A cumulative meta-analysis of endoscopic papillary balloon dilation versus endoscopic sphincterotomy for removal of common bile duct stones

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Bibliography

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ABSTRACT

Background Endoscopic papillary balloon dilation (EPBD) was introduced to overcome the risk of adverse events associated with endoscopic sphincterotomy in the removal of common bile duct (CBD) stones. We performed a meta-analysis of randomized controlled trials (RCTs) comparing efficacy and safety of EPBD vs. endoscopic sphincterotomy, focusing on stone size, balloon diameter, and balloon dilation time.

Methods A multiple database search was performed, including MEDLINE, EMBASE and Cochrane Library, from their inception date until October 2017. RCTs comparing the efficacy and safety of EPBD vs. endoscopic sphincterotomy in the removal of CBD stones were included. Cumulative meta-analyses over time, and subgroup analyses according to stone size, and balloon diameter and dilation time were carried out.

Results 25 RCTs met the inclusion criteria. Despite the cumulative meta-analysis showing a trend over time in favor of endoscopic sphincterotomy in studies published up to 2004, the conventional meta-analysis revealed that EPBD was equally efficacious compared with endoscopic sphincterotomy in stone removal at first attempt (odds ratio [OR] 0.95, 95 % confidence interval [CI] 0.65 – 1.38). Endoscopic sphincterotomy was superior to EPBD in terms of overall stone clearance (OR 0.65, 95 %CI 0.43 – 0.99) in studies published since 2002, but no differences emerged in studies using large (≥ 10 mm) balloons (OR 1.37, 95 %CI 0.72 – 2.62). No statistically significant difference in pancreatitis occurrence emerged between EPBD and endoscopic sphincterotomy (OR 1.35, 95 %CI 0.90 – 2.03). Pancreatitis was more common with EPBD than with endoscopic sphincterotomy in studies using balloons < 10 mm (OR 1.78, 95 % CI 1.07 – 2.97), whereas no difference emerged in studies using large balloons (OR 0.84, 95 %CI 0.46 – 1.53). EPBD had lower rates of bleeding and cholecystitis.

Conclusions Our latest data confirm that EPBD is currently inferior to endoscopic sphincterotomy in terms of overall stone clearance. However, EPBD using large balloons (≥ 10 mm) was as effective as endoscopic sphincterotomy, both in stone clearance and the need for endoscopic mechanical lithotripsy, without carrying an increased risk of pancreatitis.

Introduction

Endoscopic papillary balloon dilation (EPBD) is an alternative to endoscopic sphincterotomy for the removal of bile duct stones in the context of endoscopic retrograde cholangiopancreatography (ERCP). EPBD, which was first proposed in 1983 by Staritz et al. [1], has several potential advantages over endoscopic sphincterotomy. Primarily, EPBD avoids cutting the biliary sphincter, thus reducing early adverse events such as bleeding and perforation. Furthermore, it may be a reasonable option in patients with coagulopathy or surgically altered anatomy who cannot undergo sphincterotomy [2, 3]. Despite the potential advantages, the significantly higher reported risk of pancreatitis in the literature when this maneuver is performed [4 – 7] has led many to prefer endoscopic sphincterotomy over EPBD [8 – 9].

Several systematic reviews and meta-analyses of randomized controlled trials (RCTs) have compared the safety and efficacy of EPBD and endoscopic sphincterotomy [4, 7, 10 – 13]. These reviews generally found that EPBD was inferior to endoscopic sphincterotomy in terms of overall stone removal; however, it was associated with a lower risk of bleeding when compared with endoscopic sphincterotomy. The latter meta-analysis by Park et al. [13] also showed that there was no significant increased risk of post-ERCP pancreatitis (PEP) with EPBD compared with endoscopic sphincterotomy. This supports the hypothesis of some earlier papers suggesting that the risk of EPBD-associated PEP may be lower than originally thought [14 – 15].

However, these meta-analyses did not evaluate whether the safety and efficacy of EPBD vs. endoscopic sphincterotomy differed according to stone size, or according to the size of the balloon or its dilation time. A consensus guideline [16] for endoscopic papillary large (≥ 12 mm) balloon dilation (EPLBD) showed that EPLBD can be used as the initial method when a large bile duct stone (> 15 mm) has been identified on ERCP or cross-sectional imaging [16].

The aim of this study, therefore, was to perform a cumulative meta-analysis of the results of RCTs comparing the efficacy and safety of EPBD vs. endoscopic sphincterotomy, with special focus on stone size, balloon diameter, and balloon dilation time.

Methods

This systematic review and meta-analysis was carried out according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [17] (see Supplementary material 1).

Identification and selection of studies

Inclusion criteria were RCTs that compared the efficacy and safety of EPBD vs. endoscopic sphincterotomy for removal of common bile duct (CBD) stones found on ERCP in patients aged 18 years old or older.

Studies were excluded if they were nonrandomized studies, studies analyzing post-sphincterotomy balloon dilation, and studies considering patients who had undergone previous treatment for CBD stones.

Search strategy

A literature search was performed in EMBASE, MEDLINE, the Cochrane library, and the Cochrane Central Register of Controlled Trials (CENTRAL) from their inception date to October 2017 (see Supplementary material 2 for search strategy). For the sake of completeness, we searched references of relevant literature. After removal of duplicates, titles and abstracts were screened by two authors (A. Tringali and M. Rota) to identify potentially eligible studies. Differences were resolved by discussion.

Data collection

Data were extracted using a standardized form. The following data were extracted.

Descriptive data – first author last name, year of publication, country of origin (grouped into Western and Asian), study setting, number of patients, age and sex distribution of patients, previous ERCP, altered anatomy (e. g. Billroth II), presence of perivaterian diverticulum, stone size, stone number, CBD size, mean follow-up time, balloon diameter, duration of balloon dilation, pressure of balloon dilation.

Outcome data – primary outcome measures were stone clearance at the first session and overall stone clearance considering subsequent stone extraction attempts. Secondary outcome measures included the need for endoscopic mechanical lithotripsy (EML), pancreatitis, bleeding, perforation, cholangitis, cholecystitis, recurrence of CBD stones, 30-day procedure mortality, overall short-term procedure-related complication rate (defined as composite outcomes of all complications), and procedure time (defined as elapsed time from ERCP to the end of the procedure).

Qualitative data – random sequence generation, allocation concealment, blinding of participants and personnel, blinding outcome assessment, incomplete outcome data, selective reporting, and loss to follow-up.

Quality appraisal

Each included study was appraised for quality by two independent evaluators (A. Tringali and M. Rota). Quality appraisal was performed using the risk of bias tool as recommended by the Cochrane collaboration [18].

Statistical analysis

Dichotomous outcomes were evaluated in terms of crude odds ratio (ORs) with their 95 % confidence intervals (CIs), and summarized across studies through a random-effects model. Briefly, each study-specific log (OR) was weighted by the inverse of its variance plus an estimate of the between-study variance component τ^2 computed through the DerSimonian and Laird moment estimator [19]. If no between-study heterogeneity was evident – resulting in a null τ^2 estimate – the pooled estimate from the random-effects model would be equal to the one derived from a fixed-effects model. The procedure time was analyzed using the Hedges' standardized mean difference estimator.

The 95 % prediction intervals, which estimate the expected effect in future studies, were also computed.

Cumulative meta-analyses were performed to investigate the effect of publication year on the pooled estimates. Briefly, in a cumulative meta-analysis, studies were added one at a time according to publication year (earliest to the most recent), and results were displayed in a forest plot showing the pooled estimate each time the results of a new study were added over time.

Between-studies heterogeneity was assessed through the Q test based on the chi-squared statistics, and inconsistency was quantified through the I^2 statistic [20]. In order to assess potential sources of heterogeneity, we first performed a sensitivity analysis by removing each study in turn (leave-one-out method) to evaluate its influence on the final pooled estimate.

Stratified analyses were carried out according to the geographic area of the study (Asian vs. Western), balloon diameter (< 10 vs. ≥ 10 mm), and dilation time (≤ 1 vs. > 1 minute), and according to the largest CBD stone size (< 10 vs. ≥ 10 mm) when reported in the original publications.

Publication bias was assessed by visual inspection of funnel plots for asymmetry and through the Egger's test for asymmetry [21].

Data were synthesized using the "metafor" library of R version 3.4.0 (R foundation for Statistical Computing, Vienna, Austria).

Results

Study selection

A total of 1267 unique studies were identified through the systematic review of the literature. Following screening of abstracts and titles, we identified 59 potentially eligible studies for which full-text reading was required. Finally, 25 articles [2, 5, 22 – 44] were included (▶ **Fig. e1**, available online).

Characteristics of the included studies

The main characteristics of the 25 included studies [2, 5, 22 – 44] are reported in ▶ **Table 1**. The studies were published between 1995 and 2017, and included a total of 3360 patients, 1665 of whom were randomized to EPBD and 1695 to endoscopic sphincterotomy. The majority of the studies (n = 18) were performed in Asian countries [22, 25 – 27, 29 – 31, 33 – 43], and the remaining ones [2, 5, 23 – 24, 28, 32, 44] were conducted in Western countries (the Netherlands, USA, Germany, UK, and Egypt). Seven studies only used balloons that were ≥ 10 mm in diameter [32, 38 – 40, 42 – 44], whereas the majority of the remaining studies used a balloon with a diameter of 8 mm [2, 5, 22 – 25, 27 – 31, 33 – 37, 41]. The balloon dilation lasted for more than 1 minute in half of the studies [22, 25, 27 – 30, 33 – 36, 39 – 41].

The risk of bias evaluation according to the Cochrane risk of bias tool did not show significant bias (▶ **Fig. e2**, available online).

Primary outcomes

A total of 18 studies, including 1262 EPBD and 1284 endoscopic sphincterotomy patients, reported the success rate of stone clearance at the first session (▶ **Table 2**). There was no statistically significant difference between EPBD and endoscopic sphincterotomy (OR 0.95, 95 %CI 0.65 – 1.38), with no single study influencing the pooled estimate. However, the cumulative meta-analysis showed a statistically significant change over time (P < 0.01) in the success rate of stone clearance at the first session (▶ **Fig. 3a**). In detail, the OR for studies published up to 2004 (n = 11) was 0.63 (95 %CI 0.45 – 0.87), showing that endoscopic sphincterotomy was superior to EPBD at the first session. Conversely, the OR for studies published after 2004 (n = 7) was 1.97 (95 %CI 1.31 – 2.97), showing a two-fold increased success rate at the first session for patients undergoing EPBD compared with those undergoing endoscopic sphincterotomy.

In terms of overall stone clearance (▶ **Table 2**), endoscopic sphincterotomy was superior to EPBD (OR 0.65, 95 %CI 0.43 – 0.99). The cumulative meta-analysis showed that endoscopic sphincterotomy performed better than EPBD starting from 2002, although the change in overall stone clearance over time was not significant (P = 0.13) between the two endoscopic techniques (▶ **Fig. 3b**).

Secondary outcomes

The results of secondary outcomes are provided in ▶ **Table 2** (see ▶ **Table e3**, available online, for study-specific data). There were 23 studies, involving 1507 EPBD and 1531 endoscopic sphincterotomy patients, reporting the need for EML for CBD stone removal. The pooled OR was 1.24 (95 %CI 0.92 – 1.67), showing that the need for EML was slightly more common in the EPBD group compared with the endoscopic sphincterotomy group (▶ **Fig. e4**, available online). The leave-one-out sensitivity analysis showed that the pooled estimate was statistically significant after the exclusion of the study by Kogure et al. [43]. The cumulative meta-analysis (▶ **Fig. 5**) showed that the increased need for EML for EPBD vs. endoscopic sphincterotomy significantly reduced over time (P < 0.01). In fact, the need for EML in EPBD progressively decreased vs. endoscopic sphincterotomy, losing its statistical significance beyond 2015.

A total of 22 studies, including a total of 1420 EPBD and 1448 endoscopic sphincterotomy patients, reported PEP data. There was a slightly, but not statistically significant, increased odds of PEP in EPBD vs. endoscopic sphincterotomy patients (OR 1.35, 95 %CI 0.90 – 2.03; ▶ **Fig. e6**, available online). The leave-one-out sensitivity analysis showed that the odds of PEP was statistically significantly higher (OR 1.52, 95 %CI 1.05 – 2.18) after the exclusion of the Fu et al. study [39]. The cumulative meta-analysis (▶ **Fig. 7a**) did not show a statistically significant change over time (P = 0.23), although the odds of PEP was lower for studies published before 2003 (OR 1.17, 95 %CI 0.65 – 2.10) compared with those published after (OR 1.49, 95 %CI 0.81 – 2.75).

▶ **Table 1** Main characteristics of the studies included in the meta-analysis.

Study and country	Patient characteristics					Balloon characteristics		
	Patients, n	Age, years[1]	Sex, M/F, n	Stones, n[1]	Stones size, mm[1]	Balloon diameter, mm	Balloon dilation time	Balloon dilation pressure, atm
Minami et al., 1995 [22] Japan (Asian)	EPBD 20 EST 20	64 ± 11.2 71.3 ± 14	13/7 9/11	N/A	< 12 < 12	8	3 min	1 – 1.3
Bergman et al., 1997 [23] The Netherlands (Western)	EPBD 101 EST 101	72 (27 – 98) 71 (29 – 96)	43/58 45/56	2 (1 – 14) 1 (1 – 15)	10 (3 – 36) 9 (427)	8	45 – 60 s	N/A
Chen et al., 1998 [24] USA (Western)	EPBD 47 EST 46	52 ± 20 47 ± 17	12/34 16/31	2.7 ± 4.6 2.3 ± 3	< 10 < 10	6 – 10	N/A	N/A
Cho et al., 1998 [25] Korea (Asian)	EPBD 42 EST 42	58.9 57.1	N/A	2.3 2.2	15.6 (5 – 32) 16.9 (6 – 35)	8	60 – 120 s	12
Iwata et al., 1998 [26] Japan (Asian)	EPBD 37 EST 41	N/A	N/A	N/A	7.9 ± 2.7 8 ± 3.0	N/A[2]	N/A	N/A
Ochi et al., 1999 [27] Japan (Asian)	EPBD 55 EST 55	62.6 ± 15.9 66.3 ± 14.3	34/21 31/24	2.1 ± 1.9 1.7 ± 1.2	8.1 ± 3.4 8.8 ± 4.2	8	60 s × 3	8
Arnold et al., 2001 [28] Germany (Western)	EPBD 30 EST 30	54.2 ± 18.5 58.5 ± 18.5	11/19 13/17	1.6 ± 1.1 1.8 ± 1.5	7.0 ± 3.5 10 ± 4.7	8	60 s × 2	10
Bergman et al., 2001 [2] The Netherlands (Western)	EPBD 16 EST 18	73 (43 – 84) 72 (61 – 84)	12/4 18/0	2 (1 – 10) 2 (1 – 10)	9 (5 – 22) 8 (4 – 20)	8	45 – 60 s	N/A
Yasuda et al., 2001 [29] Japan (Asian)	EPBD 35 EST 35	69.5 (42 – 86) 69.4 (43 – 88)	16/19 21/14	3.7 (1 – 16) 3.3 (1 – 16)	12.4 (4 – 24) 12.3 (5 – 24)	8	1 min × 2	6
Natsui et al., 2002 [30] Japan (Asian)	EPBD 70 EST 70	64.5 (23 – 87) 67.1 (38 – 88)	33/37 33/37	2.7 (1 – 15) 2.6 (1 – 15)	9.2 (3 – 22) 9.7 (3 – 17)	8	2 min	8
Fujita et al., 2003 [31] Japan (Asian)	EPBD 138 EST 144	66.8 (26 – 93) 68.4 (31 – 93)	75/63 92/52	2.4 ± 2.5 2.4 ± 2.9	7.0 ± 3.1 7.3 ± 3.4	4 – 8	15 s	N/A
Vlavianos et al., 2003 [32] UK (Western)	EPBD 103 EST 99	60.8 ± 20.5 61.9 ± 18.3	25/78 35/64	N/A	N/A	10	30 s	12
Disario et al., 2004 [5] USA (Western)	EPBD 117 EST 120	47 ± 19 54 ± 19	41/76 31/89	1 (1 – 100) 1 (1 – 10)	6 (0.5 – 10) 5 (0.5 – 14)	8	1 min	N/A
Lin et al., 2004 [33] Taiwan (Asian)	EPBD 51 EST 53	64 (28 – 90) 65 (28 – 88)	28/23 31/22	N/A	8 ± 6 8 ± 6	8 – 12	2 – 5 min	3 – 12
Takezawa et al., 2004 [34] Japan (Asian)	EPBD 46 EST 45	70 (40 – 90) 69 (41 – 93)	32/14 30/15	1 (1 – 7) 1 (1 – 7)	10 (1 – 35) 11 (3 – 27)	8	2 min	8

▶ **Table 1** (Continuation)

Study and country	Patient characteristics					Balloon characteristics		
	Patients, n	Age, years[1]	Sex, M/F, n	Stones, n[1]	Stones size, mm[1]	Balloon diameter, mm	Balloon dilation time	Balloon dilation pressure, atm
Tanaka et al., 2004 [35] Japan (Asian)	EPBD 16 EST 16	67.2 (50 – 78) 70.6 (49 – 87)	10/6 13/3	2 (1 – 12) 2 (1 – 4)	10.2 ± 3.5 12.4 ± 6.0	8	2 min	8
Watanabe et al., 2007 [36] Japan (Asian)	EPBD 90 EST 90	69.1 ± 13.1 70.2 ± 8.1	51/39 49/41	2.7 ± 2.8 2.5 ± 2.7	8.1 ± 3.2 7.7 ± 2.9	8	2 min	7
Yasuda et al., 2010 [37][3] Japan (Asian)	EPBD 138 EST 144	68.5 (26 – 93) 71 (31 – 93)	75/63 92/52	1(1 – 16) 1(1 – 24)	6.5 (2 – 15) 7 (2 – 16)	4 – 6 – 8	15 s	N/A
Oh et al., 2012 [38] Korea (Asian)	EPBD 40 EST 43	72.3 ± 9.5 68.7 ± 12.9	20/20 23/20	N/A	13.2 ± 3.6 13.1 ± 3.9	10 – 18	10 – 60 s	N/A
Fu et al., 2013 [39] China (Asian)	EPBD 103 EST 103	61.8 ± 17.4 60.5 ± 14.7	52/51 45/58	2.2 ± 1.4 1.9 ± 1.4	8.4 ± 2.7 7.7 ± 2.4	10 – 12	3 min	N/A
Minakari et al., 2013 [40] Iran (Asian)	EPBD 80 EST 80	56.4 ± 15.3[4]	39/41 42/38	N/A	10 – 20 10 – 20	12 – 15	1 min × 3	N/A
Seo et al., 2014 [41] Korea (Asian)	EPBD 62 EST 70	32.1 ± 7.3 33.2 ± 5.8	27/35 32/38	1.5 (1 – 5) 1.8 (1 – 8)	7.2 ± 2.1 7.6 ± 3.1	6 – 10	90 – 120 s	N/A
Guo et al., 2015 [42] China (Asian)	EPBD 85 EST 85	62 ± 17 59 ± 16	45/40 43/42	N/A	10 (10 – 30) 10 (10 – 40)	10 – 15	N/A	N/A
Kogure et al., 2015 [43] Japan (Asian)	EPBD 82 EST 82	> 60 > 60	N/A	N/A	≥ 10 ≥ 10	> 10	N/A	N/A
Omar et al., 2017 [44] Egypt (Western)	EPBD 61 EST 63	47.8 ± 14.5 44.8 ± 13.9	26/35 25/38	2.3 ± 1.5 2.1 ± 1.4	13.9 ± 2.4 13.1 ± 2.6	12 – 15	30 – 60 s	N/A

EPBD, endoscopic papillary balloon dilation; EST: endoscopic sphincterotomy; N/A: not available.
[1] Quantitative variables are expressed as mean ± Standard deviation or median (range).
[2] For the analyses we assumed that a balloon with a diameter of < 10 mm was used.
[3] This study reported the long-term outcomes of the Fujita et al., 2003 [31] study. It was not considered in the analyses for the endoscopic mechanical lithotripsy outcome to avoid data duplication.
[4] Mean age of all patients included in the study. Age was not separately reported for patients undergoing EPBD and EST.

The odds of bleeding were statistically significantly lower in EPBD vs. endoscopic sphincterotomy (OR 0.30, 95 %CI 0.16 – 0.55). Although recurrence of CBD stones was less common after EPBD than after endoscopic sphincterotomy, there was no statistically significant difference (OR 0.77, 95 %CI 0.52 – 1.13).

EPBD had a lower occurrence of short-term cholecystitis than endoscopic sphincterotomy (OR 0.35, 95 %CI 0.13 – 0.93).

A total of 23 studies, including a total of 1477 EPBD and 1505 endoscopic sphincterotomy patients, reported overall short-term complications. There was no statistically significant difference in the incidence of overall short-term complications (OR 0.94, 95 %CI 0.64 – 1.36) in EPBD vs. endoscopic sphincterotomy (▶ **Fig. e8**, available online). The cumulative meta-analysis (▶ **Fig. 7b**) did not show a statistically significant difference ($P = 0.73$) over the time span from the first considered study published in 1995 [22] to the latest one published in 2017 [44].

Subgroup analyses

The main results for subgroup analyses are reported in ▶ **Fig. 9** (see also ▶ **Table e4**, ▶ **Table e5**, ▶ **Table e6**, ▶ **Table e7**, available online). In terms of overall stone clearance (▶ **Fig. 9a**), endoscopic sphincterotomy was superior to EPBD in Asian (OR 0.45, 95 %CI 0.24 – 0.84) but not in Western studies (OR 0.81, 95 %CI 0.40 – 1.66), in studies using a balloon with a diameter < 10 mm (OR 0.42, 95 %CI 0.25 – 0.72), and in studies where the balloon was dilated for more than 1 minute (OR 0.34, 95 % CI 0.18 – 0.67).

▶ **Table 2** Pooled meta-analytic odds ratios for the comparison of endoscopic papillary balloon dilation vs. endoscopic sphincterotomy for bile duct stone removal.

Outcomes	No. of studies	Events/Patients, n EPBD vs. EST	OR (95 %CI)	I^2, %	Prediction interval
Primary outcomes					
Stone clearance at the first session	18	1013/1262 vs. 1034/1284	0.95 (0.65 – 1.38)	63[1]	0.25 – 3.67
Overall stone clearance	20	1109/1185 vs. 1157/1202	0.65 (0.43 – 0.99)[1]	3	0.37 – 1.14
Secondary outcomes					
Need for EML	23	309/1507 vs. 271/1531	1.24 (0.92 – 1.67)	41[1]	0.47 – 3.25
PEP	22	105/1420 vs. 72/1448	1.35 (0.90 – 2.03)	24	0.46 – 3.93
Bleeding	19	8/1234 vs. 51/1264	0.30 (0.16 – 0.55)[1]	0	0.15 – 0.57
Perforation	16	3/1113 vs. 5/1142	0.89 (0.37 – 2.13)	0	0.34 – 2.32
Short-term cholangitis	12	18/884 vs. 16/893	1.06 (0.51 – 2.18)	0	0.46 – 2.41
Long-term cholangitis	5	5/400 vs. 10/412	0.67 (0.22 – 2.06)	0	0.11 – 4.14
Short-term acute cholecystitis	6	4/460 vs. 17/474	0.35 (0.13 – 0.93)[1]	0	0.09 – 1.39
Long-term acute cholecystitis	7	8/396 vs. 16/402	0.52 (0.22 – 1.26)	0	0.16 – 1.66
CBD stone recurrence	13	57/816 vs. 75/836	0.77 (0.52 – 1.13)	0	0.50 – 1.18
30-days procedure-related mortality	22	5/1441 vs. 2/1465	1.22 (0.55 – 2.68)	0	0.53 – 2.81
Overall short-term complications	23	165/1477 vs. 178/1505	0.94 (0.64 – 1.36)	52[1]	0.24 – 3.69
Procedure time	9	529 vs. 548	0.12 (– 0.12 to 0.37)[2]	83[1]	– 0.67 to 0.92

CBD, common bile duct; CI, confidence interval; EML, endoscopic mechanical lithotripsy; EPBD, endoscopic papillary balloon dilation; EST, endoscopic sphincterotomy; OR, odds ratio; PEP, post-endoscopic retrograde cholangiopancreatography pancreatitis.
[1] Statistically significant at $\alpha = 0.05$.
[2] Standardized mean difference (95 %CI)

There was no statistically significant difference in the need for EML (▶ **Fig. 9b**) between EPBD and endoscopic sphincterotomy in both Asian (OR 1.26, 95 %CI 0.91 – 1.76) and Western studies (OR 1.13, 95 %CI 0.52 – 2.42). The need for EML was required less with endoscopic sphincterotomy than with EPBD in studies using a balloon with a diameter < 10 mm (OR 1.72, 95 % CI 1.33 – 2.23), whereas in studies using larger balloons, the need for EML was less frequent with EPBD than with endoscopic sphincterotomy (OR 0.62, 95 %CI 0.42 – 0.91). Conversely, endoscopic sphincterotomy required less EML than EPBD in studies where the balloon was dilated for more than 1 minute (OR 1.66, 95 %CI 1.21 – 2.27). Moreover, the need for EML was less frequent with endoscopic sphincterotomy than with EPBD (OR 2.66, 95 %CI 1.31 – 5.40) for stones < 10 mm, but no statistically significant differences emerged for stones ≥ 10 mm (OR 1.07, 95 %CI 0.52 – 2.22).

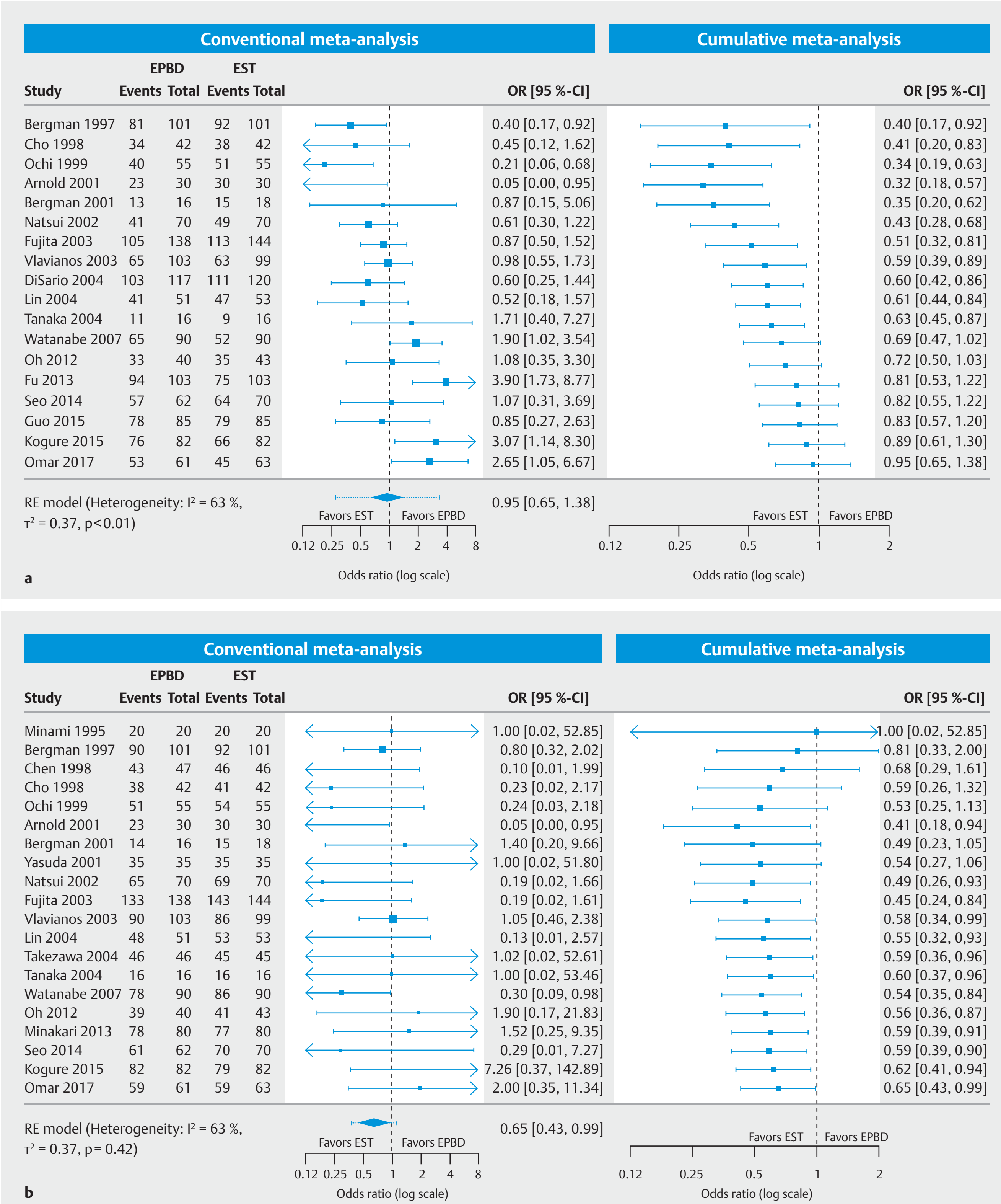
A slightly higher occurrence of PEP (▶ **Fig. 9c**) emerged for EPBD vs. endoscopic sphincterotomy in studies from Western countries (OR 2.33, 95 %CI 1.00 – 5.42) but not in those from Asian countries (OR 1.12, 95 %CI 0.72 – 1.76). The odds of PEP were statistically significantly higher for EPBD vs. endoscopic sphincterotomy in studies using a balloon with a diameter < 10 mm (OR 1.78, 95 %CI 1.07 – 2.97), whereas there was no statistically significant difference in PEP occurrence (OR 0.84, 95 %CI 0.46 – 1.53) in studies using larger balloons. PEP was more common with EPBD (OR 2.29, 95 %CI 0.93 – 5.62) than with endoscopic sphincterotomy in studies with a short (≤ 1 minute) balloon dilation, whereas no difference in PEP occurrence emerged in studies where the balloon was dilated for more than 1 minute (OR 1.12, 95 %CI 0.68 – 1.85).

Publication bias

Visual inspection of funnel plots for overall stone clearance and overall short-term complications showed no evidence of asymmetry (▶ **Fig. e10**, available online). As a confirmation, the Egger's test for funnel plot asymmetry gave a *P* value of 0.49 and 0.61, respectively, showing no potential publication bias for the two considered outcomes.

Discussion

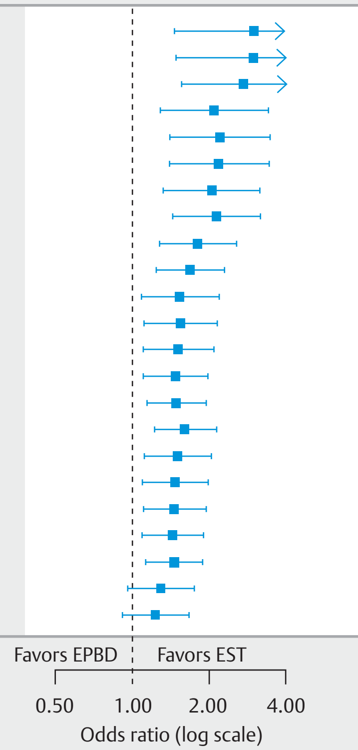
We carried out a cumulative meta-analysis to investigate how the efficacy and safety of EPBD vs. endoscopic sphincterotomy in CBD stone removal varied over time and to study, for the first time, the impact of balloon characteristics (e. g. balloon diameter and dilation time) and stone size on overall stone clearance,



▶ **Fig. 3** Forest plots showing the results of conventional and cumulative meta-analyses of endoscopic papillary balloon dilation (EPBD) vs. endoscopic sphincterotomy (EST) for the removal of common bile duct stones. **a** Stone clearance at the first session. **b** Overall stone clearance. In the conventional meta-analysis, the summary odds ratio (OR) is represented through a diamond and its tips represents the 95 % confidence interval (CI), whereas the prediction interval is represented through a dashed thin line. In the cumulative meta-analysis, a summary OR was calculated each time the results of a new study were added. The rate of successful stone clearance at the first session was not significantly different between EPBD and endoscopic sphincterotomy starting from 2007, whereas endoscopic sphincterotomy was superior to EPBD in terms of overall stone clearance since 2002.

Study	EPBD Events*	EPBD Total*	EST Events*	EST Total*	OR [95 %-CI]
Bergman 1997	31	101	13	101	3.00 [1.46, 6.16]
+ Chen 1998	32	148	13	147	3.00 [1.49, 6.05]
+ Cho 1998	51	190	24	189	2.73 [1.56, 4.77]
+ Iwata 1998	68	227	42	230	2.10 [1.29, 3.42]
+ Ochi 1999	75	282	44	285	2.21 [1.40, 3.48]
+ Arnold 2001	75	312	44	315	2.19 [1.39, 3.44]
+ Bergman 2001	78	328	48	333	2.05 [1.32, 3.16]
+ Yasuda 2001	95	363	57	368	2.14 [1.44, 3.19]
+ Natsui 2002	124	433	84	438	1.81 [1.29, 2.56]
+ Fujita 2003	144	571	101	582	1.69 [1.24, 2.30]
+ Vlavianos 2003	151	674	112	681	1.54 [1.09, 2.19]
+ DiSario 2004	153	791	113	801	1.55 [1.12, 2.15]
+ Lin 2004	154	842	115	854	1.52 [1.10, 2.10]
+ Takezawa 2004	170	888	129	899	1.48 [1.11, 1.98]
+ Tanaka 2004	178	904	135	915	1.49 [1.14, 1.95]
+ Watanabe 2007	254	994	193	1005	1.62 [1.22, 2.14]
+ Oh 2012	258	1034	202	1048	1.51 [1.11, 2.05]
+ Fu 2013	261	1137	206	1151	1.48 [1.10, 1.99]
+ Minakari 2013	263	1217	208	1231	1.47 [1.11, 1.96]
+ Seo 2014	268	1279	214	1301	1.45 [1.10, 1.90]
+ Guo 2015	280	1364	222	1386	1.46 [1.13, 1.89]
+ Kogure 2015	303	1446	260	1468	1.29 [0.96, 1.75]
+ Omar 2017	309	1507	271	1531	1.24 [0.92, 1.67]

*Cumulative number of patients are presented



▶ **Fig. 5** Forest plot showing the results of a cumulative meta-analysis comparing use of mechanical lithotripsy (EML) between endoscopic papillary balloon dilation (EPBD) and endoscopic sphincterotomy (EST) for removal of common bile duct stones. In the cumulative meta-analysis, a summary odds ratio (OR) was calculated each time the results of a new study were added. No statistically significant difference in the use of EML between EPBD and endoscopic sphincterotomy appeared after 2015. CI, confidence interval.

EML use, and PEP. With respect to the conventional approach, cumulative meta-analysis allowed us to study the differences between EPBD and endoscopic sphincterotomy over time. In particular, we were able to assess the impact of each new study on the pooled estimate, and thus to pinpoint the first time a difference in outcome becomes statistically significant.

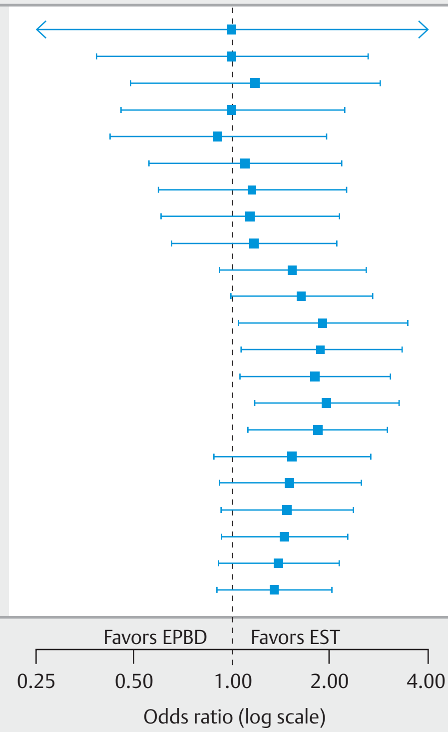
In line with the latest published meta-analysis [13], our results, which importantly included additional RCTs [24 – 26, 40, 43 – 44] not previously considered, showed that there was an absence of evidence of a meaningful difference between EPBD and endoscopic sphincterotomy in terms of successful stone removal rates at the index procedure. Of note, the cumulative meta-analysis clearly evidenced a trend over time in favor of endoscopic sphincterotomy up to 2004, and thereafter no significant difference emerged between the two endoscopic techniques. As shown in studies published after 2004, it is possible that increasing experience with EPBD reduced the difference in stone removal rates at first attempt compared with endoscopic sphincterotomy. This finding could possibly be related to better selection of patients for endoscopic sphincterotomy and to a greater use of large-diameter (≥ 10 mm) balloons for EPBD after 2004, which showed an improved clearance at the index procedure compared with endoscopic sphincterotomy in previous studies [45 – 46], as in our investigation.

EPBD was inferior to endoscopic sphincterotomy in terms of overall stone clearance in studies published since 2002, and more frequently required EML probably because bile duct dilation may not be sufficient for CBD stone removal in all patients [13]. Notably, in studies using large (≥ 10 mm) balloons, EPBD appeared superior to endoscopic sphincterotomy in terms of overall stone clearance, requiring less EML use. Although only a few studies have reported data stratified by stone size, use of EML was more frequently required for removal of small (≤ 10 mm) stones in EPBD than with endoscopic sphincterotomy. This may be due to inadequate papillary dilation caused by the use of small balloons to potentially limit the risk of PEP.

Although PEP was more common with EPBD than with endoscopic sphincterotomy in studies published since 2003, our data confirmed an absence of evidence of a difference in PEP occurrence in the EPBD group compared with the endoscopic sphincterotomy group; this finding was also reported by Seo et al. [47], who suggested that papillary balloon dilation may not in itself be a cause of PEP. The development of PEP might be related to the trauma to the papilla following balloon dilation rather than to the balloon dilation itself [47].

Subgroup analyses revealed an increased, though not significant, PEP risk in studies where papillary dilation lasted for less than 1 minute. This in accordance with the results of an RCT

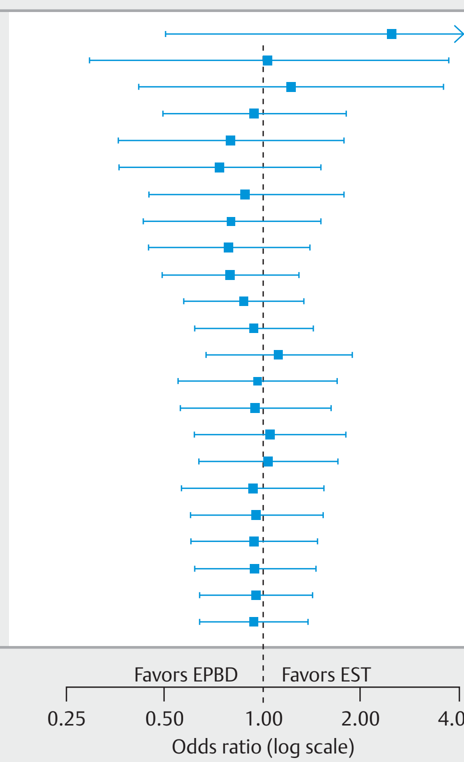
Study	EPBD Events*	EPBD Total*	EST Events*	EST Total*	OR [95 %-CI]
Minami 1995	2	20	2	20	1.00 [0.13, 7.89]
+ Bergman 1997	9	121	9	121	1.00 [0.38, 2.61]
+ Chen 1998	12	168	10	167	1.18 [0.49, 2.87]
+ Iwata 1998	14	205	14	208	1.00 [0.45, 2.22]
+ Ochi 1999	14	256	16	262	0.91 [0.42, 1.95]
+ Arnold 2001	20	286	19	292	1.10 [0.56, 2.17]
+ Bergman 2001	21	302	19	310	1.15 [0.59, 2.25]
+ Yasuda 2001	23	337	21	345	1.14 [0.60, 2.14]
+ Natsui 2002	27	407	24	415	1.17 [0.65, 2.10]
+ Fujita 2003	42	545	28	559	1.54 [0.91, 2.58]
+ Vlavianos 2003	47	648	29	658	1.64 [0.99, 2.72]
+ DiSario 2004	65	765	30	778	1.91 [1.05, 3.48]
+ Lin 2004	65	816	30	831	1.88 [1.06, 3.34]
+ Tanaka 2004	68	832	33	847	1.80 [1.06, 3.06]
+ Watanabe 2007	77	922	35	937	1.96 [1.17, 3.26]
+ Oh 2012	79	962	38	980	1.84 [1.12, 3.02]
+ Fu 2013	82	1050	49	1068	1.54 [0.88, 2.68]
+ Minakari 2013	91	1130	56	1148	1.51 [0.91, 2.50]
+ Seo 2014	96	1192	61	1218	1.48 [0.92, 2.36]
+ Guo 2015	98	1277	63	1303	1.45 [0.93, 2.27]
+ Kogure 2015	102	1359	68	1385	1.39 [0.91, 2.13]
+ Omar 2017	105	1420	72	1448	1.35 [0.90, 2.03]



*Cumulative number of patients are presented

a

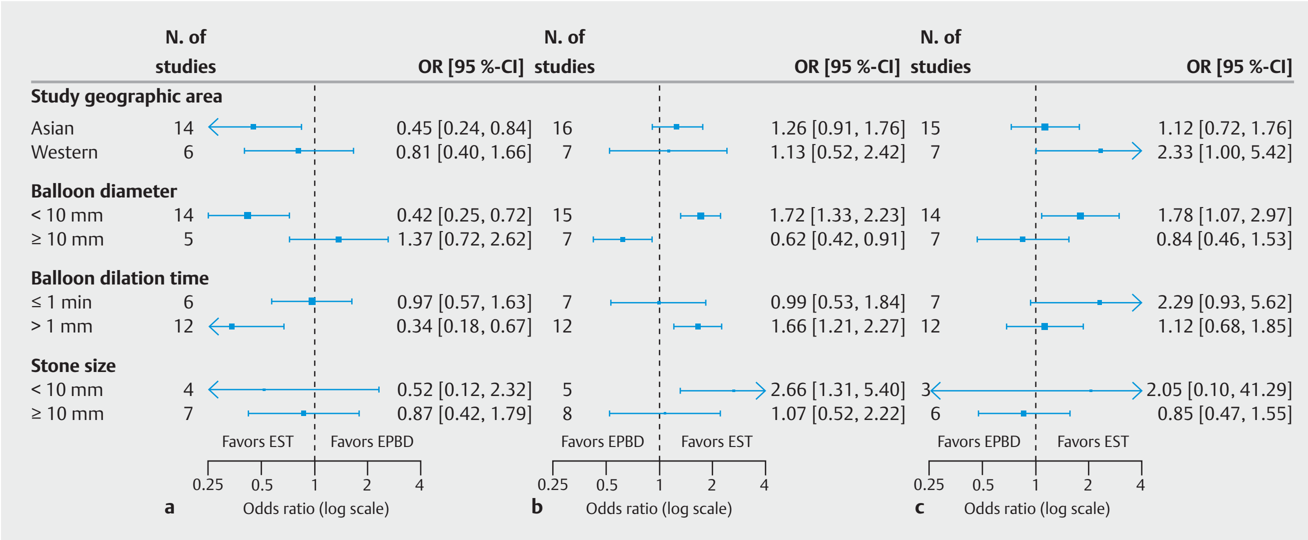
Study	EPBD Events*	EPBD Total*	EST Events*	EST Total*	OR [95 %-CI]
Minami 1995	6	20	3	20	2.43 [0.51, 11.51]
+ Bergman 1997	23	121	27	121	1.04 [0.30, 3.57]
+ Chen 1998	26	168	28	167	1.21 [0.42, 3.48]
+ Cho 1998	32	210	35	209	0.94 [0.50, 1.77]
+ Iwata 1998	34	247	45	250	0.80 [0.37, 1.74]
+ Ochi 1999	35	298	48	304	0.74 [0.37, 1.48]
+ Arnold 2001	44	328	53	334	0.89 [0.45, 1.74]
+ Bergman 2001	47	344	60	352	0.80 [0.43, 1.49]
+ Yasuda 2001	49	379	63	387	0.79 [0.45, 1.37]
+ Natsui 2002	56	449	71	457	0.80 [0.50, 1.28]
+ Fujita 2003	76	587	88	601	0.88 [0.58, 1.32]
+ Vlavianos 2003	83	690	91	700	0.94 [0.62, 1.41]
+ DiSario 2004	104	807	95	820	1.11 [0.67, 1.84]
+ Lin 2004	105	858	109	873	0.96 [0.56, 1.67]
+ Tanaka 2004	108	874	113	889	0.95 [0.56, 1.60]
+ Watanabe 2007	120	964	116	979	1.05 [0.62, 1.76]
+ Oh 2012	129	1004	127	1022	1.04 [0.64, 1.68]
+ Fu 2013	132	1107	141	1125	0.93 [0.57, 1.52]
+ Minakari 2013	142	1187	149	1205	0.96 [0.60, 1.51]
+ Seo 2014	147	1249	157	1275	0.94 [0.61, 1.45]
+ Guo 2015	151	1334	161	1360	0.95 [0.62, 1.43]
+ Kogure 2015	159	1416	169	1442	0.95 [0.64, 1.41]
+ Omar 2017	165	1477	178	1505	0.94 [0.64, 1.36]



*Cumulative number of patients are presented

b

▶ **Fig. 7** Forest plots showing the results of cumulative meta-analyses of endoscopic papillary balloon dilation (EPBD) vs. endoscopic sphincterotomy (EST) for the removal of common bile duct stones. **a** Post-endoscopic retrograde cholangiopancreatitis pancreatitis (PEP). **b** Overall short-term complications. In the cumulative meta-analysis, a summary odds ratio (OR) was calculated each time the results of a new study were added. Although significance was not achieved, PEP was more common after EPBD than after endoscopic sphincterotomy since 2003, whereas the incidence of overall short-term complications did not differ over time between the two endoscopic techniques. CI, confidence interval.



▶ **Fig. 9** Forest plots showing the results from subgroup analyses according to the geographic area of the study (Asian vs. Western), balloon diameter (< 10 vs. ≥ 10 mm), balloon dilation time (≤ 1 vs. > 1 minute), and stone size (< 10 vs. ≥ 10 mm). **a** Overall stone clearance. **b** Use of mechanical lithotripsy **c** Post-endoscopic retrograde cholangiopancreatitis pancreatitis. CI, confidence interval; OR, odds ratio.

[48] and a meta-analysis by Liao et al., which showed that EPBD duration is inversely associated with pancreatitis risk [15] and that EPBD with adequate duration (about 5 minutes) had a lower complication rate than the current standard of endoscopic sphincterotomy [49]. Inadequate dilation of the sphincter of Oddi from short-duration EPBD or by the use of small balloons, could be responsible for the limited volume expansion, which could worsen compression of the pancreatic duct from post-EPBD edema, increasing the pancreatitis risk [48]. Consistent with our findings, a smaller degree of CBD dilation has been shown to be associated with PEP [46]. Although large balloons did not affect the development of post-EPBD pancreatitis [46 – 50], it is still unclear whether the balloon diameter is the major factor in the induction of pancreatitis, as practice patterns with regard to balloon diameter vary widely among endoscopists. A sufficiently large dilation of the papilla may avoid the stress caused to the papilla by mechanical lithotripsy at stone removal, reducing pancreatitis risk [51]; nevertheless, the relationship between dilation time, balloon diameter, and PEP is poorly understood.

Some authors [52 – 53] have suggested that endoscopic sphincterotomy could lead to long-term complications such as cholecystitis and recurrence of CBD stones because of damage to papillary function. Based on the results of our meta-analysis, there was a trend, without statistical significance, toward an increased risk of long-term cholangitis, cholecystitis, and stone recurrence in patients undergoing endoscopic sphincterotomy compared with those undergoing EPBD. Moreover, EPBD may be preferred in terms of patient comfort, as it requires fewer sessions of repeat ERCP compared with endoscopic sphincterotomy. This in turn would result in cost savings for the healthcare system, as fewer reinterventions are needed [54].

This meta-analysis has some limitations. Our literature search considered several medical literature databases allowing us to search across conference proceedings, but we chose to consider only English language publications for inclusion in this systematic review and meta-analysis. It is unlikely, however, that the potential exclusion of non-English publications has biased our results. In fact, previous investigations generally found no evidence of bias from the use of language restrictions in systematic review-based meta-analyses [55 – 56]. We did not try to contact study investigators to retrieve additional data because a previous study showed unsuccessful attempts [57]. From a statistical perspective, we used the OR instead of the relative risk as an association measure to enable comparison between our results and those from previously published meta-analyses [4, 7, 10 – 13]. Between-study heterogeneity may be a concern in meta-analyses [20]. Thus, we performed stratified analyses according to the geographic area of the study, stone size, balloon diameter, and dilation time to explore potential sources of heterogeneity. Indeed, the limited number of studies reporting data according to stone size represents a limitation, while the use of a priori data-driven cutoffs for balloon diameter (10 mm) and balloon dilation time (1 minute) may have introduced bias.

Our results highlight the need of further RCTs aimed at studying efficacy and safety of EPBD vs. endoscopic sphincterotomy by balloon diameter, dilation time, stone size, number of attempts, cannulation time, and stone recurrence rate. Moreover, new studies should perform subgroup analyses that also consider patients with altered anatomy and perivaterian diverticulum.

In conclusion, although our latest data confirm that EPBD is currently inferior to endoscopic sphincterotomy in terms of overall stone clearance, this is the first meta-analysis to report an absence of evidence of a difference in efficacy when EPBD was performed with large (≥ 10 mm) balloons. EPBD with large balloons (≥ 10 mm) also increased clearance and reduced the need for EML, while longer dilation time (>1 minute) reduced pancreatitis risk. For these reasons, EPBD should be considered as an alternative treatment for CBD stone removal, especially in patients with altered anatomy, perivaterian diverticulum, coagulopathy, and cholecystitis, and in patients with higher risk of bleeding.

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Competing interests

None.

References

[1] Staritz M, Ewe K, Meyer zum Buschenfelde KH. Endoscopic papillary dilation (EPD) for the treatment of common bile duct stones and papillary stenosis. Endoscopy 1983; 15: 197 – 198

[2] Bergman JJ, van Berkel AM, Bruno MJ et al. A randomized trial of endoscopic balloon dilation and endoscopic sphincterotomy for removal of bile duct stones in patients with a prior Billroth II gastrectomy. Gastrointest Endosc 2001; 53: 19 – 26

[3] Liao WC, Huang SP, Wu MS et al. Comparison of endoscopic papillary balloon dilatation and sphincterotomy for lithotripsy in difficult sphincterotomy. J Clin Gastroenterol 2008; 42: 295 – 299

[4] Baron TH, Harewood GC. Endoscopic balloon dilation of the biliary sphincter compared to endoscopic biliary sphincterotomy for removal of common bile duct stones during ERCP: a metaanalysis of randomized, controlled trials. Am J Gastroenterol 2004; 99: 1455 – 1460

[5] Disario JA, Freeman ML, Bjorkman DJ et al. Endoscopic balloon dilation compared with sphincterotomy for extraction of bile duct stones. Gastroenterology 2004; 127: 1291 – 1299

[6] Freeman ML, DiSario JA, Nelson DB et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. Gastrointest Endosc 2001; 54: 425 – 434

[7] Weinberg BM, Shindy W, Lo S. Endoscopic balloon sphincter dilation (sphincteroplasty) versus sphincterotomy for common bile duct stones. Cochrane Database Syst Rev 2006: CD004890

[8] Williams EJ, Green J, Beckingham I et al. Guidelines on the management of common bile duct stones (CBDS). Gut 2008; 57: 1004 – 1021

[9] Maple JT, Ikenberry SO et al. ASGE Standards of Practice Committee. The role of endoscopy in the management of choledocholithiasis. Gastrointest Endosc 2011; 74: 731 – 744

[10] Feng Y, Zhu H, Chen X et al. Comparison of endoscopic papillary large balloon dilation and endoscopic sphincterotomy for retrieval of choledocholithiasis: a meta-analysis of randomized controlled trials. J Gastroenterol 2012; 47: 655 – 663

[11] Zhao HC, He L, Zhou DC et al. Meta-analysis comparison of endoscopic papillary balloon dilatation and endoscopic sphincteropapillotomy. World J Gastroenterol 2013; 19: 3883 – 3891

[12] Jin PP, Cheng JF, Liu D et al. Endoscopic papillary large balloon dilation vs endoscopic sphincterotomy for retrieval of common bile duct stones: a meta-analysis. World J Gastroenterol 2014; 20: 5548 – 5556

[13] Park CH, Jung JH, Nam E et al. Comparative efficacy of various endoscopic techniques for the treatment of common bile duct stones: a network meta-analysis. Gastrointest Endosc 2018; 87: 43 – 57 e10

[14] Tsujino T, Kawabe T, Isayama H et al. Efficacy and safety of low-pressured and short-time dilation in endoscopic papillary balloon dilation for bile duct stone removal. J Gastroenterol Hepatol 2008; 23: 867 – 871

[15] Liao WC, Tu YK, Wu MS et al. Balloon dilation with adequate duration is safer than sphincterotomy for extracting bile duct stones: a systematic review and meta-analyses. Clin Gastroenterol Hepatol 2012; 10: 1101 – 1109

[16] Kim TH, Kim JH, Seo DW et al. International consensus guidelines for endoscopic papillary large-balloon dilation. Gastrointest Endosc 2016; 83: 37 – 47

[17] Liberati A, Altman DG, Tetzlaff J et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009; 339: b2700

[18] Higgins JP, Altman DG, Gotzsche PC et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343: d5928

[19] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986; 7: 177 – 188

[20] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002; 21: 1539 – 1558

[21] Egger M, Davey Smith G, Schneider M et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997; 315: 629 – 634

[22] Minami A, Nakatsu T, Uchida N et al. Papillary dilation vs sphincterotomy in endoscopic removal of bile duct stones. A randomized trial with manometric function. Dig Dis Sci 1995; 40: 2550 – 2554

[23] Bergman JJ, Rauws EA, Fockens P et al. Randomised trial of endoscopic balloon dilation versus endoscopic sphincterotomy for removal of bileduct stones. Lancet 1997; 349: 1124 – 1129

[24] Chen YK, Deguzman L, Godil A et al. Prospective randomized trial of endoscopic balloon dilation versus sphincterotomy for extraction of bile duct stones. Gastrointest Endosc 1998; 47: AB111

[25] Cho YD, Hong SJ, Moon JH et al. Endoscopic papillary balloon dilatation versus endoscopic sphincterotomy for removal of common bile duct stones. Gastrointest Endosc 1998; 47: AB111

[26] Iwata F, Miyaki T, Yamada J et al. Effect of endoscopic papillary balloon dilation for the management of common bile duct stones in the elderly. Gastroenterology 1998; 114: A524

[27] Ochi Y, Mukawa K, Kiyosawa K et al. Comparing the treatment outcomes of endoscopic papillary dilation and endoscopic sphincterotomy for removal of bile duct stones. J Gastroenterol Hepatol 1999; 14: 90 – 96

[28] Arnold JC, Benz C, Martin WR et al. Endoscopic papillary balloon dilation vs. sphincterotomy for removal of common bile duct stones: a prospective randomized pilot study. Endoscopy 2001; 33: 563 – 567

[29] Yasuda I, Tomita E, Enya M et al. Can endoscopic papillary balloon dilation really preserve sphincter of Oddi function? Gut 2001; 49: 686 – 691

[30] Natsui M, Narisawa R, Motoyama H et al. What is an appropriate indication for endoscopic papillary balloon dilation? Eur J Gastroenterol Hepatol 2002; 14: 635 – 640

[31] Fujita N, Maguchi H, Komatsu Y et al. Endoscopic sphincterotomy and endoscopic papillary balloon dilatation for bile duct stones: a prospective randomized controlled multicenter trial. Gastrointest Endosc 2003; 57: 151 – 155

[32] Vlavianos P, Chopra K, Mandalia S et al. Endoscopic balloon dilatation versus endoscopic sphincterotomy for the removal of bile duct stones: a prospective randomised trial. Gut 2003; 52: 1165 – 1169

[33] Lin CK, Lai KH, Chan HH et al. Endoscopic balloon dilatation is a safe method in the management of common bile duct stones. Dig Liver Dis 2004; 36: 68 – 72

[34] Takezawa M, Kida Y, Kida M et al. Influence of endoscopic papillary balloon dilation and endoscopic sphincterotomy on sphincter of oddi function: a randomized controlled trial. Endoscopy 2004; 36: 631 – 637

[35] Tanaka S, Sawayama T, Yoshioka T. Endoscopic papillary balloon dilation and endoscopic sphincterotomy for bile duct stones: long-term outcomes in a prospective randomized controlled trial. Gastrointest Endosc 2004; 59: 614 – 618

[36] Watanabe H, Yoneda M, Tominaga K et al. Comparison between endoscopic papillary balloon dilatation and endoscopic sphincterotomy for the treatment of common bile duct stones. J Gastroenterol 2007; 42: 56 – 62

[37] Yasuda I, Fujita N, Maguchi H et al. Long-term outcomes after endoscopic sphincterotomy versus endoscopic papillary balloon dilation for bile duct stones. Gastrointest Endosc 2010; 72: 1185 – 1191

[38] Oh MJ, Kim TN. Prospective comparative study of endoscopic papillary large balloon dilation and endoscopic sphincterotomy for removal of large bile duct stones in patients above 45 years of age. Scand J Gastroenterol 2012; 47: 1071 – 1077

[39] Fu BQ, Xu YP, Tao LS et al. Endoscopic papillary balloon intermittent dilatation and endoscopic sphincterotomy for bile duct stones. World J Gastroenterol 2013; 19: 2425 – 2432

[40] Minakari M, Samani RR, Shavakhi A et al. Endoscopic papillary balloon dilatation in comparison with endoscopic sphincterotomy for the treatment of large common bile duct stone. Adv Biomed Res 2013; 2: 46

[41] Seo YR, Moon JH, Choi HJ et al. Comparison of endoscopic papillary balloon dilation and sphincterotomy in young patients with CBD stones and gallstones. Dig Dis Sci 2014; 59: 1042 – 1047

[42] Guo Y, Lei S, Gong W et al. A preliminary comparison of endoscopic sphincterotomy, endoscopic papillary large balloon dilation, and combination of the two in endoscopic choledocholithiasis treatment. Med Sci Monit 2015; 21: 2607 – 2612

[43] Kogure H, Kawahata S, Mukai T et al. OP211 A multicenter randomized trial of endoscopic papillary large balloon dilation alone versus endoscopic sphincterotomy for removal of bile duct stones: MARVELOUS trial. United European Gastroenterol J 2015; 3: A69

[44] Omar MA, Abdelshafy M, Ahmed MY et al. Endoscopic papillary large balloon dilation versus endoscopic sphincterotomy for retrieval of large choledocholithiasis: a prospective randomized trial. J Laparoendosc Adv Surg Tech A 2017; 27: 704 – 709

[45] Akiyama D, Hamada T, Isayama H et al. Superiority of 10-mm-wide balloon over 8-mm-wide balloon in papillary dilation for bile duct stones: a matched cohort study. Saudi J Gastroenterol 2015; 21: 213 – 219

[46] Youn YH, Lim HC, Jahng JH et al. The increase in balloon size to over 15 mm does not affect the development of pancreatitis after endoscopic papillary large balloon dilatation for bile duct stone removal. Dig Dis Sci 2011; 56: 1572 – 1577

[47] Seo YR, Moon JH, Choi HJ et al. Papillary balloon dilation is not itself a cause of post-endoscopic retrograde cholangiopancreatography pancreatitis; results of anterograde and retrograde papillary balloon dilation. J Gastroenterol Hepatol 2013; 28: 1416 – 1421

[48] Liao WC, Lee CT, Chang CY et al. Randomized trial of 1-minute versus 5-minute endoscopic balloon dilation for extraction of bile duct stones. Gastrointest Endosc 2010; 72: 1154 – 1162

[49] Mac MathunaP, Siegenberg D, Gibbons D et al. The acute and long-term effect of balloon sphincteroplasty on papillary structure in pigs. Gastrointest Endosc 1996; 44: 650 – 655

[50] Shim CS, Kim JW, Lee TY et al. Is endoscopic papillary large balloon dilation safe for treating large CBD stones? Saudi J Gastroenterol 2016; 22: 251 – 259

[51] Fujisawa T, Kagawa K, Hisatomi K et al. Is endoscopic papillary balloon dilatation really a risk factor for post-ERCP pancreatitis? World J Gastroenterol 2016; 22: 5909 – 5916

[52] Doi S, Yasuda I, Mukai T et al. Comparison of long-term outcomes after endoscopic sphincterotomy versus endoscopic papillary balloon dilation: a propensity score-based cohort analysis. J Gastroenterol 2013; 48: 1090 – 1096

[53] Lu Y, Wu JC, Liu L et al. Short-term and long-term outcomes after endoscopic sphincterotomy versus endoscopic papillary balloon dilation for bile duct stones. Eur J Gastroenterol Hepatol 2014; 26: 1367 – 1373

[54] Paik WH, Ryu JK, Park JM et al. Which is the better treatment for the removal of large biliary stones? Endoscopic papillary large balloon dilation versus endoscopic sphincterotomy Gut Liver 2014; 8: 438 – 444

[55] Juni P, Holenstein F, Sterne J et al. Direction and impact of language bias in meta-analyses of controlled trials: empirical study. Int J Epidemiol 2002; 31: 115 – 123

[56] Morrison A, Polisena J, Husereau D et al. The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. Int J Technol Assess Health Care 2012; 28: 138 – 144

[57] Tringali A, Hassan C, Rota M et al. Covered vs. uncovered self-expandable metal stents for malignant distal biliary strictures: a systematic review and meta-analysis. Endoscopy 2018; 50: 631 – 641