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Original Article

Small endoscopic biliary sphincterotomy facilitates long-term recurrence of common bile duct stones

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Abstract: Common bile duct (CBD) stones occur in 10% to 15% of patients with CBD disease. However, there has been no consensus achieved on the treatment of CBD stones to date. The current study aimed to assess the effect of endoscopic biliary sphincterotomy (EST) on the long-term recurrence of CBD stones. Clinical and recurrence-free data of 112 patients with concomitant gallbladder and CBD stones who received laparoscopic cholecystectomy (LC)+laparoscopic CBD exploration (LCBDE) or LC+endoscopic retrograde cholangiopancreatography (ERCP) as an initial treatment were retrospectively reviewed and the prognostic risk factors were identified with univariate and multivariate analyses. Our findings showed EST as an independent risk factor for the recurrence of CBD stones. Patients receiving LC+ERCP had a median follow-up period of 31.3 months (range, 8-49 months), a median recurrence-free period of 25 months (range, 8-49 months), and 1-, 2- and 3-year recurrence-free rates of 87%, 50%, and 42%, respectively, while those undergoing LC+LCBDE had a median follow-up period of 28.7 months (range, 4-52 months), a median recurrence-free period of 24 months (range, 17-48 months), and 1-, 2-, and 3-year recurrence-free rates of 96%, 72%, and 67%, respectively. Multivariate analysis identified CBD diameter (≥1 cm), angulated CBD (angle ≤145) and initial treatment options (LC+ERCP or LC+LCBDE) as independent risk factors for the recurrence of CBD stones (all *P* values <0.05). It is considered that EST should be employed carefully, especially for patients with small stones that were not hard to retrieve, and LC+LCBDE seem to be a more suitable option to avoid the long-term recurrence of CBD stones.

Keywords: Common bile duct stones, endoscopic biliary sphincterotomy, recurrence, risk factor, laparoscopic exploration

Introduction

Common bile duct (CBD) stones occur in 10% to 15% of patients with CBD disease [1]. Meanwhile, approximately 8% to 15% of the patients with gallbladder stones have simultaneous choledocholithiasis [2], a leading cause of acute pancreatitis. Currently, there are several options for the treatment of CBD stones; However, no consensus has been achieved to date [1]. The conventional surgical management of CBD stones consists of choledochotomy and T-tube drainage by open or laparoscopic approach [3]. Since endoscopic retrograde cholangiopancreatography (ERCP) was introduced in 1974 [4], it has become the mainstay in the management of CBD stones, particularly for patients refusing surgery [5]. During the ERCP procedures, endoscopic biliary sphincterotomy (EST) has been widely used to enlarge the papillary orifice and facilitate the removal of stones, and this technique has been proved to effectively reduce the risk of developing iatrogenic pancreatitis [1, 5]. However, EST suffers from the problems of a 15% risk of developing post-ERCP pancreatitis and a 1% to 2% risk of bleeding [6-10]. In addition, endoscopic approach is difficult to remove the stones that are too large or located above the stricture [11], when ERCP requires to be repeated and large EST needs to be performed, resulting in an increase in the risk of perforation development [8].

A 6.4% to 24% short-term recurrence of CBD stones is reported [12, 13]. In recent years, the function of the sphincter of Oddi has been paid

much attention [14]. It has been demonstrated that EST may damage the physiological function of the sphincter of Oddi and cause the subsequent duodenobiliary reflux and infection, which, theoretically, induces the long-term recurrence of stones [15-17]. Laparoscopic CBD exploration (LCBDE), which is minimally invasive to remove CBD stones, may reduce the duration of hospital stay relative to endoscopic treatment [18, 19], and such a technique may retain the function of the sphincter of Oddi and have no iatrogenic reflux [20].

It has been demonstrated that LCBDE and ERCP+EST have comparable effectiveness for removing CBD stones [21]. Large EST has been identified as a risk factor for the recurrence of CBD stones [22]. However, there is little knowledge on the long-term recurrence of CBD stones in patients with small EST [5]. In these studies, the residual muddy stones were hardly differentiated from the recurrent stones. This retrospective study was therefore designed with aims to evaluate the effectiveness of small EST on the long-term recurrence of CBD stones.

Subjects and methods

Study subjects

A total of 223 consecutive patients with CBD and gallbladder stones were retrospectively reviewed, and all cases under went laparoscopic cholecystectomy (LC)+LCBDE or perioperative LC+ERCP at the Department of Hepato-Biliary-Pancreatic Surgery, Nave General Hospital of Chinese People's Liberation Army (Beijing, China) between January 2012 and December 2014. Patients that met the following criteria were enrolled in this study: (1) The subjects with CBD stones undergoing LC+ LCBDE or LC+ERCP as an initial treatment; (2) CBD stones were considered not to be difficult to remove preoperatively; (3) In subjects undergoing LC+ERCP, only small EST was performed during ERCP procedures; And (4) all imaging and laboratory testing results were available. Patients that met the following criteria were excluded from this study: (1) CBD stones were estimated to be difficult to remove preoperatively; (2) The CBD stones were too small to perform LCBDE (diameter <8 mm); (3) The subjects undergoing LC and ERCP did not have the same duration of hospital stay; And (4) the subjects had contraindications of ERCP or laparoscopy.

Of all participants, 44 patients with difficult CBD stones were excluded. Difficult CBD stones were identified based on the stone size (diameter >10 to 15 mm), shape (multiple or barrel shape) and location (proximal to strictures). In the remaining 130 patients undergoing LC+ ERCP, we excluded 63 cases without EST and 4 cases with failure in endoscopic treatment. Finally, 49 subjects undergoing LC+LCBDE and 63 subjects undergoing LC+ERCP were included in this retrospective analysis.

In this study, acute cholangitis was diagnosed if patients had Charcot's triad (upper abdominal pain, fever and jaundice) and leukocytosis, and acute pancreatitis was diagnosed if patients had upper abdominal pain, fever, elevated blood amylase level and edematous pancreas on computed tomography (CT) scans.

Preoperative assessment

Blood samples were collected from each subject. Liver function was evaluated by measuring serum total bilirubin (TBIL), direct bilirubin (DBIL), indirect bilirubin (IBIL), albumin (ALB), alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and gamma-glutamyltranspeptidase (GGT) levels. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were measured to test liver function and surgical safety. Tumor markers including alpha fetoprotein (AFP), carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA-19-9) were examined routinely. Kidney function was evaluated by measuring serum urea nitrogen, creatinine, uric acid, and electrolyte levels. Chest X-ray scan was performed to evaluate signs of pulmonary disease. Abdominal ultrasonography, CT scan or magnetic resonance cholangiopancreatography (MRCP) were employed to evaluate the size and location of CBD stones. In patients at ages of over 60 years or with a history of pulmonary or cardiovascular disease, pulmonary function test and cardiovascular Doppler ultrasound were performed to evaluate signs of any contraindications to resection.

Methods

Patients with CT or MRCP evidence of CBD stones were recommended for LCBDE or ERCP. All subjects chose their initial treatment after they were informed of the surgical risk completely.

LC+LCBDE

All subjects received general anesthesia, and nasogastric tube and catheter were routinely inserted preoperatively. Anesthesia was induced by administration of midazolam (NhwaPharmaceutical Corporation Ltd.; Xuzhou, China), etomidate (NhwaPharmaceutical Corporation Ltd.; Xuzhou, China), sufentanil (Humanwell Healthcare (Group) Co.; Wuhan, China) and rocuronium bromide (Merck Sharp & Dohm; Kenilworth, NJ, USA), and then endotracheal intubation was performed. Sevoflurane (Maruishi Pharmaceutical Co., Ltd.; Osaka, Japan), propofol (Biomedica Foscama Chemical Pharmaceutical Industry; Rome, Italy) and remifentanil (Humanwell Healthcare (Group) Co.; Wuhan, China) were administered for the maintenance of anesthesia. We used a 10-mm trocar below the belly button, a 10-mm trocar below the xiphoid and two 5-mm subcostal trocars for the laparoscopy. Laparoscopic pneumoperitoneum pressure was maintained at 11 to 13 mmHg. Firstly, cholecystectomy was performed in the patients whose Calot's triangle was easily distinguished, while retrograde cholecystectomy or partial cholecystomy was used as an alternative. Then, the anterior wall of CBD was cut by a bipolar electrotome and choledochoscopy was performed to explore the CBD and remove the stones. A T-tube was routinely inserted into the CBD, and then cholangiography was conducted through the T-tube after 4 to 6 weeks to identify the residual CBD stones. If no residual CBD stones were detected, the T-tube was removed; Otherwise, additional choledochoscopy was performed to remove the stones.

EST

All cases received local anaesthesia by oral administration of lidocaine hydrochloride mucilage and underwent intravenous anesthesia perioperatively through intravenous administration of propofol (Biomedica Foscama Chemical Pharmaceutical Industry; Rome, Italy) at a dose of 1.5 to 2 mg/kg and sufentanil (Humanwell Healthcare (Group) Co.; Wuhan, China) at a dose of 0.1 μg/kg. Dosing frequency was adjusted based on the depth of anesthesia. A triple lumen sphincterotome with a guide wire was used to perform cannulation of the CBD, and cholangiography was employed to confirm the stone size and location. Then, a needle-knife sphincterogomy was performed. Small EST was defined as 1/3 of the distance to the papillary roof [23]. All patients receiving ERCP were given a nasobiliary drainage tube in order to relieve the biliary pressure in CBD. Within 3 days after successful ERCP, LC was performed.

Follow-up

All patients were recommended ursodeoxycholic acid (UDCA) therapy and conventionally followed up. Patients underwent monitoring of stone recurrence once every three months by measurement of the liver function, complete blood count, and MRCP. If there was no recurrence in the first 2 years, routine follow-up was then conducted once every 6 months.

Ethical statement

The study was approved by the Ethics Review Committee of Navy General Hospital of Chinese People's Liberation Army (permission number: HJZYY20140017). Written informed consent was obtained from all participants following a detailed description of the purpose of the study.

Statistical analyses

All data were entered into Microsoft Excel version 2007 (Microsoft; Seattle, WA, USA), and all statistical analyses were performed using the statistical software SPSS version 18.0 software (SPSS, Inc.; Chicago, IL, USA). The measurement data were expressed as mean ± standard deviation (SD), while categorical data were described as number or proportion. Comparison of the measurement data was performed with Student *t* test, while differences of the proportions were tested for statistical significance with chi-square test or Fisher's exact test. The long-term recurrence of stones was estimated using the Kaplan-Meier method, and compared between groups using the log-rank test. Multivariate analysis was performed using the Cox proportional hazards model to identify independent prognostic factors, and factors with a P value of <0.05 in the univariate analysis were included in the multivariate Cox regression analysis. Recurrence-free period was defined as the duration from the day of treatment to the first follow-up visit when stone

Table 1. Baseline characteristics of the study subjects

Variable	ERCP+LC (*n*=63)	LC+LCBDE (*n*=49)	*P* value
Gender (M:F)	18:31	20:43	0.725
Age (Year)	66.50±13.629	56.52±14.332	0.001
Child-Pugh score (*n*)			
5	61	48	0.712
6	2	1	
TBIL>17.1 (μmol/L)	39	42	0.196
DBIL>6.1 (μmol/L)	37	46	0.477
ALB (g/L)	34.13±7.66	36.22±5.71	0.112
PT>13 s (*n*)	14	17	0.201
ALT>44 U/L (*n*)	45	39	0.646
AST>38 U/L (*n*)	40	37	0.147
CA19-9>39 μg/L (*n*)	19	29	0.201
WBC ($\times 10^9$/L)	4.75±1.67	6.59±2.61	<0.001
RBC ($\times 10^{12}$/L)	4.82±1.65	4.23±2.41	0.134
HGB (g/L)	130.64±16.11	131.25±18.97	0.871
PLT ($\times 10^9$/L)	209.64±67.40	203.65±73.12	0.699
Postoperative hospital stay (d)	2.75±0.595	4.00±0.793	<0.001
Maximal diameter of CBD (cm)	1.2±0.75	1.4±0.69	0.012
Clinical presentations (*n*)			
Cholangitis	35	28	1.000
Pancreatitis	27	19	0.702
Abnormal LFT	45	42	0.108
None	11	7	0.797

TBIL, total bilirubin; DBIL, direct bilirubin; ALB, albumin; PT, prothrombin time; ALT, alanine transaminase; AST, aspartate aminotransferase; GGT, gamma glutamyltranspeptidase; WBC, white blood cell; RBC, red blood cell; PLT, platelet; HGB, hematoglobulin; LFT, liver function test. CA19-9, carbohydrate antigen 19-9.

Table 2. Comparison of post-surgical complications between LC+ERCP and LC+LCBDE

Complication	ERCP+LC (*n*=63)	LC+LCBDE (*n*=49)
Hemorrhage	0	0
Perforation	0	0
Pancreatitis after ERCP	9	0
Bile leakage	0	1

recurrence was detected, or the latest follow-up visit. A *P* value of <0.05 was considered statistically significant.

Results

Patient characteristics

The subjects' demographic and clinical features are shown in **Table 1**. The subjects receiving LC+ERCP had a mean age of 66.5±13.6 years, and those with LC+LCBDE had a mean age of 56.5±14.3 years (*P*<0.01). A significantly lower mean white blood cell count was detected in the subjects undergoing LC+ERCP than in those with LC+LCBDE (*P*<0.01), while no significant difference was observed in the red blood cell count between the two treatments (*P*=0.134). In addition, a significantly shorter duration of postoperative hospital stay was seen in the subjects undergoing LC+ERCP relative to the subjects undergoing LC+LCBDE (*P*<0.01). All subjects had a Child-Pugh class A liver function.

Follow-up outcomes

There were 9 cases with LC+ERCP and 7 cases with LC+LCBDE lost to follow up. The patients undergoing LC+ERCP had a mean follow-up period of 31.3 months (range, 8-49 months), a median recurrence-free period of 25 months (range, 8 to 49 months), and 1-, 2- and 3-year recurrence-free rates of 87%, 50% and 42%, respectively, while the subjects with LC+LCBDE had a mean follow-up period of 28.7 months (range, 4-52 months), a median recurrence-free period of 24 months (range, 17 to 48 months), and 1-, 2- and 3-year recurrence-free rates of 96%, 72% and 67%, respectively (*P*<0.01).

Efficacy and complications

The success rate of ERCP was 96% in this study. This rate was higher than most reports, which may attribute to the exclusion of patients with difficult CBD stones from the study [13]. The patients with LC+ERCP had a 14.3% incidence of post-surgical complications (*n*=9), which were all post-ERCP pancreatitis with serum amylase elevation, and no other complications, such as bleeding or perforation, occurred in these patients (**Table 2**).

All surgeries were performed successfully in the subjects receiving LC+LCBDE. The most

Table 3. Univariate analysis of risk factors for long-term recurrence of CBD stones

Variables		Recurrence-free rate (%)		*P* value
		1-year	3-year	
Age (years)	<60	92	51	0.129
	≥60	95	56	
WBC (×10^9/L)	>10	94	53	0.765
	≤10	95	51	
CA19-9 (μg/L)	>120	89	49	0.029
	≤120	94	58	
TBIL (μmol/L)	>17.1	89	47	0.021
	≤17.1	95	56	
ALB (g/L)	<35	96	50	0.781
	≥35	93	56	
ALT (U/L)	>44	88	52	0.103
	≤44	92	60	
AST (U/L)	>38	89	53	0.117
	≤38	95	63	
ALP (U/L)	>129	88	50	0.018
	≤129	92	62	
GGT (U/L)	>64	86	44	<0.001
	≤64	94	62	
PLT (×10^9/L)	<100	92	54	0.498
	≥100	89	56	
PT (s)	>13	90	51	0.765
	≤.7	87	59	
Number of stones	≥2	91	51	0.119
	1	92	59	
Diameter of the largest stone (cm)	≥1	83	43	0.001
	<1	97	65	
Diameter of CBD (cm)	≥1	79	40	<0.001
	<1	97	69	
Angle of angulated CBD ()	≤145°	86	45	<0.001
	>145°	95	66	
Thickness of the gallbladder wall (cm)	≥4	86	49	0.044
	<4	93	54	
Initial treatment	LC+ERCP	87	42	<0.001
	LC+LCBDE	96	67	

CA19-9, carbohydrate antigen 19-9; TBIL, total bilirubin; DBIL, direct bilirubin; ALB, albumin; PT, prothrombin time, ALT, alanine transaminase; AST, aspartate aminotransferase; GGT, gamma glutamyltranspeptidase; ALP, alkaline phosphatase; WBC, white blood cell; CBD, common bile duct.

common postoperative complication was biliary leakage (*n*=1) (**Table 2**), which was cured by an additional ERCP to insert a plastic stent.

Risk factors for CBD stone recurrence

We examined the possible correlations between the recurrence-free period and 16 variables using the Kaplan-Meier method (**Table 3**). Since focal inflammation has been identified as a negative factor of LCBDE, we chose the thickness of the gallbladder wall, which can be easily measured prior to treatment, as a marker of inflammatory edema. Univariate analysis revealed that CA19-9, TBIL, ALP, GGT, diameter of the largest stone, CBD diameter, thickness

Table 4. Multivariate analysis of risk factors for the recurrence of CBD stones

Variables	β	SE	Sig	*HR*	95% *CI* for *HR*
CBD diameter	0.545	0.241	0.013	1.835	1.112-2.969
Angulated CBD	0.819	0.229	<0.001	2.331	1.391-3.721
Initial treatment option	0.576	0.249	0.018	1.819	1.108-2.779

B, partial regression coefficient; SE, standard error; Sig, significance; *HR*, hazard ratio; *CI*, confidence interval.

of gallbladder wall, angulated CBD and initial treatment option were potential risk factors for the recurrence of CBD stones.

Multivariate analysis showed that CBD diameter (≥1 cm) (*P*=0.013; Hazard ratio=1.835, 95% *CI*: 1.112-2.969), angulated CBD (angle≤ 145°) (*P*<0.001; Hazard ratio=2.331, 95% *CI*: 1.391-3.712), initial treatment (LC+ERCP or LC+LCBDE) (*P*=0.018; Hazard ratio=1.819, 95% *CI*: 1.108-2.779) were independent risk factors for the recurrence of CBD stones (**Table 4**).

Discussion

CBD stone is a common clinical problem which may cause serious complications, such as acute cholangitis and pancreatitis [1]. To date, there have been several strategies proposed for the management of CBD stones [1]. Open CBD exploration (OCBDE) was the standard treatment of CBD stones before the introduction of laparoscopy and endoscopy [24], and is still of great treatment values nowadays [3]. Currently, the best option for the management of CBD stones is still in debate; However, ERCP and LCBDE are widely accepted as mainstays for the management of the disorder [5]. Since primary CBD stones have a high risk of recurrence [22], the long-term recurrence is an important factor to assess the effectiveness of the treatment.

Compared with LCBDE, ERCP is currently the most commonly used approach to retrieve stones in CBD due to minimally invasive procedures [5]. As a common technique performed during ERCP, EST is effective, notably for difficult CBD stones, such as large stones (diameter >15 mm), multiple stones, and Mirizzi's syndrome [25]. In addition, a combination of EST and endoscopic papillary large-balloon (12 to 20 mm) dilation (EPLBD) is also a well-known procedure for the treatment of CBD stones [25]. However, repeated ERCP and lithotripsy are usually required due to operational difficulties in patients with difficult CBD stones [26]. Small or muddy residual stones often occur in these cases, which is likely to result in incorrect estimation of the exact time of relapse. Therefore, we chose the patients with small CBD stones that were not difficult to remove. In these patients, we observed the recurrence of CBD stones except the confounding existence of residual stones. In addition, stone migration from gallbladder is considered as one of the major causes for the recurrence of CBD stones [27]. It has been reported that development of gallbladder stones affects the pressure on the CBD and the function of the Oddi's sphincter, which is associated with stones recurrence [28]. Hence, we recruited the patients requiring LC with the same duration of hospital stay in order to exclude the effect of gallbladder stones.

ERCP and LCBDE have been found to have the comparative effectiveness for the treatment of CBD stones [21]. In this retrospective study, ERCP and LCBDE were found to show a similar success rate for extracting CBD stones completely. T-tube drainage after choledochotomy has been linked with bile leakage and suture, and focal inflammation around CBD shows adverse effects on choledochotomy [29]. Endoscopic treatments also have multiple disadvantages to retrieve stones such as hemorrhage and perforation of duodenum wall [30]. However, both ERCP and LCBDE showed a low incidence of complications in this study. In addition, we found higher occurrence of dilated CBD in subjects undergoing LC+LCBDE than in those with LC+ERCP, and a lower mean age was observed in subjects with LC+LCBDE relative to those with LC+ERCP. These demographic and clinical characteristics were consistent with clinical practices, since LCBDE has a higher risk than simple LC, which remains a challenge for elderly patients, and it is easier and safer to perform LCBDE and insert a T-tube into a dilated CBD [17].

Currently, most clinical studies regarding the use of laparoscopy and ERCP for the treatment of CBD stones focus on the short-term postoperative effectiveness, complications and safety

[2, 11, 20-22]. There are few reports comparing the long-term recurrence of CBD stones between the LCBDE and EST groups, and little knowledge is available on the risk factors for the recurrence of CBD stones. Results from prospective randomized trials have shown efficacy of stone clearance and safety between the LC+LCBDE and LC+ERCP treatment groups; However, the long-term efficacy and risk factors for stone recurrence were not investigated [31, 32]. Long-term follow-up of 221 patients with gallstones and CBD stones showed 9.5% and 2.1% incidence of recurrent CBD stones in the LC+ERCP and LC+LCBDE groups, respectively; However, stone size and CBD diameter were not stratified in this study [33]. In this study, 13% and 4% one-year recurrence rates of CBD stones were seen in the LC+ERCP and LC+LCBDE groups, which were higher than previous reports [31-33]. To ensure the homogeneity between the two treatment groups, the subjects with a CBD diameter of <8 mm that were hard to receive LCBDE were excluded from the study, which may be responsible for the high incidence of CBD stone recurrence.

Based on long-term follow-up outcomes, a Cox proportional hazards model was employed to identify the risk factors for the long-term recurrence of CBD stones, and multivariate analysis identified CBD diameter, angulated CBD and initial treatment options as independent risk factors for the recurrence of CBD stones (all *P* values <0.05). The patients with LC+ERCP were found to have a significantly higher 1, 2 and 3 years recurrence rates of CBD stones than those with LC+LCBDE. Since all patients undergoing LC+ERCP received EST during endoscopic treatments, it is therefore considered that EST may pose a positive contributor of CBD stone recurrence.

The sphincter of Oddi works as a barrier to prevent reflux from the duodenum [14]. EST enlarges the orifice of sphincter of Oddi and damages its function, resulting in duodenobiliary reflux [14]. A recent study reported the incidence of duodenobiliary reflux in patients with recurrent CBD stones after ERCP [27], and after EST, the incidence of pneumobilia was estimated to be 19% to 42% and bacteriobilia was detected in 88% to 100% patients [34]. Subsequent duodenobiliary reflux tends to cause repeated chronic cholangitis which has a positive effect on recurrence of CBD stones [35, 36]. Therefore, preserving the role of the sphincter of Oddi should be considered.

In the current study, we identified CBD diameter and angulated CBD as independent risk factors for the recurrence of CBD stones. These two factors have been recognized as risk factors for cholestasis and lithogenesis [27, 37]. Before CBD meets duodenum, distal CBD turns to the right side and forms an angle. Distal CBD angulation is associated with cholestasis, which tends to be more severe if distal CBD angle becomes more acute [38]. The diameter of CBD≥1 cm indicates an increased pressure in CBD, which is also a result of abnormal function of the sphincter of Odd and secondary cholestasis. This may be evidence implying the role of the sphincter of Odd in the CBD disease. It is suggested that the function of the sphincter of Oddi should be preserved during the management of CBD stones.

This study also has some limitations. (1) During the retrieval of the CBD stones with ERCP, EPLBD alone is considered to maintain the integrity of the sphincter of Oddi, and facilitate the maintenance of its function. Due to the small sample size, this study did not compare the rate of long-term stone recurrence between EST and EPLBD. (2) To ensure the homogeneity, the effectiveness for the incision of the sphincter of Oddi was not compared among EST. (3) This study was a single-center, non-randomized study with limited study subjects, and all participants enrolled in this study had no difficult CBD stones. Therefore, further large-scale randomized controlled trials are required to validate the findings from this study.

In conclusion, the results of this study demonstrate that LC+LCBDE may be a more suitable approach to reduce the long-term recurrence of CBD stones and small EST may be a positive factor facilitating stone recurrence. It is suggested that the function of the sphincter of Oddi should be preserved as much as possible and small EST should be employed cautiously, notably during ERCP.

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Disclosure of conflict of interest

None.

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