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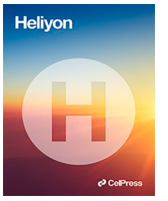

Research article

Clinical application of ERCP concurrent laparoscopic cholecystectomy in the treatment of cholecystolithiasis complicated with extrahepatic bile duct stones

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ABSTRACT

Objective: To compare the clinical efficacy of endoscopic retrograde cholangiopancreatography (ERCP) combined with laparoscopic cholecystectomy (LC) and laparoscopic common bile duct exploration and lithotomy (LCBDE) in the treatment of cholecystolithiasis combined with bile duct stones.

Methods: From September 2018 to January 2022, 195 patients with cholecystolithiasis complicated with extrahepatic bile duct stones from Department of Department of General Surgery, Shanghai Jiading Central Hospital met the inclusion criteria, including 60 cases in the LC group and 86 cases in the LCBDE group. The general condition, operation success rate, complications and residual stone rate of the two groups were retrospectively analyzed.

Results: In the simultaneous operation group, 58 patients successfully performed ERCP, and the indwelling rate of the abdominal drainage tube (41.7 % vs. 95.3 %) was significantly better than that in the LCBDE group. There was no significant difference in the conversion rate to open surgery, operation time, and intraoperative blood loss between the two groups. In the simultaneous surgery group, 4 patients (6.7 %) developed pancreatitis after ERCP, which was cured by conservative treatment. The pain score at 6 h after operation was significantly lower than that in the LCBDE group (3.9 ± 1.6 vs 6.5 ± 2.4). There were no significant differences in biliary leakage (1.7 % vs. 4.7 %), postoperative cholangitis (5.0 % vs. 5.8 %), incision infection (3.3 % vs. 3.5 %), and bile duct stone residue rate (5.0 % vs 3.5 %) between the two groups. There was no severe pancreatitis, second operation or death. The duration of hospital stay was shortened in the concurrent operation group (5.1 ± 2.3d vs 7.9 ± 3.7d), and the operation cost was significantly higher than that in the LCBDE group (48839.9 ± 8549.5 vs 34635.9 ± 5893.7 yuan).

Conclusion: ERCP combined with LC and LCBDE are both safe and effective methods for the treatment of cholecystolithiasis combined with extrahepatic bile duct stones. The simultaneous operation group has certain advantages in patient comfort and rapid rehabilitation, which can be popularized in qualified units.

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1. Introduction

Cholecystolithiasis combined with extrahepatic bile duct stones is one of the common diseases in general surgery [1]. With the development of minimally invasive surgery, ERCP, laparoscopy, choledochoscopy, Spyglass lithotripsy and other technologies, various innovative solutions were provided: for example, ERCP followed by LC, LC simultaneously with common bile duct exploration and choledocholithotomy, and choledochoscopic lithotripsy via T-tube sinus tract, besides, the emergence of the composite operating room offers facilitate for this procedure [2]. In this study, 195 patients diagnosed with gallbladder and extrahepatic bile duct stones were retrospectively analyzed to explore the feasibility and safety of ERCP and simultaneous surgery.

A common clinical gallbladder condition, gallstones typically cause biliary colic, persistent distention discomfort, and right upper abdominal pain [3]. Studies indicate that 10%–15 % of patients with cholecystolithiasis also have extrahepatic bile duct stones, requiring prompt treatment to prevent liver abscesses, cirrhosis, acute bile duct obstruction, and other complications. The surgical removal of extrahepatic bile duct stones is the standard treatment for cholecystolithiasis. Stone removal and clinical symptom relief are the primary goals of surgery [4]. Although the therapeutic efficacy was impressive, the laparotomy procedure was utilized in the past. The risks of upper T tube drainage include bile duct haemorrhage and loss, a lengthy recovery period for patients, and significant surgical stress. Minimally invasive treatments are on the rise because of developments in science and medical technology. A typical treatment is endoscopic retrograde cholangiopancreatography (ERCP) in conjunction with lithotomy [5]. To start, endoluminal cholangiopancreatography (ERCP) is useful for surgical procedures since it may clearly and comprehensively provide angiographic pictures of the biliary tract. Avoiding incisions of the common bile channel is possible with ERCP and lithotomy, which also helps prevent complications and their effects. Laparoscopic cholecystectomy (LC) is a widely recognised method for gallstone treatment [3–5].

2. Material and methods

Ethical approval

This study protocol was approved by the Ethics Committee of Shanghai University of Medicine and Health Sciences (20180910SU).

General data: A total of 195 patients were diagnosed with gallbladder and extrahepatic bile duct stones in Shanghai Jiading District Central Hospital from September 2018 to January 2022. This study was approved by the Ethics Committee of the hospital. 146 patients were enrolled including 60 cases undergoing ERCP concurrent LC and 86 cases undergoing LCBDE (Fig. 1). There were no significant differences in gender, age, body mass index, or preoperative jaundice (total bile >34.2 μmol/L) between the two groups, as shown in Table 1.

Inclusion criteria: ① Adult patients over 18 years old; ② Preoperative CT or MRCP or ultrasound images showed gallbladder and extrahepatic bile duct stones, and bile duct diameter >6 mm; ③ Maximum diameter of bile duct stones <2.5 cm; ④ Patients could tolerate general anesthesia.

Exclusion criteria: ① Patients combined with acute pancreatitis; ② Patients underwent ERCP, biliary enterostomy or

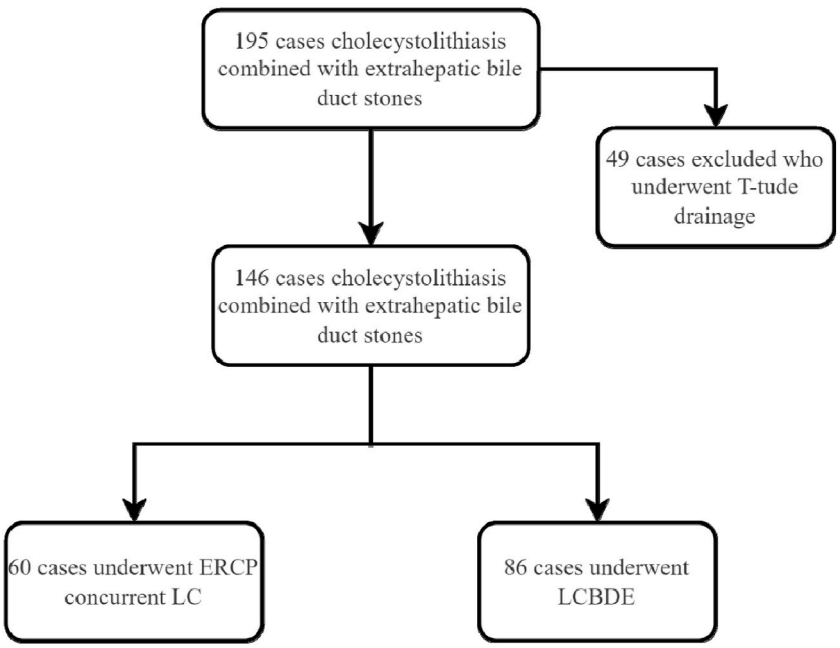

Fig. 1. Flow chart of patients with choledocholithiasis combined with cholecystolithiasis.

Table 1
General information of the two groups.

	ERCP concurrent LC group (n = 60)	LCBDE group (n = 86)	χ2 (t)	P values
Gender (male/female)	27/33	48/38	1.654	>0.05
Age (years)	53.6 ± 11.4	61.2 ± 13.7	1.573	>0.05
Body mass index (kg/m2)	23.2 ± 4.5	20.9 ± 3.8	0.948	>0.05
Complicated with jaundice (cases/%)	4 (6.7 %)	7 (8.1 %)	0.110	>0.05
Operation cost (Yuan)	48839.9 ± 8549.5	34635.9 ± 5893.7	5.732	<0.05
Length of hospital stay (days)	5.1 ± 2.3	7.9 ± 3.7	4.551	<0.05

gastrointestinal anastomosis; ③ Preoperative CT and MRCP showed gallbladder atrophy, Mirizzi syndrome, suspected gallbladder or bile duct tumor, etc; ④ Pregnant or lactating women or patients can not cooperate with ERCP.

Surgical methods: Both groups were operated on under general anesthesia with endotracheal intubation. ERCP concurrent LC group: ① First, ERCP was performed in the prone position with Olympus TJF-180/260 electronic duodenoscope, and CO_2 was injected to reduce abdominal distension and prevent interference to laparoscopic operation [1]. In case of difficulty in intubation during the operation, pancreatic sphincter papillectomy (TPS) and pancreatic duct stent were placed to reduce postoperative pancreatitis (PEP) after ERCP [2]. ② After successful biliary cannulation, sphincterotomy (EST) or combined with papillary balloon dilatation (EPBD) was performed. In the case of large stones, Spyglass-guided hydraulic electro-lithotripsy and nasociliary duct (ENBD) or bile duct stent (ERBD) were placed. ③ Turn over the patient and keep them in the supine position, then perform LC. Generally, the three-hole method or four-hole method is used to dissect the gallbladder triangle, ligation the cystic duct and the gallbladder artery, and remove the gallbladder from the xiphoid process or umbilical incision after stripping, and determine whether to place negative pressure drainage.

LCBDE group: ① CO_2 pneumoperitoneum was established by supraphilical/subumbilical troca puncture the gallbladder triangle was dissected and the choledochal duct was fully exposed by the four-hole method. ② The cystic duct and the gallbladder artery were ligated, the upper section of the common bile duct was slit longitudinally for 6–10 mm, and the stones were removed with a net basket after electronic choledochoscopy. In the case of difficult cases such as incarcerated stones or large stones, the hydraulic electric lithotripter was used. ③ The degree of bile duct inflammation, bile duct diameter, etc., determined whether phase 1 suture was placed T tube; the cystic duct and artery were dissected then the gallbladder [Fig. 2(A-E)].

Perioperative management: ① Routine examination was completed and surgical contraindications were excluded in both groups; fasting for more than 6 h and water restriction for more than 2 h before operation, fasting at least 1 day after operation, with parenteral

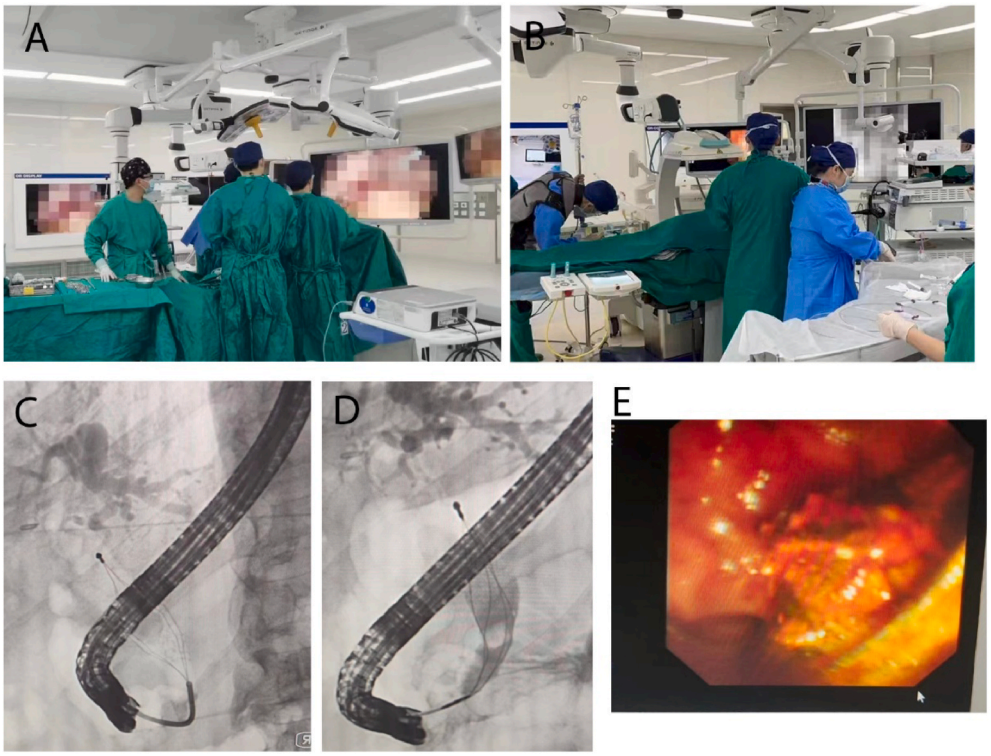

Fig. 2. A. Live performance of laparoscopic common bile duct exploration and lithotomy (LCBDE) in an integrated operating room, B. Live performance of endoscopic retrograde cholangiopancreatography (ERCP) in an integrated operating room, C and D. X-ray of basket-extracting for the bile stones, and E. Endoscopic view of basket-extracting for the bile stones.

nutrition support. ② In the ERCP concurrent LC group, abdominal pain, abdominal distension and vomiting were observed. After the exclusion of PEP assessed by blood amylase, fluid/semi-fluid food was allowed to be eaten 24 h after the operation. ③ In the LCBDE group, observe whether T-tube drainage is unobstructed, whether negative pressure drainage has bleeding or bile leakage, etc., the next day fluid/semi-fluid food was allowed; the T-tube will be removed after 6–8 weeks by ruling out residual stones by angiography/choledochoscopy. ④ After discharge, the patients were followed up for 2–6 weeks, and B ultrasound, liver and kidney function were rechecked.

Observation Indicators: ① General conditions: operation cost, length of hospital stay; ② Intraoperative conditions: ERCP successful rate, conversional rate to open surgery, drainage tube indwelling rate, operational time, blood loss; ③ Postoperative efficacy: VAS pain score (6 h after operation), bile leakage, postoperative cholangitis, incision infection, bile duct stone residue rate, PEP rate, exhaust time.

Statistical analysis: Data were analyzed by the SPSS 23.0 software package, and measurement data were in the form of mean ± standard deviation, and a *t*-test was used. X2 test was used for counting data (rate and constituent ratio), and $P < 0.05$ was considered statistically significant.

3. Results

General Information: The operation cost of the ERCP concurrent LC group was significantly higher than that of the LCBED group (48839.9 ± 8549.5 vs 34635.9 ± 5893.7 yuan, $P < 0.05$), however, the length of hospital stay was significantly shortened (5.1 ± 2.3 vs 7.9 ± 3.7days, $P < 0.05$), as shown in Table 1.

Intraoperative conditions: 58 cases (96.7 %) successfully performed ERCP concurrent LC during the same period, showing a significant advantage in the indwelling rate of the drainage tube (41.7 % vs 95.3 %) ($P < 0.05$), and the conversion rate to open surgery was also lower than that in the LCBDE group (1.7 % vs 7.0 %), but with no statistical difference ($P > 0.05$). There were no significant differences in operation time and intraoperative blood loss between the two groups, as shown in Table 2.

Postoperative efficacy: ERCP concurrent LC group significantly reduced postoperative pain (3.9 ± 1.6 vs 6.5 ± 2.4, $P < 0.05$). There were no significant differences in bile leakage, postoperative cholangitis, incision infection, bile duct residual stone rate, and postoperative exhaust time between the two groups. There were no severe post-ERCP pancreatitis, second operation and death cases. In the ERCP + LC group, 4 cases (6.7 %) of PEP were mild and cured by conservative treatment, as shown in Table 2. Preoperative and postoperative biochemistry findings demonstrated no significant difference between the ERCP concurrent LC group and the LCBDE group (Table 3).

4. Discussion

In the ERCP concurrent LC group, the surgical sequence initiated with prone ERCP, followed by interventions for stone removal. Subsequently, the patient was repositioned for laparoscopic cholecystectomy using standard methods. Katsinelos et al. [6] research work showed that the primary success is significantly higher in guided wire ERCP but it may take more time in cannulation 4.48 ± 0.32 min versus 3.53 ± 0.32 min) as compared to the standard one. A study conducted by Tae Hoon Lee et al. [7] has pointed out that the post ERCP pancreatitis is lower in guided wire and it has shown to be acting as protective factor from multivariate analysis, in preventing post ERCP pancreatitis [2,3].

It provides evidence that preoperative endoscopic retrograde cholangiopancreatography sphincterotomy plus laparoscopic cholecystectomy (ERCP/S + LC) and laparoscopic cholecystectomy plus laparoscopic common bile duct exploration (LC + LCBDE) are

Table 2
Comparison of intraoperative conditions and postoperative outcomes.

	ERCP concurrent LC group (n = 60)	LCBDE group (n = 86)	χ2 (t)	P values
ERCP success rate (example/%)	58 (96.7 %).	/	/	/
Stone Characteristics				
Number of stones	1.87 ± 0.54	1.57 ± 0.84	1.978	>0.05
Diameter of stones	0.75 ± 0.27	0.72 ± 0.31	2.014	>0.05
Diameter of CBD	0.93 ± 0.47	0.96 ± 0.27	2.086	>0.05
Conversion to open surgery (cases/%)	1 (1.7 %).	6 (7.0 %)	2.183	>0.05
Indwelling drainage tube (example/%)	25 (41.7 %)	82 (95.3 %)	52.025	<0.05
Operation time (min)	85.7 ± 27.3	61.2 ± 18.6	2.035	>0.05
Blood loss (ml)	19.5 ± 8.6	36.3 ± 14.7	1.961	>0.05
VAS score (6h)	3.9 ± 1.6	6.5 ± 2.4	4.462	<0.05
Bile leakage (case/%)	1 (1.7 %).	4 (4.7 %)	0.952	>0.05
Postoperative cholangitis (cases/%)	3 (5.0 %)	5 (5.8 %)	0.045	>0.05
Incision infection (cases/%)	2 (3.3 %)	3 (3.5 %)	0.003	>0.05
Bile duct residual stone rate (cases/%)	3 (5.0 %)	3 (3.5 %)	0.205	>0.05
PEP (example/%)	4 (6.7 %)	/	/	/
Bleeding (example/%)	2 (3.3 %)	0	/	/
Exhaust time (h)	22.5 ± 9.8	35.6 ± 12.7	1.047	>0.05

Note: Visual analogue scale (VAS) was utilized for clinical assessment of pain, with 0 indicating no pain and 10 indicating unbearable and severe pain.

Table 3
Comparison of preoperative and postoperative biochemistry findings.

	ERCP concurrent LC group (n = 60)	LCBDE group (n = 86)	P values
Preoperative biochemistry findings			
NE%	83.61 ± 11.28	81.94 ± 9.54	>0.05
Leukocyte (10^9/L)	13.18 ± 2.35	12.52 ± 1.98	>0.05
TBIL (μmol/L)	57.42 ± 42.75	64.24 ± 46.21	>0.05
DBIL(μmol/L)	31.28 ± 21.19	33.54 ± 19.58	>0.05
ALT (U/L)	61.28 ± 28.19	57.81 ± 31.42	>0.05
AST (U/L)	68.41 ± 38.75	71.29 ± 45.85	>0.05
GGT	341.75 ± 216.87	364.91 ± 231.28	>0.05
ALP	153.29 ± 57.26	167.42 ± 61.46	>0.05
Postoperative biochemistry findings			
NE%	75.21 ± 8.61	76.65 ± 9.12	>0.05
Leukocyte (10^9/L)	8.17 ± 2.18	8.46 ± 2.35	>0.05
TBIL (μmol/L)	20.31 ± 16.49	19.81 ± 15.55	>0.05
DBIL(μmol/L)	12.54 ± 5.21	11.98 ± 6.17	>0.05
ALT (U/L)	34.51 ± 16.21	36.27 ± 18.39	>0.05
AST (U/L)	38.34 ± 14.46	37.87 ± 16.22	>0.05
GGT	84.32 ± 25.19	91.28 ± 29.37	>0.05
ALP	69.21 ± 31.19	73.67 ± 27.84	>0.05

NE neutrocyte, **TBIL** total bilirubin, **DBIL** direct bilirubin, **ALT** aspartate transaminase, **AST** oxaloacetic transaminase, **GGT** gamma-glutamyl transpeptidase, **ALP** A Lkaline Phosphatase.

highly effective in detecting and removing common bile duct stones. As this both procedures are effective in terms of efficacy and costing, both procedures are selected. If the patients are diagnosed with cholecystitis in Gastroenterology, then, they are mostly given ERCP while the patients diagnosed in hepatobiliary department, are usually given LCBDE. The outcomes of these both cases are almost equal (there is no significant difference between the outcomes between these cases) in terms of efficacy and complications [3,4]. LC enhances the lesion laparoscopically, making it easy to examine and operate. It is less traumatic and has an excellent prognosis. Few studies have studied the impact of ERCP and lithotomy and LC on the discomfort and prognosis of extrahepatic bile duct stones in cholecystolithiasis patients. The study found that ERC and lithotomy and LC may be better for these patients. Roux-EN-Y gastric bypass patients had a 95.9 % stone-removal rate after ERCP and LC. The observation group had notably higher stone clearance and lower stone recurrence rates than the control group [3,4]. This study also found that the observation group had a longer surgery duration, smaller incisions and blood loss than the control group. Results suggest that ERCP along with lithotomy and LC efficiently treat gallstones and enhance surgical indications. The ERCP is effective at diagnosing biliary and pancreatic disorders. It can clearly show the bile duct and its lesions, calculi position and shape, and lesions location, degree, and kind to efficiently remove calculi, reduce residual, and reduce relapse. When conventional CBDS methods fail, endoscopic electrohydraulic lithotripsy could be used. An electrohydraulic shock wave generator transmits high-frequency hydraulic pressure forces over a spacious operational channel that fits a 4.5 Fr calibre probe. It is imperative to place the probe near the stone as possible to avoid damaging any nearby tissues. A rate of stone removal between 74 % and 98 % is possible. Large stones can be fragmented under fluoroscopic visualisation using endoscopic laser lithotripsy to avoid heat-induced biliary injury [8,9]. However, the treatment of gallbladder stones with extrahepatic bile duct stones has failed to reach a consensus because of a lot of choices: ERCP with subsequent LC, ERCP with simultaneous LC [3], LCBDE (T tube drainage or one stage suture after CBD incision and exploration) and so on. The focus of contradictions should be: endoscopic lithotomy or cholangiotomy for extrahepatic bile duct stones. In other words, which procedure causes less damage, incision of Oddi's sphincter or destroying bile duct integrity [5]. Fundamentally, imaging makes it difficult to determine whether cholangiolithiasis is primary or secondary (except for a few patients with disease course characteristics), and physiologically there is a lack of safe and effective manometry of Oddi's sphincter [5]. In this context, there are inevitable differences in the selection, which are highlighted by the differences in technique and equipment [9]. Patients who are diagnosed in the Department of Gastroenterology generally tend to undergo ERCP, while in the Department of hepatobiliary surgery tend to undergo LCBDE or even open surgery.

A meta-analysis involving 1545 patients suggested [10] that the LCBDE group was superior to the ERCP concurrent LC group in terms of the complication rate, stone recurrence rate and hospitalization cost. Another meta-analysis involving 5 pieces of literature and 860 patients [11] suggested that in addition to the increased bile leakage rate, the LCBDE group was superior to the ERCP concurrent LC group in the rate of stone clearance, complications and enhanced recovery after surgery (ERAS). So why is LCBDE still not the gold standard for the treatment of cholecystolithiasis with extrahepatic cholangiolithiasis? The author believes that the product derivation, standard training and technical improvement of ERCP, including the promotion of Spyglass, the use of hydroelectric lithotripsy, and the re-recognition and prevention of complications (the use of domain embolus and pancreatic duct stent), have greatly improved the effectiveness and safety of ERCP [12]. In this study, patients after gastrointestinal or biliary diversion surgery [13], patients with large stones over 2.5 cm, patients with acute pancreatitis or narrow bile ducts (<6 mm), and patients with a history of ERCP surgery were excluded to minimize the selection bias of patients.

Why did previous research report the disadvantage in length of stay and cost in the ERCP concurrent LC group [9,14]. It is inferred that limited by technique and equipment conditions, most units adopted ERCP with subsequent LC [9,15], which undoubtedly increases the waiting time, the length of hospital stay, and the impact of second anesthesia. In this study, 60 ERCP patients undergoing LC surgery at the same time, compared with the LCBDE group, the length of hospital stay, postoperative pain score and the proportion of

drainage tube indwelling were significantly shortened, which showed certain advantages in minimally invasive and ERAS. Thanks to the cooperation of the anesthesia and nursing team, the operation time was not significantly prolonged despite the need to change the position during the operation. LC does not involve the incision of the bile duct wall, so the amount of blood loss and conversion to open surgery rate is superior to LCBDE.

Surgical safety is one of the most important factors in technical evaluation. Does ERCP concurrent LC cause more complications than LCBDE? Bile leakage is the most common complication after LCBDE [16], while PEP is an unavoidable problem after ERCP, therefore, it is hard to compare equally. In terms of LCBDE, whether to choose a stage I suture remains to be discussed: if the first-stage suture is selected, the biliary pressure will be increased, and so will the rate of postoperative bile leakage. In some cases, secondary bile duct stenosis and recurrent cholangitis will occur [17]. Therefore, for those with fine bile duct, thin bile duct wall, bile duct complicated with obstruction, and oral glucocorticoids, the author will choose T-tube external drainage and gradual clamping T-tube after 2–3 weeks. In terms of ERCP, how do we reduce PEP? Timely indwelling of pancreatic duct stents and preoperatively use of Nonsteroidal Anti-inflammatory Drugs (NSAIDs) are the standard measures recommended by domestic and foreign guidelines [18]. In this study, there were 4 cases of mild PEP in the ERCP concurrent LC group who recovered after conservative treatment, which fully indicated that strict accordance with the indications, standardizing the surgical process and improving the technical level are effective measures to reduce complications.

There are two experiences to share: firstly, CO_2 was suggested to be used to avoid the influence on the field of view of the following LC. It is not advisable to perform LC before ERCP [19]. Secondly, after stone removal in ERCP, 5Fr pigtail stent was indwelled in the bile duct, instead of nasociliary drainage, which improved postoperative comfort and was in line with the concept of ERAS. One month after the operation, the stent was pulled out under a gastroscope if still existed.

In conclusion, ERCP concurrent LC and LCBDE are both safe and effective methods for the treatment of gallbladder stones combined with extrahepatic bile duct stones, and the ERCP concurrent LC group has advantages in postoperative pain, ERAS and comfort, which can be recommended in qualified medical centers.

Data availability

The data could be obtained by request to the corresponding author.

Informed consent

Written informed consent was obtained from all patients.

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CRediT authorship contribution statement

Jiang-Bo Shen: Writing – review & editing, Writing – original draft. **Peng-Cheng Chen:** Writing – review & editing, Writing – original draft. **Jin-Gen Su:** Data curation. **Qing-Chun Feng:** Validation, Software, Formal analysis. **Pei-Dong Shi:** Supervision, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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