META-ANALYSIS AND SYSTEMATIC REVIEWS

Endoscopic papillary balloon dilatation versus endoscopic sphincterotomy in the treatment for choledocholithiasis: A meta-analysis

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Abstract

Background and Aim: Endoscopic papillary balloon dilatation (EPBD) and endoscopic sphincterotomy (EST) are two common nonsurgical treatments for choledocholithiasis. The aim of this study was to compare the efficacy and safety of EPBD and EST in the treatment for choledocholithiasis, confining the analysis to work reported in the last decade.

Methods: The rate of overall postoperative complications was chosen as the primary outcome, and 10 other outcomes were secondary outcomes. Relative risk (RR) or Peto odds ratio (OR) were computed as the measures of pooled effects. We planned sensitivity analyses a priori for examining the change in robustness of the sensitivity to excluding studies with some inappropriate objects, technique defects or without full-text acquisition.

Results: For complete stone removal, EPBD was similar to EST (95% vs. 96%, P = 0.36) and overall postoperative complications (14.0% vs. 11.7%, P = 0.53). The incidence of post-ERCP cholangitis (2.5% vs. 1.8%, P = 0.40), basket impaction (0.9% vs. 0%, P = 0.16) and perforation (0.0% vs. 0.4%, P = 0.17) were equivalent between EPBD and EST. On the other hand, EPBD caused more post-ERCP pancreatitis (PEP) (9.4% vs. 3.3%, P < 0.00001), but less hemorrhage (0.1% vs. 4.2%, P < 0.00001). People undergoing EPBD required more use of endoscopic mechanical lithotripsy (35.0% vs. 26.2%, P = 0.0004). The results of sensitivity analyses showed no substantial change.

Conclusion: EPBD is comparable to EST for stone extraction, though it requires more endoscopic mechanical lithotripsy (EML). EPBD may outweigh EST for patients with coagulopathy; however, it may cause more PEP.

Key words
balloon dilation, choledocholithiasis, endoscopic retrograde cholangiopancreatography, endoscopic sphincterotomy, meta-analysis.

Introduction

With the development of endoscopic technology, endoscopic treatment has become a preferred method for the treatment of common bile duct (CBD) stones around the world. Endoscopic papillary balloon dilatation (EPBD) and endoscopic sphincterotomy (EST) are the most important endoscopic techniques. As early as 1983, Staritz et al. proposed that EPBD could be an alternative to EST for stone extraction. However, EPBD had not provoked extensive attention until 1994 when May et al. started trying to use EPBD as a less invasive technology instead of EST.

The common complications of endoscopic management with endoscopic retrograde cholangiopancreatography (ERCP) for CBD stones are hemorrhage, pancreatitis, cholangitis, and occasionally, basket impaction. EPBD has been found to have less post-ERCP pancreatitis (PEP) bleeding but higher post-ERCP pancreatitis (PEP). In addition, Weinberg et al. have found that EPBD had poorer success of stone extraction, which has been otherwise in other clinical trials. We therefore conducted a meta-analysis to compare the efficacy and safety of EPBD and EST in randomized clinical trials (RCT).
Methods

Search strategy and study selection

A systemic research was conducted on PubMed/MEDLINE, EMBASE, Cochrane Library, Wiley Library, BIOSIS previews/ISI web of knowledge, Web of Science, and ScienceDirect databases, for medical reports published between 2000 and 2011. The following search terms were used: balloon dilation, sphincterotomy, endoscopy sphincterotomy. Expanded search was done via scholar search engines (Google and Scirus) and e-mails to authors. In the case of two different articles reporting the same clinical trial, the publication with more information was selected.

The eligible studies enrolled in the meta-analysis should satisfy the following criteria: (i) prospective clinical randomized controlled trials (RCT); (ii) studies comparing the success of stone clearance and/or post-ERCP complications of EPBD with EST in patients with similar clinical setting and features; and (iii) published reports providing enough data to count numbers of success and total individuals, and/or numbers of separate complication. Exclusion criteria were as follows: (i) clinical trials comparing EPBD and EST in patients with significantly different clinical settings and characteristics, i.e. non-corrected coagulopathy; and (ii) studies using a single therapy or combined treatments.

Data extraction

Two reviewers independently extracted data by using a predefined form (SH. L and K. X.), and disagreements were resolved by discussion and consensus by a third reviewer (PZ. S.). Information was collected in each selected study as possible, concerning first author, publication year, research type, publication type, the number of subjects, complete stone removal achieved, post-ERCP complications and recurrence of bile duct stones.

Statistical analysis

Two reviewers independently assessed the quality of all eligible studies using Jadad scale.6 Heterogeneity between studies was assessed using both the χ² test with a P-value < 0.10 and inconsistency index (I²) with a cut-off of ≥ 50%.7,8 Pooled effects with 95% CIs were derived using a fixed effect model,9 unless significant heterogeneity was present, in which case a random effect model was applied.10 Poored relative risk (RR) with 95% CIs was computed for the measurement of complete stone removal achieved, the use of endoscopic mechanical lithotripsy (EML), overall post-ERCP complications and the recurrence of bile duct stones. Peto odds ratio (OR) with 95% CIs was for separate post-ERCP complications, including PEP, perforation, hemorrhage, cholangitis and basket impaction, since it could generate the least biased pooled results of studies with zero event in both groups.11,12 Among these 11 outcomes, overall postoperative complications was chosen as the primary outcome, and the rest of the 10 outcomes as secondary ones.

Subgroup analysis was conducted to explore the incidence of mild/moderate and severe pancreatitis. We planned sensitivity analyses a priori for examining the change in the robustness of the sensitivity to excluding studies with some patients with coagulopathy, Billroth II gastrectomy, or studies without full texts. Furthermore, sensitivity analyses were done after excluding studies using balloons of different sizes. If exclusion of these studies, which might generate biased effects, made no substantive difference to the primary outcome, they were left in the final analyses.

Statistical analyzes were executed by STATA version 11.0 (STATA Corporation, College Station, TX, USA) and Revman version 5.0 (The Cochrane Collaboration, Oxford, UK).

Results

Descriptive assessment and study characteristics

Out of 379 citations generated by the initial published report search, 10 prospective RCTs with 1451 patients were finally enrolled in the meta-analysis according to the screening criteria, including eight full texts14-21 and two abstracts22,23 (Fig. 1, Table 1). Two studies were excluded because of comparison in...
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<td>EST 53</td>
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<td>EPBD 86</td>
<td>EPBD 76</td>
<td>EST 58</td>
<td>EPBD 58</td>
<td>EST 2</td>
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<td>EST 53</td>
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<td>EST 58</td>
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<td>EST 3</td>
<td>EPBD 9</td>
<td>EPBD 2</td>
<td>EPBD 8</td>
<td>EST 2</td>
<td>EPBD 1</td>
<td>EST 0</td>
<td>EPBD 3</td>
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<td>EPBD 8</td>
<td>EPBD 2</td>
<td>EPBD 3</td>
<td>EST 0</td>
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<td>EPBD 1</td>
<td>EST 0</td>
<td>EPBD 0</td>
<td>EST 0</td>
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<td>EPBD 0</td>
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<td>EST 0</td>
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<td>EPBD 0</td>
<td>EPBD 0</td>
<td>EST 0</td>
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<td>EPBD 0</td>
<td>EPBD 0</td>
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<td>Basket impaction</td>
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EPBD, endoscopic papillary balloon dilatation; EST, endoscopic sphincterotomy; NA, no data available.
special situations, i.e. periamputellar diverticulum and coagulopathy,24,25 and three comparative studies were excluded due to non randomization (Fig. 1).26-28 As is shown in Table 1, raw data were extracted as possible, including numbers of complete stone removal (10 studies), use of EML (seven studies), recurrence of bile duct stones (four studies), overall postoperative complications (10 studies) and the incidence of PEP (10 studies), mild/moderate pancreatitis (five studies), severe pancreatitis (four studies), post-ERCP cholangitis (seven studies), perforation (seven studies), hemorrhage (eight studies), and basket impaction (three studies).

Pooled effects of RCTs in the last decade

All of the eligible RCTs were of high quality, with average Jadad scores of 3.9 ± 0.3162 (Table 1). Table 2 summarized pooled effects of all the outcome measures. There was significant heterogeneity between studies in the summary results of overall morbidity (I² ≥ 50 and P < 0.1).

As is shown in Table 2, EPBD was equivalent to EST with respect to complete stone removal achieved (94.6% vs. 95.9%, RR 0.99, 95% CI = 0.98 to 1.01, P = 0.36) and recurrence of bile duct stone (5.5% vs. 8.8%, RR 0.67, 95% CI = 0.36 to 1.24, P = 0.20). People undergoing EPBD required more EML (35.0% vs. 26.2%, RR 1.31, 95% CI = 0.46 to 118.13, P = 0.0004).

Peto OR was selected as the assessment of summary effects of overall PEP, perforation, hemorrhage and basket impaction, because the incidence of these events was zero in both groups in some studies. The overall complications were similar between EPBD and EST (14.0% vs. 11.7%, RR 1.19, 95% CI = 0.69 to 2.07, P = 0.53, Fig. 2), the same with the incidence of post-ERCP cholangitis (2.5% vs. 1.8%, Peto OR 1.42, 95% CI = 0.63 to 3.18, P = 0.40). Both EPBD and EST caused equivalently little perforation (0.0% vs. 0.4%, Peto OR 0.14, 95% CI = 0.01 to 2.32, P = 0.17) and basket impaction (0.9% vs. 0%, Peto OR 7.39, 95% CI = 0.46 to 118.13, P = 0.16). EPBD caused less hemorrhage (0.2% vs. 4.6%, Peto OR 0.06 to 0.31, P < 0.00001). The morbidity of overall PEP was more common in EPBD groups (9.4% vs. 3.3%, Peto OR 2.82, 95% CI = 1.85 to 4.32, P < 0.00001). The subgroup analysis by the severity of pancreatitis showed that mild/moderate PEP (8.14% vs. 1.96%, Peto OR 3.97, 95% CI = 1.81 to 8.68, P = 0.0005) and severe PEP (2.94% vs. 0.00%, RR 3.97, 95% CI = 1.81 to 8.68, P = 0.03) were more prevalent in the EPBD group as well (Table 2).

There was no strong evidence for publication bias in the results of these 11 outcomes, since their values of Pr > I² (continuity corrected) were all larger than 0.1, according to the Begg’s rank correlation test.

Sensitivity analysis

We conducted the sensitivity analysis by excluding studies without full texts. Pooled results of these eight full texts showed no substantial change to the original results of all eligible studies (Table 2).

Different from the other nine RCTs, the study by Bergman21 included patients with a prior Billroth II gastrectomy, and it might affect the treatment effects. Therefore, we did another analysis by excluding this study. Table 3 shows that the results demonstrated no significant difference to the primary outcomes.

Balloons of different sizes were applied in three studies,15,18,22 whilst 8-mm balloons were used in the other seven studies. Since balloon size might be responsible for the incidence of PEP, we repeated the analysis for the measurement of PEP, to find no substantial change (0.11% vs. 0.44%, Peto OR 2.56, 95% CI = 1.55 to 4.22, P = 0.0002). On the other hand, Lin15 had not excluded patients with coagulopathy and it might increase post-ERCP hemorrhage. Therefore, another analysis was done after rejecting this study with respect to post-ERCP hemorrhage, and it showed no significant difference (0% vs. 0.02%, Peto OR 0.13, 95% CI = 0.04 to 0.47, P = 0.002).

In brief, the results of sensitivity analyses manifested no substantial difference to the primary outcomes of all eligible studies.

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<th>EPBD</th>
<th>EST</th>
<th>Risk Ratio</th>
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<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
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<td>3</td>
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<td>7</td>
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<td>Bergman 2001</td>
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<td>Arnold 2001</td>
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<td>Natsui 2002</td>
<td>7</td>
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<td>Fujita 2003</td>
<td>21</td>
<td>138</td>
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<td>Vlavianos 2003</td>
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<td>Tanaka 2004</td>
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<td>Disario 2004</td>
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<td>Lin 2004</td>
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<td>Watanabe 2007</td>
<td>13</td>
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<td>Total (95% CI)</td>
<td>724</td>
<td>727</td>
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<td>1.19 [0.69, 2.07]</td>
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<td>Total events</td>
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<td>Heterogeneity: Tau² = 0.48; x² = 27.18, df = 9 (P = 0.001); I² = 67%</td>
<td>Test for overall effect: Z = 0.63 (P = 0.53)</td>
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Figure 2 Forest plot of relative risk (RR), with 95% confidence interval (CI), for overall postoperative complications in all randomized controlled trials.
<table>
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<th>Outcomes</th>
<th>All 10 RCTs</th>
<th>Eight full texts</th>
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<th>RR/Peto OR (95% CI)</th>
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<td>Removal</td>
<td>EPBD 685/724 (94.6%)</td>
<td>EST 697/727 (95.9%)</td>
<td>1451 (10) 26% (P = 0.20) RR 0.99 (0.98,1.01)</td>
<td>0.764</td>
<td>1109 (8) 42% (P = 0.10) RR 0.99 (0.98,1.01)</td>
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<td></td>
<td>EPBD 146/236 (43.5%)</td>
<td>EST 108/234 (32.3%)</td>
<td>670 (8) 14% (P = 0.33) RR 1.31 (1.12,1.53)</td>
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<td>EPBD 111/137 (8.0%)</td>
<td>EST 121/139 (9.6%)</td>
<td>276 (3) 0% (P = 0.96) RR 0.94 (0.45,1.96)</td>
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<td>EPBD 15/275</td>
<td>558 (4) 0% (P = 0.46) RR 0.67 (0.36,1.24)</td>
<td>1.000</td>
<td>EPBD 47/56 (8.5%)</td>
<td>EST 17/56 (11.4%)</td>
<td>1.31 (1.12,1.53)</td>
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<td>EST 25/283 (8.8%)</td>
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<td>EPBD 518/556</td>
<td>932 (8) 42% (P = 0.10) RR 0.99 (0.98,1.01)</td>
<td>1.000</td>
<td>EPBD 47/56 (8.5%)</td>
<td>EST 17/56 (11.4%)</td>
<td>1.31 (1.12,1.53)</td>
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<td>EPBD 71/566</td>
<td>1109 (8) 73% (P = 0.0005) RR 1.09 (0.51,2.30)</td>
<td>1.000</td>
<td>EPBD 47/56 (8.5%)</td>
<td>EST 17/56 (11.4%)</td>
<td>1.31 (1.12,1.53)</td>
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<td>EST 63/653 (11.4%)</td>
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<td><strong>PEP (overall)</strong></td>
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<td>EPBD 25/326</td>
<td>653 (4) 0% (P = 0.80) RR 1.31 (1.12,1.53)</td>
<td>1.000</td>
<td>EPBD 47/56 (8.5%)</td>
<td>EST 17/56 (11.4%)</td>
<td>1.31 (1.12,1.53)</td>
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<td>EST 4/327 (1.2%)</td>
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<td><strong>Cholangitis</strong></td>
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<td>(mild/moderate)</td>
<td>EPBD 88/724 (11.7%)</td>
<td>EST 91/727 (12.0%)</td>
<td>1451 (10) 67% (P = 0.001) RR 1.19 (0.69,2.07)</td>
<td>1.000</td>
<td>EPBD 47/56 (8.5%)</td>
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<td>EPBD 10/340 (2.9%)</td>
<td>EST 14/340 (3.9%)</td>
<td>679 (4) 0% (P = 0.48) RR 3.97 (1.81,8.68)</td>
<td>0.462</td>
<td>EPBD 47/56 (8.5%)</td>
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<td><strong>Pancreatitis</strong></td>
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<tr>
<td>(severe)</td>
<td>EPBD 9/309 (3.0%)</td>
<td>EST 6/309 (2.0%)</td>
<td>619 (3) 0% (P = 0.70) RR 1.31 (1.12,1.53)</td>
<td>1.000</td>
<td>EPBD 47/56 (8.5%)</td>
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<td>EPBD 8/310 (2.6%)</td>
<td>EST 5/310 (1.6%)</td>
<td>619 (3) 0% (P = 0.70) RR 1.31 (1.12,1.53)</td>
<td>1.000</td>
<td>EPBD 47/56 (8.5%)</td>
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<td><strong>Hemorrhage</strong></td>
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<tr>
<td>EPBD 0/396</td>
<td>0.0% (P = 0.98) RR 0.14 (0.01,2.32)</td>
<td>1.000</td>
<td>EPBD 8/396 (2.1%)</td>
<td>EST 7/395 (1.8%)</td>
<td>1.36 (0.63,3.98)</td>
</tr>
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<td>EST 0/396 (0%)</td>
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<td><strong>Basket impaction</strong></td>
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<tr>
<td>EPBD 0/396</td>
<td>0.0% (P = 0.98) RR 0.14 (0.01,2.32)</td>
<td>1.000</td>
<td>EPBD 8/396 (2.1%)</td>
<td>EST 7/395 (1.8%)</td>
<td>1.36 (0.63,3.98)</td>
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<td>EST 0/396 (0%)</td>
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</table>
| CI, confidence interval; EML, endoscopic mechanical lithotripsy; EPBD, endoscopic papillary balloon dilatation; EST, endoscopic sphincterotomy; OR, odds ratio; PEP, post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis; RR, relative risk.
| Outcomes                  | Incidence (n/N) | No. patients (studies) | I² (%) | RR/Peto OR (95% CI) | Pr>|z| | Incidence (n/N) | No. patients (studies) | I² (%) | RR/Peto OR (95% CI) | Pr>|z| |
|--------------------------|-----------------|------------------------|--------|----------------------|-----|-----------------|----------------|--------|---------------------|-----|-----------------|-----|
| Complete stone removal   | EPBD 685/724    | 1451 (10)              | 26%    | (P = 0.20) RR       | 0.99 (0.98,1.01) | 0.764 | EPBD 671/708    | 1417 (9)            | 33%    | (P = 0.15) RR       | 0.99 (0.98,1.01) |
|                          | EST 697/727     | 952 (7)                | 26%    | (P = 0.44) RR       | 1.31 (1.13,1.51) | 1.000 | EST 163/458     | 918 (6)             | 8%    | (P = 0.37) RR       | 1.32 (1.10,1.57)  |
| Utility of EML           | EPBD 186/474    | 558 (4)                | 0%     | (P = 0.46) RR       | 0.67 (0.36,1.24) | 0.283 | EPBD 15/275     | 558 (4)             | 0%     | (P = 0.46) RR       | 0.67 (0.36,1.24)  |
|                          | EST 125/478     | 26%                    | (26.2%)|                     |                 |       | EST 121/460     | 26%                    | (26.3%)            | 0%     | (P = 0.46) RR       | 0.67 (0.36,1.24)  |
| Recurrence               | EPBD 18/275     | 952 (7)                | 0%     | (P = 0.46) RR       | 0.67 (0.36,1.24) | 0.283 | EPBD 15/275     | 952 (7)             | 0%     | (P = 0.46) RR       | 0.67 (0.36,1.24)  |
|                          | EST 25/283      | 558 (4)                | 0%     | (P = 0.46) RR       | 0.67 (0.36,1.24) | 0.283 | EST 25/283      | 558 (4)             | 0%     | (P = 0.46) RR       | 0.67 (0.36,1.24)  |
| Overall morbidity        | EPBD 101/724    | 1451 (10)              | 67%    | (P = 0.001) RR      | 1.19 (0.89,2.07) | 1.000 | EPBD 987/08     | 1417 (9)             | 68%    | (P = 0.002) RR      | 1.31 (0.73,2.33)  |
|                          | EST 81/727      | (14.0%)                | (11.7%)|                     |                 |       | EST 78/708      | (13.8%)               | (11.0%)            | 0%     | (P = 0.015) RR      | 2.79 (1.82,4.27)  |
| PEP (overall)            | EPBD 69/724     | 1415 (10)              | 28%    | (P = 0.20) Peto OR  | 2.82 (1.84,3.32) | 0.764 | EPBD 28/340     | 679 (4)             | 0%     | (P = 0.51) RR       | 3.58 (1.81,7.09)  |
|                          | EST 24/727      | 9.4%                   | (0.3%) |                     |                 |       | EST 7/339       | 2.1%                    | (2.1%)             | 0%     | (P = 0.51) RR       | 3.58 (1.81,7.09)  |
| Pancreatitis (mild/moderate) | EPBD 23/356 | 713 (5)                | 0%     | (P = 0.48) RR       | 3.97 (1.81,8.68) | 0.462 | EPBD 20/340     | 679 (4)             | 0%     | (P = 0.51) RR       | 3.58 (1.81,7.09)  |
|                          | EST 7/357       | (0.1%)                 | (0.0%) |                     |                 |       | EST 7/339       | (2.1%)               | (2.1%)            | 0%     | (P = 0.51) RR       | 3.58 (1.81,7.09)  |
| Pancreatitis (severe)    | EPBD 10/340     | 679 (4)                | 0%     | (P = 0.87) RR       | 6.02 (2.1,26.90) | 0.308 | EPBD 10/340     | 679 (4)             | 0%     | (P = 1.00) RR       | 6.02 (1.36,26.52) |
|                          | EST 0/039       | (2.9%)                 | (0.0%) |                     |                 |       | EST 0/039       | (0.0%)               | (0.0%)            | 0%     | (P = 1.00) RR       | 6.02 (1.36,26.52) |
| Cholangitis              | EPBD 14/564     | 1133 (7)               | 25%    | (P = 0.24) RR       | 1.36 (0.63,3.18) | 1.000 | EPBD 14/564     | 1133 (7)             | 25%    | (P = 0.24) RR       | 1.42 (0.63,3.18)  |
|                          | EST 10/569      | (2.5%)                 | (1.8%) |                     |                 |       | EST 10/569      | (2.5%)               | (1.8%)            | 0%     | (P = 0.98) RR       | 1.14 (0.07,2.00)  |
| Perforation              | EPBD 0/498      | 1003 (7)               | 0%     | (P = 0.98) Peto OR  | 0.14 (0.01,2.32) | 1.000 | EPBD 0/498      | 975 (6)             | 0%     | (P = 0.98) Peto OR  | 0.14 (0.07,2.00)  |
|                          | EST 2511        | (0.9%)                 | (0.4%) |                     |                 |       | EST 0/498       | (0.2%)               | (0.2%)            | 0%     | (P = 0.98) Peto OR  | 0.14 (0.07,2.00)  |
| Hemorrhage               | EPBD 1/515      | 1035 (8)               | 0%     | (P = 1.00) Peto OR  | 0.14 (0.06,0.31) | 0.452 | EPBD 14/98     | 1000 (7)            | 0%     | (P = 1.00) Peto OR  | 0.14 (0.06,0.33)  |
|                          | EST 24/520      | (0.2%)                 | (4.6%) |                     |                 |       | EST 21/502      | (4.2%)               | (4.2%)            | 0%     | (P = 1.00) Peto OR  | 0.14 (0.06,0.33)  |
| Basket impaction         | EPBD 2/211      | 424 (3)                | 0%     | (P = 1.00) Peto OR  | 7.39 (0.46,118.13) | 1.000 | EPBD 2/211      | 424 (3)             | 0%     | (P = 1.00) Peto OR  | 7.39 (0.46,118.13) |
|                          | EST 0/213       | (0.9%)                 | (0.0%) |                     |                 |       | EST 0/213       | (0.0%)               | (0.0%)            | 0%     | (P = 1.00) Peto OR  | 7.39 (0.46,118.13) |

CI, confidence interval; EML, endoscopic mechanical lithotripsy; EPBD, endoscopic papillary balloon dilation; EST, endoscopic sphincterotomy; OR, odds ratio; PEP, post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis; RR, relative risk.
Discussion

The treatment of CBD stones has advanced from surgical choledochotomy to nonsurgical endoscopic management.\textsuperscript{20,29,30} Endoscopic papillary balloon dilation for CBD stones has a success rate of over 90\%.\textsuperscript{29,30} and there are two important techniques, EPBD and EST. Our meta-analysis compared the efficacy and safety of EPBD with both of the standard endoscopic therapy, EST, for the patients with choledocholithiasis.

Endoscopic papillary balloon dilation was demonstrated to have equivalently great success for complete stone removal to EST (94.7\% and 94.4\%, respectively). However, EPBD required more EML, which would probably add up to extra therapeutic cost.

The overall post-ERCP complications along with the incidence of cholangitis, perforation and basket impaction were found to be similar between EPBD and EST. EPBD caused less hemorrhage (0.1\% vs. 4.2\%, \( P < 0.00001 \)). Compared with EPBD, EST is somehow more invasive since it needs sphincterotomy, so we should be deliberate in the options of EST in patients with coagulopathy. Lin et al.\textsuperscript{15} have included patients with coagulation disorders, which have been corrected before ERCP, and they found that post-ERCP bleeding was more frequent in the EST group (26.4\% vs. 2\%, \( P < 0.01 \)). Considering this study might influence the results, we did a sensitivity analysis by omitting this study, but no substantial change happened. On the other hand, Park et al.\textsuperscript{27} have compared EPBD and EST for the treatment of CBD stones in patients with coagulopathy, and EST generated significantly higher postoperative hemorrhage than EPBD did (30\% vs. 0\%, \( P = 0.009 \)). Therefore, EPBD may be optimal for patients with coagulopathy, i.e. those with liver cirrhosis, intake of anti-coagulater drugs, etc.\textsuperscript{31}

We found that overall PEP, mild/moderate and severe PEP were more prevalent in the EPBD group. The risk factors for PEP are the entry of contrast media into pancreatic duct, poor minor papilla function, long procedure time and high balloon inflation pressure of > 5 atm.\textsuperscript{12,33} and thus it may be effective for lowering the incidence and extent of PEP to shorten the duration of balloon dilation and lower the dilation pressure.\textsuperscript{31} On the other hand, balloon size may be another factor responsible for PEP, since it may influence the dilation pressure. Among the 10 enrolled RCTs, 8-mm balloons were applied in seven trials, while balloons of various sizes were used in three other trials\textsuperscript{15,18,22} which were excluded in the sensitivity analysis. The results appeared to be substantially similar, EPBD favoring PEP. Thus it requires more studies to demonstrate the probable role of balloon size in the incidence of PEP.

In the study by Bergman\textsuperscript{21} studying patients with prior Billroth II gastrectomy, complete stone clearance are lower than the results of our meta-analysis in both EPBD and EST, but no significant difference is figured out between them (88\% vs. 83\%, \( P = 0.73 \)). It is likely to increase the difficulty and hazards during ERCP in these patients, because dramatic changes have happened to the upper gastrointestinal anatomy especially the position of major duodenal papilla. Thus we rejected this study and re-synthesized data, finding no substantial change, so it is safe to include this study in the meta-analysis.

Our meta-analysis illustrated that EPBD and EST caused equally low recurrence of bile duct stones (5.5\% vs. 8.8\% respectively). Concerns that have been provoked about the long-term complications of EST are the potential complications of recurrent bile duct stone duct stone, perhaps as a consequence of bacterial colonization of the biliary tree, and stenosis of the biliary orifice.\textsuperscript{34-36} However, it requires more studies in regard to the contributory role of the numbers of stones and maximal stone size on the performance of EPBD and EST, including their impact on the success for stone removal, use of EML, basket impaction and recurrence of bile duct stones.

Both EST and EPBD are similar in their complications and efficacy for removal of bile duct stones during ERCP. While hemorrhage occurs more frequently after EST, post-ERCP pancreatitis seems to be more common after EPBD. EPBD may be preferable in patients with coagulopathy.

Acknowledgments

The authors thank the following colleagues for their helpful advice for and encouragement in this study: Dr Bo Jiang (Nanfang Hospital) and Dr Side. Liu (Nanfang Hospital).

References

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