenous glucagon or butylscopolamine was tried. Only patients with cholangiographic findings confirming large CBDS, which were not amenable or failed to be flushed, were randomized to one of the two study groups. Failure of dissection of the Calot's triangle and performing an IOC cancel the procedure and convert to open surgery. LC was performed according to the SAGES Safe Cholecystectomy Program.

### ERCP

ERCP was performed in the prone position after finishing the LC and removing the ports by the same surgeon. Deep cannulation was attempted with a biliary cannula, a sphincterotome, or a precut needle. The endoscopic sphincterotomy was performed using a sphincterotome. The balloon sphincteroplasty was performed when indicated. A retrieval balloon or basket catheter removed stones under fluoroscopic

**Figure 1**




Flow of participants in the RCT According to CONSORT. MRCP: magnetic resonance cholangiopancreatography; IOC: intraoperative cholangiogram; LC-intraERCP: laparoscopic cholecystectomy- intraoperative endoscopic retrograde cholangiopancreatography; LC-LCBDE: laparoscopic cholecystectomy-laparoscopic common bile duct exploration.

guidance. Large stones (>15 mm) were removed with mechanical lithotripsy. After biliary tract irrigation, a balloon occlusion cholangiogram was performed to ensure complete clearance of the CBD. Biliary or pancreatic drainage stents were inserted if indicated. Intraoperative ‘rendezvous’ facilitation of cannulation via a 0.035-inch guidewire introduced through the cystic duct down through the sphincter of Oddi and into the duodenum was tried in cases of failed standard cannulation.

#### LCBDE

LCBDE was performed either through a trans-cystic or trans-choledochal approach, based on the anatomy and size of the cystic and common bile ducts as well as the number, size, and location of the CBDS. The trans-choledochal approach was used when the CBD diameter was >8 mm, cystic duct anatomy was unfavourable, large CBDS (>10 mm), multiple CBDS (>4), proximal CBDS, impacted CBDS, or after the failure of a trans-cystic approach [16]. The trans-cystic procedure was performed under fluoroscopic guidance, while the trans-choledochal procedure was undertaken either under fluoroscopic guidance or direct vision using a 5-mm flexible choledochoscope when available. Stone extraction was usually performed with saline flushing, a retrieval basket, and a retrieval balloon catheter. No electrohydraulic lithotripsy was used. Choledochorraphy was performed with or without biliary drainage. Completion cholangiography was routinely performed in all patients after clearance of CBDS.

#### Postoperative assessment

Oral fluids were administered as tolerated. All patients received 3rd generation cephalosporin for 5–7 days postoperatively. The subhepatic drain was removed in the absence of discharge. The patient was discharged once oral fluid was tolerated, and the pain was controlled with oral analgesia. If a T-tube was inserted, a trans-tubal cholangiogram was performed on the 14th postoperative day. If the cholangiogram was clear, the T-tube was removed, while if there was a retained stone, the patient was prepared for ERCP.

### Follow-up

The patients were followed-up at the outpatient clinic on the 7th, 14th, and 30th postoperative days and then annually. The follow-up evaluation included a clinical examination, bilirubin level, abdominal ultrasound, and T-tube cholangiography. MRCP was done when indicated. The patients were advised to return if they complained of recurring symptoms or suspected complications at any time.

### Outcomes

The primary outcome was a technical success, while conversion to open surgery, operative time, morbidity, mortality, length of hospital stay, and cost were considered secondary outcomes. Technical success was defined as removing the gallbladder and CBDS by the intended procedure [5,8]. Potential causes of failure included a failed planned approach, retained stones, or the need for conversion to other procedures [5,8]. Morbidity was defined as any intraoperative or postoperative adverse event that altered the clinical course or needed reintervention [17,18]. Morbidity was graded according to the Clavien-Dindo system [19]. Retained or recurrent stones are any biliary tract stones detected within or after 2 years of the procedure [15]. Procedure time is from randomization to the completion cholangiography in the LC-LCBDE group and from the duodenoscope introduction to the occlusion cholangiography in the LC-intraERCP group. The operative time was from the start of anesthesia to its end. We considered the morbidity and mortality rates as the primary measures of safety and the success rates as an indicator of efficacy [4].

### Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS 25.0, Inc., Chicago, IL, USA).

**Table 1 Patients demographics and clinical characteristics**

| Variables | LC-intraERCP (*n*=109) | LC-LCBDE (*n*=109) | *P* value |
|---|---|---|---|
| **Age** (years)[1] | 47.19±8.22 | 46.75±8 | 0.69 |
| **Sex** (Female)[2] | 63 (57.8) | 65 (59.6) | 0.78 |
| **BMI** (Kg/m$^2$)[1] | 26.83±2.32 | 26.9±2.28 | 0.81 |
| **ASA score**[2] | | | 0.26 |
| I | 69 (63.3) | 58 (53.2) | |
| II | 29 (26.6) | 40 (36.7) | |
| III | 11 (10.1) | 11 (10.1) | |
| **Laboratory findings** | | | |
| Bilirubin (mg/dl)[3] | 7 (4.5-8) | 7 (4-8) | 0.98 |
| Alkaline phosphatase (IU/l)[3] | 198 (114-256) | 213 (127-271) | 0.08 |
| **CBD diameter**[1] | 13.28±5.01 | 12.1±4.37 | 0.07 |
| **CD diameter**[1] | 3.58±1.12 | 3.47±0.88 | 0.42 |
| **CBDS number**[2] | | | 0.89 |
| Single | 36 (33) | 35 (32.1) | |
| Multiple | 73 (67) | 74 (67.9) | |
| **CBDS size**[1] | 7.65±2.65 | 7.88±2.31 | 0.50 |
| **Preoperative diagnosis**[2] | | | 0.96 |
| Obstructive jaundice | 83 (76.1) | 83 (76.1) | |
| Biliary colic | 9 (8.3) | 10 (9.2) | |
| Asymptomatic | 17 (15.6) | 16 (14.7) | |
| **Preoperative imaging**[2] | | | 0.91 |
| Ultrasonography | 109 (100) | 109 (100) | |
| MRCP | 109 (100) | 109 (100) | |
| CT | 7 (6.4) | 6 (5.5) | |

ASA, American Society of Anesthesiologists; BMI, body mass index; CBD, common bile duct; CBDS, common bile duct stone; CD, cystic duct; CT, computed tomography; LC-intraERCP, laparoscopic cholecystectomy- intraoperative endoscopic retrograde cholangiopancreatography; LC-LCBDE, laparoscopic cholecystectomy-laparoscopic common bile duct exploration; MRCP, magnetic resonance cholangiography.

[1]mean±SD.

[2]no (%).

[3]median (IQR1–IQR 3).

Normally distributed data were confirmed using the Shapiro-Wilk test. Categorical variables are expressed as frequencies (n) and percentages (%) and were compared using the chi-square test. Normally distributed variables are expressed as mean±standard deviation (SD) and were compared using the Student's *t*-test. Non-normally distributed variables are defined as the median and interquartile range (IQR, Q1-Q3) and were compared using the Mann-Whitney *U* test. A *P* value of 0.05 or less was considered statistically significant.

## Results

### Patient flow

Between February 2019 and October 2022, 323 consecutive patients with suspected cholecysto-choledocholithiasis were evaluated for eligibility. After applying the inclusion and exclusion criteria, 218 patients were randomly assigned to the LC-intraERCP and LC-LCBDE groups ($n$=109). The analysis was based on the intention to treat regardless of failed procedures or loss of follow-up (Fig. 1). The median follow-up was 19 months until April 2023. Table 1 shows the two groups' patient demographics and clinical characteristics; no significant differences existed (Table 1).

LC-intraERCP was successful in 103 patients (94.5%) and failed in 6 patients (5.5%). LCBDE managed failed cases in five patients and open surgery in one patient. LC-LCBDE was successful in 95 patients (87.2%) and failed in 14 (12.8%). In order to manage failed cases, 12 patients underwent open surgery, and 2 patients underwent postoperative ERCP. Although the success rate was higher in the LC-intraERCP, both groups had no significant difference. There was no significant difference in the conversion to other procedures between both groups (5.5% vs. 12.8%, $P$=0.059); however, the conversion rate to open surgery was significantly higher in the LC-LCBDE group (0.9% vs. 11%, $P$<0.0001).

Also, although the proportion of patients with complications was more than double in the LC-LCBDE group compared with that in the LC-intraERCP group (20.2% vs. 8.3%), this was not significantly different ($P$=0.17). In the LC-intaERCP group, complications occurred in 9 patients (8.3%), and 6 patients had more than one complication. Four patients had minor complications, which were managed medically. Five patients had major complications. Four patients had retained ($n$=2), and recurrent stones ($n$=2) were managed with ERCP and stone extraction, and one patient had basket trapping and was managed with LCBDE. In the LC-LCBDE group, complications occurred in 22 patients (20.2%), and 17 patients had more than one complication. Seven patients had minor complications, which were managed medically. Twelve patients had major complications. Six patients presented with biliary colic and obstruction due to retained or recurrent CBDS at 3, 5, 11, 19, 25, and 33 postoperative months. They were managed with ERCP and stone extraction. Two patients presented with repeated cholangitis due to biliary stricture, and they were treated with ERCP and a biliary plastic stent. Biliary peritonitis occurred in one patient; he explored, and CBD was repaired over a plastic stent. One patient experienced subhepatic collection, and he received percutaneous drainage treatment. One patient had excessive intraoperative bleeding that could not be controlled laparoscopically, and he converted to open surgery. Finally, one patient developed a migrated CBD stent, and ERCP extracted it. The incidence of overall complications was significantly higher in the LC-LCBDE group (13.8% vs. 36.7%; $P$<0.012); however, the incidence of major complications was not significantly different between both groups (4.6% vs. 11%; $P$<0.07). There were no deaths in both groups (Tables 2 and 3).

The mean operative time (113 vs. 160 min, $P$<0.001), the length of hospital stay (2 vs. 3 days, $P$<0.001), and the total cost (26,064 vs. 33,192 E£, $P$<0.001) were significantly lower in the LC-intraERCP (Table 2). Also, the median number of abdominal ports (4 vs. 5 ports, $P$<0.01), the use of an abdominal drain (33.9% vs. 89%, $P$<0.01), the procedure operative time (40 vs.

**Table 2 Primary and secondary outcomes**

| Variables | LC-intraERCP ($n$=109) | LC-LCBDE ($n$=109) | $P$ value |
|---|---|---|---|
| **Success rate**[1] | 103 (94.5) | 95 (87.2) | 0.061 |
| **Conversion to open surgery**[1] | 1 (0.9) | 12 (11%) | 0.0001 |
| **Total operative time** (min)[2] | 113.92±20.84 | 160.73±34.07 | **0.001** |
| **Complications**[1] | 9 (8.3) | 22 (20.2) | 0.17 |
| **Mortality**[1] | 0 | 0 | 0 |
| **Hospital stay** (days)[3] | 2 (1-2) | 3 (2-3) | **0.001** |
| **Cost** (E£)[2] | 26064.22 ±3086.04 | 33192.66 ±7331.41 | **0.001** |

E£, Egyptian pound; LC-intraERCP, laparoscopic cholecystectomy-intraoperative endoscopic retrograde cholangiopancreatography; LC-LCBDE, laparoscopic cholecystectomy-laparoscopic common bile duct exploration.
[1]no (%).
[2]mean±SD.
[3]median (IQR1–IQR 3).
Bold numerals indicate a statistically significant difference.

**Table 3 Comparison between LC intra-ERCP and LC-LCBDE**

| Variables | LC-intraERCP (*n*=109) | LC-LCBDE (*n*=109) | *P* value |
|---|---|---|---|
| **Causes of failure**[1] | 6 (5.5) | 14 (12.8) | 0.059 |
| Failed stone extraction. | 2 | 9 | |
| Difficult LC | 1 | 2 | |
| Excessive bleeding | 0 | 1 | |
| Retained stone | 0 | 2 | |
| Failed cannulation | 2 | 0 | |
| Basket trapping | 1 | 0 | |
| **Conversion to other procedure**[1] | 6 (5.5) | 14 (12.8) | 0.059 |
| LCBDE | 5 | 0 | |
| OC-OCBDE | 1 | 11 | |
| Post-ERCP | 0 | 2 | |
| OC-OCD | 0 | 1 | |
| **Complications**[1] | 15 (13.8)* | 40 (36.7)** | **0.012** |
| **Grade I** | 5 (4.6) | 19 (17.4) | **0.001** |
| Bile leak | 2 | 10 | 0.12 |
| Wound infection | 2 | 6 | 0.07 |
| Fever | 1 | 3 | |
| **Grade II** | 5 (4.6) | 9 (8.3) | |
| Pancreatitis | 4 | 1 | |
| Paralytic ileus | 0 | 1 | |
| Adhesive intestinal obstruction | 0 | 1 | |
| T-tube related complications | 0 | 2 | |
| Other | 1 | 4 | |
| **Grade III a/b** | 5 (4.6) | 12 (11) | |
| Bile leak | 0 | 1 | |
| Biliary stricture | 0 | 2 | |
| Retained stones. | 2 | 4 | |
| Recurrent stones | 2 | 2 | |
| Sub hepatic collection | 0 | 1 | |
| Stent migration | 0 | 1 | |
| Bleeding | 0 | 1 | |
| Basket trapping | 1 | 0 | |
| **Complications** | | | 0.09 |
| Short-term | 11 (10.1) | 30 (27.5) | |
| Long-term | 4 (3.7) | 10 (9.2) | |
| **Number of abdominal ports**[1] | | | **0.01** |
| Three | 22 (20.2) | 0 (0) | |
| Four | 87 (79.8) | 37 (33.9) | |
| Five | 0 (0) | 72 (66.1) | |
| **Blood loss** (ml)[2] | 80 (50–100) | 100 (100–120) | 0.09 |
| **Blood transfusion**[1] | 1 (0.9) | 3 (2.8) | 0.313 |
| **Abdominal drain**[1] | 37 (33.9) | 97 (89) | **0.01** |
| **Readmissions**[1] | 4 (3.7) | 13 (11.9) | **0.023** |
| **Reinterventions**[1] | 4 (3.7) | 12 (11) | **0.038** |

DVT, deep venous thrombosis; LC-intraERCP, laparoscopic cholecystectomy- intraoperative endoscopic retrograde cholangiopancreatography; LC-LCBDE, laparoscopic cholecystectomy-laparoscopic common bile duct exploration; OC-OCBDE, open cholecystectomy-open common bile duct exploration; OC-OCD, open cholecystectomy-open choledochoduodenostomy; post-ERCP, postoperative ERCP.
[1]no (%).
[2]median (IQR1–IQR 3).
*6 patients have more than one complication.
**17 patients have more than one complication.
Bold numerals indicate a statistically significant difference.

128 min, $P<0.001$), readmission (3.7% vs. 11.9%, $P<0.023$), and reintervention (3.7% vs. 11%, $P<0.038$) were significantly lower in the LC-intraERCP. The median blood loss and the patient's need for transfusion were higher in the LC-LCBDE group (100 vs. 80 ml and 3 vs. 1 patient, respectively); however, the differences did not reach statistical significance (Table 3).

Three patients were shown to have no CBDS after cannulation and ES, and two of them were managed with CBD stents due to suspected strictures. Also, two patients failed to show CBDS after choledochotomy, although the IOC was positive, and a choledochoscope confirmed this. Tables 4 and 5 report specific ERCP and LCBDE outcomes (Tables 4 and 5).

## Discussion

For several years, the standard management for cholecysto-choledocholithiasis was open cholecystectomy and open CBD exploration. Recently, with the development of laparoscopy and endoscopy, many minimally invasive options, either LC plus ERCP (pre, intra, or postoperative) or LCBDE, have become available. However, the best treatment option is still controversial [8].

**Table 4 ERCP outcomes**

| Variable | ERCP (*n*=109) |
|---|---|
| **Successful cannulation**[1] | 106 (97.2) |
| **Technique of cannulation**[1] | |
| Standard sphincterotomy | 97 (89) |
| Precut sphincterotomy | 7 (6.4) |
| Rendezvous technique | 2 (1.8) |
| **Methods of extraction**[1] | |
| Basket extraction | 55 (50.5) |
| Balloon extraction | 22 (20.2) |
| Combined balloon and basket extraction | 16 (14.7) |
| Mechanical lithotripsy | 13 (11.9) |
| **Procedure time** (min)[2] | 40.6±13.2 |

ERCP, endoscopic retrograde cholangiopancreatography.
[1]no (%).
[2]mean±SD.

**Table 5 LCBDE outcomes**

| Variable | LCBDE (*n*=109) |
|---|---|
| **Rout stone extraction**[1] | |
| Trans-choledochal | 95 (87.2) |
| Trans-cystic | 11 (10.1) |
| **Visualization**[1] | |
| C-arm. | 77 (70.6) |
| Choledochoscope | 29 (26.6) |
| **Methods of extraction**[1] | |
| Irrigation | 7 (6.4) |
| Basket | 12 (11) |
| Balloon | 19 (17.4) |
| Combined | 59 (54.1) |
| **Methods of CBD closure**[1] | |
| Ante-grade CBD stent | 71 (65.1) |
| Primary | 15 (13.8) |
| T-tube | 9 (8.3) |
| **Time of LCBDE** (min)[2] | 128±22 |

CBD, common bile duct; LCBDE, laparoscopic common bile duct exploration.
[1]no (%).
[2]mean±SD.

The first option is the LC-preERCP. The European Association for the Study of the Liver recommends it [2], and currently, it is the most commonly practiced and preferred option worldwide. It is safe and highly successful (94%) in eliminating CBDS [18,20]. However, it has some drawbacks. First, Only 40–60% of patients will have stones on ERCP due to high negative results (40–70%) or spontaneous passage of small stones in the interval between the diagnosis and the ERCP. As a result, many patients may undergo unnecessary and risky ERCP [17,21]. Second, 13% of preoperative endoscopic stone clearance patients still have CBDS during LC due to previously retained or new CBD stones [22]. Third, it needs two operative interventions and occasionally two hospital admissions, which lengthen the hospital stay and raise costs [23,24]. Fourth, some patients may avoid LC if the results of preERCP are sufficient for them, which exposes them to recurrent biliary problems [25]. Finally, prior ERCP may negatively impact LC in the form of a higher risk of conversion and difficulty, a prolonged operative time, a higher postoperative infection, and a prolonged hospital stay [26].

The second option is the LC-postERCP. It is not typically regarded as the primary treatment choice for CBDS. There is still a possibility of failed ERCP (3–10%), which requires another surgical intervention [27]. It is usually indicated when CBDS is accidentally discovered during LC with no facilities for LCBDE or intraERCP [28].

The third option is LC-intraERCP. It had a comparable or better stone clearance rate than pre-ERCP but needed more expertise and experience [9]. It has several advantages. First, it is a one-stage procedure that shortens the hospital stay and minimizes costs [1]. Second, the IOC may allow the avoidance of unnecessary ERCP and its related complications in cases of negative cholangiograms or flushed small stones [17]. Third, a residual contrast from the IOC delineating the biliary system can facilitate deep biliary cannulation [15]. Fourth, Minor bile leaks demonstrated by the cholangiogram can be managed by stent insertion after stone extraction [4]. Fifth, If the procedure fails, the patient can undergo open or laparoscopic surgery in the same session [17]. Finally, a drainage procedure such as a biliary stent or T-tube was unnecessary [29]. Moreover, ERCP has a short learning curve and is available in many hospitals [21,29].

Generally, ERCP carries the risk of post-ERCP complications (5–15%), such as pancreatitis, bleeding, perforation, and cholangitis [13,30]. EST may cause sphincter dysfunction, and it is still not clear if it causes recurrent choledocholithiasis and bile duct cancer due to chronic duodenal and pancreatic fluid reflux and bacterobilia [31,32]. Also, the success rate of ERCP is low in patients with altered gastrointestinal anatomy, such as those who have undergone gastric bypass surgery [33].

The fourth option is LC-LCBDE. It has been proven safe and effective [34,35]. It has the advantages of a one-stage procedure with a successful CBDS clearance rate of 85–100% [36] and occasionally decreases the number of readmissions, shorter overall hospital stays, and lower cost [20,21]. Moreover, LCBDE preserves the function of the sphincter of Oddi and avoids post-ERCP-related complications [8]. Unfortunately, its practice and widespread use have been constrained by its technical challenges, long and complex learning curve, and availability of laparoscopic instruments and a choledochoscope at many hospitals [37,38].

Many papers reported that patients treated with one-stage procedures have a shorter hospital stay and lower hospital costs than those treated with two-stage procedures with similar therapeutic efficacy and safety [20,39]. A few studies have compared the safety and effectiveness of the one-stage procedures in managing cholecysto-choledocholithiasis [8], and they failed to demonstrate the superiority of one technique over the other [12,13]. We thought that the benefits and risks of these one-stage, minimally invasive procedures must be thoroughly analyzed [8].

In a recent meta-analysis, Zha *et al.* [8] found no significant differences between LC-intraERCP and LC-LCBDE in terms of technical success (88.6% vs. 89.6%), overall morbidity (15.3% vs. 10.8%), major morbidity (1.7% vs. 1.1%), or conversion rate (4.4% vs. 5.1). Bile leak (0.5% vs. 2.6%) and retained stones (3.6% vs. 8.5%) were significantly more common in the LC-LCBDE group. Pancreatitis (8.4% vs. 2%) was significantly more common in the LC-intraERCP group. They concluded that both groups had comparable technical success, morbidity, and conversion rates, and the choice should be based on patient characteristics, local resources, and surgeon expertise.

Another meta-analysis by Lie *et al.* [5] reported no significant differences in surgical success, overall complications, conversion to laparotomy, or operative time. The meta-analysis showed that in the LC-intraERCP group, retained stones and bile leaks were lower, while in the LC-LCBDE group, postoperative bleeding and pancreatitis were lower. They advised LC-intraERCP as the first option for cholecysto-choledocholithiasis. Vakayil *et al.* [12] conducted a retrospective analysis of 1814 patients, 34.6% of whom had LC-intraERCP and 65.3% had LC-LCBDE. They reported a significantly shorter mean operative time with LC-intraERCP (113 vs. 125 min). The morbidity, mortality (0.8% vs. 0.2%), median length of hospital stay (3 vs. 3 days), readmission rate (7.2% vs. 4.6%), and reoperation rate (1.7% vs. 2.4%) did not differ significantly. They recommended ERCP as the preferred technique due to its accessibility and shorter operative time, although LCBDE remains a good alternative, particularly in the absence of timely endoscopic intervention. Ricci *et al.* [4] conducted a meta-analysis comparing LC-preERCP, LC-intraERCP, LC-postERCP, and LC-LCBDE based on the results of 20 RCTs. The shortest operative time and the lowest overall cost were recorded for LC-LCBDE, whereas LC-intraERCP had the highest success rate, more safety, and the shortest hospital stay. They concluded that LC-intraERCP was the most successful and safest approach. Poh *et al.* [15] conducted an RCT with 52 patients in LC-intraERCP and LC-LCBDE. They found that the two groups had no statistically significant differences in the duct clearance rate (87% vs. 69%), the complication rate (27% vs. 38%), or the total operative time (112 vs. 110 min). The LC-intraERCP group had a significantly lower rate of retained stones (15% vs. 42%), a shorter procedure time (20 vs. 28 min), and a shorter median length of hospital stay (2 vs. 3 days). They determined that LC-intraERCP outperformed LC-LCBDE regarding duct clearance, retained stone rate, and length of hospital stay. González *et al.* [18] conducted a RCT comparing LC-intraERCP, LC-preERCP, and LC-LCBDE. They found no statistically significant differences in the rates of ductal stone clearance (97.8% vs. 93.3% vs. 97.7%), residual stone (2.2% vs. 11.1% vs. 2.3%), or postoperative complications (2.2% vs. 11.1% vs. 2.3%). They concluded that LC-intraERCP results in a higher stone clearance rate, shorter hospital stays, and lower morbidity. ElGeidie *et al.* [17] conducted an RCT with 111 patients in LC-intraERCP and 115 in LC-LCBDE. They reported no significant differences in the CBD clearance rate (97.2% vs. 92%), operative time (68 vs. 57 min), hospital stay (3.1 vs. 2.2 days), or complication rate

(9.3% vs. 7.1%) between both groups. In the LC-intraERCP group, retained stones were significantly lower (0.0% vs. 3.6%). They concluded that LC-intraERCP might be preferred when endoscopic resources and expertise are available.

In contrast, a recent RCT by Liu *et al.* [40] evaluated 207 patients randomly assigned to either LC-intraERCP or LC-LCBDE. They reported a significantly higher success rate (93.3% vs. 82.5%), short operative time (151 vs. 171 min), less blood loss (179 vs. 384 ml), low morbidity (18% vs. 30%), short hospital stay (4 vs. 6 days), and lower cost (18,000 vs. 29,000) in LC-LCBDE. They concluded that LC-LCBDE was safer and more effective than LC-intraERCP; however, it is not a suitable replacement for LC-intraERCP in all patients, and both techniques should be considered complementary, with their relative advantages in a given patient depending on local resource availability and expertise.

The success rate is one of the most important indicators for evaluating the feasibility and effectiveness of surgery [5]. In our study, the overall success rate was higher in the LC-intraERCP group than in the LC-LCBDE group (94.5% vs. 87.2%); however, there was no statistically significant difference. The high LC-intraERCP success rate may be attributed to some factors. First, in the LC-LCBDE group, the acute presentation of some patients caused inflammation and scarring in the Calot's triangle. This made it difficult to remove stones through the trans-cystic and trans-choledochal routes. Second, in the LC-intraERCP group, due to a high rate of successful CBD cannulation and a low rate of retained stones. There were no significant differences regarding failure rate and conversion to other procedures. However, failed cases in the LC-intraERCP group showed a significantly lower conversion rate to open surgery (0.9% vs. 11%).

Many studies reported no significant differences in operative time [5,15,17]. Riccie *et al.* [4] reported a longer operative time with LC-intraERCP [4,15]. They attributed this to the logistical factors, i.e., installation of the endoscopy unit and the C-arm X-ray set, calling the endoscopist, repositioning the patient, and sometimes changing the operative room [4,15]. Vakayil *et al.* [12] reported that the operative times for LC-intraERCP performed by two different surgical and endoscopic teams were similar (120 min), and the operative times for LC-intraERCP performed by the same surgical team were significantly shorter (108 min) than those for LC-LCBDE (125 min). In our study, the LC-intraERCP had a significantly shorter operative time (113 vs. 160 min). This may be due to the short ERCP procedure time (40 vs. 128 min) and the good logistics, as the same surgeon performed the entire LC-intraERCP in one well-equipped operating room.

Our study revealed a higher complication rate in the LC-LCBDE group (8.3% vs. 20.2%); however, these differences were insignificant. The present study showed that LC-intraERCP was associated with a higher rate of pancreatitis, and LC-LCBDE was associated with a higher rate of bile leak and wound infection. In LC-IntraERCP, accidental cannulation and opacification of the pancreatic duct are risk factors for post-ERCPP pancreatitis [30]. However, most cases were mild and were treated conservatively, which is in line with other studies [41,42]. In LC-LCBDE, the trans-choledochal approach is associated with a higher rate of postoperative bile leakage. This result was consistent with many studies [5,33]. Most studies focused on short-term complications (within 30 postoperative days). A very important prognostic factor for these patients is the long-term complications, such as recurrent stones due to reflux of duodenal juice after endoscopic sphincterotomy and biliary stricture after the closure of choledochotomy [24]. Our study revealed higher long-term postoperative complications in the LC-LCBDE group (3.7% vs. 9.2%), resulting in high readmission (3.7% vs. 11.9%) and reintervention rates (3.7% vs. 11%).

Poh *et al.* [15] said that the number of retained stones is probably a better measure of success than duct clearance because it depends less on how duct clearance is interpreted at the end of the procedure, which may be more subject to differences between observers. Many studies [4,5,15] reported that the ERCP group had a low retained stone rate. They said the endoscopic sphincterotomy may allow spontaneous passage of small missed CBDS. In contrast, in the LCBDE group, this was not possible with an intact sphincter of Oddi. Our study revealed a double rate of retained stones in the LC-LCBDE group (1.8% vs. 3.7%). In contrast, some papers reported no differences in retained stone rates between both groups [17,27,43].

There was a significantly shorter median hospital stay in the LC-intraERCP group (2 vs. 3 days). This finding concorded with many studies [4,15,18]. On the contrary, other studies [12,17,27] reported no statistically significant difference in hospital stay between both groups. Our result noted significantly lower costs in the LC-intraERCP group. Hong *et al.* [27] reported no statistically significant difference in total cost between both groups, while others [4,11] reported significantly lower costs for LC-LCBDE. Recent healthcare cost modeling analyses [12,44] have shown that ERCP may be more cost-effective after considering aspects like short operative time, hospital stay, high success rate, and lower complications rate.

Our study revealed a highly successful ERCP cannulation rate (97.2%), which may be attributed mainly to a residual IOC, which would map a road that facilitates biliary cannulation [15] and use different cannulation techniques and several stone extraction techniques. This finding was consistent with many studies [15,17,27].

The authors reported that some organizational and technical issues had impeded the adoption of the LC-intraERCP.

First, let's assume that the IOC discovers the stones by accident. In this case, it is often hard to ensure that an endoscopist is available quickly and that all endoscopic needs are met, which could result in a long operative time or postpone the ERCP after LC [17,33]. We did not have this problem because all cases were known to have a strong suspicion of CBDS before surgery. Our operating rooms are equipped with both laparoscopic and endoscopic equipment; thus, performing an LC-intraERCP requires minimal setup and time [45]. Al-Mansour *et al.* [46] said that the surgeon's skills, such as interpreting cholangiograms, using electrosurgical current safely, handling tissue gently, and recognizing and dealing with complications, could improve the ERCP procedure [46]. Fortunately, the two authors are surgeons who are highly experienced in laparoscopy and ERCP, and this reduces the need for cross-coordination between surgeons and endoscopists, making the combined technique in the current series possible and more effective [45]. Numerous studies concurred with our conclusion that when carried out by experienced laparo-endoscopic surgeons, LC-intraERCP has a high success rate, a short operative time, and acceptable rates of complications. Otherwise, it requires much work and planning [1,46,47]. The second was the supine position of the patient, which may interfere with the cannulation of the papilla [48,49]. However, some studies reported no effect of the supine position on the success rate [47,50]. In our study, we turned the patient after finishing the LC, and all ERCPs were performed in the prone position. The third was proximal small bowel distension from the insufflated air during ERCP, which may make LC more challenging [48,49]. Ghazal *et al.* [21] reported that bowel distension caused mild LC difficulty but did not prevent safe completion. Getting rid of bowel distension was suggested in many ways, such as finishing gallbladder dissection before starting ERCP [51], using a laparoscopic bowel clamp on the first jejunal loop [52], and reducing inflation and extending aspiration before removing the endoscope [53]. In our study, we finished the LC before the ERCP.

The laparo-endoscopic rendezvous techniques were reported to facilitate CBD cannulation [52]. Cavina *et al.* [54] reported a success rate of 100% of CBDS clearance with a Dormia basket passed through the cystic duct down to the duodenum to pull and guide the sphincterotome into the bile duct. Enochsson *et al.* [49] and Iodice *et al.* [55] reported a success rate of 94% of CBDS clearance with a guidewire passed through the IOC catheter into the cystic duct down to the duodenum to guide the ERCP cannula or sphincterotome over it into the CBD. Moreover, anterograde cannulation of the papilla with laparo-endoscopic rendezvous techniques avoids inadvertent pancreatic duct cannulation, reducing the risk of post-ERCP pancreatitis [27,50]. However, it has some technical problems; it may fail to pass through the spiral valve of the cystic duct or through the papilla due to an impacted CBD stone. Also, it may result in cystic duct injury during manipulation [23]. Therefore, the authors have recommended the rendezvous technique only for cases where the standard cannulation has failed [17,51]. We used rendezvous techniques only with two patients and cannot comment on the previous finding.

In LC-LCBDE, the trans-choledochal approach was associated with an improved bile duct clearance rate [31]. However, it is associated with an increased incidence of postoperative bile leaks compared to trans-cystic LCBDE and ERCP [33,56]. In our study, the trans-cystic approach was used in 12 patients (11%), while the trans-choledochal approach was used in 97 patients (89%), but we did not compare the safety of both techniques. Recently, with technological advancements such as small choledochoscopes, the Laser-Assisted Bile duct Exploration by Laparoendoscopy (LABEL) technique, FREDDY laser lithotripsy, Basket-in-catheter access, and the Multichannel Instrument Guide, many surgeons reported increasing trans-cystic efficacy in dealing with large stones [57–59]. Poh *et al.* [15] reported that CBDS removal is much facilitated by direct visualization with a choledochoscope and enables more precise duct clearance assessment. Our study used the C-arm in 77 patients (70.6%), while the choledochoscope was used in 29 patients (26.6%), but we did not compare the efficacy of both techniques.

### Strengths and limitations

Our study has several strengths. This study is one of the few randomized controlled studies evaluating the outcomes of the LC-intraERCP and LC-LCBDE done by the same surgeons for managing cholecysto-choledocholithiasis. This trial was a multicenter study with a large sample size and high statistical power. Finally, the data collected from our collaborating centers had an exact, homogeneous timing and endpoint. However, this study has some limitations. First, cholangiograms could have been interpreted imprecisely, which could have affected the study results. Second, we did not use choledochoscopy in all LC-LCBDE, which may decrease the success of LCBDE. Finally, intraoperative ERCP and expert endoscopists are not routinely available in all hospitals.

## Conclusion

Our study concluded that LC-intraERCP and LC-LCBDE have comparable success, morbidity, and mortality rates. No procedure can replace the other in all patients, and both procedures should be considered complementary to one another, with the advantages of each for a specific patient based on the patient's characteristics, local resource availability, expertise, and cost-effectiveness. However, centers with available ERCP services, especially with expert laparo-endoscopic surgeons, should consider LC-intraERCP as the first option, as LC-intraERCP is safer, more effective, and associated with significantly reduced operative time, length of hospital stay, and total cost. Considering the lower rates of LCBDE and the inexperience of most surgeons with endoscopic surgery, we recommend that all future surgical training programs for residents and postgraduate surgeons offer advanced LCBDE and ERCP skills training.

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### Conflicts of interest

The authors declare that there is no conflict of interest.

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