**Medicine**

# A retrospective cohort study on the optimal interval between endoscopic retrograde cholangiopancreatography and laparoscopic cholecystectomy

Huan Liu, MD[a],[*] , Wenjun Pan, MD[b], Guoqiang Yan, MD[b], Zhongmin Li, MD[b]

**Abstract**

Endoscopic retrograde cholangiopancreatography (ERCP) and laparoscopic cholecystectomy (LC) are the most important procedures for patients with choledocholithiasis and gallstones. Many studies recommend early LC after ERCP; however, there is still no consensus on the optimal interval between the two. The purpose of this study was to investigate the appropriate timing of LC after ERCP in patients with choledocholithiasis and cholecystolithiasis.

We retrospectively reviewed all ERCPs in our institution from November 2014 to August 2021. All eligible 261 patients were divided into ERCP-LC1 (≤3 days), ERCP-LC2 (3–7 days), and ERCP-LC3 (>7 days). We also reviewed 90 patients with elective LC as the LC group. Procedures, treatment outcomes, and postoperative adverse events were evaluated.

In a total of 1642 ERCPs, 261 eligible patients were divided into ERCP-LC1 (n = 102), ERCP-LC2 (n = 113), and ERCP-LC3 (n = 46). The ERCP-LC groups had no difference in operation time, postoperative adverse events, and open conversion rate with the LC group, but the total hospital stay and hospital stay after LC were longer than the LC group. There were no differences between the ERCP-LC groups in operation time, hospital stay after LC, open conversion rate, postoperative adverse events, and efficacy. However, LC within 7 days and even 3 days after ERCP had significant advantages in improvement in total length of stay and medical expenses. Furthermore, we also found an increased risk of gallbladder gangrene and perforation in LC >7 days after ERCP.

LC within 7 days and even 3 days after ERCP is a safe, effective, and economical method for patients with choledocholithiasis and gallstones.

**Abbreviations:** CBD = common bile duct, EBS = endoscopic biliary stenting, ENBD = endoscopic nasobiliary drainage, EPBD = endoscopic papillary balloon dilation, ERCP = endoscopic retrograde cholangiopancreatography, EST = endoscopic sphincterotomy, LC = laparoscopic cholecystectomy.

**Keywords:** adverse events, endoscopic retrograde cholangiopancreatography (ERCP), laparoscopic cholecystectomy (LC), the optimal interval

## 1. Introduction

Gallstones are an extremely common disease, and 5% to 21% of these patients have choledocholithiasis.[1,2] However, its incidence is extremely high in patients with choledocholithiasis, reaching 95%.[2] We know that most common bile duct (CBD) stones are secondary, which come from the intrahepatic bile duct and gallbladder, while primary CBD stones are rare. For those patients with choledocholithiasis and gallstones who only deal with choledocholithiasis, the recurrence rate of choledocholithiasis after surgery is 11% to 47%.[3,4] Similarly, 2 studies

reported that while waiting for gallbladder surgery after endoscopic retrograde cholangiopancreatography (ERCP), 20% of patients will have gallstone-related complications.[5,6] Therefore, patients with choledocholithiasis and gallstones usually require procedures for both diseases.

Laparoscopic cholecystectomy (LC) has become the standard procedure for gallstones, unless there are complicated conditions such as severe abdominal adhesions. There are many methods for choledocholithiasis, including laparoscopic CBD exploration + stone removal, ERCP, and choledochoscopy. However, ERCP has become the preferred procedure for choledocholithiasis.

a Department of General Surgery, Zhongshan Hospital of Traditional Chinese Medicine, Zhongshan City, China, b Department of General Surgery, Liaoyang Central Hospital, China Medical University, Liaoyang City, Liaoning Province, China.

* Correspondence: Huan Liu, Department of General Surgery, Zhongshan Hospital of Traditional Chinese Medicine, No. 3 Kangxin Rd., West District, Zhongshan City, Guangdong Province 528400, China (e-mail: cmuliuhuan@outlook.com).

Therefore, ERCP and LC have become the most important methods for patients with choledocholithiasis and gallstones. However, the optimal interval between ERCP and LC is still controversial, which varies in different institutions. However, the trend is consistent that more and more surgeons prefer shorter intervals and waiting times. Considering the recurrence of CBD stones and its associated complications, and the increased financial burden due to repeated hospitalizations, ERCP and LC during the same hospital stay have become the main method. Moreover, even if ERCP and LC are performed in the same hospitalization, many studies advocate performing LC earlier after ERCP, although this "early" varies from days to months in different studies.[7–13] There are also many studies that try to perform ERCP and LC during the same anesthesia. However, we know that ERCP requires not only specially trained endoscopists but also specialized equipment, which means that it is only performed in large institutions, where specialties are more refined, leading to ERCP and LC in 2 departments. Extending the operation time, increasing the difficulty of the operation due to intestinal dilation, coordination between different departments,[9,14] changing equipment, and posture and other factors limit the completion of ERCP and LC during the same anesthesia. Therefore, even if it has begun to perform ERCP and LC during the same anesthesia before decades, a recent study also confirmed that it is safe and effective,[11] but it is performed in 2 stages during a hospital stay in most institutions. At present, there are many studies on the optimal interval between ERCP and LC during a hospitalization. However, there is still no consensus, which varies in institutions and countries. Moreover, there are few cases in these studies, and there are few comparative studies with elective LC.

The purpose of this study was to investigate the appropriate timing of LC after ERCP in patients with choledocholithiasis and cholecystolithiasis.

## 2. Methods

### 2.1. Patients

The study is a single-center retrospective cohort study, which was approved by the Ethics Committee of Liaoyang Central Hospital of China Medical University and waived the ethical requirements due to its retrospective study. All patients obtained written informed consent. We reviewed all ERCPs in our institution, a tertiary medical center, from November 2014 to August 2021. These data include the patient's clinical characteristics, procedure-related characteristics, postoperative outcomes, and adverse events. Total length of stay was defined as the time from admission on day 1 to discharge or death. Procedure-related characteristics include ERCP (endoscopic sphincterotomy [EST], endoscopic papillary balloon dilation [EPBD], endoscopic nasobiliary drainage [ENBD], and endoscopic biliary stenting [EBS]), the interval between ERCP and LC, and LC (methods of cholecystectomy, postoperative peritoneal drainage, postoperative fever, and postoperative hospital stay). Postoperative hospital stay was defined as the time from the day of cholecystectomy to discharge or death.

The inclusion criteria of eligible patients in the ERCP-LC groups were as follows:

age ≥18 years
patients with choledocholithiasis and gallstones
ERCP and LC during a hospital stay.

Its exclusion criteria were as follows:

malignant bile duct obstruction
patients with choledocholithiasis and without gallstones or cholecystitis
patients who underwent ERCP only
patients who underwent cholecystectomy before ERCP
patients who underwent choledochoscopy bile duct exploration + stone removal.

The ERCP-LC groups were divided into ≤3 days (ERCP-LC 1), 3 to 7 days (ERCP-LC 2), and >7 days (ERCP-LC 3). We proportionally reviewed patients with gallstones in the same period as the ERCP-LC groups, who had similar clinical characteristics as those in the ERCP-LC group, as the LC group.

### 2.2. Procedures

#### 2.2.1. ERCP procedures. All ERCPs were performed by surgeons with extensive experience (performing >250 ERCP procedures per year). All patients were anesthetized with diazepam and propofol, and anisodamine reduced intestinal motility. ERCP was performed in the prone position using a standard duodenoscope (TJF-260V; Olympus, Tokyo, Japan). After anesthesia, selective CBD catheterization and 30% iohexol choledochography to clarify the condition of the CBD and its stones, and then selectively perform EST (≤5 mm) and (or) EPBD (≤10 mm) to facilitate its stone extraction. Afterward, we used a basket or balloon to perform mechanical lithotripsy and stone removal and performed choledochography again to ensure that it has been removed and then placed ENBD or bile duct stents (including plastic and metal). Finally, we confirmed the condition of CBD drainage and duodenal papilla before withdrawing the duodenoscope.

#### 2.2.2. LC procedures All patients with LC, including the ERCP-LC and the LC groups, followed the standardized LC method. Patients with pre-LC pancreatitis performed LC after its symptoms improved and serum amylase levels were normal. Surgeons decided whether to convert to open, whether the gallbladder was completely removed, and whether to drain according to the inflammation and adhesion during the operation and the patient's condition.

#### 2.2.3. Postoperative management The management of all patients after LC was consistent. Routine blood tests such as complete blood count, liver function tests, and serum amylase were performed within 48 hours after LC. The indication for removal of abdominal drainage was drainage <10 mL and asymptomatic such as fever (>37.5°C) and abdominal pain. All patients performed abdominal ultrasound to confirm peritoneal effusion before removal of abdominal drainage, and performed abdominal ultrasound, computed tomography, and magnetic resonance cholangiopancreatography when needed.

### 2.3. Statistical analysis

In our studies, continuous variables were described by mean ± standard deviation, which was statistically analyzed by the Student $t$ test or Mann–Whitney $U$ test according to its distribution. Categorical variables were described by frequency (percentage), which were statistically analyzed by chi-square tests or Fisher exact tests as optimal. We used appropriate statistical methods above to analyze the following variables: treatment outcome, length of hospital stay, operative time and method, proportion of gangrenous cholecystitis, proportion of complete cholecystectomy, postoperative fever and drainage time, and proportion of adverse events (biliary fistula, postoperative pancreatitis, postoperative intraperitoneal, incision, and bile duct infection). $P$ value ≤.05 was considered statistically significant. All statistics were performed with SPSS 25.0.

## 3. Results

The review and grouping of the cases in our study were shown in Figure 1. Our institution performed 1642 ERCPs, including 333 (20.3%) patients with malignant diseases and 1309 patients
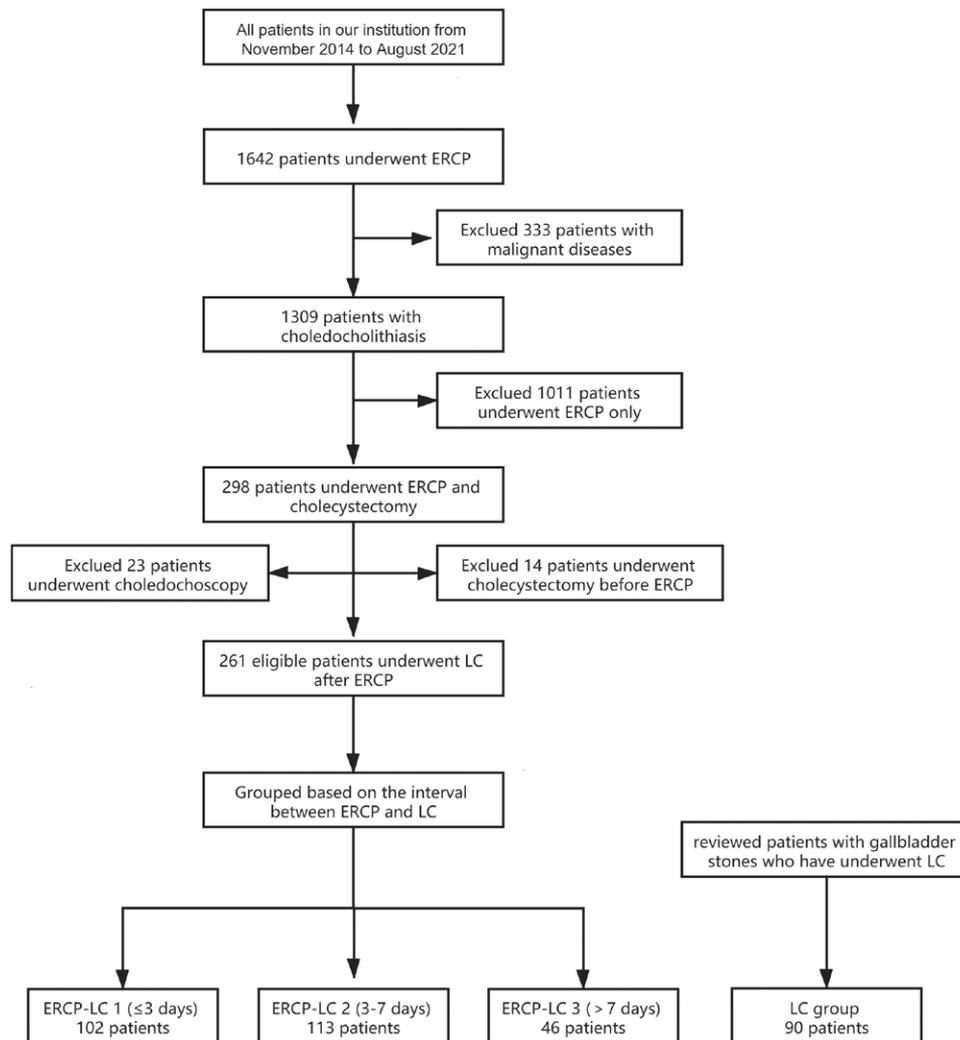
**Figure 1.** Flowchart of review and grouping of eligible patients in our study. ERCP = endoscopic retrograde cholangiopancreatography, LC = laparoscopic cholecystectomy.

with choledocholithiasis, from November 2014 to August 2021. Among the 1309 patients with choledocholithiasis, 1011 patients with ERCP only, 23 patients who underwent choledochoscopy and 14 patients who underwent LC before ERCP were excluded, and there were 261 eligible patients. These patients were divided into ERCP-1 group (n = 102), ERCP-LC2 group (n = 113), and ERCP-LC3 group (n = 46). To compare whether there is a difference between LC after ERCP and elective LC, we proportionally selected 90 elective LC patients as the LC group.

The characteristics of all patients who underwent ERCP were shown in Table 1. Among all 1642 patients, 333 (20.3%) and 1309 (79.7%) had undergone ERCP for malignant disease and choledocholithiasis, respectively. Among patients with CBD stones, there were 892 (68.1%) patients with gallstones or cholecystitis, 141 (10.8%) patients without gallstones or cholecystitis, and 276 (21.1%) patients with gallbladder removed, respectively. We also saw that 86.4% (892/1033) of patients with choledocholithiasis had gallstones or cholecystitis. However, only 33.4% (298/892) of these patients dealt with both disorders during a hospital stay, including 261 (87.6%) who underwent LC after ERCP, 14 (4.7%) who underwent LC before ERCP, and 23 (7.7%) who underwent choledochoscopy.

The clinical characteristics of the ERCP-LC and the LC groups are shown in Table 2. The average interval between ERCP and LC was $1.9 \pm 0.9$, $5.6 \pm 1.1$, and $10.9 \pm 3.1$ days in ERCP-LC1, 2, and 3, respectively. We saw no statistical difference between

the ERCP-LC and the LC groups in gender, diabetes, dementia or paralysis, and treatment outcome. However, there were statistical differences in age, history of abdominal surgery, preoperative pancreatitis, and intrahepatic bile duct stones. There were no statistical differences between the ERCP-LC groups in age and preoperative pancreatitis, while there were statistical differences in the history of abdominal surgery, intrahepatic bile duct stones.

The ERCP-related characteristics in the ERCP-LC groups were shown in Table 3. We saw no significant differences in the proportion of severe cholangitis, CBD diameter, type, and size of CBD stones among the 3 ERCP-LC groups. In terms of ERCP procedures, there was also no statistically significant difference in the choice of EST, ENBD, and EBS, except for EPBD.

The procedures and postoperative adverse events of the ERCP-LC groups and the LC group were shown in Table 4. There was no statistical difference between the ERCP-LC and the LC groups in treatment outcome, surgical methods, complete gallbladder resection, postoperative fever, postoperative infection, postoperative bile duct fistula, and postoperative pancreatitis. However, there were statistical differences in postoperative hospital stay, operation time, gangrenous cholecystitis, and postoperative drainage time. There were statistically significant differences in gangrenous cholecystitis among the 3 ERCP-LC groups but no differences in operative time and postoperative drainage time.

**Table 1**

**Clinical characteristics of all patients undergoing ERCP.**

| Clinical characteristics | N (%) |
|---|---|
| Causes of ERCP | |
|   Malignant diseases | 333 (20.3) |
|   Choledocholithiasis | 1309 (79.7) |
|     ERCP | 1011 |
|       CBDS | 141 (13.9) |
|       CBDS + GR | 276 (27.3) |
|       CBDS + GD | 594 (58.8) |
|     ERCP + cholecystectomy | 298 |
|       ERCP + LC | 261 (87.6) |
|       LC + ERCP | 14 (4.7) |
|       ERCP + BDE | 23 (7.7) |
| Choledocholithiasis | 1309 |
|   GD | 892 (68.1) |
|     Cholecystectomy | 298 (33.4) |
|     No cholecystectomy | 594 (66.6) |
|   No GD | 141 (10.8) |
|   GR | 276 (21.1) |

CBDS = CBD stones, BDE = Bile duct exploration, ERCP = endoscopic retrograde cholangiopancreatography, GD = gallstones or cholecystitis, GR = gallbladder removed, LC = laparoscopic cholecystectomy.

## 4. Discussion

Gallstones are a common disease in general surgery. In clinical practice, we noticed that the proportion of choledocholithiasis in patients with gallstones is not very high. However, the proportion of gallstones in patients with choledocholithiasis is extremely high because most choledocholithiasis are secondary stones, usually from the gallbladder and intrahepatic bile ducts. In our study, the proportion reached 68.1% without excluding 21.1% of patients with gallbladder removed, which is consistent with previous studies.[2] At present, for patients with choledocholithiasis and gallstones or cholecystitis, procedures are recommended for both disorders.[9,15,16] However, there is no consensus on the interval between CBD and gallbladder surgery. After anti-infection and CBD stone removal, the patient's clinical manifestations such as jaundice, fever, nausea, and abdominal pain were significantly relieved or even disappeared, which led many patients to dismiss the problem of gallstones and be reluctant to continue gallbladder surgery. Even though we actively educated and recommended surgery for all patients with CBD stones and gallstones. In our study, we saw that only 33.4% (298/892) of patients had undergone CBD and gallbladder surgery. However, while waiting for gallbladder surgery, adverse events may occur in patients such as recurrence of choledocholithiasis, gallbladder gangrene, and perforation, which will increase the risk of medical disputes. We have recently encountered 2 medical disputes, both of which were caused by the patient's refusal to perform gallbladder surgery after ERCP, which resulted in gallbladder gangrene and perforation. Even after the gallbladder procedures were finally performed, both of them were admitted to the intensive care unit due to abdominal infection, sepsis, and acute respiratory distress syndrome. Moreover, there is no clear consensus on the interval between ERCP and gallbladder surgery, which also causes our surgeons to be at a disadvantage in such medical disputes even if we have no medical negligence. Therefore, we aim to find the optimal interval between ERCP and LC based on our practice.

The average interval between ERCP and LC for ERCP-LC1, 2, and 3 was $1.9 \pm 0.9$, $5.6 \pm 1.1$, and $10.9 \pm 3.1$ days. In terms of total hospital stay, ERCP-LC3 was significantly longer than ERCP-LC1 and 2 ($23.6 \pm 8.7$ vs $14.7 \pm 6.8$ days, $P(1,3) \leq .001$; $23.6 \pm 8.7$ vs $16.8 \pm 5.3$ days, $P(2,3) \leq .001$), while there was no statistical difference between ERCP-LC1 and 2 ($14.7 \pm 6.8$ vs $16.8 \pm 5.3$ days, $P(1,2) = .075$). The hospital stays of ERCP-LC1, 2, and 3 after LC were $8.7 \pm 5.2$, $8.0 \pm 5.0$, and $9.2 \pm 5.5$ days, respectively. Among them, ERCP-LC2 and 3 were the shortest and longest, respectively, but there was no statistical difference among the 3 groups ($P = .386$). The postoperative hospital stay in the ERCP-LC groups was longer than that in the LC group ($P = .018$), and ERCP-LC1 and 3 were significantly different from the LC group ($8.7 \pm 5.2$ vs $6.3 \pm 2.4$ days, $P(1,4) = .014$; $9.2 \pm 5.5$ vs $6.3 \pm 2.4$ days, $P(3,4) = .013$), and ERCP-LC2 was also longer than the LC group, but there was no statistical difference ($8.0 \pm 5.0$ vs $6.3 \pm 2.4$ days, $P(2,4) = .098$). In a retrospective study, including the interval between ERCP and LC within 2 weeks, 2 to 6 weeks, and >6 weeks, we found that there was no difference in the hospital stay after LC.[17] Similarly, another study found that patients with LC

**Table 2**

**Clinical characteristics in ERCP-LC and LC groups.**

| | ERCP-LC groups | | | |
|---|---|---|---|---|
| | ERCP-LC 1 | ERCP-LC 2 | ERCP-LC 3 | LC group |
| N | 102 | 113 | 46 | 90 |
| Gender | | | | |
|   Male, n (%) | 48 (47.1) | 53 (46.9) | 22 (47.8) | 38 (42.2) |
|   Female, n (%) | 54 (52.9) | 60 (53.1) | 24 (52.2) | 52 (57.8) |
| Age, yr (mean ± SD) | 57.9 ± 14.2 | 61.5 ± 12.3 | 58.3 ± 12.2 | 54.1 ± 13.5 |
| ERCP-LC interval, d (mean ± SD) | 1.9 ± 0.9 | 5.6 ± 1.1 | 10.9 ± 3.1 | - |
| Diabetes | | | | |
|   Yes, n (%) | 12 (11.8) | 16 (14.2) | 4 (8.7) | 6 (6.7) |
|   No, n (%) | 90 (88.2) | 97 (85.8) | 42 (91.3) | 84 (93.3) |
| Previous abdominal surgery | | | | |
|   Yes, n (%) | 15 (14.7) | 28 (24.8) | 5 (10.9) | 8 (8.9) |
|   No, n (%) | 87 (85.3) | 85 (75.2) | 41 (89.1) | 82 (91.1) |
| Preoperative pancreatitis | | | | |
|   Yes, n (%) | 18 (17.6) | 23 (20.4) | 16 (34.8) | 0 (0) |
|   No, n (%) | 84 (82.4) | 90 (79.6) | 30 (65.2) | 90 (100) |
| Dementia or paralysis | | | | |
|   Yes, n (%) | 3 (2.9) | 2 (1.8) | 2 (4.3) | 0 (0) |
|   No, n (%) | 99 (97.1) | 111 (98.2) | 44 (95.7) | 90 (100) |
| Intrahepatic bile duct stones | | | | |
|   Yes, n (%) | 9 (8.8) | 1 (0.9) | 1 (2.2) | 0 (0) |
|   No, n (%) | 93 (91.2) | 112 (99.1) | 45 (97.8) | 90 (100) |

ERCP = endoscopic retrograde cholangiopancreatography, LC = laparoscopic cholecystectomy.

## Table 3

**ERCP-related characteristics in the ERCP-LC groups.**

| | ERCP-LC groups | | |
|---|---|---|---|
| Severe cholangitis | | | |
| Yes, n (%) | 3 (2.9) | 2 (1.8) | 1 (2.2) |
| No, n (%) | 99 (97.1) | 111 (98.2) | 45 (97.8) |
| CBD stones | | | |
| Single, n (%) | 37 (36.3) | 25 (22.1) | 14 (30.4) |
| Multiple, n (%) | 54 (52.9) | 79 (69.9) | 26 (56.5) |
| Sludge, n (%) | 11 (10.8) | 9 (8.0) | 6 (13.1) |
| CBD diameter, cm (mean ± SD) | 1.1 ± 0.4 | 1.2 ± 0.3 | 1.1 ± 0.3 |
| Stone diameter, cm (mean ± SD) | 0.7 ± 0.5 | 0.8 ± 0.4 | 0.7 ± 0.3 |
| EST | | | |
| Yes, n (%) | 87 (85.3) | 92 (81.4) | 37 (80.4) |
| No, n (%) | 15 (14.7) | 21 (18.6) | 9 (19.6) |
| EPBD | | | |
| Yes, n (%) | 49 (48.0) | 91 (80.5) | 38 (82.6) |
| No, n (%) | 53 (52.0) | 22 (19.5) | 8 (17.4) |
| ENBD | | | |
| Yes, n (%) | 100 (98.0) | 112 (99.1) | 46 (100) |
| No, n (%) | 2 (2.0) | 1 (0.9) | 0 (0) |
| Stents* | | | |
| Yes, n (%) | 2 (2.0) | 3 (2.7) | 3 (6.5) |
| No, n (%) | 100 (98.0) | 110 (97.3) | 43 (93.5) |

CBD = common bile duct; ENBD = endoscopic nasobiliary drainage, EPBD = endoscopic papillary balloon dilation, ERCP = endoscopic retrograde cholangiopancreatography, EST = endoscopic sphincterotomy, LC = laparoscopic cholecystectomy.

* Including plastic and metal.

within 24 hours after ERCP had a shorter total hospital stay than those with LC after 24 hours (2 [2–3] vs 4 [4–7] days; $P < .001$); however, there was no difference in the length of hospital stay after LC ($1.5 ± 1.0$ vs $1.7 ± 1.3$ days; $P = .402$).[16] In terms of treatment outcomes, 1 patient in the ERCP-LC1 group eventually died of multiple organ dysfunction syndrome due to difficulty in stone removal, and 1 patient in the ERCP-LC2 group died of sepsis due to biliary fistula after LC, but there was no significant difference among the 3 ERCP-LC groups.

The length of hospital stay is related to the patient's condition, and the characteristics of surgery are also a relatively direct indicator. In our study, we saw that the mean operation time was significantly shorter in the LC group than in the ERCP-LC group ($82.6 ± 35.7$ vs $72.2 ± 25.1$ min, $P(1, 4) ≤ .001$; $82.3 ± 36.8$ vs $72.2 ± 25.1$ min, $P(2,4) ≤ .001$, $98.2 ± 57.4$ vs $72.2 ± 25.1$ min, $P(3,4) ≤ .001$); however, there was no difference between the ERCP-LC group ($P = .211$). Similarly, many studies found that the interval between ERCP and LC had no correlation with the length of LC procedures.[13,16–18] The length of procedures varies based on the severity of diseases, medical equipment, and surgeons' experience. However, it also reflects the difficulty of procedures to a certain extent. In clinical practice, many surgeons tend to postpone gallbladder surgery because they are worried that ERCP may cause edema and adhesion of the gallbladder and its surrounding tissues, resulting in unclear anatomy and increasing the difficulty of the procedure. However, some studies found that contrast agents may increase the risk of infection, and directly lead to fibrosis around the hepatic portal over time,[4,19] resulting in increased operative time in patients with delayed gallbladder surgery.[20] The adhesion of the gallbladder,

## Table 4

**Procedures and postoperative adverse events.**

| | ERCP-LC groups | | | | LC group | P value |
|---|---|---|---|---|---|---|
| | ERCP-LC 1 | ERCP-LC 2 | ERCP-LC 3 | *P* value | | |
| Total hospital stay, d (mean ± SD) | 14.7 ± 6.8 | 16.8 ± 5.3 | 23.6 ± 8.7 | .001* | 9.2 ± 2.9 | .001 |
| Postoperative hospital stay, d (mean ± SD) | 8.7 ± 5.2 | 8.0 ± 5.0 | 9.2 ± 5.5 | .386 | 6.3 ± 2.4 | .018† |
| Treatment outcome | | | | | | |
| Death, n (%) | 1 (1.0) | 1 (0.9) | 0 (0) | .999 | 0 (0) | .999 |
| Cure, n (%) | 101 (99.0) | 112 (99.1) | 46 (100) | | 90 (100) | |
| Operation time, min (mean ± SD) | 82.6 ± 35.7 | 82.3 ± 36.8 | 98.2 ± 57.4 | .211 | 72.2 ± 25.1 | .024* |
| Surgical methods | | | | | | |
| Laparoscopy | 98 (96.1) | 112 (99.1) | 46 (100) | .206 | 90 (100) | .115 |
| Open‡ | 4 (3.9) | 1 (0.9) | 0 (0) | | 0 (0) | |
| Gangrenous cholecystitis | | | | | | |
| Yes, n (%) | 4 (3.9) | 3 (2.7) | 7 (15.2) | .005* | 8 (8.9) | .013* |
| No, n (%) | 98 (96.1) | 110 (97.3) | 39 (84.8) | | 82 (91.1) | |
| Cholecystectomy | | | | | | |
| Complete, n (%) | 101 (99.0) | 112 (99.1) | 46 (100) | .999 | 89 (98.9) | .999 |
| Partial, n (%) | 1 (1.0) | 1 (0.9) | 0 (0) | | 1 (1.9) | |
| Postoperative fever, d (mean ± SD) | 0.7 ± 1.2 | 0.8 ± 1.3 | 0.5 ± 1.2 | .376 | 0.4 ± 0.8 | .150 |
| Postoperative drainage, d (mean ± SD) | 4.9 ± 2.9 | 4.7 ± 3.3 | 5.5 ± 5.4 | .441 | 3.1 ± 1.3 | ≤.001* |
| Postoperative infection | | | | | | |
| Yes, n (%) | 4 (3.9) | 5 (4.4) | 3 (6.5) | .796 | 2 (2.2) | .645 |
| Intraperitoneal | 1 (1.0) | 1 (0.9) | 0 (0) | | 1 (1.1) | |
| Incision | 1 (1.0) | 1 (0.9) | 0 (0) | | 1 (1.1) | |
| Cholangitis | 2 (1.9) | 3 (2.6) | 3 (6.5) | | 0 (0) | |
| No, n (%) | 98 (96.1) | 108 (95.6) | 43 (93.5) | | 88 (97.8) | |
| Bile duct fistula | | | | | | |
| Yes, n (%) | 0 (0) | 1 (0.9) | 1 (2.2) | .474 | 0 (0) | .394 |
| No, n (%) | 102 (100) | 112 (99.1) | 45 (97.8) | | 90 (100) | |
| Postoperative pancreatitis | | | | | | |
| Yes, n (%) | 1 (1.0) | 0 (0.0) | 0 (0.0) | .567 | 0 (0) | .678 |
| No, n (%) | 101 (99.0) | 113 (100.0) | 46 (100.0) | | 90 (100) | |

ERCP = endoscopic retrograde cholangiopancreatography, LC = laparoscopic cholecystectomy.

* $P(1,2,3) = .001$: $P(1,2) = .075$, $P(1,3) ≤ .001$, $P(2,3) ≤ .001$; $P(1,2,3,4) = .024$: $P(1,4) ≤ .001$, $P(2,4) ≤ .001$, $P(3,4) ≤ .001$; $P(1,2,3) = .013$: $P(1,2,3) = .005$: $P(1,3) = .036$, $P(2,3) = .007$, $P(3,4) = .265$; $P(1,2,3,4) ≤ .001$: $P(1,4) ≤ .001$, $P(2,4) ≤ .001$, $P(3,4) = .033$.

† $P(1,2,3,4) = .018$: $P(1,4) = .014$, $P(2,4) = .098$, $P(3,4) = .013$.

‡ Including open and laparoscopic conversion to open.

bile duct, and surrounding tissues after ERCP is difficult to evaluate clearly. A study based on the adhesion severity scale recommended by Ercan et al[21] found that the degree of adhesions in early LC after ERCP was lower than in delayed LC, but it was not statistically different.[13] However, ultrasound results showed that the gallbladder wall thickness in early LC after ERCP was significantly thinner than in delayed LC, and the pathological results also showed that the microscopic indicators such as collagen deposition, fibrosis, leukocyte infiltration, and mucosal damage in early LC were lower than in delayed LC, and all were statistically significant.[13]

Does delayed LC after ERCP increase open conversion rates? We found in the article by Vaccari et al[22] that history of ERCP (P = .16; odds ratio [OR] = 1.7) was a risk factor for open conversion rate. In our study, we saw that the conversion rate was higher in ERCP-LC1 (≤3 days) and 2 (3–7 days) than elective LC, although the difference was not statistically significant. This may be due to bias due to the small sample size of our study. However, its open conversion rate was also not statistically different between the ERCP-LC groups (P = .206). Moreover, many studies have also confirmed that there is no correlation between the length of the interval between ERCP and LC and its open conversion rate.[16,17,23] During LC, if the gallbladder was severely adhered to surrounding tissues or organs and cannot be completely removed, we usually preferred partial cholecystectomy and electrocoagulation of the remaining gallbladder tissue to avoid excessive dissection, which may cause damage to liver or bile duct. We saw that there was no difference in the complete gallbladder resection rate between the ERCP-LC and the LC groups. Currently, many surgeons in clinical practice prefer to postpone LC due to concerns that early LC after ERCP may increase the difficulty of its procedure and the risk of intraoperative injury. However, our study does not support these concerns of surgeons. In our study, there were no significant differences in the operation time, open conversion rate, and complete resection rate among the ERCP-LC group. However, the proportion of gallbladder gangrene was significantly higher in the ERCP-LC group 3 (>7 days) than in the ERCP-LC groups 1 (≤3 days) and 2 (3–7 days), and it was statistically different (15.2% vs 3.9%, P = .036; 15.2% vs 2.7%, P = .007). Moreover, its proportion was also higher than that of elective LC, although it was not statistically significant (15.2% vs 8.9%, P = .265). In contrast, the proportion of gallbladder gangrene was lower in the ERCP-LC1 (≤3 days) and 2 (3–7 days) groups than in elective LC, although it was not statistically significant (3.9% vs 8.9%, P = .165; 2.7% vs 8.9%, P = .064). CBD stones block the passage of bile from the gallbladder or liver to the duodenum, which in turn increases the pressure of the bile duct and disrupts its pressure gradient, leading to bile reflux and bile duct infection. Compared with elective LC, symptoms of cholangitis in patients with choledocholithiasis and cholecystolithiasis may provide an indication of early LC before the onset of cholecystitis. Because biliary dilatation caused by choledocholithiasis and EST, EPBD, ENBD, and EBS during ERCP increase the chance of intestinal bacteria entering the gallbladder after ERCP, cholecystitis manifests as more rapidly and more severely once it occurs in delayed LC. The difference in the proportion of gallbladder gangrene in our study supports this point to some extent.

In our study, all gallbladder procedures were performed in accordance with the standard LC method. More severe intra-abdominal adhesions inevitably lead to larger surgical scope, resulting in more postoperative exudation and longer duration of fever. Therefore, the duration of postoperative fever and drainage can indicate abdominal adhesion and exudation to a certain extent. There was no difference in the duration of postoperative fever between the ERCP-LC and the LC groups. There were statistical differences between the LC and the ERCP-LC groups in terms of postoperative

drainage (P(1,4) ≤ .001, P(2,4) ≤ .001, P(3,4) = .033), but there were no differences among the ERCP-LC groups. Therefore, from the perspective of postoperative drainage, ERCP has an effect on LC itself to a certain extent, while the interval between ERCP and LC is not significant for it. Previous studies have indicated that preoperative ERCP increases the risk of post-LC infections, including wound infections and intra-abdominal abscesses, at least 3-fold. However, in our study, there were no statistically significant differences between the ERCP-LC groups and the LC group in postoperative cholangitis, pancreatitis, biliary fistula and incision, and intraperitoneal infection. Moreover, we also saw that the earlier the LC was performed after ERCP, the lower the incidence of postoperative adverse events, although there was no statistical difference between the ERCP-LC groups. Similarly, many studies revealed that there is no difference in postoperative complications between early and delayed LC after ERCP.[16,17,24] Moreover, a study also has shown that the incidence of postoperative complications in delayed LC after ERCP is significantly higher than that in early LC.[13] Two studies also showed that the proportion of postoperative complications in the 1-stage procedure and the 2-stage procedure was similar, and there was no significant statistical difference.[11,25] A study showed that the incidence of postoperative adverse events in LC after ERCP and elective LC was similar, which is consistent with our study.[23] Surgeons are concerned that early LC after ERCP may increase the incidence of perihilar injury and postoperative adverse events, which are important factors that predispose them to delayed LC. However, many studies found that the incidence of postoperative adverse events and bile duct damage in early LC after ERCP is similar or even lower than that of delayed LC, and few studies showed that it is higher.

A study found that ≥2 CBD stones (OR = 2.20) were a risk factor for open conversion rate.[26] Another study also showed that cholecystectomy after EST for symptomatic CBD stones is more difficult and requires longer operation time, which may increase open conversion rate.[3] However, in our study, there were no statistical differences in the proportion of severe cholangitis, CBD stone characteristics, CBD diameter, CBD stone size, and the proportion of EST, EPBD, ENBD, and EBS between the ERCP-LC groups.

Our study also has its own limitations as its results are hypothetical findings from a retrospective study; therefore, further prospective studies are warranted to confirm these results.

## 5. Conclusions

In our study, although the operation time and hospital stay of LC after ERCP were significantly longer than that of elective LC, there was no statistical difference in postoperative adverse events and open conversion rate. LC within 7 days and even 3 days after ERCP is a safe, effective, and more economical method, and there was no statistical difference with LC >7 days in operation time, hospital stay after LC, open conversion rate, postoperative adverse events, and treatment outcomes. However, it had significant advantages in total hospital stay and medical expenses. Moreover, we also saw a significant increase in the risk of gallbladder gangrene perforation in LC >7 days after ERCP.

## Author contributions

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