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ORIGINAL ARTICLE—LIVER, PANCREAS, AND BILIARY TRACT

Comparison of endoscopic papillary large balloon dilation and endoscopic sphincterotomy for retrieval of choledocholithiasis: a meta-analysis of randomized controlled trials

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Abstract
Background Endoscopic sphincterotomy (EST) is the most frequently used technique for removal of stones from the bile duct. In recent years, endoscopic papillary large balloon dilation (EPLBD) has been shown to be a safe and effective technique for the removal of large or difficult common bile duct stones. However, comparison of EPLBD and EST for effectiveness in bile duct stone removal has given inconsistent results. The present meta-analysis was carried out to compare the effect of EPLBD and EST in retrieval of choledocholithiasis.
Methods A literature search was performed using Medline, PubMed, EMBase and the Cochrane Central Register of Controlled Trials (CENTRAL) for relevant articles published in English. A meta-analysis was performed on the retrieved studies.
Results Seven randomized controlled trials and 790 patients were involved. EPLBD compared with EST resulted in similar outcomes for overall successful clearance rates of bile duct stones (97.35 vs. 96.35%, OR 1.28, 95% CI 0.58–2.82, $P = 0.54$), stone clearance in the first ERCP session (87.87 vs. 84.15%, OR 1.31, 95% CI 0.81–2.11, $P = 0.21$) and removal of large sized stones (OR 1.08, 95% CI 0.21–5.64, $P = 0.49$). EPLBD performed with either a short or a long ballooning time did not increase the bile duct stone clearance rate. EPLBD decreased overall usage of mechanical lithotripsy in the bile duct stone removal process (OR 0.51, 95% CI 0.30–0.86, $P = 0.01$). However, no significant difference was found between EPLBD and EST in the use of mechanical lithotripsy for the removal of large sized stones (OR 0.67, 95% CI 0.34–1.28, $P = 0.22$). Compared with EST, EPLBD did not show a short ERCP duration (WMD −0.75, 95% CI −1.57 to 0.08, $P = 0.08$). EPLBD was associated with fewer overall complications than EST (5.8 vs. 13.1%, OR 0.41, 95% CI 0.24–0.68, $P = 0.0007$). Hemorrhage occurred less frequently with EPLBD than with EST (OR 0.15, 95% CI 0.04–0.50, $P = 0.002$). There was no significant difference in post-ERCP pancreatitis, perforation and cholangitis.
Conclusions EPLBD is an effective and safe method for the removal of large or difficult common bile stones. EPLBD should be considered as an alternative to EST for patients in whom EST could not be routinely performed. Based on EPLBD causing fewer cases of hemorrhaging, EPLBD is also recommended for removal of large or difficult common bile duct stones in patients with an underlying coagulopathy or need for anticoagulation following ERCP. The long-term prognosis of EPLBD need to be further investigated.

Keywords Endoscopic papillary large balloon dilation · EST · Retrieval of choledocholithiasis · Randomized controlled trials · Meta-analysis

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Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) has become one of the most important techniques for the

diagnosis and treatment of choledocholithiasis. Endoscopic sphincterotomy (EST) and endoscopic papillary balloon dilatation (EPBD) are basic treatments for common bile duct (CBD) stones. These two techniques, however, are associated with complications, such as bleeding, perforation and pancreatitis. In approximately 10% of patients, CBD stones cannot be removed using either EST or EPBD alone combined with standard basket and balloon extraction [1]. Endoscopic treatment for difficult CBD stones with conventional EST or EPBD remains challenging. Stone extraction failure generally occurs with stones larger than 15 mm, stones impacted in the bile duct, intrahepatic stones, post-gastrectomy or mechanical lithotripter use [2]. Methods such as mechanical basket lithotripsy, intraductal shock-wave lithotripsy, extracorporeal shock-wave lithotripsy or, if those fail, biliary stent placement with repeated ERCP or even surgery are applied for removal of difficult CBD stones [2, 3]. However, these methods are not widely available and there is limited data regarding their effectiveness. To facilitate removal of large or difficult CBD stones, a larger opening of the common bile duct orifice seems to be necessary, while the extent of biliary orifice dilation with conventional EST or EPBD is limited [2–4]. For the purpose of removal of large or difficult stones, endoscopic papillary large balloon dilation (EPLBD) with large-diameter (12–20 mm) dilation balloons has been applied in clinical practice. EPLBD, first attempted in 2003 by Ersoz et al. [5] would theoretically combine the advantages of sphincterotomy and balloon dilation by increasing the efficacy of stone extraction while minimizing the complications of both EST and conventional EPBD.

In recent years, a few studies have revealed the encouraging effect of EPLBD for CBD stone removal. However, EST has been accepted as the standard technique for treatment of CBD stones and is most frequently used in retrieval of choledocholithiasis. There are few published reports on comparisons of EPLBD and EST with the outcomes varying among different institutions. We performed the present meta-analysis to evaluate comparisons between EPLBD and EST in the removal of bile duct stones by systematically viewing the published randomized trials.

Methods

Literature search and inclusion criteria

Since EPLBD was first reported in 2003 [5], a Medline, PubMed, EMBase and Cochrane Central Register of Controlled Trials (CENTRAL) search for the years 2003–2011 was carried out to identify relevant articles published in English. Text words and medical subject headings (MeSH) included "endoscopic retrograde cholangiopancreatography", "endoscopic papillary balloon dilation", "large balloon dilation", "endoscopic sphincterotomy" and "removal of common bile duct stone". Boolean operators ('NOT','AND'and'OR') were used in succession to narrow or widen the search. The search result was limited to human studies and clinical trials with no language restrictions. Case report and abstracts from major gastrointestinal meetings were also searched. We searched reference lists and contacted ERCP experts.

The following inclusion criteria were employed in our meta-analyses: (1) studies that evaluated a comparison of EPBD and EST in the removal of CBD stones; (2) studies that were randomized and controlled; (3) studies on humans; (4) data not duplicated in other randomized controlled trials; and (5) EPBD performed with large sized (12–20 mm) balloons. Exclusive criteria were the following: (1) incorrect method of randomization; (2) repetitive publications; (3) studies without complete raw data; (4) intervention differences among intervention groups; and (5) EPLBD or EST for removal of pancreatic duct stones.

Quality assessment

The Jadad score [6], a valid tool for assessing the quality of randomized trials, was applied to the quality assessment of included trials by two investigators (Yadong Feng and Hong Zhu) independently. Scores ranged from 1 to 5: a score of ≤ 2 indicated a lower study quality, whereas studies achieving a rating of ≥ 3 were considered of higher quality and were used as part of the sensitivity analysis. When a discrepancy was encountered, a third reviewer (Xiaoxing Chen) was recruited and a decision was made through discussion.

Data extraction

Two reviewers independently extracted data from each paper fulfilling the inclusion criteria. Discrepancies were resolved through discussion. A flow diagram was employed to identify randomized controlled trials (RCTs) that were eligible for the meta-analysis. Publication year, study population, interventional method, study design, successful rate of CBD stone removal and complications recorded in each included article were extracted.

Statistical analysis

The meta-analysis was conducted using Review Manager 4.2.8 software. Crude analysis and subgroup analysis were performed for included outcomes. The odds ratio (OR) or the weighted mean difference (WMD) and the 95%

confidence interval (CI) for major outcomes were estimated for each study with a random-effects model or a fixed-effects model. For each outcome, between-study heterogeneity was evaluated by Q and I^2 statistics. A P value of <0.05 was considered significant for the χ^2-based Q testing and I^2 was interpreted as the proportion of the total variation contributed by the between-study variation. In the case of clinical heterogeneity concerning the study population and therapeutic modalities, the results were assessed using subgroup analyses or descriptive statistics.

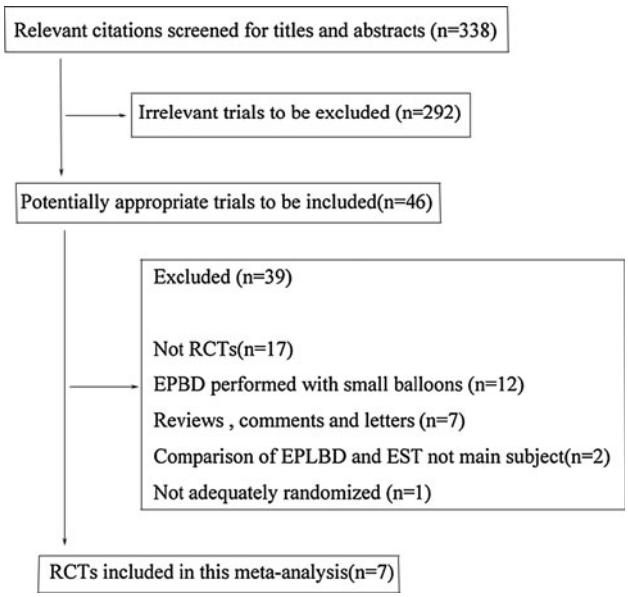

Fig. 1 Flowchart of study selection, exclusion and inclusion processes

Results

Characteristics of included studies

Details of the literature search and selection process are shown in Fig. 1. The literature search with Medline, PubMed, EMBase and CENTRAL yielded 338 articles. Among these citations, we included seven RCTs [7–13] with 790 patients for the meta-analysis. All articles had full text available. Characteristics of the included seven RCTs are listed in Table 1. The Jadad score was used to evaluate the quality of the included studies. As shown in Table 2, four studies had a Jadad score of 5, one study had a Jadad score of 4 and the other two studies had a Jadad score of 3. The included studies were all of high quality and were of reasonable methodological quality.

Outcomes of CBD stones clearance rate

All 790 patients were included in the meta-analysis of bile duct stone clearance. There was no significant heterogeneity ($\chi^2 = 4.62$, $df = 5$, $P = 0.46$) and a fixed-effects model analysis was performed. With regards to the CBD stone overall successful clearance rate, there was no significant difference between the EPLBD group and EST group (OR 1.28, 95% CI 0.58–2.82, $P = 0.54$, Fig. 2). The overall successful clearance rate of bile duct stones was 368/378 (97.35%) in the EPLBD group, while it was 397/412 (96.35%) in the EST group. Meta-analysis was then performed by stratified settings (Table 3). Complete CBD stone clearance in the first ERCP session was reported in five studies [7–9, 11, 12]. The Q test of heterogeneity between the five studies was not significant. The meta-analysis did not show any significant difference in bile duct stones clearance in the first ERCP session

Table 1 Characteristics of the included 7 RCTs

Studies	Location	Patients (n)	Intervention	Allocation concealment
Lin et al. [7]	Taiwan	104	Group 1 ($n = 51$) EPLBD Group 2 ($n = 53$) EST	Adequate
Heo et al. [8]	Korea	200	Group 1 ($n = 100$) small EST plus EPLBD Group 2 ($n = 100$) EST	Adequate
Itoi et al. [9]	Japan	101	Group 1 ($n = 53$) small EST plus EPLBD Group 2 ($n = 48$) EST	Unclear
García-Cano et al. [10]	Spain	91	Group 1 ($n = 31$) small EST plus EPLBD Group 2 ($n = 60$) EST	Unclear
Kim et al. [11]	Korea	55	Group 1 ($n = 27$) small EST plus EPLBD Group 2 ($n = 28$) EST	Adequate
Kim et al. [12]	Korea	149	Group 1 ($n = 72$) small EST plus EPLBD Group 2 ($n = 77$) EST	Not clear
Stefanidis et al. [13]	Greece	90	Group 1 ($n = 45$) full EST plus EPLBD Group 2 ($n = 45$) EST plus ML	Adequate

EPLBD endoscopic papillary large balloon dilation, *EST* endoscopic sphincterotomy, *ML* mechanical lithotripsy

Table 2 Jadad score evaluation of included RCTs

Studies	Setting	Blinded	Randomization	Withdraws	Jadad score
Lin et al. [7]	Single center	Double	Adequate	Clear	5
Heo et al. [8]	Single center	Double	Adequate	Clear	5
Itoi et al. [9]	Single center	Single	Not clear	Clear	3
García-Cano et al. [10]	Single center	Double	Not clear	Clear	4
Kim et al. [11]	Single center	Double	Adequate	Clear	5
Kim et al. [12]	Single center	Single	Not clear	Clear	3
Stefanidis et al. [13]	Single center	Double	Adequate	Clear	5

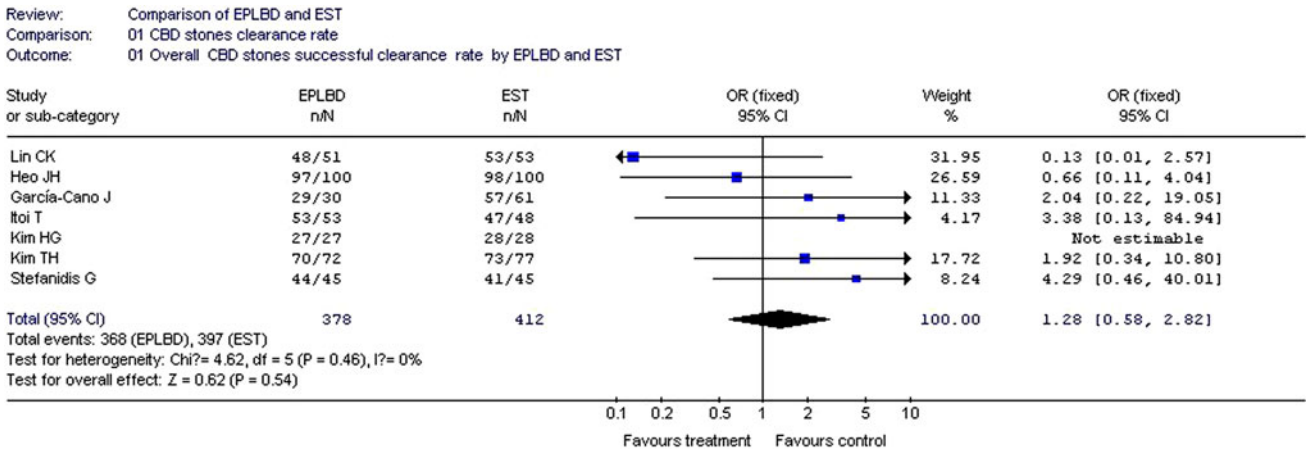

Fig. 2 Fixed-effects model of odds ratios for overall CBD stone successful clearance rates: EPLBD versus EST

Table 3 Stratified subgroup analysis of CBD stone clearance by EPLBD and EST

Setting	Methods	Patients (*n*)	OR (95% CI)	*Z*	*P*	Heterogeneity		
						χ^2	*df*	*P*
CBD stones clearance in first ERCP	EPLBD	295	1.31 (0.81–2.11)	1.10	0.27	5.91	4	0.21
	EST	299						
Removal of large size CBD stones	EPLBD	91	1.08 (0.21–5.64)	0.09	0.93	0.48	1	0.49
	EST	87						
Different ballooning time for EPLBD								
Shot BT (<60 s)	EPLBD	170	2.77 (0.80–9.61)	1.61	0.11	0.34	2	0.85
	EST	170						
Long BT (≥1 min)	EPLBD	181	0.56 (0.18–1.78)	0.98	0.33	1.68	2	0.43
	EST	213						

EPLBD endoscopic papillary large balloon dilation, *EST* endoscopic sphincterotomy, *BT* ballooning time

between the EPLBD and EST groups (OR 1.31, 95% CI 0.81–2.11, $P = 0.21$). The CBD stone clearance rates in the first ERCP session were 261/297 (87.87%) and 255/303 (84.15%) in the EPLBD and EST groups, respectively. Comparison of EPLBD and EST for removal of large sized (≥15 mm) CBD stones was evaluated and three studies [8, 11, 13] with 178 patients were included. The heterogeneity was not significant and there was no significant difference according to a fixed-effects model analysis (OR 1.08, 95% CI 0.21–5.64, $P = 0.49$). Different ballooning times were reported in six studies [7–10, 12, 13] and three studies [9, 12, 13] were about short ballooning times (<60 s) and the

other three studies [7, 8, 10] were about long ballooning times (≥1 min) for EPLBD. The Q test of heterogeneity between studies was not significant. When studies were stratified by different ballooning times, meta-analysis did not indicate a significant difference in bile duct clearance between EST and EPLBD, despite EPLBD being performed with either short times (OR 2.77, 95% CI 0.80–9.61, $P = 0.11$) or long times (OR 0.56, 95% CI 0.18–1.78, $P = 0.33$). The bile duct stone clearance rate was 167/170 (98.23%) and 174/181 (96.13%) in short ballooning time and long ballooning time subgroups, respectively.

Meta-analysis for mechanical lithotripsy and ERCP duration

Six studies [7–9, 11–13] with 698 patients were included in the meta-analysis for use of mechanical lithotripsy during the CBD stone removal process. The trials were heterogeneous ($\chi^2 = 27.76$, $df = 5$, $P < 0.0001$). A random-effects model analysis was performed. The results indicated no significant difference in mechanical lithotripsy between EPLBD and EST (OR 0.26, 95% CI 0.06–1.03, $P = 0.06$, Fig. 3). A subgroup analysis was then performed by excluding the study by Stefanidis et al. [13] because use of mechanical lithotripsy was not followed EPLBD in this study. In the subgroup analysis, heterogeneity disappeared ($\chi^2 = 5.38$, $df = 4$, $P = 0.25$). The results of the subgroup analysis showed that the application of EPLBD decreased the need for use of mechanical lithotripsy during whole CBD stone removal using the ERCP process (OR 0.51, 95% CI 0.30–0.86, $P = 0.01$, Fig. 4). For use of mechanical lithotripsy in the removal of large sized stones, data were extracted from three studies [8, 11, 12]. The Q test indicated that studies were homogeneous ($\chi^2 = 3.19$, $df = 2$, $P = 0.20$). Meta-analysis did not show any significant difference in mechanical lithotripsy between the two groups (OR 0.67, 95% CI 0.34–1.28, $P = 0.22$, Fig. 5). Three studies compared EPLBD and EST for ERCP duration of the removal of bile duct stones [7, 9, 11]. These trials included 256 patients for meta-analysis. The Q test of heterogeneity for the included studies was not significant ($\chi^2 = 0.35$, $df = 2$, $P = 0.84$). Meta-analysis was performed using a fixed-effects model. The meta-analysis

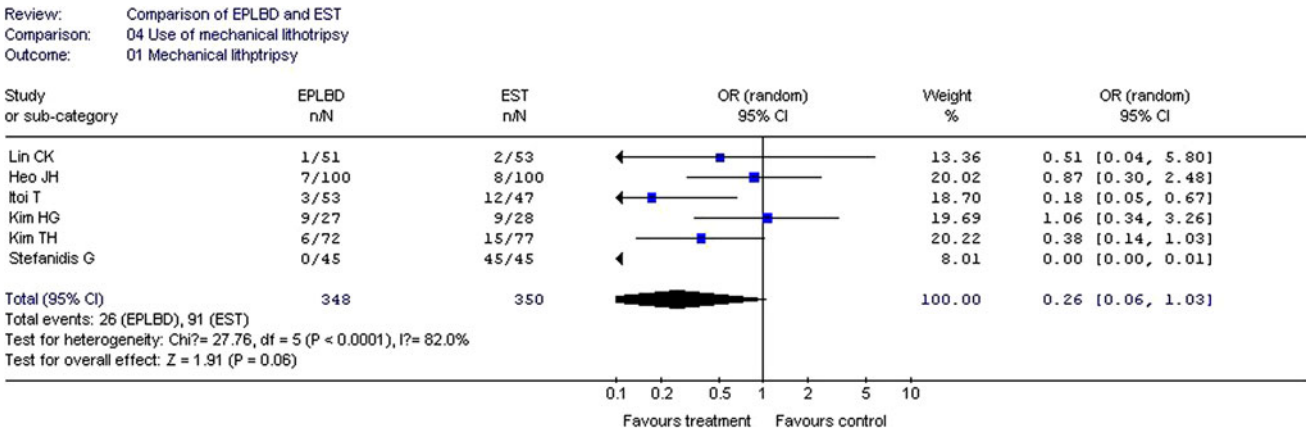

Fig. 3 Random-effects model of odds ratios for mechanical lithotripsy during CBD stone removal processes: EPLBD versus EST

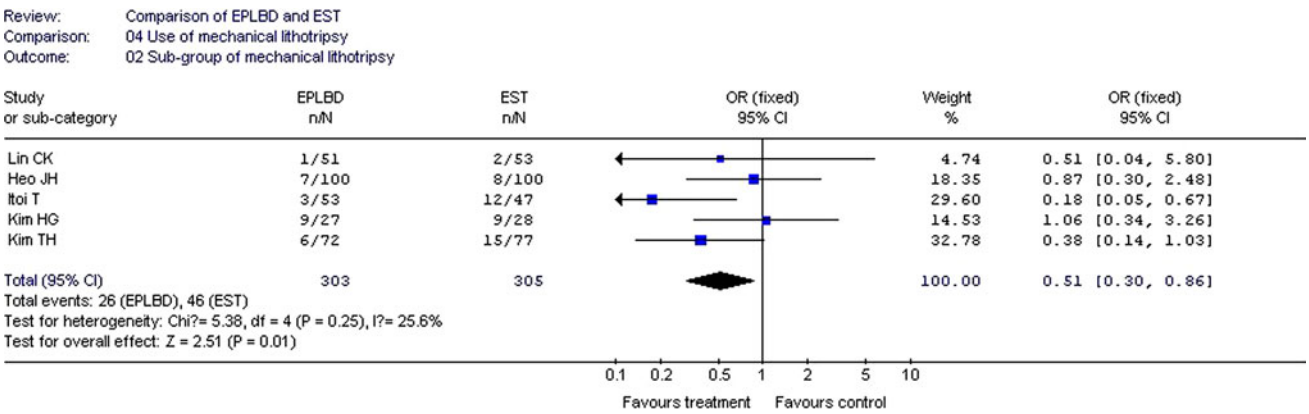

Fig. 4 Fixed-effects model of odds ratio for mechanical lithotripsy during CBD stones removal process: EPLBD versus EST (subgroup analysis)

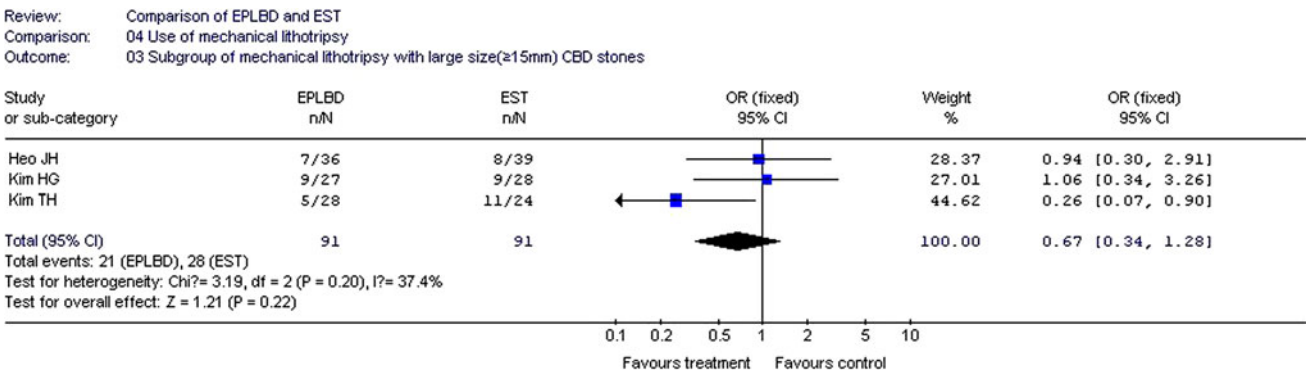

Fig. 5 Fixed-effects model of odds ratios for mechanical lithotripsy in the removal of large CBD stones: EPLBD versus EST

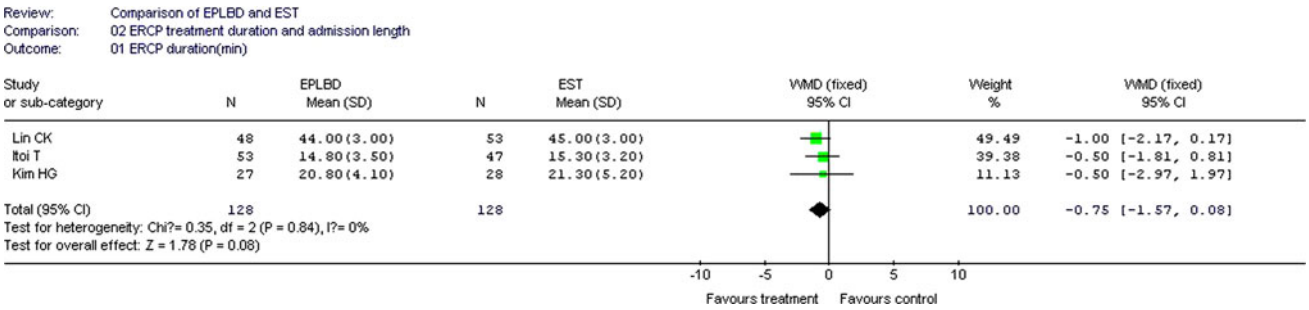

Fig. 6 Fixed-effects model of weighted mean differences for ERCP duration of removal of CBD stones: EPLBD versus EST

revealed no significant difference in ERCP duration (WMD −0.75, 95% CI −1.57 to 0.08, $P = 0.08$, Fig. 6).

Outcomes of related complications

Complications were determined according to consensus guidelines, including post-ERCP pancreatitis, hemorrhage, perforation and cholangitis [14, 15]. All seven studies with 790 patients were included. For overall complications, the Q test for heterogeneity demonstrated no statistical significant difference ($\chi^2 = 6.97$, $df = 6$, $P = 0.32$). Meta-analysis showed that EPLBD (22/378, 5.8%) caused fewer complications than EST (54/412, 13.1%; OR 0.41, 95% CI 0.24–0.68, $P = 0.0007$, Fig. 7). Complications were stratified for subcategory analysis (Table 4). There was no significant heterogeneity in each subgroup. Meta-analysis indicated a significant reduction for hemorrhage in the EPLBD group (OR 0.15, 95% CI 0.04–0.50, $P = 0.002$). There was no significant difference in post-ERCP pancreatitis, perforation and cholangitis.

Discussion

In recent years, EPLBD has been shown to be effective for the removal of large or difficult common bile duct stones. However, EST remains as the "gold standard" therapy technique for removal of CBD stones and is widely used during ERCP. Conventional EPBD appears to be an alternative for the removal of CBD stones and seems to offer some advantages over EST. Since conventional EPBD is performed with small balloons (<10 mm), its use is always limited, especially in the removal of large CBD stones [16]. According to the concept of combining the advantages of EST with those of EPBD, EPLBD is always performed with EST plus large balloon dilation and has been applied in the extraction of large or difficult CBD stones. Theoretically, as an excellent procedure for large and difficult common bile duct stones removal, EPLBD would facilitate the removal of CBD stones and result in a lower risk for complications [8, 17]. Additionally, dilating the papilla using a large balloon without prior addition of EST was also reported. No matter prior addition EST is performed or not, EPLBD has been reported to come out with satisfactory results for large or difficult common bile duct stones [18]. Although some published studies compared EPLBD and EST for extraction of CBD stones, the efficacies and the complication rates of these two methods differ. Our present meta-analysis was to compare EPLBD with EST for the treatment of large or difficult common bile duct stones.

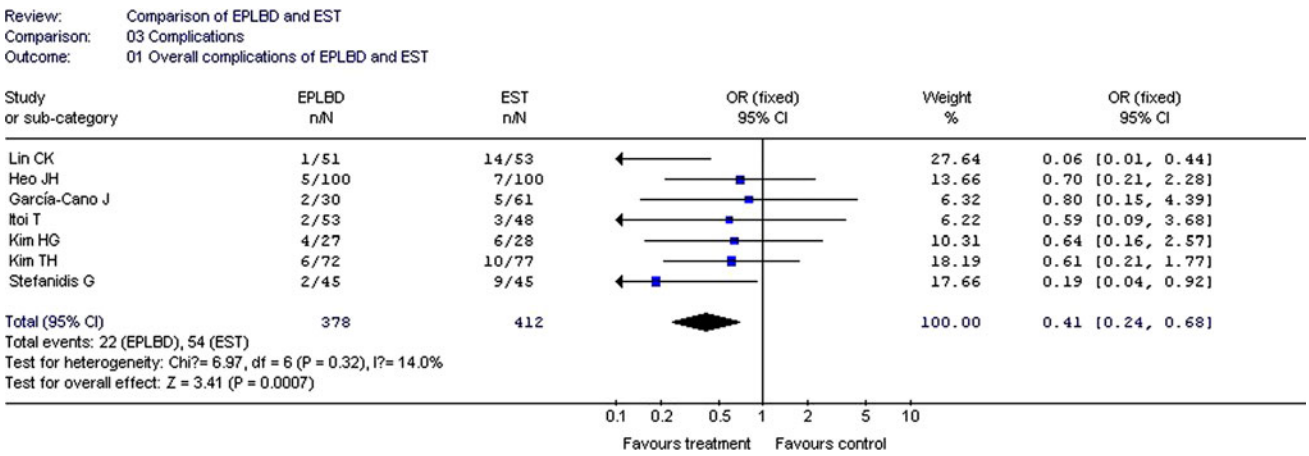

Fig. 7 Fixed-effects model of odds ratios for overall complications: EPLBD versus EST

Table 4 Stratified subgroup analysis of complications with EPLBD and EST

Setting	Methods	Patients (*n*/*N*)	OR (95% CI)	*Z*	*P*	Heterogeneity		
						χ^2	*df*	*P*
Hemorrhage	EPLBD	2/378	0.15 (0.04–0.50)	3.09	0.002	2.83	3	0.42
	EST	20/412						
Post-ERCP pancreatitis	EPLBD	17/378	1.17 (0.58–2.36)	0.44	0.66	5.05	5	0.41
	EST	16/412						
Perforation	EPLBD	0/378	0.34 (0.03–3.31)	0.93	0.35	0.00	1	0.97
	EST	2/412						
Cholangitis	EPLBD	3/378	0.46 (0.15–1.39)	1.38	0.17	3.69	4	0.45
	EST	9/412						

In this meta-analysis, the overall success rate of CBD stone clearance was similar in the EPLBD and EST groups (97.35 vs. 96.35%). The data was consistent with previous studies [7–13]. Then the CBD stone clearance rate in first ERCP session was compared. According to the results, EPLBD did not show any advantage in successful clearance of bile duct stones over EST in the first ERCP session. This result was not consistent with the studies by Itoi et al. [9] and Kim et al. [12]. Regarding this discrepancy, it may be associated with factors such as study design, balloon size, the size or shape of the CBD stones and the extent of EST. In patients whose CBD stones could not be completely removed in the first ERCP session, the cause was mainly large or multiple stones or anatomical difficulties [8, 12]. As for removal of large sized CBD stones, comparison of the results for EPLBD and EST showed the two procedures were similar. Our result was consistent with the included RCTs [8, 11, 13]. However, it has been reported that EPLBD may reveal better results in the removal of large sized stones [5]. This difference may be related to the forementioned factors. Ballooning time remains controversial in EPLBD. According to the present results, EPLBD was performed with longer durations, which did not affect the success rate of CBD stone clearance. In conventional EPBD [19], a longer duration of conventional EPBD may improve the efficacy of CBD stone extraction. In conventional EPBD, the papilla is dilated with a 10 mm or smaller balloon, thus longer dilations may offer a larger orifice and facilitate stone extraction. In EPLBD, the biliary sphincter is dilated with a large diameter (12–20 mm) balloon, which can create a very large orifice [4]. In all included studies for this meta-analysis, EPLBD was performed under endoscopic and fluoroscopic guidance to observe the gradual disappearance of the waist in the balloon. Once the waist disappeared, the balloon remained inflated for different times. Theoretically, EPLBD with a long duration may be beneficial to stone extraction. However, according to the present meta-analysis, EPLBD ballooning time did not seem to alter the success rate of CBD stone clearance. Regarding this difference, EPLBD is a different procedure than conventional EPBD, which can offer a large orifice and facilitate removal of large bile duct stones [4, 5].

Mechanical lithotripsy has been the traditional choice for the management of large bile duct stones. In this

meta-analysis, the use of mechanical lithotripsy was less frequent in the EPLBD group than in the EST group. However, mechanical lithotripsy usage in large size stones was similar. In the included studies by Itoi et al. [9] and by Kim et al. [12], mechanical lithotripsy might be used more often in the EST group compared to the EPLBD group. Our results were consistent with other included studies [7, 8, 11]. For relatively smaller CBD stones, lower rates of mechanical lithotripsy usage were reported [20, 21]. Despite orifice dilation with a large balloon, removing large stones may be difficult, especially in patients with a tapered distal common bile duct [22]. It was notable that in the study by Kim [11], a stone fragmentation method such as mechanical lithotripsy was needed, despite the orifice being dilated with a CRE balloon (maximum 18 mm). Use of lithotripsy was shown to be related to ERCP duration and fluoroscopic time [23]. In this meta-analysis, ERCP duration was not shorter in the EPLBD group compared to the EST group. The use of mechanical lithotripsy may be related to stone size, the extent of EST, the shape of the stones and the bile duct. The extent of EST may be the important factor in reducing the use of mechanical lithotripsy. Full EST was considered as the most important factor in removal of large bile-duct stones [8], the degree of sphincterotomy before EPBD remains to be determined [24]. Although the technical aspects of EST have been well established, it is difficult to evaluate the adequacy of a sphincterotomy, so the criteria for creating an adequate sphincterotomy for removal large stones are not described [5]. In this meta-analysis (Table 1), EPLBD was performed without prior EST in the study by Lin et al. [7], while in the study by Stefanidis et al. [13] full EST was added prior to the use a large-diameter balloon dilation, and small EST was performed prior to EPLBD in the other five studies [8–12]. Although the extent of EST varied in the reported studies [5, 7–13, 16, 17, 20–22], ranging from limited to extended, the results of successful rates and complication rates were acceptable. Compared with conventional EST or EPBD, EPLBD may seem to be a different procedure in removal of large or difficult CBD stones. Use of a large-diameter balloon would be expected to tear the sphincter and offer an adequate orifice for removal of large stones.

Endoscopic retrograde cholangiopancreatography-related complications were evaluated in the meta-analysis. Compared with EST, EPLBD was associated with fewer complications. EPLBD is thought to have remarkably less risk of complications than EST [4]. Stratified subgroup analysis showed that EPLBD might reduce the risk of hemorrhage. Risks of pancreatitis, perforation and cholangitis were not significantly different in the EPLBD and EST groups. So EPLBD is always applied to patients with prior sphincterotomy [25] and patients with periampullary diverticula [26]. Although post-ERCP complications occur less frequently in EPLBD, it should be mentioned that EPLBD may cause very serious bleeding [27] and perforation [28]. The most likely explanation would be that dilation with a large balloon would tear the ducts and result in bleeding and perforation. It is logical that the size of a balloon, the size and shape of stones and the patient's anatomy should be taken into account [3].

The function of the biliary sphincter after EPLBD is still not clear, while it should be necessarily considered. The function of the sphincter of Oddi is destroyed by EST, leading to duodenobiliary reflux. So in EST, long-term complications, such as cholangitis, recurrent stones and possibility of increasing risk of cholangiocarcinoma have been reported [24, 29]. Papillary function after EPBD is preserved and greater than it after EST [30]. There is no data available if papillary function was altered after EPLBD. Late complications of EPLBD remains not clear, and there is no data in this meta-analysis. It is important to investigate clinical benefits for late complications and long prognosis of EPLBD.

The present meta-analysis has some limitations. First, data regarding EPLBD are relatively limited. The sample size included for this meta-analysis was not sufficiently large. Second, as for subcategory analysis such as ballooning time, stone size and the extent of EST, data were limited because of the relatively small sample size. Third, the included studies had different study designs. Furthermore, based on high quality studies, our present meta-analysis might have selection and negative results bias.

In conclusion, EPLBD is an effective and safe method for the removal of large or difficult common bile stones. EPLBD might reduce the usage of mechanical lithotripsy in bile duct stone removal procedures. EPLBD is as effective as EST in the removal of large sized or difficult common bile duct stones. In patients with large or difficult common bile duct stones, if EST could not be routinely performed, EPLBD should be considered as an alternative treatment method, because of a wider orifice of the papilla. Since EPLBD causes fewer complications than EST, EPLBD should also be considered as an alternative for EST in patients with prior sphincterotomy and with periampullary diverticula. As for treatment of large or difficult common bile duct stones in patients with an underlying coagulopathy or need for anticoagulation following ERCP, EPLBD is recommended, because of less risk of hemorrhage than EST. Since relatively limited data regarding EPLBD are available, the efficiency and long-term prognosis of EPLBD for removal of large or difficult common bile duct stones still need to be further investigated.

Conflict of interest The authors declare that they have no conflict of interest.

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