Comparable Safety of ERCP in Symptomatic and Asymptomatic Patients with Common Bile Duct Stones: A Propensity-Matched Analysis

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Research article

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Abstract

Background: The safety of endoscopic retrograde cholangiopancreatography (ERCP) for asymptomatic common bile duct (CBD) stones patients has not been fully studied. This study aimed to compare the incidence and severity of ERCP complications in patients with asymptomatic and symptomatic CBD stones and to provide evidence for the treatment of asymptomatic CBD stones.

Methods: The clinical data of patients were retrospectively analyzed. These patients were divided into the asymptomatic CBD stones group and the symptomatic CBD stones group. Propensity score matching (PSM) was used to match the two groups. The incidence and severity of postoperative complications of ERCP in the two groups were analyzed.

Results: A total of 79 patients who had asymptomatic CBD stones and 795 patients who had symptomatic CBD stones were included in this study. After PSM, 79 patients from asymptomatic CBD group and 316 patients from the symptomatic CBD stones group were identified. Before and after PSM, there were no significant differences in the incidence and severity of post-ERCP pancreatitis (PEP) between the two groups (P> 0.05). Besides, the incidence and severity of other complications including acute cholangitis, bleeding and perforation in the two groups was no differences before and after PSM (P>0.05).

Conclusions: Patients with asymptomatic CBD stones are not at higher risk of getting ERCP-related complications when compared with those with symptomatic ones. ERCP is as safe and effective for asymptomatic CBD stones as for symptomatic patients.

Background

Common bile duct (CBD) stones can cause abdominal pain, jaundice, biliary pancreatitis, acute cholangitis, and even life-threatening. Commonly, CBD stones causing symptoms require active treatment\[1–3\]. Endoscopic retrograde cholangiopancreatography (ERCP) has become a first-line treatment for CBD stones due to its advantages of small trauma, quick recovery, and repeatable operation\[4\]. Nevertheless, ERCP itself has the risk to cause some complications. The previous studies reported that the overall incidence of complications of ERCP is 4%~14%, mainly including post-ERCP pancreatitis (PEP), cholangitis, bleeding, and perforation\[5, 6\]. For asymptomatic CBD stones, there is no consensus for its treatment strategy because of its unclear natural history. To prevent the serious adverse consequences of asymptomatic CBD stones, several guidelines recommend that patients with asymptomatic CBD stones should be treated as long as they are able to tolerate the operation\[1–3\]. However, unlike endoscopic treatment for symptomatic CBD stones, ERCP plays a preventative role in patients with asymptomatic CBD stones. In other words, since the patients don't have any discomfort related to CBD stones before ERCP, the expectation of safety is higher. If any complications related to ERCP operation occurred, it would be more difficult to accept. Although a few studies compared the incidence of ERCP related complications between patients with asymptomatic and symptomatic CBD stones, suggesting that patients with asymptomatic CBD stones were more susceptible to postoperative complications. However, more evidence is needed to reach an agreement. \[7–10\].

This study retrospectively analyzed the data of patients who underwent ERCP for CBD stones in West China Hospital of Sichuan University in the past five years to compare the occurrence of post-ERCP complications in patients with asymptomatic and symptomatic CBD stones.

Methods
Patient selection

We retrospectively reviewed all medical records of patients who underwent ERCP for CBD stones at West China Hospital of Sichuan University from January 2014 to December 2018. The exclusion criteria were as follows: (1) patients under the age of 18; (2) patients with ampulla tumor; (3) patients who had undergone papillary treatment; (4) patients with malignant tumors of biliary tract or pancreas; (5) patients with Billroth II surgery or Roux-en-Y reconstruction; (6) patients with liver transplantation; (7) patients who had preexisting gastrointestinal bleeding; (8) patients who had preexisting pancreatitis; (9) patients who had preexisting acute cholangitis; (10) patients who had preexisting gastrointestinal perforation; (11) patients who were pregnant; (12) patients in whom unable to distinguish the symptoms from cholecystolithiasis or CBD stones; (13) patients whose clinical data were incomplete.

Endoscopic procedures

All the ERCP operations were performed by 4 endoscopic doctors who independently complete more than 300 ERCP operations per year using a side-viewing duodenoscope (TJF-240/260; Olympus Optical Corporation, Tokyo, Japan). After successful cannulation into the CBD, a 25% diluted ominipaque solution was injected for cholangiography to obtain the size, number, and diameter of CBD stones. The endoscopic doctors selected endoscopic sphincterotomy (EST), endoscopic papillary balloon dilation (EPBD), mechanical lithotripsy, or balloon to help remove the stone according to the specific situation. If the CBD stones are not removed completed or residual CBD stones are suspected, endoscopic nasobiliary drainage (ENBD) or endoscopic retrograde biliary drainage (ERBD) will be performed.

Definitions

Symptomatic CBD stone

Symptomatic CBD stone is defined as CBD stone causes abdominal pain, obstructive jaundice, cholangitis or acute pancreatitis, or abnormal liver tests. In our study, we excluded patients with acute cholangitis or acute pancreatitis before ERCP to obtain accurate diagnosis of postoperative complications.

Asymptomatic CBD stone

Asymptomatic CBD stone is defined as CBD stone that did not cause corresponding symptoms, and the blood data associated with CBD stones was normal at the time of ERCP.

Difficult biliary cannulation

More than 10 minutes of deep cannulation were defined as difficult biliary intubation[11].

ERCP related complications and its severity

ERCP related complications include PEP, bleeding, perforation and cholangitis. The definition and severity of PEP, bleeding, and perforation based on the consensus of Cotton et al[12]. The definition and severity of cholangitis based on the Tokyo Guidelines 2018 (TG2018) [13].

Outcome

The primary outcome was the incidence of PEP and its severity in patients with asymptomatic or symptomatic CBD stones. The secondary outcome was the incidence of other ERCP related complications including acute cholangitis,
bleeding, and perforation and their severity in these patients.

**Matching method and statistical analyses**

We carried out propensity score matching (PSM) to reduce the effects of selection bias and potential confounding on measured outcomes due to differences in baseline characteristics between the groups. The propensity score was calculated using a multivariable logistic regression model. The following patients’ characteristics which were reported as risk factors for ERCP-related complications were included in the model: age, gender, periampullary diverticulum, non-dilated CBD, history of pancreatitis, precut sphincterotomy, EST, ERBD, difficult cannulation, using anticoagulants before ERCP [14-19]. By using these propensity scores, patients in the asymptomatic CBD stones group were matched at a 1:4 ratio with those in the symptomatic CBD stones group. PSM analyses were performed using R version 3.6.1 (free to download from http://www.r-project.org).

We used SPSS (version 23.0; SPSS Inc, Chicago, Ill, USA) for data analysis. The t-test or Mann–Whitney U test was used to assess continuous data. Fisher’s exact test or the chi-squared test was used to evaluate differences of categorical data. P <0.05 was considered statistically significant.

**Results**

A total of 1690 patients underwent ERCP for CBD stones from January 2014 to December 2018. Among these patients, 816 were excluded based on the exclusion criteria. After screening, 874 patients were included in our study: 79 patients who had asymptomatic CBD stones and 795 patients who had symptomatic CBD stones. PSM was then conducted at a ratio of 1:4, and consequently 79 patients from asymptomatic CBD group and 316 patients from the symptomatic CBD stones group were identified (Fig. 1).

**Patients Characteristics**

Before PSM, the proportions of the female (51 (64.6%) vs 412 (51.8%), P =0.031) and cholecystectomy history (60 (76.9%) vs 428 (54.0%), P <0.001) were significantly higher in the asymptomatic group than in the symptomatic group. Levels of prothrombin time (PT) [11.6 (10.8,12.2) vs 11.7 (11.1,12.3) seconds, P =0.020], international normalized ratio (INR) [1.0 (1.0,1.1) vs 1.0 (1.0,1.1), P =0.040], total bilirubin (TB) [13.5 (11.1,16.9) vs 21.2 (13.5,50.0) umol/L, P <0.001], alanine aminotransferase (ALT) [27.0 (17.0,46.0) vs 58.0 (24.0,138.0) IU/L, P <0.001], and aspartate transpeptidase (AST) [26.0 (20.0,35.0) vs 40.0 (25.0,100.0 IU/L), P <0.001] in the asymptomatic group was lower than those in symptomatic group. The remaining characteristics such as ages, patients’ underlying diseases, and the levels of blood cells did not differ significantly between the two groups (P >0.05). The intergroup differences between female proportion and the value of PT and INR were no longer present after PSM. But there were still significant statistical differences in the proportion of cholecystectomy and the levels of TB, ALT, and AST between the two groups (Table 1).
|                                | Total cohort                                      | Matched cohort                                      | P     | Total cohort                                      | Matched cohort                                      | P     |
|--------------------------------|---------------------------------------------------|----------------------------------------------------|-------|---------------------------------------------------|----------------------------------------------------|-------|
|                                | Asymptomatic group (N=79)                         | Symptomatic group (N=795)                          | P     | Asymptomatic group (N=79)                         | Symptomatic group (N=316)                          | P     |
| Age (year)                     | 62.6±14.7                                        | 59.6±16.7                                         | 0.086 | 62.6±14.7                                        | 61.8±15.4                                         | 0.669 |
| Sex female%                    | 51 (64.6%)                                       | 412 (51.8%)                                       | 0.031 | 51 (64.6%)                                       | 218 (69.0%)                                       | 0.450 |
| Symptoms                       |                                                   |                                                   |       |                                                   |                                                   |       |
| Abdominal pain                 | -                                                | 515 (64.8%)                                       | -     | -                                                | 229 (72.5%)                                       | -     |
| Obstructive jaundice           | -                                                | 227 (28.5%)                                       | -     | -                                                | 70 (22.2%)                                        | -     |
| Abdominal pain and obstructive jaundice | -                                                | 53 (6.7%)                                         | -     | -                                                | 17 (5.4%)                                         | -     |
| Underlying diseases            |                                                   |                                                   |       |                                                   |                                                   |       |
| Hypertension                   | 17 (21.5%)                                       | 173 (21.8%)                                       | 0.960 | 17 (21.5%)                                       | 77 (24.4%)                                        | 0.595 |
| Diabetes mellitus              | 10 (12.7%)                                       | 97 (12.2%)                                        | 0.906 | 10 (12.7%)                                       | 46 (14.6%)                                        | 0.665 |
| Ischemic heart disease         | 5 (6.3%)                                         | 45 (5.7%)                                         | 1.000 | 5 (6.3%)                                         | 22 (7.0%)                                         | 0.842 |
| Cerebrovascular accident       | 2 (2.5%)                                         | 22 (2.8%)                                         | 1.000 | 2 (2.5%)                                         | 9 (2.8%)                                          | 1.000 |
| Chronic kidney disease         | 2 (2.5%)                                         | 18 (2.3%)                                         | 1.000 | 2 (2.5%)                                         | 9 (2.8%)                                          | 1.000 |
| Cirrhosis                      | 3 (3.8%)                                         | 37 (4.7%)                                         | 0.948 | 3 (3.8%)                                         | 16 (5.1%)                                         | 0.860 |
| Cholecystectomy history        | 60 (76.9%)                                       | 428 (54.0%)                                       | <0.001| 60 (76.9%)                                       | 177 (56.0%)                                       | 0.001 |
| Laboratory findings            |                                                   |                                                   |       |                                                   |                                                   |       |
| Hb (g/L)                       | 129.0±15.8                                       | 129.0±19.0                                       | 0.975 | 129.0±15.8                                       | 126.1±17.8                                       | 0.187 |
| PLT (10^9/L)                   | 169.4±68.1                                       | 177.9±76.3                                       | 0.373 | 169.4±68.1                                       | 176.8±74.3                                       | 0.420 |
| WBC (10^9/L)                   | 5.6±1.7                                         | 5.7±1.5                                          | 0.714 | 5.6±1.7                                         | 5.5±1.5                                          | 0.530 |
| PT (s)     | 11.6 (10.8,12.2) | 11.7 (11.1,12.3) | 0.020 | 11.6 (10.8,12.2) | 11.7 (11.1,12.3) | 0.051 |
|------------|------------------|------------------|-------|------------------|------------------|-------|
| INR        | 1.0 (1.0,1.1)    | 1.0 (1.0,1.1)    | 0.040 | 1.0 (1.0,1.1)    | 1.0 (1.0,1.1)    | 0.138 |
| APTT (s)   | 28.7 (26.6,30.3) | 28.6 (26.1,31.3) | 0.586 | 28.7 (26.6,30.3) | 28.0 (25.7,30.6) | 0.564 |
| TB (umol/L)| 13.5 (11.1,16.9) | 21.2 (13.5,50.0) | <0.001| 13.5 (11.1,16.9) | 18.4 (13.4,37.1) | <0.001|
| ALT (IU/L) | 27.0 (17.0,46.0) | 58.0 (24.0,138.0)| <0.001| 27.0 (17.0,46.0) | 51.0 (22.0,116.5) | <0.001|
| AST (IU/L) | 26.0 (20.0,35.0) | 40.0 (25.0,100.0)| <0.001| 26.0 (20.0,35.0) | 38.0 (24.0,80.0) | <0.001|

GS: gallstone; CBDS: common bile duct stone; Hb: hemoglobin; PLT: plate; WBC: white blood cell; PT: prothrombin time; INR: international normalized ratio; APTT: activated partial thromboplastin time; TB: total bilirubin; ALT: alanine aminotransferase; AST: aspartate transpeptidase

Findings and procedures of ERCP

Among the included 874 patients, the findings of ERCP including presence of periampullary diverticulum (PAD), the proportion of non-dilated CBD, the number of CBD stone, and the diameter of largest stone was not significantly different between the asymptomatic and symptomatic group. Similarly, there were no significant differences in ERCP procedures including the proportion of precut sphincterotomy, difficult biliary cannulation, performed EPBD, ENBD, EST, ERBD, mechanical lithotripsy, and the proportion of patients requiring more than 30 minutes procedure time were observed between the two groups. What is more, complete stone removal in one session were no significant difference in two groups. After PSM, there was still no statistical difference in the above indicators (Table 2).
### Table 2 Baseline characteristics of findings and procedures of ERCP

|                               | Total cohort                      | Matched cohort                  |
|--------------------------------|-----------------------------------|---------------------------------|
|                               | Asymptomatic group (N=79)         | Symptomatic group (N=795)       |
|                               | Symptomatic group (N=795)         | P                               |
| Pad                           | 23/29.1%                         | 228/28.6%                       | 0.935                           |
|                               | 228/28.6%                        | 100/31.6%                       | 0.664                           |
| Number of CBD stone           | 0.344                             | 0.508                           |
| Single                        | 48/60.8%                         | 439/55.2%                       | 48/60.8%                        |
|                               | 439/55.2%                        | 48/60.8%                        | 179/56.6%                       |
| Multiple ≥ 2                  | 31/39.2%                         | 356/44.8%                       | 31/39.2%                        |
|                               | 356/44.8%                        | 31/39.2%                        | 137/43.4%                       |
| CBDD (≤ 1.0 cm/ ≥ 1.0 cm)     | 17(21.5%)/181(22.8%)             | 0.800                           |
|                               | 181(22.8%)/614(77.2%)            | 17(21.5%)/52(16.5%)             |
|                               | 62(78.5%)/614(77.2%)             | 62(78.5%)/264(83.5%)            |
| Largest diameter of stone (cm)| 1.0±0.6                          | 1.1±0.6                         | 0.523                           |
|                               | 1.1±0.6                          | 1.0±0.6                         | 1.1±0.6                         |
|                               | 0.523                            | 1.0±0.6                         | 0.647                           |
| Precut sphincterotomy         | 4/5.1%                           | 32/4.0%                         | 0.884                           |
|                               | 32/4.0%                          | 4/5.1%                          | 14/4.4%                         |
| Difficult cannulation         | 17/21.5%                         | 198/24.9%                       | 0.505                           |
|                               | 198/24.9%                        | 17/21.5%                        | 63/19.9%                        |
|                               | 0.505                            | 63/19.9%                        | 0.754                           |
| EPBD                           | 27/34.2%                         | 286/36.0%                       | 0.751                           |
|                               | 286/36.0%                        | 27/34.2%                        | 112/35.4%                       |
| ENBD                           | 64/81.0%                         | 677/85.2%                       | 0.328                           |
|                               | 677/85.2%                        | 64/81.0%                        | 270/85.4%                       |
| EST                            | 70/88.6%                         | 686/86.3%                       | 0.565                           |
|                               | 686/86.3%                        | 70/88.6%                        | 279/88.3%                       |
| ERBD                           | 11/13.9%                         | 85/10.7%                        | 0.381                           |
|                               | 85/10.7%                         | 11/13.9%                        | 30/9.5%                         |
| Mechanical lithotripsy        | 29/36.7%                         | 243/30.6%                       | 0.261                           |
|                               | 243/30.6%                        | 29/36.7%                        | 99/31.3%                        |
| Procedure time (>30 min)      | 24/30.4%                         | 174/21.9%                       | 0.085                           |
|                               | 174/21.9%                        | 24/30.4%                        | 72/22.8%                        |
| Complete stone removal in one | 66/83.5%                         | 663/83.4%                       | 0.973                           |
| session                        | 663/83.4%                        | 66/83.5%                        | 257/81.3%                       |

PAD: periampullary diverticulum; CBD: common bile duct; CBDD: diameter of common bile duct; EPBD: endoscopic papillary balloon dilation; ENBD: endoscopic nasobiliary drainage; EST: endoscopic sphincterotomy; ERBD: endoscopic retrograde biliary drainage.

**PEP and its severity**

PEP occurred in 6 patients in the asymptomatic group (6/79, 7.6%) and 55 patients in the symptomatic group (55/795, 6.9%). The incidence of PEP was not statistically different between the two groups (P=0.822). After PSM, there was still no significant difference in the incidence of PEP between the two groups (P=0.854) (Table 3).
Further analysis of the severity of PEP in the two groups revealed that all the 6 patients with PEP in the asymptomatic group were mild, and the number and proportion of patients with mild, moderate and severe PEP in the symptomatic group were 45 (81.8%), 9 (16.4%) and 1 (1.8%), respectively. There was no statistically significant difference in the severity of PEP between the two groups (P=0.258). After PSM, there was still no statistical difference in the severity of PEP between the two groups (P=0.199) (Table 3).

|                     | Total cohort                   | Matched cohort       |
|---------------------|--------------------------------|----------------------|
|                     | Asymptomatic group (N=79)     | Symptomatic group (N=795) | P  | Asymptomatic group (N=79) | Symptomatic group (N=316) | P    |
| Incidence           | 6 (7.6%)                       | 55 (6.9%)            | 0.822 | 6 (7.6%)                       | 26 (8.2%)                   | 0.854 |
| **Severity**        |                                |                      |       |                                |                             |      |
| Mild                | 6 (100%)                       | 45 (81.8%)           |       | 6 (100%)                       | 20 (76.9%)                   |      |
| Moderate            | 0 (0.0%)                       | 9 (16.4%)            |       | 0                               | 6 (23.1%)                    |      |
| Severe              | 0 (0.0%)                       | 1 (1.8%)             |       | 0                               | 0 (0.0%)                     |      |

**Table 3 Incidence and severity of PEP in all patients and matched patients**

ERCP related other complications and its severity

ERCP related cholangitis, bleeding and perforation was noted in 1 (1.3 %), 3(3.8%) and 0 patients in the asymptomatic group respectively. In the symptomatic group, ERCP related cholangitis, bleeding and perforation occurred in 7(0.9%), 13(1.6%) and 2 patients (0.3%), respectively. The incidence of cholangitis and bleeding in the asymptomatic group was higher than that in the symptomatic group, and the incidence of perforation was lower than that in the symptomatic group. But these differences between the two groups were not statistically different. After PSM, the incidence of cholangitis, bleeding, and perforation between the two groups had no statistical difference either (Table 4).

|                     | Total cohort                   | Matched cohort       |
|---------------------|--------------------------------|----------------------|
|                     | Asymptomatic group (N=79)     | Symptomatic group (N=795) | P  | Asymptomatic group (N=79) | Symptomatic group (N=316) | P    |
| Incidence           | 1 (1.3%)                       | 7 (0.9%)             | 0.533 | 1 (1.3%)                       | 3 (0.9%)                    | 1.000 |
| Bleeding            | 3 (3.8%)                       | 13 (1.6%)            | 0.354 | 3 (3.8%)                       | 3 (0.9%)                    | 0.181 |
| perforation         | 0                              | 2 (0.3%)             | 1.000 | 0                              | 2 (0.6%)                    | 1.000 |
| **Severity**        |                                |                      |       |                                |                             |      |
| Mild                | 4 (100%)                       | 12 (54.5%)           |       | 4 (100%)                       | 6 (75.0%)                    |      |
| Moderate            | 0 (0.0%)                       | 8 (36.4%)            |       | 0 (0.0%)                       | 2 (25.0%)                    |      |
| Severe              | 0 (0.0%)                       | 2 (9.1%)             |       | 0 (0.0%)                       | 0 (0.0%)                     |      |

**Table 4 Incidence and severity of other ERCP related complications in all patients and matched patients**
Then we compared the severity of the other complications (cholangitis, bleeding, and perforation) between two groups of patients. All 4 complications in the asymptomatic group were mild. In the symptomatic group, 12 (54.5%) complications were mild, 8 (36.4%) were moderate, 2 (9.1%) were severe. There was no statistical difference in the severity of the other complications between the two groups (P=0.098). After PSM, we found that there was still no statistical difference in the severity of complications between the two groups (P=0.294) (Table 4).

Discussion

Nearly 90% of CBD stones could be treated by ERCP and it has become the preferred method for the treatment of CBD stones[20, 21]. However, ERCP related complications are still of concern, especially in asymptomatic patients. Only a few reports focus on the ERCP related complications in patients with asymptomatic CBD stones[7–10]. Therefore, we performed this study to compare the incidence and severity of ERCP related complications between patients with asymptomatic CBD stones and symptomatic ones. The study revealed that there was no significant difference in the incidence and severity of ERCP related complications between asymptomatic and symptomatic patients.

PEP is the most common complication after ERCP, and its risk factors are divided into patient-related and operation-related factors. Female and patients with a history of pancreatitis are patient-related risk factors of PEP, while precut sphincterotomy, non-dilatation of the CBD, and difficult biliary cannulation are operation-related risk factors of PEP [5, 14, 15, 22–24]. In our study, the proportion of female patients in the asymptomatic group (64.6%) was higher than that in the symptomatic group (51.8%), and the difference was statistically significant (P = 0.031). Other risk factors related to PEP were no significant differences between the two groups. The incidence of PEP in the asymptomatic group (7.6%) was higher than that in the symptomatic group (6.9%), but the difference was not statistically significant (P = 0.822). After conducting PSM, we found that the PEP related risk factors and the incidence of PEP were both no significant difference. The outcome was not consistent with previous studies. Xu et al[10]. and Saito et al[8]. found that the incidence of PEP in asymptomatic patients with CBD stones was significantly higher than that in the symptomatic patient. In their studies, there was a significant statistical difference between the two groups of patients with difficult biliary cannulation, a risk factor for PEP, and the number of patients with difficult biliary cannulation in the asymptomatic stone group was significantly higher than that in the symptomatic group. In addition, in Xu et al.'s study, the proportion of patients with CBD dilatation was lower in the asymptomatic group than that in the symptomatic group. These differences may explain why the incidence of PEP was higher in the asymptomatic group than that in the symptomatic group in the previous two studies. A study from Japan also used PSM to compare the incidence of PEP between asymptomatic and symptomatic CBD stones patients. After PSM, the incidence of PEP in the asymptomatic group and the symptomatic groups were 15.2% and 3.2%, respectively. There was a significant statistical difference in the incidence of PEP between the two groups (P < 0.01). Before PSM, the proportion of difficult biliary cannulation and non-dilated bile duct in the asymptomatic group was higher than that in the symptomatic group, which may be the reason for the higher incidence of PEP. After PSM, the above differences disappeared between the two groups. They believed that asymptomatic CBD stone itself was a risk factor for PEP[9]. Previous reports have explained why the incidence of difficult biliary cannulation and non-dilated CBD is higher in asymptomatic patients with CBD stones than in symptomatic patients: for asymptomatic CBD stones patients, they usually had no cholestasis, and the biliary tract pressure is low, so their biliary tract is not easy to occur expansion and the papillary orifices are small, which is a related factor for difficult biliary cannulation [25]. However, there was no statistical difference both in the non-dilated CBD and the incidence of difficult biliary cannulation between the two groups in our study. History of cholecystectomy is an important factor leading to CBD dilatation[26, 27]. In our study, patients with a history of cholecystectomy in the asymptomatic group is significantly higher than that in symptomatic group (P < 0.001), which may lead to the proportion of biliary tract dilatation between two groups no difference. In
addition, the incidence of two groups of patients with difficult biliary cannulation was no different. We think that it may be related to the rich experience of endoscopic doctors. Hence, we think that for doctors who are skilled in ERCP, there may be no increased risk of PEP in asymptomatic patients with CBD stones.

The incidences of mild, moderate, and severe PEP in symptomatic patients were 81.8%, 16.4% and 1.8%, respectively, which is consistent with previous study [28]. In asymptomatic patients, the severity of all PEP cases was mild (100%). There was no statistical difference in the incidence of mild, moderate, and severe PEP between the asymptomatic group and the symptomatic group before and after PSM. So, we believed that the presence of symptoms of CBD stones would not affect the severity of PEP. However, because the sample size of patients with asymptomatic CBD stones in this study was relatively small compared with that of symptomatic patients, further study is needed to confirm the outcome.

The incidence of ERCP related cholangitis, bleeding, and perforation were no significant differences between patients with asymptomatic CBD stones and patients with symptomatic CBD stones. For patients who had ERCP related bleeding, we found there was a statistical difference in the indicators related to coagulation function (PT and INR) between the two groups before PSM. After PSM, the difference was disappeared. In all 13 patients with bleeding in the symptomatic group, obstructive jaundice was present in 10 patients and coagulation dysfunction was observed in 9 patients. So, we think cholestasis may have an influence on coagulation function. These results indicated that clinicians should be alert to bleeding when ERCP is performed on patients with jaundice or abnormal coagulation function. However, the analysis of the results is uncertain since there were few patients suffering from these complications.

The major limitation of this study was that it is in a retrospective and single-center study which had a small number of asymptomatic patients. Further large, multicenter studies are needed to confirm the risk of performing ERCP in asymptomatic CBD stones patients.

**Conclusions**

The present study revealed that there was no significant difference in the incidence and severity of ERCP related complications between asymptomatic and symptomatic patients. Thus, we concluded that the safety of ERCP for asymptomatic patients with CBD stones was comparable to those for symptomatic patients.

**Abbreviations**

ERCP
Endoscopic retrograde cholangiopancreatography; CBD: Common bile duct; PSM: Propensity score matching; PEP: Post-ERCP pancreatitis; EST: Endoscopic sphincterotomy; EPBD: Endoscopic papillary balloon dilation; ENBD: Endoscopic nasobiliary drainage; ERBD: Endoscopic retrograde biliary drainage; PT: Prothrombin time; INR: International normalized ratio; TB: Total bilirubin; ALT: Alanine aminotransferase; AST: Aspartate transpeptidase; PAD: Periampullary diverticulum (PAD).

**Declarations**

**Ethics approval and consent to participate**

This research protocol was approved by the Ethics Committee on Biomedical Research, West China Hospital of Sichuan University.
Consent for publication
Not applicable.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests
The authors declare that they have no competing interests.

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Authors’ contributions
LNX contributed to conception and design of study, acquisition of data, analysis and interpretation of data, drafting the article; CG contributed to acquisition of data, drafting the article; XL contributed to acquisition of data, drafting the article; YNL contributed to critical revision; CHW contributed to conception and design of study, critical revision. All authors issued final approval for the version to be submitted.

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**Figures**

**Figure 1**

Flowchart of patient selection. ERCP: Endoscopic retrograde cholangiopancreatography; CBD: common bile duct stones; PSM: Propensity score matching.