The effect of duration time on the efficacy and safety during endoscopic papillary balloon dilation for choledocholithiasis treatment

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Abstract

Background

Endoscopic papillary balloon dilation (EPBD) has been widely accepted as an alternative to endoscopic sphincterotomy (EST) during therapeutic endoscopic retrograde cholangiopancreatography (ERCP) for choledocholithiasis treatment. No consensus has been established to define the precise duration of EPBD.

Methods

The PubMed, EMBASE, Cochrane Library database were systematically searched up to 31 May 2019 for research comparing short duration (≤ 30 seconds) and long duration (≥ 1 minute) of EPBD.

Results

Seven studies demonstrated that EPBD with long duration was superior than short duration in the stone clearance rate during the first ERCP (OR 0.61, 95%CI [0.48, 0.77], $P < 0.001$). Long duration exhibited a trend of higher efficacy in total stone removal across all ERCP sessions (OR 0.98, 95%CI [0.73, 1.31], $P = 0.89$), less frequency of mechanical lithotripsy use (OR 1.22, 95%CI [0.79, 1.89], $P = 0.37$). Compared with long duration, short balloon time had lower rate of overall complications (OR 0.85, 95%CI [0.70, 1.04], $P = 0.11$) and post-ERCP pancreatitis (OR 0.81, 95%CI [0.63, 1.03], $P = 0.09$). No significance was identified in hemorrhage (OR 0.86, 95%CI [0.30, 2.44], $P = 0.77$), perforation (OR 0.54, 95%CI [0.14, 2.14], $P = 0.38$) and cholangitis (OR 1.15, 95%CI [0.80, 1.66], $P = 0.44$).

Conclusion

Long duration (≥ 1 minute) could significantly increase the efficacy of EPBD in stone removal rate during first ERCP session, manifesting higher rate of total CBD stone clearance and less mechanical lithotripsy. Short EPBD contributed to less overall complications than long EPBD but not significantly.

Background

Approximately 10% of the global adult are diagnosed with symptomatic gallstones and common bile duct stones (CBDs) accounted for 10%-15% symptomatic cholelithiasis[1]. For patients with choledocholithiasis, the therapeutic effect and prophylaxis has been obviously improved with the rapid progress of endoscopic techniques. Endoscopic sphincterotomy (EST) was firstly implemented in 1975 and gradually accepted as a common technique to enlarge the sphincter of Oddi (SO) during endoscopic retrograde cholangiopancreatography (ERCP)[2]. But EST also demonstrated failure of stone removal and post-procedure complications including post-ERCP pancreatitis (PEP), hemorrhage, perforation, cholangitis. As a potential method for preserving the function of SO, endoscopic papillary balloon dilation (EPBD) was invented and suggested as an alternative intervention to sphincterotomy for efficient and safe removal of CBDs with less hemorrhage events[3–7]. But higher incidence of PEP was reported in patients suffering EPBD. Recently, EPBD appears to be combined with preceding EST to treat large or difficult CBD stones, which could improve efficacy of stone removal and reduce the risk of related complications[8–11].

Although EPBD has been widely adopted for removal and extraction of CBD stones, no consensus of accurate duration time has been established. ERCP guideline of European Society of Gastrointestinal Endoscopy (ESGE) weakly recommends ≥ 2 -minute papillary dilation should be maintained after waist disappearance[4]. Endoscopic guideline for common bile duct stones of ESGE illustrated that EPBD duration should be maintained between 30 and 60 seconds from waist disappearance[12]. Conflicting conclusions were drawn from present published data. A network meta-analysis illustrated that EPBD with long dilation duration is safer than EPBD with short dilation duration and EST because ≤ 1 -minute dilation could increase the risk of PEP and long EPBD had a lower rate of overall complications[13]. Another meta-analysis indicated no significant difference in CBD stone clearance between endoscopic papillary large balloon dilation (EPLBD) and EST, despite EPLBD being taken with either short dilation time (≤ 30 seconds) or long dilation time (≥ 1 minute)[14]. Besides, it was reported that 30-second ballooning duration showed a lower tendency in the incidence of post-procedural pancreatitis than 2-minute ballooning duration[15].

Our meta-analysis and systematic review will aim to evaluate the efficacy and safety between short dilation duration (≤ 30 seconds) or long dilation duration (≥ 1 minute) during removal of CBD stones by EPBD.

Methods

Our analysis was implemented on the basis of the Cochrane Handbook for Systematic Reviews of Interventions and presented according to Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines[16].

Literature search

We searched and identified research from PubMed, EMBASE, and Cochrane Library (including CENTRAL) database from the January 1st, 1990 to May 31st, 2019. Besides, we broaden the search for available or similar studies from review articles and academic conferences. No language restriction was achieved during our searching. The following keywords involved in our searching were “endoscopic retrograde cholangiopancreatography”, “ERCP”, “endoscopic papillary balloon dilation”, “endoscopic papillary large balloon dilation” and “endoscopic sphincterotomy”. The titles and abstracts of literature research was independently conducted and screened by two authors (Y.N.W., M.Q.). Discrepancies were resolved by consensus and a final decision was made by the third author (J.B.H.).

Study selection

Inclusion criteria were: (1) both randomized controlled trials (RCTs) and retrospective cohort trials (RCSs) comparing ballooning dilation duration with ≤ 30 seconds vs ballooning dilation duration with ≥ 1 minute; (2) trials enrolling CBD stones removed by ERCP for patients with choledocholithiasis; (3) trials following Cotton consensus guideline to assess post-ERCP complications[17]; (4) full-length article. And exclusion criteria were: (1) systematic reviews, meta-analysis and case reports involved in commenting EPBD duration; (2) trials comparing both groups with long duration (≥ 1 minute) of balloon dilation; (3) trials aiming for other diseases, such as biliary stenosis or biliary tumor.

Data extraction and quality assessment

Extracted outcome includes from included studies: (1) total CBD stone clearance rate during ERCP; (2) CBD stones clearance rate during the first ERCP; (3) frequency of mechanical lithotripsy used; (4) frequency of overall post-procedural complication; (5) frequency of PEP, bleeding, perforation and cholangitis.

According to Cochrane guideline and consensus, we collected baseline clinical data from included research and converted them to a common data extraction form[16, 18]. Baseline information includes first author, publication year, trial design, country, male proportion, patients age, past history of cholecystectomy, existence of periampullary diverticula, balloon diameter, proportion of single CBD stone, size of the largest CBD stone, CBD diameter, the usage of EST or post-ERCP pancreatic stents. Data were independently extracted by two reviewers (Y.N.W., M.Q.) and confirmed by a third reviewer (J.B.H.) for agreement. We tried to contact the authors if detailed supplementary information of included trials cannot be accurately extracted.

The quality of RCTs was evaluated on the basis of Cochrane risk-of-bias criteria (Version 5.1.0)[16]. The following 7 points were assessed: (1) randomization sequence generation; (2) allocation concealment; (3) blinding of participants and researchers; (4) blinding of the outcome assessors; (5) selective outcome reporting; (6) attrition bias; (7) other biases. The quality of RCSs was assessed by using the nine-point Newcastle-Ottawa Scale (NOS) scale to assess the following three fundamental aspects of methodology: study participant selection (0–4), confounder adjustment (0–2), and outcome indicator determination (0–3). A RCS with ≥ 7 points NOS score was defined as a highly qualified study and included in final analysis[19].

Statistical analysis

A pooled odds ratio (OR) and 95% confidence interval (CI) was adopted in our statistical analysis. The pooled continuous data are presented as a form of means $\pm$ standard error. Two-tailed with $P < 0.05$ was considered statistically significant. Subgroup analysis was performed to assess the effect of prior EST, large balloon and 5-minute strategy on the efficacy and safety of EPBD. We also assessed publication bias via funnel plot asymmetry and Egger test[20]. $P \geq 0.1$ was considered to indicate no significant publication bias. The statistical heterogeneity was evaluated by Higgins I^2 statistic and the chi square-based Q statistic [21]. Heterogeneity was defined to be not significant when $P > 0.1$ and $I^2 < 50\%$. Fixed-effect model was selected without significant heterogeneity and random-effect model was used if heterogeneity is significant. Sensitivity analysis was also performed to confirm the stability of our results. All the analyses described above were performed with STATA 15.0 statistical software (Stata Corp., College Station, TX, USA).

Results

Literature search and basic characteristics of included trials

A total of 644 potentially eligible articles were identified from PubMed, EMBASE and Cochrane Library database. After screening titles, abstracts and full text, seven full-length published trials were ultimately selected (Fig. 1), including five RCTs (2263 subjects)[22–26] and two nonrandomized studies (1255 subjects) [15, 27]. A summary of detailed baseline characteristics from all included trials are reviewed and presented in Table 1.

Table 1

Baseline characteristics of included studies. RCT, randomized controlled trial; RCS, retrospective cohort study; EPBD, endoscopic papillary balloon dilation; EP, endoscopic papillary large balloon dilation; ESD, endoscopic sphincterotomy plus balloon dilation; ESLBD, endoscopic sphincterotomy plus large balloon dilation; NA, not available.

Author with country	Study type	Centers involved, n	Study design (sample size, n)	Male, n (%)		Age, y		Balloon diameter, mm		Maximum size of stones, mm		CBD diameter, mm		Multiple stone (%)	
				< 30 s	> 1 min	< 30 s	> 1 min	< 30 s	> 1 min	< 30 s	> 1 min	< 30 s	> 1 min	< 30 s	> 1 min
Tsujino 2008 (Japan)	RCS	6	EPBD 15 s (324) vs 2 min (324)	191 (59.0%)	191 (59.0%)	70.0 ± 11.83	69.3 ± 12.83	NA	NA	7.1 ± 3.8	7.2 ± 5.0	10.6 ± 5.2	11.1 ± 5.5	NA	NA
Bang 2010 (Korea)	RCT	1	EPBD 20 s (35) vs 1 min (35)	16 (45.7%)	19 (54.3%)	63.3 ± 13.6	66.2 ± 17.4	9.6 ± 2.4	9.7 ± 2.6	8.2 ± 3.3	8.1 ± 3.5	13.1 ± 4.2	12.3 ± 3.1	14 (40%)	19 (54)
Paspatis 2013 (Greece)	RCT	1	ESLBD 30 s (64) vs 1 min (60)	23 (35.9%)	27 (45.0%)	75.1 ± 11.9	74.7 ± 13.2	15.08 ± 1.12	15.22 ± 1.45	15.8 ± 4.3	15.7 ± 5.2	17.1 ± 4.8	18.4 ± 5.4	NA	NA
Sun 2014 (China)	RCT	1	EPLBD 0 s (27) vs 1min + 5 min (62)	12 (44.4%)	32 (51.6%)	63.3 ± 10.71	69.2 ± 11.1	15.33 ± 1.78	14.7 ± 1.87	18.7 ± 3.6	16.2 ± 3.6	17.6 ± 3.2	16.9 ± 3.6	24 (88.9%)	53 (85)
Shavakhi 2015 (Iran)	RCT	1	ESBD 5 s (31) vs 1 min (29)	10 (32.3%)	14 (48.3%)	55.74 ± 20.7	54.97 ± 19.83	12.22 ± 2.16	12.22 ± 2.08	7.74 ± 2.96	8.1 ± 3.65	12.97 ± 4.54	12.86 ± 4.8	3 (9.7%)	7 (24)
Hakuta 2017 (Japan)	RCS	5	EPBD 15 s (450) vs 5 min (157)	272 (60.4%)	106 (67.5%)	73.5 ± 15.0	75.12 ± 17	NA	NA	6 ± 5.67	5 ± 3.17	10 ± 4.17	9 ± 2.67	NA	NA
Meng 2019 (China)	RCT	15	ESBD 0s + 30 s (755) vs 1min + 3min + 5 min (1165)	343 (45.4%)	572 (49.1%)	64.5 ± 17.1	64.7 ± 16.1	NA	NA	10 ± 3.0	10 ± 3.3	12 ± 3.7	12 ± 3.7	387 (51.3%)	62 (53)

Five RCTs were conducted in following countries: two in China; one in Korea, Greece and Iran, respectively. Both two RCSs are from Japan. Three trials were multicentered research including two RCSs[15, 26, 27]. There are three trials involved in endoscopic sphincterotomy with balloon dilation (ESBD)[23, 25, 26] including one trial implementing endoscopic sphincterotomy with large balloon dilation (ESLBD)[23]. Large balloon dilation was used in two trials[23, 24]. Five-minute strategy in EPBD dilation was involved in three trials[24, 26, 27]. No significant publication bias was identified by funnel plot (Figure S1) and Egger's test ($P = 0.45$, Figure S2).

Efficacy comparison

All included trials reported total CBD stone clearance rate across all ERCP sessions, which was compared between short duration group and long duration group. As shown in Fig. 2, pooled OR (0.98, 95%CI [0.73, 1.31], $P = 0.89$) demonstrated no significance in the rate of total stone clearance without significant heterogeneity ($I^2 = 0\%$, $P = 0.73$). And the rate of complete stone removal during the first ERCP procedure was assessed between two groups after excluding three RCTs without reporting relevant data. No significant heterogeneity was shown ($I^2 = 32.4\%$, $P = 0.22$). Figure 3 revealed that ≥ 1 -minute duration group significantly had higher successful rate of complete stone clearance than < 30 -second duration group during the first ERCP session (OR 0.61, 95%CI [0.48, 0.77], $P < 0.001$). A total of five studies[15, 22, 24, 26, 27] were included to compare the frequency of mechanical lithotripsy use during ERCP. The heterogeneity was statistically significant ($I^2 = 62.9\%$, $P = 0.03$). In spite of no significance, ≤ 30 -second duration group implemented mechanical lithotripsy more frequently compared with ≥ 1 -minute duration group (OR 1.22, 95%CI [0.79, 1.89], $P = 0.37$) by using a random-effect model (Fig. 4). The information of procedure time

was available in only three studies[24, 26, 27]. Obvious heterogeneity was exhibited ($I^2 = 91.3\%$, $P < 0.001$). The weighted mean difference (WMD) was -1.61 (95%CI $[-7.05, 3.83]$, $P = 0.56$) measured by the random-effect model.

Safety comparison

The rate of overall early complications was compared between two groups. Our meta-analysis without significant heterogeneity ($I^2 = 0\%$, $P = 0.61$) revealed short duration group had a relatively lower rate of early complication although statistical significance was not generated (OR 0.85, 95%CI $[0.70, 1.04]$, $P = 0.11$, Fig. 5). In addition, common complications were analyzed, respectively. No significance between two groups was demonstrated in the rate of PEP (OR 0.81, 95%CI $[0.63, 1.03]$, $P = 0.09$, Fig. 6), hemorrhage (OR 0.86, 95%CI $[0.30, 2.44]$, $P = 0.77$), perforation (OR 0.54, 95%CI $[0.14, 2.14]$, $P = 0.38$) and cholangitis (OR 1.15, 95%CI $[0.80, 1.66]$, $P = 0.44$). And all analysis of common complications showed no significant heterogeneity.

Subgroup analysis

As shown in Table 2, Subgroup analyses were conducted to investigate the effect of EST, use of large balloon dilation and 5-minute strategy in the efficacy and safety between two groups. The results demonstrated that there was no significant difference (OR 0.96, 95%CI $[0.55, 1.69]$, $P = 0.90$) between ≤ 30 -second duration and ≥ 1 -minute duration in the subgroup taking balloon dilation with prior EST, which indicated prior EST potentially increased the efficacy of stone removal in short duration group during the first ERCP session. And the subgroup analysis of EPLBD, short duration group had longer procedure time than long duration group (WMD 13.10, 95%CI $[9.39, 16.81]$, $P < 0.001$) but this result was produced by only one trials which was also the potential source of heterogeneity. Additionally, no significant difference was shown in the rate of overall early complications (OR 0.94, 95%CI $[0.75, 1.18]$, $P = 0.58$) and pancreatitis (OR 0.90, 95%CI $[0.68, 1.18]$, $P = 0.44$) between < 30 -second duration group and ≥ 1 -minute duration group with 5-minute duration involvement. This result implied that 5-minute duration could reduce the risk of early complications and PEP. Besides, prior EST, large balloon dilation and 5-minute duration had no significant effect on other outcomes concerning the efficacy and safety of EPBD.

Table 2

Subgroup analysis for the effect of prior EST, large balloon dilation and 5-minute strategy on the efficacy and safety of EPBD between short dilation duration group and long dilation duration group. EST, endoscopic sphincterotomy; ERCP, Endoscopic Retrograde Cholangiopancreatography.

Results	Outcome	Subgroup analysis (OR/WMD [95%CI])					
		Prior EST		Large balloon dilation		5-minute strategy involvement	
		Yes	No	Yes	No	Yes	No
Efficacy	Total stone clearance rate	1.04 [0.76, 1.43] $P = 0.82$	0.73 [0.35, 1.51] $P = 0.393$	1.08 [0.40, 2.93] $P = 0.88$	0.97 [0.72, 1.31] $P = 0.85$	0.98 [0.70, 1.36] $P = 0.89$	0.98 [0.53, 1.82] $P = 0.96$
	Rate of complete stone removal during first ERCP session	0.96 [0.55, 1.69] $P = 0.90$	0.55 [0.42, 0.72] $P < 0.001$	No Subgroup analysis		0.60 [0.42, 0.86] $P = 0.005$	0.61 [0.44, 0.85] $P = 0.003$
	Mechanical lithotripsy use	1.00 [0.76, 1.32] $P = 0.99^*$	1.39 [0.63, 3.04] $P = 0.41$	1.17 [0.32, 4.29] $P = 0.81^*$	1.24 [0.76, 2.02] $P = 0.39$	1.49 [0.69, 3.22] $P = 0.31$	0.88 [0.62, 1.25] $P = 0.47$
	Procedure time	0.00 [-1.42, 1.42] $P = 1.00^*$	-2.48 [-13.36, 8.40] $P = 0.66$	3.10 [-0.61, 6.81] $P = 0.10^*$	-3.85 [-11.68, 3.99] $P = 0.34$	No subgroup analysis	
Safety	Overall complications	0.90 [0.71, 1.14] $P = 0.364$	0.75 [0.53, 1.08] $P = 0.12$	0.74 [0.29, 1.87] $P = 0.53$	0.86 [0.70, 1.05] $P = 0.14$	0.94 [0.75, 1.18] $P = 0.58$	0.61 [0.40, 0.93] $P = 0.02$
	Pancreatitis	0.84 [0.62, 1.13] $P = 0.24$	0.74 [0.47, 1.15] $P = 0.18$	0.94 [0.13, 6.86] $P = 0.95^*$	0.81 [0.63, 1.03] $P = 0.09$	0.90 [0.68, 1.18] $P = 0.44$	0.52 [0.30, 0.92] $P = 0.03$
	Hemorrhage	0.67 [0.19, 2.30] $P = 0.52$	1.84 [0.19, 17.66] $P = 0.60$	0.45 [0.08, 2.56] $P = 0.37^*$	1.31 [0.33, 5.15] $P = 0.70$	1.03 [0.22, 4.94] $P = 0.97$	0.74 [0.18, 3.03] $P = 0.67$
	Perforation	0.71 [0.09, 5.61] $P = 0.75$	0.43 [0.07, 2.73] $P = 0.37$	0.94 [0.06, 15.32] $P = 0.96^*$	0.45 [0.09, 2.25] $P = 0.33$	0.42 [0.05, 3.59] $P = 0.43$	0.65 [0.11, 3.91] $P = 0.64$
	Cholangitis	1.20 [0.79, 1.82] $P = 0.39$	1.02 [0.50, 2.11] $P = 0.95$	1.43 [0.23, 8.85] $P = 0.70^*$	1.14 [0.79, 1.65] $P = 0.48$	1.20 [0.80, 1.78] $P = 0.38$	0.99 [0.42, 2.30] $P = 0.97$
* Only one trial was included in the subgroup							

Discussion

EPBD has been widely accepted as a potential method for preserving the function of SO during ERCP but no consensus is established to define explicit duration of EPBD. Our review and meta-analysis were the first systematic investigation to figure out the effect of EPBD duration on the efficacy and safety of therapeutic ERCP for choledocholithiasis by comparing short duration dilation (≤ 30 seconds) and long duration (≥ 1 minute) dilation. There were also some potentially confounding factors including preceding EST, the use of large balloon dilation and 5-minute long duration. Subgroup analyses were taken to identify their effect on the efficacy and safety of ERCP for CBD stones. Both RCTs and RCSs were included in our analysis due to limited number of trials showing the comparison between short and long dilation time.

During the first ERCP session, a significantly higher efficiency in complete removal of CBD stones was shown in the EPBD group with long dilation duration. Intriguingly, subgroup analysis indicated that the efficacy of stone removal during the first ERCP session was improved by preceding EST especially for ≤ 30 -second dilation because there was no significance in the rate of stone removal between short- and long-time dilation with preceding EST. Recently, a network meta-analysis has identified ESBD has a significant higher rate of stone removal during the first endoscopic session compared with EST and EPBD[28]. Besides, ≥ 1 -minute dilation duration of EPBD demonstrated a trend of higher rate of total stone clearance and less frequency of mechanical lithotripsy use although no significance was verified.

After comparing the efficiency between two groups, we compared a total rate of overall early complications. The result revealed that short duration of EPBD could have a trend to reduce the risk of overall complications and pancreatitis compared with long duration of EPBD. Our result was opposed to an earlier meta-analysis demonstrating duration of EPBD is inversely associated with pancreatitis risk[13]. Their results were mainly based on indirect comparison with EST and only one trial was included in the comparison between short and long EPBD despite Bayesian statistical approach was used. And subgroup analysis implied that five-minute duration in the group with long duration dilation could potentially reduce the incidence of overall complications and PEP. Our result agreed on the results of the randomized research illustrating that five-minute duration of EPBD triggered a significant lower risk of overall complications and pancreatitis than one-minute duration of EPBD[29]. There are many disputes on the issue of the relationship between EPBD time and subsequent complications. Short duration dilation may restrict the enlargement and expansion of SO, which increase a risk of PEP[29]. Other influence factors include difficult biliary cannulation and operation without gentleness, which could induce papillary irritation[30]. But now prophylactic pancreatic stents have been proven to effectively reduce the incidence of PEP[31]. EPBD is an effective approach to avoid the short-term complications of perforation and bleeding. And hemorrhage, perforation and cholangitis did not show any significance between two groups in our results.

No significant heterogeneity was proven among most results. But significant heterogeneity existed in the comparison of mechanical lithotripsy use and procedure time. Selection bias in a RCS was figured out as the main source of heterogeneity[27]. All included patients undergoing EPBD with short duration were from 2008 to 2013 and all EPBD operation with long duration were performed after 2013. Lack of operational experience and imperfect technique and equipment may contribute to more frequent use of lithotripsy and longer procedure time.

The results of our meta-analysis could provide an instructive clinical significance but also have some inevitable limitations. Firstly, relatively insufficient number of trials and small sample size may potentially reduce the quality and reliability of the evidence. More RCTs are required to identify the better choice for EPBD duration. Secondly, one to three-minute or five-minute duration were mainstream strategies of long EPBD. The comparative results could also be impacted by the time span in group with long duration of EPBD although no significant heterogeneity was proven. In our analysis, subgroup analysis for five-minute strategy was used to discuss the effect of different time choice in the group with long EPBD duration on final results and conclusions. Thirdly, the safety of EPBD duration we discussed only referred to short-term/early complications. Long-term/late complications also are required to be focused on. Only one RCT systematically reported no significant difference in recurrent choledocholithiasis and hepatobiliary complications between 1-minute and 5-minute EPBD group[32]. More comparative analyses of late complications after EPBD should be conducted in the future.

Conclusions

Long duration (≥ 1 minute) could significantly increase the efficacy of EPBD in stone removal rate during first ERCP session compared with short duration. Long duration EPBD group demonstrated higher rate of total CBD stone clearance and less mechanical lithotripsy although not significantly. Moreover, short EPBD contributed to less overall complications and PEP than long EPBD but not significantly. Prophylactic pancreatic stent placement could be an effective strategy against PEP nowadays. For long duration of EPBD, 5-minute duration may potentially reduce the rate of overall complications and pancreatitis.

Abbreviations

EPBD, Endoscopic papillary balloon dilation; EST, endoscopic sphincterotomy; ERCP, endoscopic retrograde cholangiopancreatography; CBDS, common bile duct stones; SO, sphincter of Oddi; PEP, post-ERCP pancreatitis; ESGE, European Society of Gastrointestinal Endoscopy; EPLBD, endoscopic papillary large balloon dilation; RCT, randomized controlled trial; RCS, retrospective cohort trial; ESBD, endoscopic sphincterotomy with balloon dilation; ESLBD, endoscopic sphincterotomy with large balloon dilation;

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication All authors read and approved the final manuscript.

Availability of data and material Not applicable.

Competing Interests The authors declare no conflict of interest.

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Authors' contributions HJB and WYN participated the design of this meta-analysis. WYN conducted literature searching, data extraction, data analysis and interpretation, drafted the manuscript. QM and HYZ participated in study design and the revision process of the manuscript. HJB participated in the critical revision of the manuscript.

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Supplementary Figure Captions

Figure S1. Funnel plot assessing for publication bias.

Figure S2. Egger’s test assessing for publication bias.

Figures

Figure 1

Flow diagram for selecting eligible studies to include in the meta-analysis.

Figure 2

Forrest plot of included studies demonstrating the effect of EPBD duration on total CBD clearance rate during all ERCP sessions.

Figure 3

Forrest plot of included studies demonstrating the effect of EPBD duration on stone removal rate during the first ERCP session.

Figure 4

Forrest plot of included studies demonstrating the effect of EPBD duration on the frequency of mechanical lithotripsy use.

Figure 5

Forrest plot of included studies demonstrating the effect of EPBD duration on overall post-ERCP complications.

Figure 6

Forrest plot of included studies demonstrating the effect of EPBD duration on post-ERCP pancreatitis.

Supplementary Files

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