



Title	Assessment of postoperative common bile duct stones after endoscopic extraction and subsequent cholecystectomy
Author(s)	Sugiura, Ryo; Nakamura, Hideaki; Horita, Shoichi; Meguro, Takashi; Sasaki, Kiyotaka; Kagaya, Hidetoshi; Yoshida, Tatsuya; Aoki, Hironori; Morita, Takayuki; Fujita, Miyoshi; Tamoto, Eiji; Fukushima, Masayuki; Ashitate, Yoshitomo; Ueno, Takashi; Tsutaho, Akio; Kuwatani, Masaki; Sakamoto, Naoya
Citation	Surgical endoscopy and other interventional techniques, 36(9), 6535-6542 <a href="https://doi.org/10.1007/s00464-022-09017-z">https://doi.org/10.1007/s00464-022-09017-z</a>
Issue Date	2022-09-01
Doc URL	<a href="http://hdl.handle.net/2115/90370">http://hdl.handle.net/2115/90370</a>
Rights	This version of the article has been accepted for publication, after peer review (when applicable) and is subject to Springer Nature 's AM terms of use, but is not the Version of Record and does not reflect post-acceptance improvements, or any corrections. The Version of Record is available online at: <a href="http://dx.doi.org/10.1007/s00464-022-09017-z">http://dx.doi.org/10.1007/s00464-022-09017-z</a>
Type	article (author version)
File Information	Surg Endosc s00464-022-09017-z.pdf



[Instructions for use](#)

# **Assessment of postoperative common bile duct stones after endoscopic extraction and subsequent cholecystectomy**

**Short title:** Assessment of postoperative bile duct stones

Ryo Sugiura, MD, PhD<sup>1,2</sup>, Hideaki Nakamura, MD, PhD<sup>1</sup>, Shoichi Horita, MD<sup>1</sup>, Takashi Meguro, MD, PhD<sup>1</sup>, Kiyotaka Sasaki, MD, PhD<sup>1</sup>, Hidetoshi Kagaya, MD, PhD<sup>1</sup>, Tatsuya Yoshida, MD<sup>1</sup>, Hironori Aoki, MD, PhD<sup>1</sup>, Takayuki Morita, MD<sup>3</sup>, Miyoshi Fujita, MD<sup>3</sup>, Eiji Tamoto, MD, PhD<sup>3</sup>, Masayuki Fukushima, MD<sup>3</sup>, Yoshitomo Ashitate, MD, PhD<sup>3</sup>, Takashi Ueno, MD, PhD<sup>3</sup>, Akio Tsutaho, MD<sup>3</sup>, Masaki Kuwatani, MD, PhD<sup>2</sup>, Naoya Sakamoto, MD, PhD<sup>2</sup>

1. Department of Gastroenterology, Hokkaido Gastroenterology Hospital, Sapporo, Japan
2. Department of Gastroenterology and Hepatology, Hokkaido University Faculty of Medicine and Graduate School of Medicine, Sapporo, Japan
3. Department of Gastroenterological Surgery, Hokkaido Gastroenterology Hospital, Sapporo, Japan

**Correspondence to:** Ryo Sugiura, MD, PhD

Department of Gastroenterology, Hokkaido Gastroenterology Hospital

Address: 1-2-10, 1-jo Honcho, Higashi-ku, Sapporo, Japan

Phone: +81-11-784-1811, Fax: +81-11-784-1838, E-mail: [ryou99sugi@yahoo.co.jp](mailto:ryou99sugi@yahoo.co.jp)

ORCID number: 0000-0003-4156-8025

## **Abstract**

**Background:** Common bile duct stones (CBDSs) occasionally cause serious diseases, and endoscopic extraction is the standard procedure for CBDS. To prevent biliary complications, cholecystectomy is recommended for patients who present with gallbladder (GB) stones after endoscopic CBDS extraction. However, CBDS can occasionally recur. To date, the occurrence of CBDS after endoscopic CBDS extraction and subsequent cholecystectomy is not fully understood. Hence, the current study aimed to evaluate the incidence of postoperative CBDSs.

**Methods:** This retrospective observational study included consecutive patients who underwent postoperative endoscopic retrograde cholangiography after endoscopic CBDS extraction and subsequent cholecystectomy between April 2012 and June 2021 at our institution. After endoscopic CBDS extraction, a biliary plastic stent was inserted to prevent obstructive cholangitis. Endoscopic retrograde cholangiography was performed to evaluate postoperative CBDSs after cholecystectomy until hospital discharge. The outcomes were the incidence of postoperative CBDSs and CBDSs/sludge. Moreover, the predictive factors for postoperative CBDSs were evaluated via univariate and multivariate analyses.

**Results:** Of eligible 204 patients, 52 patients (25.5%) presented with postoperative CBDSs. The incidence rate of CBDS/sludge was 36.8% (n = 75). Based on the univariate analysis, the significant predictive factors for postoperative CBDSs were  $\geq 6$  CBDSs, presence of cystic duct stones, and  $\geq 10$  GB stones ( $P < 0.05$ ). Moreover, male sex and  $< 60$ -mm minor axis in GB might be predictive factors

( $P < 0.10$ ). Based on the multivariate analysis,  $\geq 6$  CBDSs (odds ratio = 6.65,  $P < 0.01$ ), presence of cystic duct stones (odds ratio = 4.39,  $P < 0.01$ ), and  $\geq 10$  GB stones (odds ratio = 2.55,  $P = 0.01$ ) were independent predictive factors for postoperative CBDSs.

**Conclusions:** The incidence of postoperative CBDS was relatively high. Hence, patients with predictive factors for postoperative CBDS must undergo imaging tests or additional endoscopic procedure after cholecystectomy.

**Keywords:** Cholecystectomy; Common bile duct stone; Cystic duct stone; Endoscopic stone extraction; Gallbladder stone; Postoperative common bile duct stone

## **Introduction**

Common bile duct (CBD) stones (CBDSs) occasionally causes serious diseases such as acute cholangitis, gallstone pancreatitis, and severe obstructive jaundice. Endoscopic retrograde cholangiography (ERC) with endoscopic CBDS extraction is performed worldwide. In addition, to prevent biliary complications such as cholecystitis, gallstone pancreatitis, and CBDS recurrence, subsequent cholecystectomy is recommended for patients who present with gallbladder (GB) stones after endoscopic CBDS extraction [1]. However, CBDS can occasionally recur even after endoscopic CBDS extraction and subsequent cholecystectomy, as observed in 2%–10% of cases [1, 2]. This phenomenon may be attributed to several reasons, which include incomplete CBDS extraction during ERC procedure, migrated GB stones during surgery, and newly formed CBDS. However, it is challenging to separate them completely. Previous studies have focused on residual CBDSs [3], which persist within 6 months after ERC, and recurrent CBDS [4-6], which persists for more than 6 months after ERC. A recent study focused on postoperative CBDS after endoscopic CBDS extraction and subsequent cholecystectomy [7]. Nevertheless, this research had few limitations. First, postoperative ERC procedure was performed if there were filling defects caused by cholangiography via the nasobiliary tube. Second, some independent predictive factors for postoperative CBDS were correlated with not all the biliary tract (CBD, GB, and cystic duct) but also the CBD. The postoperative CBDS after endoscopic CBDS extraction and subsequent cholecystectomy is not fully understood.

In our institution, after endoscopic CBDS extraction, we routinely insert a biliary plastic stent

to prevent obstructive cholangitis during the perioperative period in all patients with GB stones who will undergo subsequent cholecystectomy. After surgery, the plastic stent was removed, and ERC was performed to evaluate postoperative CBDSs until hospital discharge.

The current study aimed to evaluate the incidence of CBDSs diagnosed after endoscopic CBDS extraction and subsequent cholecystectomy. Moreover, the predictive factors for postoperative CBDS were discussed.

## **Methods**

The study protocol was in accordance with the ethical guidelines of the 1975 Declaration of Helsinki (revised in 2013), and it was approved by the Institutional Review Board of Hokkaido Gastroenterology Hospital (20210826-1). Informed consent was obtained from the patients or their families using an opt-out form.

## **Study design**

This retrospective observational study was conducted at Hokkaido Gastroenterology Hospital in Sapporo, Japan. A collected database was searched for consecutive patients who underwent cholecystectomy following ERC and endoscopic CBDS extraction between April 2012 and June 2021, which was an inclusion criterion. The exclusion criteria were the following: 1) patients who did not undergo additional ERC after cholecystectomy, 2) those with GB stones not confirmed on any

preoperative imaging studies and surgically resected specimens, 3) those who underwent surgical CBDS extraction, 4) those who underwent incomplete CBDS extraction before cholecystectomy, and 5) those who refused to enroll in the study.

### **Preoperative endoscopic procedures**

ERC was performed while the patients were sedated (midazolam and pethidine) using the standard station approach with a therapeutic duodenoscope (TJF-240, JF-260V, or TJF-260V; Olympus Medical Systems, Tokyo, Japan). Bile duct cannulation was performed using contrast-assisted or wire-guided cannulation per the endoscopist's discretion. Then, the bile duct was filled with a contrast medium until CBDSs were visualized. After ERC, endoscopic sphincterotomy, endoscopic papillary balloon dilatation, and/or endoscopic papillary large balloon dilatation using a  $\geq 12$ -mm dilation balloon was performed based on the endoscopist's discretion. CBDSs were extracted using a balloon catheter and/or a basket with or without mechanical lithotripsy as necessary. To prevent obstructive cholangitis during the perioperative period, a 7-Fr plastic stent was inserted and positioned with its distal end lying free in the duodenum at the end of the procedure.

### **Postoperative endoscopic procedures**

After cholecystectomy, the plastic stent was removed using forceps. Subsequently, ERC and balloon sweeping were performed to confirm CBDSs. If the presence of CBDSs or sludge was confirmed,



balloon extraction was performed with or without basket extraction as necessary. Postoperative ERC was performed until hospital discharge.

## **Definitions**

Sludge was not considered as CBDS and GB stone in the current study because biliary sludge can improve with conservative treatment and it does not necessarily require endoscopic treatment. The periampullary diverticulum was classified as type I, II, or III according to the position of the major papilla [8]. Cystic duct patterns were classified into three groups (I, II, or III), as shown in a previous report [9]. Cystic duct stone was confirmed via computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasonography (EUS), or preoperative ERC. GB size was measured using the surgically resected specimens.

## **Outcome measures**

The primary outcome was the incidence of postoperative CBDSs. The secondary outcome was the incidence of postoperative CBDSs/sludge. The predictive factors for postoperative CBDSs were evaluated via a multivariate analysis using baseline characteristics and endoscopic and surgical procedure details.

## **Statistical analysis**

Statistical analyses were performed using EZR, which is a free statistical software [10]. Data were presented as percentages for categorical variables and medians (interquartile range) for nonparametric variables. Categorical variables were compared using the chi-square test or the Fisher's exact test, as appropriate. The Mann–Whitney U test was used to compare median values between two groups. The predictive factors for postoperative CBDSs were analyzed via the logistic regression analysis. Factors with a *P* value of < 0.10 in the univariate analysis were then included in the multivariate analysis. The number of CBDSs was measured using the receiver operating characteristic curve, and the cutoff value for the predictive factors for postoperative CBDS was assessed. A *P* value of < 0.05 was considered statistically significant.

## **Results**

In total, 281 patients underwent cholecystectomy following ERC and endoscopic CBDS extraction during the study period. Among them, 204 consecutive patients who fulfilled the study criterion without the exclusion criteria were included in the final analyses (Fig. 1). Moreover, 52 (25.5%) patients presented with postoperative CBDSs (the postoperative CBDS group), and the remaining 152 (74.5%) patients did not (the no CBDS group).

### **Baseline characteristics of participants**

Table 1 shows the baseline characteristics of patients. The postoperative CBDS group had greater

numbers of CBDSs and GB stones and was more likely to have cystic duct stone than the no CBDS group ( $P < 0.05$ ). The two groups did not significantly differ in terms of baseline characteristics, such as age, sex, anatomical factors, and type of CBDS/GB stone. Two patients in the no CBDS group underwent total gastrectomy and jejunal pouch interposition, and a therapeutic duodenoscope was inserted. Therefore, none of the patients underwent ERC procedure with a balloon-assisted endoscope.

### **Preoperative endoscopic and surgical procedure findings**

Almost all patients underwent endoscopic sphincterotomy. The main CBDS extraction method was balloon extraction. There were no significant differences between the two groups in terms of preoperative endoscopic procedure ( $P \geq 0.05$ ) (Table 2).

The median preoperative waiting periods after complete CBDS extraction (interquartile range) in the postoperative CBDS and no CBDS groups were 10.5 (8–15) and 12 (9–15) days, respectively, and were not significantly different between the two groups ( $P = 0.19$ ). In total, 50 (96.2%) patients in the postoperative CBDS group and 151 (99.3%) in the CBDS group underwent laparoscopic cholecystectomy. In one patient from each group, the procedure was converted from laparoscopic to open cholecystectomy during surgery due to strong adhesions around the GB and cystic duct. There were no significant differences in terms of surgical procedure and duration between the two groups ( $P \geq 0.05$ ).

### **Postoperative endoscopic procedures findings**

Postoperative ERC was performed to evaluate postoperative CBDSs until hospital discharge in all patients. The median waiting periods from surgery to postoperative ERC (interquartile range) in the postoperative CBDS and no CBDS groups were 4 (3–6) and 5 (3–7) days, respectively, and were not significantly different between the two groups ( $P = 0.15$ ). The median durations from preoperative ERC to postoperative ERC (interquartile range) in the two groups were 15.5 (13.5–21) and 18 (14–22) days, respectively ( $P = 0.26$ ). The incidence rate of postoperative CBDSs was 25.5% ( $n = 52$ ), and that of postoperative CBDSs/sludge was 36.8% ( $n = 75$ ) in all patients. Table 3 shows the details about postoperative CBDSs and sludge.

### **Predictive factors for postoperative CBDSs**

A univariate analysis of patient characteristics and preoperative endoscopic and surgical procedures was performed to evaluate the predictive factors for postoperative CBDS. Results showed that the significant predictive factors were  $\geq 6$  CBDSs, presence of cystic duct stones, and  $\geq 10$  GB stones ( $P < 0.05$ ) (Table 4). In addition, male sex and  $< 60$ -mm minor axis in GB might be predictive factors for postoperative CBDSs ( $P < 0.10$ ). Based on the multivariate analysis,  $\geq 6$  CBDSs, presence of cystic duct stones, and  $\geq 10$  GB stones were independent predictive factors for postoperative CBDSs (odds ratio = 6.65 [ $P < 0.01$ ], odds ratio = 4.39 [ $P < 0.01$ ], and odds ratio = 2.55 [ $P = 0.01$ ], respectively).

## Discussion

Most studies have focused on residual CBDSs [3], which persist within 6 months after ERC, and recurrent CBDS [4-6], which persists more than 6 months after ERC. The term residual CBDS indicates incomplete endoscopic CBDS extraction in several studies. However, if subsequent cholecystectomy is performed, not only incomplete endoscopic CBDS extraction but also migrated GB stones during surgery should be considered. Further, the occurrence of CBDS must be evaluated within a shorter period after surgery. The term postoperative CBDS, which first appeared in a recent study [7], comprised incomplete CBDS extraction and migrated GB stones in a short period after surgery. Therefore, the term postoperative CBDS was adopted in the current study.

Choe JW et al. [7] showed that the incidence of postoperative CBDS and that of CBDS/sludge were 17.6% and 20.1%, respectively, and these values were slightly lower than those (25.5% and 36.8%) of the current study. This finding might be attributed to two reasons. First, additional ERC and endoscopic CBDS extraction were performed only when there were any filling defects caused by cholangiography via the nasobiliary tube (n = 64/278, 23.0%). CBDSs can be missed on cholangiography, particularly when CBDSs are small or the bile duct is dilated [11]. The current study is advantageous. That is, ERC and balloon sweeping were performed to validate the presence of postoperative CBDSs in all patients. Second, the presence of cystic duct stone was not included as a factor in the previous study, which might explain the differences of the incidence rate

of postoperative CBDS between the two studies because we demonstrated the significant association between the presence of cystic duct stone and postoperative CBDS in the current study.

Moreover, the presence of  $\geq 6$  CBDSs was an independent predictive factor for postoperative CBDS in the current study. The result was similar to that of a previous study, which showed that the presence of  $\geq 3$  CBDSs was a predictive factor [7]. The current and previous studies revealed that multiple CBDSs were not completely retrieved during endoscopic CBDS extraction. Some studies showed that post-ERC CBDSs were missed on balloon-occluded cholangiography in 11%–33% of cases [3, 12, 13]. Moreover, intraductal ultrasonography [12, 13] and peroral cholangioscopy (POCS) [3] can be used to identify post-ERC CBDSs. EUS was also effective for detecting post-ERC CBDSs due to its high accuracy rate [14]. Although intraductal ultrasonography was considered, an accurate evaluation may be challenging to perform due to pneumobilia in most cases. Thus, the procedure was not routinely performed. For POCS and EUS, an additional endoscopic procedure session is required. We consider not only incomplete CBDS extraction but also migrated GB stones during surgery. Hence, we routinely perform postoperative ERC procedure, instead of preoperative POCS and EUS, after cholecystectomy at our institution.

To the best of our knowledge, the current study first showed that postoperative CBDS is common in patients with cystic duct stone. This might be attributed to two reasons. First, cystic duct stones are confirmed during pre-ERC examinations or intra-ERC procedure, and they naturally migrate into the CBD until surgery. Second, cystic duct stones migrate into the CBD during surgery.

Surgeons generally excise the cystic duct as nearly as possible to the confluence of the CBD if there is a cystic duct stone. However, the stone could be unexpectedly pushed out into the CBD due to surgical procedures.

A previous study showed that the presence of GB stone measuring  $\leq 5.5$  mm was a risk factor for the development of CBDS 6 months or more after cholecystectomy [15]. Therefore, we hypothesized that smaller GB stones were likely to migrate into the CBD during surgery. However, our univariate analysis revealed that presence of GB stones measuring  $\leq 5$  and  $\leq 10$  mm were not predictive factors for postoperative CBDS (odds ratio = 2.13 [ $P = 0.11$ ] and 3.98 [ $P = 0.19$ ], respectively) (date not shown). In practice, the presence of  $\geq 10$  GB stones was a predictive factor for postoperative CBDSs in the current study. Our study showed that numerous GB stones can occupy the lumen of the GB. Hence, these stones could be pushed out into the CBD in patients with numerous stones during surgery. Meanwhile, the current research did not accurately identify the number of GB stones. Although we attempted to count the GB stones during preoperative imaging examinations, it could not be evaluated precisely particularly if there were an extremely high number of GB stones due to the presence of biliary sludge, CT-negative GB stones, and accuracy of MRCP for detecting small GB stones. The number of GB stones was described in the surgical record, and the term several numbers was used to describe 10 or more GB stones. Therefore, the presence of  $\geq 10$  GB stones was considered a predictive factor for postoperative CBDS in the current study. Finally, a cutoff value of  $\geq 10$  GB stones was established.

A plastic biliary stent was routinely inserted in the current study. The advantage of insertion of the plastic stent is the ability to prevent obstructive cholangitis during the perioperative period, while the disadvantage of the method is the possibility of the formation of biliary sludges [16]. Previous studies showed that the rates of sludge formation due to insertion of the plastic stent were 33.3% at a mean of 33 day [17] and 43.4% at a median of 70 day [18]. There was a significant relationship between the stent indwelling time and the occurrence of sludge [18]. Considering the previous studies, the plastic stent was unlikely to form biliary sludge because durations from preoperative ERC to postoperative ERC were relatively short (median 15.5–18 days) in the current study. In addition, the difference between CBDS and sludge could be recognizable. However, it cannot be excluded that the formation of sludge due to the insertion of the plastic stent might affect the results.

Risk factors such as large CBD and CBDSs, deep CBD angulation, presence of periampullary diverticulum, low insertion of the cystic duct, and use of mechanical lithotripsy can be associated with residual CBDS and recurrent CBDS, which persist within and after 6 months after ERC [3-6]. However, based on our univariate analysis, these factors could not be used to predict the risk of postoperative CBDS after endoscopic CBD extraction and subsequent cholecystectomy.

The current study had several limitations. First, this was a single-center retrospective study with a relatively small sample size. Second, the risk of incomplete CBDS extraction during preoperative ERC cannot be excluded. Therefore, further studies must be conducted to determine the importance of migrated GB stones during surgery based on several preoperative examinations such



as POCS and EUS. Third, the possibility of formation of biliary sludge due to the insertion of a plastic stent cannot be completely excluded. Forth, the appropriate method for detecting postoperative CBDSs was not identified. Fifth, the long-term outcome was not discussed.

In conclusion, the incidence of CBDSs diagnosed after endoscopic CBDS extraction and subsequent cholecystectomy was relatively high. Thus, patients with predictive factors for postoperative CBDS must undergo imaging tests or additional ERC procedure after cholecystectomy.

**Acknowledgements:** Not applicable.

**Disclosure statement:** Drs. Ryo Sugiura, Hideaki Nakamura, Shoichi Horita, Takashi Meguro,

Kiyotaka Sasaki, Hidetoshi Kagaya, Tatsuya Yoshida, Hironori Aoki, Takayuki Morita, Miyoshi

Fujita, Eiji Tamoto, Masayuki Fukushima, Yoshitomo Ashitate, Takashi Ueno, Akio Tsutaho, Masaki

Kuwatani, and Naoya Sakamoto have no conflicts of interest or financial ties to disclose.

**Funding:** No funding was received for this article.

## References

1. Boerma D, Rauws EAJ, Keulemans YCA, Janssen IMC, Bolwerk CJM, Timmer R, Boerma EJ, Obertop H, Huibregtse K, Gouma DJ (2002) Wait-and-see policy or laparoscopic cholecystectomy after endoscopic sphincterotomy for bile-duct stones: a randomised trial. *Lancet* 360:761-765
2. Lau JY, Leow CK, Fung TM, Suen BY, Yu LM, Lai PB, Lam YH, Ng EK, Lau WY, Chung SS, Sung JJ (2006) Cholecystectomy or gallbladder in situ after endoscopic sphincterotomy and bile duct stone removal in Chinese patients. *Gastroenterology* 130:96-103
3. Itoi T, Sofuni A, Itokawa F, Shinohara Y, Moriyasu F, Tsuchida A (2010) Evaluation of residual bile duct stones by peroral cholangioscopy in comparison with balloon-cholangiography. *Dig Endosc* 22 Suppl 1:S85-89
4. Chong CC, Chiu PW, Tan T, Teoh AY, Lee KF, Ng EK, Lai PB, Lau JY (2016) Correlation of CBD/CHD angulation with recurrent cholangitis in patients treated with ERCP. *Endosc Int Open* 4:E62-67
5. Chae MK, Lee SH, Joo KR (2020) Assessment of the possible risk factors for primary common bile duct stone recurrence after cholecystectomy. *Surg Endosc*, DOI: 10.1007/s00464-020-08143-w, Nov 17, 2020.
6. Choi SJ, Yoon JH, Koh DH, Lee HL, Jun DW, Choi HS (2021) Low insertion of cystic duct increases risk for common bile duct stone recurrence. *Surg Endosc*, DOI: 10.1007/s00464-

021-08563-2, May 24, 2021.

7. Choe JW, Kim SY, Lee DW, Hyun JJ, Ahn KR, Yoon I, Jung SW, Jung YK, Koo JS, Yim HJ, Lee SW (2021) Incidence and risk factors for postoperative common bile duct stones in patients undergoing endoscopic extraction and subsequent cholecystectomy. *Gastrointest Endosc* 93:608-615
8. Boix J, Lorenzo-Zúñiga V, Añaños F, Domènech E, Morillas RM, Gassull MA (2006) Impact of periampullary duodenal diverticula at endoscopic retrograde cholangiopancreatography: a proposed classification of periampullary duodenal diverticula. *Surg Laparosc Endosc Percutan Tech* 16:208-211
9. Itoi T, Sofuni A, Itokawa F, Kurihara T, Tsuchiya T, Moriyasu F (2006) Endoscopic nasobiliary gallbladder drainage after endoscopic sphincterotomy in patients with acute cholecystitis and choledocholithiasis. *Dig Endosc* 18:S101-104
10. Kanda Y (2013) Investigation of the freely available easy-to-use software 'EZ R' for medical statistics. *Bone Marrow Transplant* 48:452-458
11. Amouyal P, Amouyal G, Lévy P, Tuzet S, Palazzo L, Vilgrain V, Gayet B, Belghiti J, Fékété F, Bernades P (1994) Diagnosis of choledocholithiasis by endoscopic ultrasonography. *Gastroenterology* 106:1062-1067
12. Ohashi A, Ueno N, Tamada K, Tomiyama T, Wada S, Miyata T, Nishizono T, Tano S, Aizawa T, Ido K, Kimura K (1999) Assessment of residual bile duct stones with use of intraductal US

during endoscopic balloon sphincteroplasty: comparison with balloon cholangiography.

Gastrointest Endosc 49:328-333

13. Tsuchiya S, Tsuyuguchi T, Sakai Y, Sugiyama H, Miyagawa K, Fukuda Y, Ando T, Saisho H, Yokosuka O (2008) Clinical utility of intraductal US to decrease early recurrence rate of common bile duct stones after endoscopic papillotomy. *J Gastroenterol Hepatol* 23:1590-1595
14. Tse F, Liu L, Barkun AN, Armstrong D, Moayyedi P (2008) EUS: a meta-analysis of test performance in suspected choledocholithiasis. *Gastrointest Endosc* 67:235-244
15. Choi YS, Do JH, Suh SW, Lee SE, Kang H, Park HJ (2017) Risk factors for the late development of common bile duct stones after laparoscopic cholecystectomy. *Surg Endosc* 31:4857-4862
16. Kwon CI, Lehman GA (2016) Mechanisms of biliary plastic stent occlusion and efforts at prevention. *Clin Endosc* 49:139-146
17. Leung JW, Liu Y, Chan RC, Tang Y, Mina Y, Cheng AF, Silva J Jr (2000) Early attachment of anaerobic bacteria may play an important role in biliary stent blockage. *Gastrointest Endosc* 52:725-729.
18. Schneider J, Hapfelmeier A, Fremd J, Schenk P, Obermeier A, Burgkart R, Forkl S, Feihl S, Wantia N, Neu B, Bajbouj M, von Delius S, Schmid RM, Algül H, Weber A (2014) Biliary endoprosthesis: a prospective analysis of bacterial colonization and risk factors for sludge

formation. PLoS One 9:e110112.

## Figure legends

### Figure 1. Study flow chart

CBD, common bile duct; CBDS, common bile duct stone; ERC, endoscopic retrograde cholangiography; GB, gall bladder

Table 1. Baseline characteristics of participants

	Postoperative CBDS (n=52)	No CBDS (n=152)	<i>P</i> value
Age, median (IQR), year	66 (60–79)	69 (59–74)	0.19
Male sex, n (%)	32 (61.5)	71 (46.7)	0.08
Concomitant diseases			
Cholangitis, n (%)	25 (48.1)	68 (44.7)	0.74
Cholecystitis, n (%)	10 (19.2)	27 (17.8)	0.84
Pancreatitis, n (%)	3 (5.8)	9 (5.9)	1
Periampullary diverticulum, n (%)	16 (30.8)	44 (28.9)	0.86
Type of periampullary diverticulum, n			0.75
I	1	5	
II	2	10	
III	13	29	
CBD diameter, median (IQR), mm	9.0 (7.6–10.6)	9.2 (7.9–11.3)	0.62
CBD diameter of $\geq 12$ mm, n (%)	8 (15.4)	25 (16.4)	1
CBD angle, median (IQR), °	132 (121–137)	131 (120–138)	0.90
CBD angle of $\geq 145^\circ$ , n (%)	6 (11.5)	16 (10.5)	0.80
Type of CBDS/sludge on preoperative ERC, n (%)			0.60
Pigmented stone	25 (48.1)	64 (42.1)	



Cholesterol stone	17 (32.7)	50 (32.9)	
Sludge	5 (9.6)	12 (7.9)	
None	5 (9.6)	26 (17.1)	
Number of CBDSs, median (IQR), n	1 (1–4)	1 (0–2)	0.02
≥2 CBDSs, n (%)	24 (46.2)	46 (30.3)	0.04
≥6 CBDSs, n (%)	11 (21.2)	4 (2.6)	<0.01
Largest CBDS diameter, median (IQR), mm			
	5.2 (3.3–8.2)	5.7 (0–7.9)	0.99
Largest CBDS diameter of ≥ 12 mm, n (%)			
	8 (15.4)	14 (9.2)	0.30
Cystic duct pattern, n (%)			0.48
I	42 (80.8)	118 (77.6)	
II	2 (3.8)	14 (9.2)	
III	8 (15.4)	20 (13.2)	
Part of cystic duct confluence, n (%)			0.99
High-level CBD	8 (15.4)	22 (14.5)	
Middle-level CBD	36 (69.2)	107 (70.4)	
Low-level CBD	7 (13.5)	20 (13.1)	
Right hepatic duct	1 (1.9)	3 (2.0)	

Presence of cystic duct stone, n (%)	17 (32.7)	14 (9.2)	<0.01
Type of GB stone, n (%)			0.33
Pigmented stone	34 (65.4)	87(57.2)	
Cholesterol stone	18 (34.6)	65 (42.8)	
Major axis of GB, median (IQR), mm	93.5 (80–100)	95 (80–105)	0.22
<100-mm major axis in GB, n (%)	32 (61.5)	83 (54.6)	0.42
Minor axis of GB, median (IQR), mm	55 (49–65)	60 (50–70)	0.06
<60-mm minor axis in GB, n (%)	28 (53.8)	59 (38.8)	0.07
≥5 GB stones, n (%)	38 (73.1)	94 (61.8)	0.18
≥10 GB stones, n (%)	17 (32.7)	14 (9.2)	0.02
Postupper gastrointestinal surgery			
Total gastrectomy + jejunal pouch interposition, n (%)			
	0	2 (1.2)	1
PTGBD until surgery, n (%)	3 (5.8)	6 (3.9)	0.70

---

CBD, common bile duct; CBDS, common bile duct stone; GB, gall bladder; IQR, interquartile range;

PTGBD, percutaneous transhepatic gallbladder drainage

Table 2. Preoperative endoscopic and surgical procedure details

	Postoperative CBDS (n=52)	No CBDS (n=152)	<i>P</i> value
Ampullary manipulation method, n (%)			0.86
ES	41 (78.9)	121 (79.6)	
EPBD	1 (1.9)	3 (2.0)	
ES + EPBD	6 (11.5)	21 (13.8)	
ES + EPLBD	3 (5.8)	5 (3.3)	
No treatment	1 (1.9)	2 (1.3)	
CBDS extraction method, n (%)			0.67
Balloon extraction	27 (51.9)	91 (59.9)	
Basket extraction	6 (11.5)	18 (11.9)	
Balloon + basket extraction	16 (30.8)	37 (24.3)	
Cholangiography alone	3 (5.8)	6 (3.9)	
Usage of mechanical lithotripsy, n (%)	5 (9.6)	7 (4.6)	0.19
≥2 endoscopic procedures until complete CBDS extraction, n (%)			
	1 (1.9)	4 (2.6)	1
Preoperative waiting period after complete endoscopic CBDS extraction, median (IQR), day			
	10.5 (8–15)	12 (9–15)	0.19
Preoperative waiting period of ≥ 11 days, n (%)			

	26 (50.0)	96 (63.2)	0.10
Surgical procedure, n (%)			0.16
Laparoscopic cholecystectomy	50 (96.2)	151 (99.3)	
Open cholecystectomy	1 (1.9)	0	
Conversion from laparoscopic to open cholecystectomy during surgery			
	1 (1.9)	1 (0.7)	
Surgical duration, median (IQR), minutes			
	70 (58–103)	68 (50–90)	0.26
Surgical duration of $\geq 120$ min, n (%)	9 (17.3)	16 (10.5)	0.22

---

CBDS, common bile duct stone; EPBD, endoscopic papillary balloon dilatation; EPLBD, endoscopic papillary large balloon dilatation; ERC, endoscopic retrograde cholangiography; ES, endoscopic sphincterotomy; IQR, interquartile range

Table 3. Postoperative CBDS and sludge

	Postoperative CBDS (n=52)	No CBDS (n=152)	<i>P</i> value
Waiting period after surgery to ERC, median (IQR), day	4 (3–6)	5 (3–7)	0.15
Pre-ERC waiting period of $\geq 5$ days, n (%)	23 (44.2)	87 (57.2)	0.11
Duration from preoperative ERC to postoperative ERC, median (IQR), day	15.5 (13.5–21)	18 (14–22)	0.26
Type of postoperative CBDS/sludge, n (%)			
Pigmented stone	34 (65.4)	0	
Cholesterol stone	18 (34.6)	0	
Sludge	0	23 (15.1)	
None	0	129 (84.9)	
Number of postoperative CBDSs, median (range, IQR), n	2 (1–20, 1–3)		
Largest postoperative CBDS diameter, median (range, IQR), mm	4.8 (1.0–11.7, 3.3–6.0)		

CBDS, common bile duct stone; ERC, endoscopic retrograde cholangiography; IQR, interquartile range

Table 4. Univariate and multivariate analyses of predictive factors for postoperative CBDSs

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>P</i> value	OR (95% CI)	<i>P</i> value
Age, $\geq 75$ vs. $< 75$ years	0.54 (0.26–1.12)	0.11		
Sex, male vs. female	1.83 (0.96–3.47)	0.06	1.80 (0.88–3.71)	0.11
Cholangitis, present vs. absent	1.14 (0.61–2.15)	0.68		
Cholecystitis, present vs. absent	1.10 (0.49–2.47)	0.81		
Pancreatitis, present vs. absent	0.97 (0.25–3.74)	0.97		
Periampullary diverticulum	1.09 (0.55–2.16)	0.80		
CBD diameter, $\geq 12$ vs. $< 12$ mm	1.79 (0.71–4.55)	0.22		
CBD angle, $\geq 145^\circ$ vs. $< 145^\circ$	1.11 (0.41–3.00)	0.84		
CBDS, cholesterol vs. others	0.99 (0.51–1.94)	0.98		
Number of CBDSs, $\geq 6$ vs. $< 6$	9.93 (3.00–32.8)	$< 0.01$	6.65 (1.84–24.0)	$< 0.01$
CBDS diameter, $\geq 12$ vs. $< 12$ mm	0.92 (0.39–2.20)	0.86		
Cystic duct pattern, I vs. II/III	1.21 (0.55–2.66)	0.64		
Cystic duct confluence, low-level CBD vs. others				
	1.03 (0.40–2.59)	0.96		
Cystic duct stone, present vs. absent	4.79 (2.15–10.6)	$< 0.01$	4.39 (1.82–10.6)	$< 0.01$
GB stone, cholesterol vs. pigmented	0.71 (0.37–1.36)	0.30		

Major axis of GB, <100 vs. ≥100 mm	1.33 (0.70–2.53)	0.39		
Minor axis of GB, <60 vs. ≥60 mm	1.84 (0.97–3.47)	0.06	1.70 (0.83–3.50)	0.15
Number of GB stones, ≥10 vs. <10	2.29 (1.18–4.43)	0.01	2.55 (1.20–5.41)	0.01
PTGBD tube, in situ vs. none	1.49 (0.36–6.18)	0.58		
ES alone vs. other methods	0.96 (0.44–2.07)	0.91		
Use of balloon extraction vs. nonuse	0.90 (0.39–2.08)	0.80		
Use of mechanical lithotripsy vs. nonuse				
	2.20 (0.67–7.27)	0.20		
Number of ERC, ≥2 vs. 1	0.73 (0.08–6.64)	0.78		
Preoperative waiting period, ≥11 vs. <11 days				
	0.58 (0.31–1.10)	0.10		
Laparoscopic vs. open cholecystectomy				
	0.17 (0.01–1.87)	0.15		
Surgical duration, ≥120 vs. <120 minutes				
	1.78 (0.73–4.31)	0.20		
Pre-ERC waiting period after surgery, ≥5 vs. <5 days				
	0.59 (0.31–1.12)	0.11		

---

CBD, common bile duct; CBDS, common bile duct stone; CI, confidence interval; ERC, endoscopic retrograde cholangiography; ES, endoscopic sphincterotomy; GB, gall bladder; OR, odds ratio; PTGBD, percutaneous transhepatic gallbladder drainage



Search of the database  
between April 2012 and June 2021



281 patients enrolled



77 patients excluded

- 60 additional ERC after cholecystectomy not performed
- 9 GB stones not confirmed
- 7 surgical CBD extraction
- 1 complete CBDS extraction not performed until cholecystectomy

204 patients analyzed