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SYSTEMATIC REVIEW

Post-ERCP pancreatitis occurs more frequently in self-expandable metallic stents than multiple plastic stents on benign biliary strictures: a meta-analysis

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ABSTRACT

Background: The occurrence of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) after using covered self-expandable metallic stents (CSEMS) and multiple plastic stents (MPS) in the therapy of benign biliary strictures (BBS) remains ambiguous, this analysis aimed to evaluate the outcomes.

Methods: A systematic search of electronic databases (PubMed, Web of Science and Cochrane Library) was conducted for randomised controlled trials (RCTs), and the included studies were published between 2008 and 2021. The primary outcome was PEP, while the secondary outcomes were stricture resolution, recurrence, overall adverse events, costs, and ERCP sessions. Pooled effect sizes were calculated with the random-effects model or fixed-effects model depending on the heterogeneity.

Results: Six RCTs contained 444 patients (221 with CSEMS, 223 with MPS) finally included in the meta-analysis. The present analysis shows that compared to MPS, PEP is more likely to occur in CSEMS (OR [odds ratio] = 3.34, 95% confidence intervals [CI]:1.44–7.77, $p = .005$). CSEMS needs fewer ERCP sessions (Mean Deviation [MD]: −1.56; 95%CI:−2.66, −0.46], $p = .006$). The difference in stricture resolution and recurrence was not significant between the two stent types (OR = 0.87, 95%CI: 0.49–1.56, $p = .64$; and OR = 2.3, 95%CI: 0.68–7.76, $p = .18$). The incidence of overall adverse events was comparable between CSEMS and the MPS group (OR = 1.49, 95% CI: 0.97–2.29, $p = .07$).

Conclusions: Compared with MPS, CSEMS caused a significantly higher incidence of PEP but fewer ERCP procedures, while the rate of stricture resolution, recurrence, and overall adverse events were comparable. Prevention methods of PEP should be further evaluated in BBS when undergoing CSEMS placement.

Systematic Review Registration: PROSPERO CRD42022314864.

KEY MESSAGES

- CSEMS and MPS placement remain a mainstay for patients with BBS, and severe complications after stent placement have not been compared.
- The incidence of PEP was higher after deployment of CSEMS compared to MPS.
- Prevention methods of PEP should be evaluated in BBS when undergoing CSEMS placement.

Abbreviations: BBS: benign biliary strictures; CI: confidence interval; CSEMS: covered self-expandable metallic stents; MPS: multiple plastic stents; OR: odds ratio; ERCP: endoscopic retrograde cholangiopancreatography; MD: mean deviation; PEP: post-ERCP pancreatitis; RCTs: randomised controlled trials

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Benign biliary strictures; covered self-expandable metallic stents; multiple plastic stents; post-ERCP pancreatitis; meta-analysis

1. Introduction

BBS derives from a multitude of aetiologies, most frequently arising from surgery or inflammation [1]. Surgery-related BBS is also called iatrogenic biliary injuries, which include predominantly orthotopic liver transplantation (OLT) and cholecystectomy (LC) [2]. While the incidence of BBS in OLT is 3–13% [3], and 0.2–0.7% in LC [4]. Chronic pancreatitis (CP) is the commonest non-surgical related BBS, with an incidence of 13–21% [5,6]. Other origins of BBS encompass bile duct diseases related to primary sclerosing cholangitis (PSC), choledocholithiasis, and IgG4-related sclerosing cholangitis [7–9]. BBS is related to a series of signs, from abdominal pain, pruritus, cholangitis, or

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elevation of liver enzymes, to complete obstruction of jaundice. It deserves endoscopic minimally invasive intervention to prevent secondary biliary cirrhosis and surgery [10].

The common treatment procedures for BBS include cholangiojejunostomy, percutaneous or endoscopic bile duct dilation, and whether or not stents are placed [11]. Endoscopic has been considered the first-line treatment of BBS [12–14]. ERCP with the placement of MPS or CSEMS has turned out to be a valid and safe method reported by the Asia–Pacific Consensus Guidelines 2017 and several meta-analyses and systematic reviews [1,15–19].

PEP is reported as the most common and severe adverse event, the incidence varying from 3% to 4% [20], while in patients with high risk, the rates range from 7% to 16% [21,22]. The majority of PEP are mild or moderate, and a few are serious, but mortality can occur, therefore, the occurrence and treatment of PEP is a topic of concern in clinical research [22,23]. However, the incidence of PEP has always been considered a secondary outcome, which varies greatly after biliary stenting (MPS or CSEMS) in previous studies [24–30].

To the best of our knowledge, there is no related meta-analysis evaluating the PEP incidence with the use of CSEMS and MPS in BBS. Recently, new RCTs and retrospective cohort studies compared the incidence of PEP, the efficacy, and the cost of CSEMS versus MPS [24,26,28,29]. Herein, we aim to perform an updated meta-analysis based on current RCTs comparing the occurrence of PEP and other results of CSEMS versus MPS in the therapy of BBS.

2. Methods

2.1. Search strategy

A systematic search of electronic databases PubMed, Web of Science, and the Cochrane Library based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines was conducted [31]. This analysis was registered in PROSPERO (registration number: CRD 42022314864). The following search terms were used: "benign biliary stricture" or "biliary stenosis" or "post-ERCP pancreatitis" or "acute pancreatitis" or "ERCP-related adverse events" and "multiple plastic stents" and "self-expandable metallic stents" or "metallic stent". Studies published between January 1, 2008 and December 31, 2021 with the use of MPS or CSEMS in the management of BBS, were included. Studies related to the treatment of BBS were manually retrieved to identify studies that met the criteria. All results were downloaded into the bibliographic database manager EndNoteX9 (Thompson ISI ResearchSoft, Philadelphia, Pennsylvania, USA).

2.2. Eligibility criteria

Inclusion criteria: a. studies included all kinds of BBS, such as laparoscopic cholecystectomy (LC), OLT, CP, and so on; b. studies compared the effects of MPS and CSEMS in the treatment of BBS; c. the patients included in the study were adults aged 18 and older; d. the stent should be positioned across the duodenal papilla; f. RCTs.

Exclusion criteria: a. suspected or confirmed malignant biliary strictures; b. using PS or SEMS only; c. studies fewer than 10 patients; d. location of the stents was completely inside the CBD; e. non-English language; f. animal studies; g. letters, comments, single case reports, conference abstracts, meta-analyses, and systematic reviews.

2.3. Data extraction

Two authors (HY and ZZY) independently extracted the related data from the included studies. The incidence of PEP was the primary outcome. The following data was extracted to evaluate the risk factors of PEP, which may obscure the correlation between stent type and PEP. These data included study type, publication year, aetiologies of stricture, stent types, stent indwell time, follow-up time, number of ERCP sessions, stricture resolution, stricture recurrence, adverse events, PEP, administration of NSAIDs, whether performed EST and pancreatic duct (PD) stent placement.

2.4. Risk of bias

Two authors (HY and ZZY) independently performed the quality assessment. The risk of bias was evaluated with the Cochrane Risk Bias tool for RCTs. Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tools was used to evaluate potential bias [32,33]. Jadad score was used to quantitatively assess the quality of the included studies [34]. All the extracted data were independently compared by two authors (HY and ZZY), and any discrepancy would be discussed to make a final decision.

2.5. Definition of PEP and endpoint outcomes

The definition of PEP was as follows: 1. Typical abdominal pain consistent with pancreatitis occurring within 24 h after endoscopy, 2. Hospitalization or prolonged hospitalization is required, 3. Serum amylase or lipase measured more than 24 h after operation was three times or more than three times the upper limit of normal. If the hospitalization is prolonged for more than 10 days, severe pancreatitis is diagnosed [35]. Stricture resolution was defined as the easy passage of an 8.5-mm balloon through the stricture and the rapid emptying of contrast material during the ERCP procedure. It could be accompanied by an improvement in liver function indicators with no need for further intervention procedures. Stricture recurrence was defined as the reappearance of biliary obstruction symptoms, with or without elevation of liver function, and cholangiographic evidence of stricture requiring subsequent reintervention after initial success [36]. PEP is the primary endpoint outcome. Secondary endpoint outcomes involved stricture resolution, stricture recurrence, ERCP sessions and overall adverse events.

2.6. Statistical analysis

All the meta-analyses were conducted using the software Review Manager 5.3 and STATA16.0. Dichotomous outcomes were calculated with a 95%CI as well as OR. ERCP sessions were analysed using the Mean Difference. These were analysed through a random-effects model or fixed-effects model depending on the heterogeneity between the studies. Cochran *Q* test and I^2 test statistics were used to assess the heterogeneity, a *P*-value $< .1$ was defined as indicating the existence of heterogeneity [31,37]. $p < .05$ was defined as statistically significant. Sensitivity analysis was conducted by deleting one study at a time to evaluate the stability of the overall results. The total ERCP times were calculated by the number of patients and mean ERCP times per patient. The cost analysis was performed by converting Eurodollars to United States dollars for studies [29]. The exchange rate depended on the month of publication. Publication bias was evaluated by Egger's test. The student's *t*-test was used to calculate the mean and standard deviation.

3. Results

3.1. Study selection

Seven hundred and forty-three studies were identified through a manual search of reference lists and an online search of electronic databases after removing

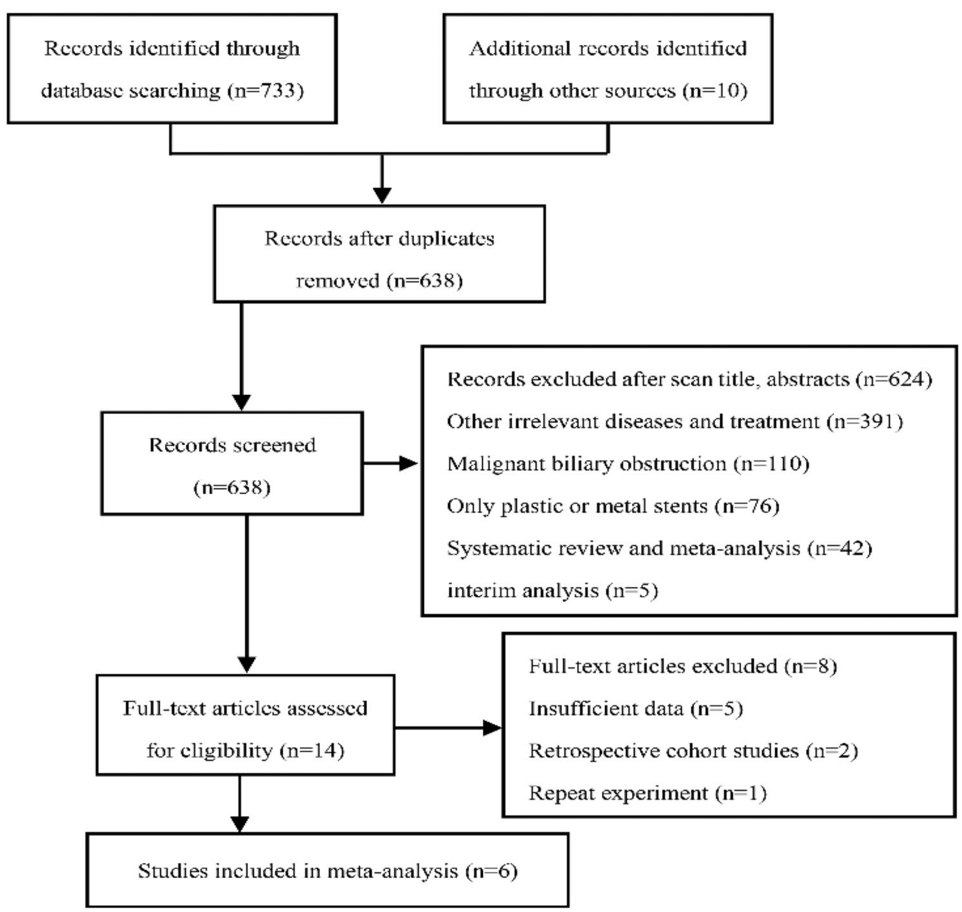


Figure 1. PRISMA flow diagram.

duplications and studies unrelated to this meta-analysis. Consequently, six RCTs met all the criteria and were included in the analysis [25,27–30,38], as shown in Figure 1.

3.2. Study characteristics

The basic characteristics of the 6 studies with 444 patients are illustrated in Table 1. The study design of the included studies was RCTs. Specifically, 223 patients received MPS and 221 patients received CSEMS treatment. All the studies reported the occurrence of PEP, stricture resolution and adverse events. Five of the six studies reported the occurrence of stricture recurrence, and ERCP sessions. Two studies compared the costs of different stent types. The risk-of-bias evaluation is shown in Tables 1 and 2.

3.3. Endpoint outcomes

3.3.1. PEP

All the included studies assessed the incidence of PEP. The overall pooled effect demonstrated that the incidence of PEP in CSEMS was significantly higher than that in MPS (OR = 3.34, 95%CI = 1.44–7.77, I^2 = 12%, $p = .33$, $Z = 2.80$, $p = .005$) (Figure 2(a)).

3.3.2. Stricture resolution

Six studies reported the stricture resolution rate. No statistically significant difference was found between CSEMS and MPS, which indicated equivalence for the initial success between the groups (OR = 0.87, 95%CI = 0.49–1.56, I^2 = 33%, $p = .20$, $Z = 0.46$, $p = .64$) (Figure 2(b)).

3.3.3. Stricture recurrence

There was no statistically significant difference between the two groups to evaluate recurrence in 402 patients who had successful initial stricture treatment (OR = 2.30, 95% CI = 0.68–7.76, I^2 = 52%, $p = .08$, $Z = 1.35$, $p = .18$) (Figure 2(c)). The heterogeneity between the studies was calculated by Cochran's *Q*-test, in which $p < .10$ indicated significant heterogeneity. The sensitivity analysis was conducted by deleting one study at a time to assess the influence of each study. While excluding studies that showed a higher recurrence for CSEMS [27], there still no statistically significant difference was noted (OR = 1.58, 95%CI =0.73–3.44, I^2 = 31%, $p = .23$, $Z = 1.15$, $p = .25$) (Figure 3(a)).

3.3.4. Adverse events

All six studies reported adverse events, including a series of symptoms, such as PEP, abdominal pain, infection, stent occlusion, cholecystitis and migration. The adverse events in the current analysis were comparable between CSEMS and MPS (OR = 1.49, 95%CI =0.97–2.29, I^2 = 0%, $p = .97$, $Z = 1.82$, $p = .07$) (Figure 3(b)).

3.3.5. Number of ERCPs

A total of 5 studies reported the ERCP sessions, including 413 patients. The number of ERCP necessary for therapy was fewer in CSEMS (MD: −1.56; 95%CI [−2.66, −0.46]) (Figure 3(c)). Although the heterogeneity exceeded 50%, the funnel plot showed little sign of treatment heterogeneity.

3.3.6. Cost analysis

A total of two studies reported the average cost of the two groups. The expenditure was converted into United States dollars. Evaluation of the average costs of the studies showed that CSEMS was more economical than MPS with average costs of \$6600.00 and \$13377.00 (Figure 4).

3.3.7. Publication bias

As shown in funnel plots (Figure 5), no obvious asymmetry was found. To further confirm this, Egger's test was performed and the P-value was 0.866, indicating no obvious publication bias with regard to the primary outcome.

4. Discussion

We conducted the first meta-analysis that compared the incidence of PEP after placement of CSEMS and MPS in the management of BBS. Our findings demonstrated that, compared with MPS, CSEMS caused a significantly higher PEP but fewer ERCP procedures, while stricture resolution, recurrence rate and overall adverse events were comparable.

PEP remains an issue for endoscopists, especially after CSEMS placement for BBS. In theory, compared to MPS, CSEMS may be related to a higher incidence of PEP owing to the larger diameter, especially FCSEMS, which may cause obstruction of the pancreatic orifice when expanded [39]. CSEMS has indeed been observed to cause a significantly higher incidence of PEP in the previous study [24]. Besides, PEP occurs more frequently in CSEMS than in MPS reported by several studies, but the difference was not significant [25–29]. What's more, PEP did not occur in

Table 1. Main characteristics of included studies.

Study	Artifon et al. [38] MPS/CSEMS	Coté et al. [25] MPS/CSEMS	Tal et al. [30] MPS/CSEMS	Martins et al. [27] MPS/CSEMS	Cantu et al. [29] MPS/CSEMS	Ramchandani et al. [28] MPS/CSEMS
Publication (y)	2012	2016	2017	2018	2021	2021
Study type	RCT	RCT	RCT	RCT	RCT	RCT
Total patients	31	112	48	59	30	164
No. of patients	16/15	55/57	24/24	29/30	15/15	84/80
Age	45.19/45.53	56.7 (11)/54.5 (10.4)	58.5 (32–72)/57 (32–69)	50 (28–71)/54 (23–73)	53 (22–68)/59 (50–67)	53 (26–74)/51 (28–74)
Sex (M vs. F)	6 vs.10/5 vs.10	38 vs.1/38 vs.19	18 vs.6/14 vs.10	20 vs.9/22 vs.8	14 vs.1/12 vs.3	72 vs.12/70 vs.10
Aetiology	Surgical procedures	OLT36/3 CP17/18 Other injury 2/2	ABS	ABS	ABS	CP
Stent type	MPS 8.5-Fr and/ or 10-Fr, 7 cm and/or 9 cm long/Partially CSEMS (Boston Medical Scientific, Natick, USA)	Maximum cumulative diameter/8 mm or 10 mm FCSEMS (WallFlex, Boston Scientific)	Maximum No. of MPS with optimal diameter at endoscopist discretion/FCSEMS with diameter of 10 mm. For retrieval, 2 stent types had a small retrieval flap a2nd 1 CSEMS had a big lasso	Maximum No. of MPS/FCSEMS (Wallflex, Boston Scientific, 10 mm in diameter, 60 or 80 mm in length)	10 Fr MPS/8 mm or 10 mm diameter FCSEMS	3 or 4 side-by-side MPS, at least two 8.5 or 10 Fr. PS/8 mm or 10 mm diameter FCSEMS (WallFlex Biliary Stent, Boston Scientific, Marlboro, MA, USA)
Indwell period (m)	6–12. Repeat ERCP at 3 months/4–5	Every 3–4 months with MPS up-sizing/6–12	Stents exchanged every 6–12 weeks and the number and diameter of the MPS were increased/4–6	ERCP repeated at 3 months intervals with an increasing number of stents until 12 months/6	Increase in number of MPS at 3 months intervals until 12 months/6	12/12
Follow-up (m)	72/72	NA	16.9 (2–39.4)/13.3 (6.3–34.9)	32.9/36.4	60 (34–80)	24/24
No. of ERCPs/ patients	NA	3.13 (±0.88)/2.21 (±0.48)	4 (3–12)/2 (2–12)	4.9 (4–6)/2 (2–2)	4 (3–7)/3 (2–8)	3.9 ± 1.3/2.6 ± 1.3
Cost	NA	NA	NA	$16095/$6903	$10659/$6297	NA
PEP	0/16 vs. 0/15	3/173 vs 3/122	0/96 vs. 0/48	3/141 vs. 8/60	3/94 vs. 1/28	0/328 vs. 2/208
BBS resolution	16/16 vs. 15/15	41/48 vs. 50/54	23/24 vs. 24/24	28/29 vs. 25/30	14/15 vs. 11/15	54/70 vs. 47/62
BBS recurrence	5/16 vs. 3/15	2/41 vs. 7/50	5/23 vs. 5/24	0/28 vs. 8/25	1/14 vs. 4/11	NA
Overall AEs	4/16 vs. 6/15	37/55 vs. 42/57	3/24 vs. 3/24	9/30 vs. 14/30	6/94 vs. 3/28	16/84 vs. 19/80
Migration	0/16 vs. 2/15	10/55 vs. 16/57	0/24 vs. 5/24	4/141 vs. 3/30	2/76 vs. 5/17	18/82 vs. 15/80
cholecystitis	0/16 vs. 0/15	0/55 vs. 0/57	0/24 vs. 0/24	0/30 vs. 0/30	0/94 vs. 0/28	1/84 vs. 3/80
PD stent	Undefined	Undefined	Undefined	Undefined	Undefined	Undefined
NSAIDs	Undefined	Undefined	Undefined	Undefined	Yes	Undefined
EST	Undefined	Undefined	Yes	Yes/No	Yes	Undefined
Jadad score	3	5	5	4	3	5

CSEMS, covered self-expandable metal stents; PEP, post-ERCP pancreatitis; MPS, multiple plastic stents; ABS, anastomotic biliary strictures; CP, chronic pancreatitis; ERCP, endoscopic retrograde cholangiopancreatography; OLT, Orthotopic Liver Transplant; $, United states dollars; PD, pancreatic duct; EST, biliary endoscopic sphincterotomy; RCT, randomised controlled trial; NA, not applicable; NSAIDs, Non-steroidal Anti-inflammatory Drugs.

Table 2. Risk of bias for included studies.

Study	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participant and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	other bias
Coté et al. [25]	Low	Low	Unclear	Low	Low	Low	Unclear
Tal et al. [30]	Low	Low	Unclear	Low	Low	Low	Unclear
Martins et al. [27]	Unclear	Low	Low	Low	Low	Low	Unclear
Cantu et al. [29]	Unclear	Unclear	Low	Low	Low	Low	Unclear
Ramchandani et al. [28]	Low	Low	Unclear	Low	Low	Low	Unclear
Artifon et al. [38]	Unclear	Unclear	Unclear	Low	Low	Low	Unclear

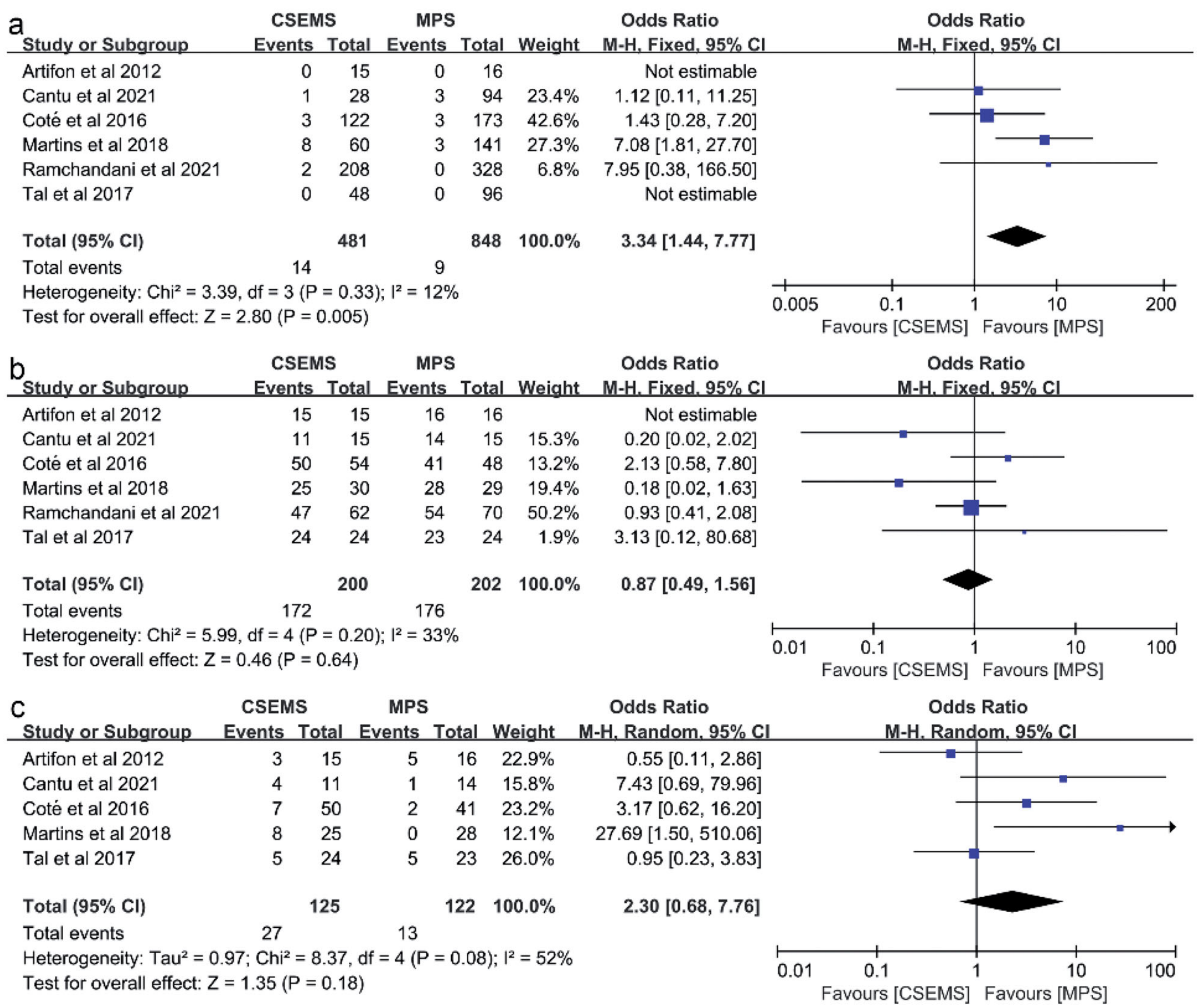


Figure 2. (a) Forest plots of results on PEP between CSEMS and MPS. (b) Forest plots of results on stricture resolution between CSEMS and MPS. (c) Forest plots of results on stricture recurrence between CSEMS and MPS. I^2, inconsistency index; MPS, multiple plastic stenting; CSEMS, covered self-expandable metal stents; M-H, Mantel-Haenszel; CI, confidence interval.

two studies with a small sample size [30,38]. Thus, these conflicting data need to be verified. Our study suggested that CSEMS was related to a significantly higher incidence of PEP in BBS patients compared to MPS. But, remarkably, PEP incidence varies greatly in these studies possibly mainly due to various aetiologies [24–30,38], as it is generally known that chronic pancreatitis (CP) may reduce the risk of PEP [40,41]. Indeed, previous studies have reported the incidence of PEP in CP patients receiving CSEMS, which ranges from 0.5% to 2.5% [28,42]. In addition, PEP risk may reduce as pancreatic duct compression by SEMS is alleviated by the separation of the pancreaticobiliary duct after EST [43]. However, some included studies

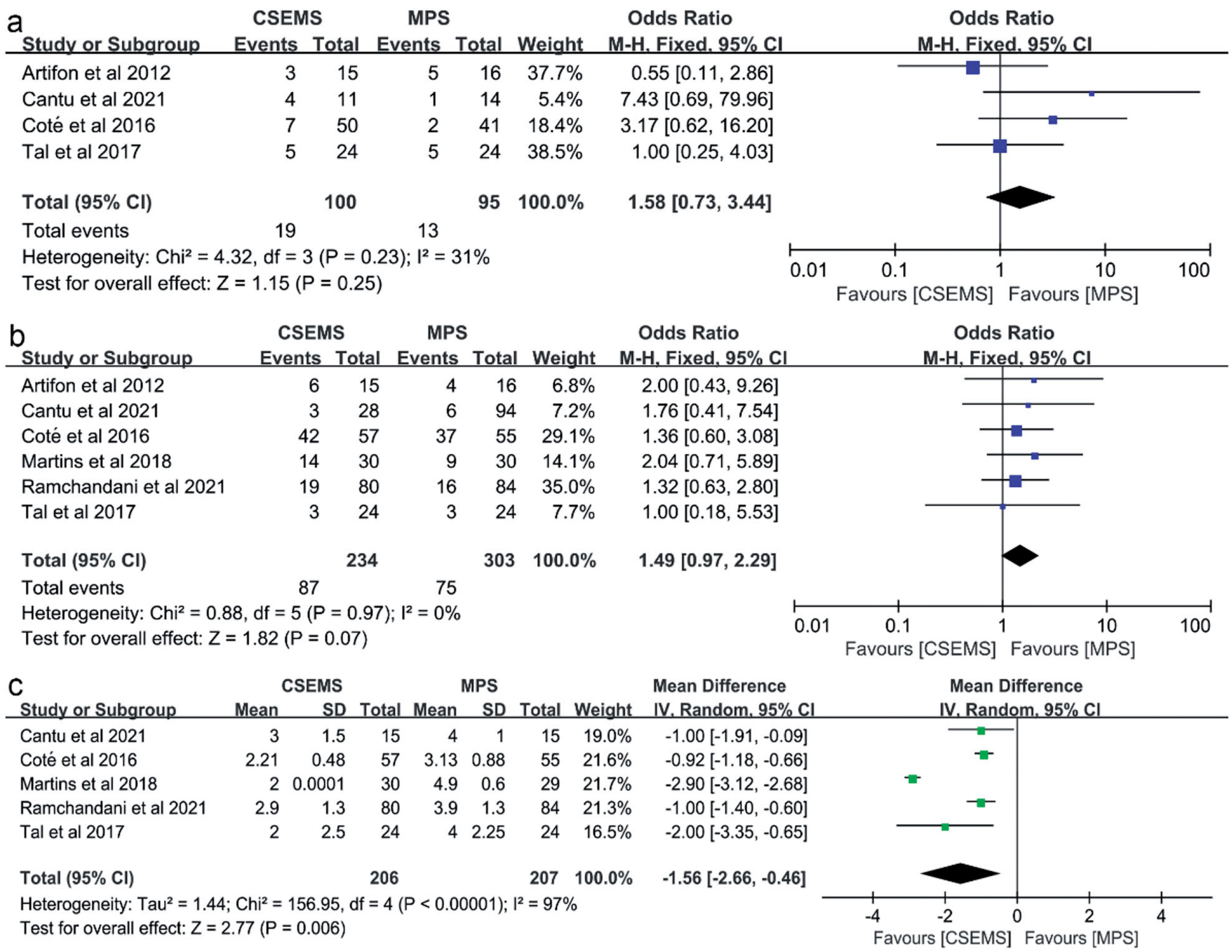
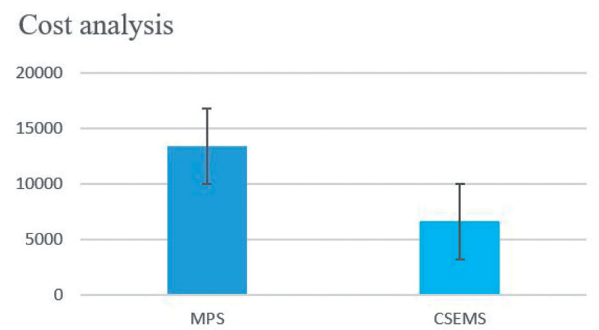


Figure 3. (a) Forest plots of results after eliminating the difference in stricture recurrence between CSEMS and MPS. (b) Forest plots of results on overall adverse events between CSEMS and MPS. (c) Forest plots of results on the number of ERCPs between CSEMS and MPS. I^2, inconsistency index; MPS, multiple plastic stenting; CSEMS, covered self-expandable metal stents; M-H, Mantel-Haenszel; I^2, inconsistency index; SD, Standard Deviation; CI, confidence interval.

did not report whether EST was performed, and the performance is undefined [27,30,38]. Similarly, only one study clearly reported the administration of NSAIDs [29]. The well-recognized precautions for PEP, prophylactic pancreatic stenting [40,41], were not systematically assessed in these studies [25,27–30,38]. Further studies with a large sample size are needed to identify the role of these prophylactic measures in BBS patients receiving biliary stents.

MPS has been recognized as an effective treatment for BBS, with resolution rates ranging from 80% to 90% [42,44]. Recently, CSEMS has aroused interest for it may achieve the same effectiveness as MPS but require fewer ERCPs [15–19,45]. In addition, CSEMS has been considered a salvage procedure when the previous PS failed [36]. As expected, no statistically significant difference was found in the stricture resolution between CSEMS and MPS in this study.

In this analysis, there was no significant difference in stricture recurrence between groups, but there was heterogeneity ($I^2 = 52\%$, $p = .08$). We performed a sensitivity analysis by deleting a study that showed a higher recurrence rate and reduced the heterogeneity ($I^2 = 31\%$, $p = .23$), indeed, there was no statistically significant difference. Stricture recurrence has also been evaluated in several meta-analyses that compared the effect of CSEMS with MPS. Zhang et al. [16] drew the conclusion that the stricture recurrence rates were comparable between CSEMS and MPS groups; Tringali et al. [15] calculated the ORs, it showed that CSEMS has a trend for a higher recurrence rate compared with MPS, with heterogeneity ($I^2 = 53\%$), but more evidence is needed to confirm this conclusion. Khan et al. [18] showed that the recurrence rate of stricture after 6 months of stent treatment was significantly lower than that after 3 months or less of stent



	MPS	CSEMS	
Cost	$13,377	$6,600	P=0.13
Standard Deviation	$3,843.82	$428.50	CI=95%

Figure 4. Graph of the cost analysis between CSEMS and MPS. $, United States dollars.

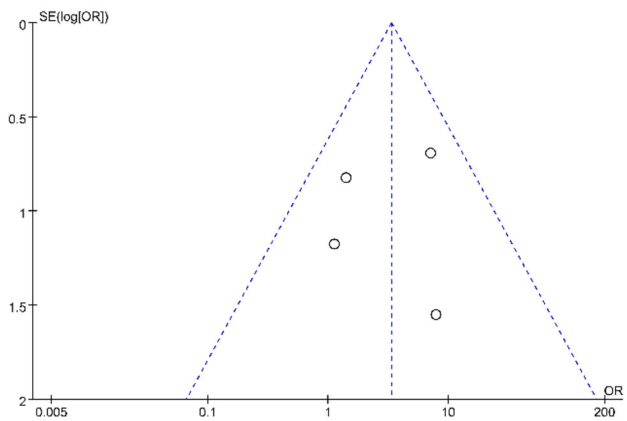


Figure 5. Funnel plot of publication bias for PEP. SE, standard error; OR, odds ratio.

treatment. Moreover, some researchers assumed that the higher rate of recurrence in the CSEMS group was attributed to shorter stent dwelling time (6 months) [27]. Visconti et al. [17] suggested that 12 months of follow-up may not be sufficient to make a reliable assumption on long-term efficacy, particularly in the CSEMS group. Some studies also indicated that the time of follow-up should be at least one year or more after sent placement [25,27,29,30]. Thus, further studies with large sample size and longer indwelling time should take these issues into account to identify the undefined results.

The overall adverse events included pancreatitis, cholangitis, perforation, haemorrhage, abdominal pain, cholecystitis, infection, and stent dysfunction such as stent occlusion, migration unravelling, and non-removability [41,46]. In the present analysis, we noticed that the adverse events were comparable between CSEMS and MPS groups. The complication of MPS is most likely owing to the procedure of exchanging stents at 3 months intervals and stent clogging [44]. Due to the strong radial force and coating material, CSEMS is mainly related to adverse events such as pancreatitis, cholecystitis and stent migration, especially when FCSEMS obstruct the cystic duct and pancreatic ducts [47]. CSEMS appears to be associated with a higher complication rate, there was also encouraging information reported in the literature [44,48–51]. The reported adverse events in CSEMS, such as cholangitis, PEP and cholecystitis, occurred at the rate of 14% to 22%. The incidence of stent migration reaches 5% even up to 38% with considerable variation [49,51,52]. MPS has been regarded as a relatively safe method for the treatment of BBS. Van Boeckel et al. reported an incidence of 20.3% [14,44]. There are also studies showing that CSEMS was as safe as PS in adverse events, either in all cases or in aetiological subgroup analyses [19]. It must be recognised that this is based on the various follow-up time, aetiologies, and stent types. To summarise, the incidence of adverse events was comparable in BBS patients receiving CSEMS and MPS.

A total of two studies reported the treatment costs, and the results showed that CSEMS was not significantly cost-effective. Generally, CSEMS was believed to be more expensive, however, CSEMS may be a more economical method for low-cost hospitalisation expenses with fewer ERCP sessions compared to MPS, and even stent implantation cost is more expensive [27]. Our data is different from the previous meta-analysis and this may be associated with the limited number of literature we included [17].

There exist several limitations in the present analysis. Firstly, although eligibility criteria have been constructed to eliminate heterogeneity, owing to confounding factors, including the lack of raw data from included studies (such as the degree and aetiology of stricture and stent types), heterogeneity was unavoidable. Secondly, the well-recognised precautions for PEP, such as EST, administration of NSAIDs and PD stenting, were not systematically evaluated in the included studies, these precautions deserve further exploration. Thirdly, the small sample size, absence of cost analysis and relatively short follow-up time may not reveal reliable data, which may affect the conclusions.

5. Conclusion

Compared with MPS, PEP occurs more frequently in BBS patients receiving CSEMS. As in previous studies, CSEMS achieves comparable stricture resolution and recurrence compared with MPS. Moreover, CSEMS is more cost-effective as it requires fewer ERCP procedures. Herein, prevention methods of PEP, such as rectal administration of diclofenac or indomethacin, prophylactic PD stent placement, and EST, should be further evaluated in BBS when undergoing CSEMS placement. Further RCTs of larger size, focussing on risk factors and prevention measures of PEP for BBS patients, are necessary.

Author contributions

JBH designed the conception and methodology. HY and ZZY wrote the original draft and collected the data for figures legends. JBH and ZZY performed the data analysis and revised the manuscript. All authors approved of the final version of the manuscript.

Disclosure statement

The authors have no conflicts of interest to disclose.

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Data availability statement

The authors elucidate that the data analysed during this study are available from the article and/or supplementary materials.

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