Systematic Review and Meta-Analysis

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Effect of covered self-expanding metal stents compared with multiple plastic stents on benign biliary stricture

A meta-analysis

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Abstract

Background: Endoscopic placement of multiple plastic stents (MPS) has been the first-line treatment for benign biliary stricture (BBS). Covered self-expanding metal stents (cSEMS) have been used in treatment of BBS; however, the efficacy has not been verified. Therefore, we conducted this meta-analysis according to PRISMA guidelines.

Methods: PubMed, Embase, and the Cochrane Library were electronically and manually searched for studies published between January 1, 1990 and April 12, 2017. Of 153 studies screened, 90 were excluded because of duplications. After scanning the title or abstract, only 24 studies were eligible for review and 6 were finally included. The investigators selected publications according to inclusion and exclusion criteria, processed the data, and assessed the quality of the selected studies. The primary endpoint outcome was stricture resolution, and the secondary endpoint outcomes included stricture recurrence rate, the number of endoscopic retrograde cholangiopancreatography (ERCP) sessions, and stent migration.

Results: A total of 6 randomized controlled trials with 330 participants were included in the current meta-analysis. There was no significant difference in stricture resolution between the cSEMS and MPS groups (odds ratio [OR] = 1.05, 95% confidence interval [CI] = 0.53–2.07, I^2 = 29%, P = .23, Z = 0.13, P = .90). Similarly, the stricture recurrence rates (OR = 1.39, 95% CI = 0.69–2.81, I^2 = 38%, P = .17, Z = 0.91, P = .36) were comparable between cSEMS and MPS groups. Stent migration rates (OR = 1.71, 95% CI = 0.84–3.50, I^2 = 4%, P = .241, Z = 1.47, P = .14) were similar between cSEMS and MPS groups. There were fewer ERCP sessions in the cSEMS group than in the MPS group.

Conclusions: This meta-analysis showed that cSEMS were comparable to MPS in achieving resolution of BBSs with fewer ERCP procedures.

Abbreviations: BBS = benign biliary stricture, CI = confidence interval, cSEMS = covered self-expanding metal stent, ERCP = endoscopic retrograde cholangiopancreatography, MPS = multiple plastic stents, OR = odds ratio, RCT = randomized controlled trial.

Keywords: benign biliary strictures, covered self-expanding metal stents, endoscopic treatment, multiple plastic stents

1. Introduction

Benign biliary stricture (BBS) is rare and most cases are caused by iatrogenic biliary injury, mainly after open or laparoscopic cholecystectomy, with reported occurrence in 0.1% to 0.5% of open procedures and 0.25% to 1.0% of laparoscopic surgeries.[1,2] The second most common cause is fibrosis at the site of surgical anastomosis after liver transplantation. Other conditions that can lead to benign bile duct obstruction include chronic pancreatitis, sclerosing cholangitis, cholelithiasis, sphincterotomy, and infection of the biliary tract.[3] The clinical symptoms present as obstructive jaundice, chronic cholestasis, and cholangitis, as well as secondary biliary cirrhosis.[4]

Endoscopic treatment rather than percutaneous transhepatic biliary drainage or surgery is considered first-line treatment for BBS. Use of multiple plastic stents (MPS) has been recommended by the European Society of Gastrointestinal Endoscopy for BBS, and uncovered self-expandable metallic stents are not recommended because of removal problems caused by embedding.[3,5] Hence, covered self-expanding metallic stents (cSEMS) are an intriguing option for treatment of BBS due to their removability.

Because they are usually fibrotic and associated with a dilated bile duct, most benign strictures cannot be fully dilated during initial endoscopic retrograde cholangiopancreatography (ERCP). An average of 3 to 4 ERCP procedures are required to dilate, deploy stents, up-size, and ultimately remove all stents once the stricture has resolved. Placement of 10-mm single cSEMS results in

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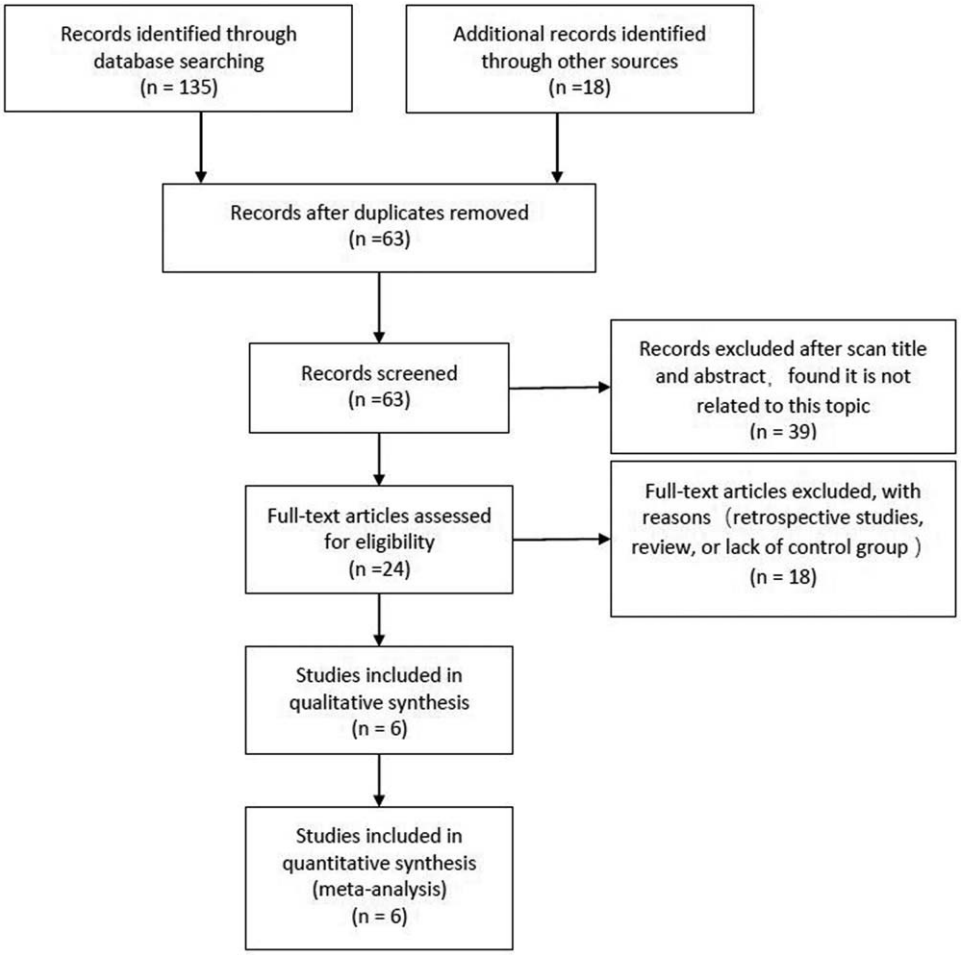

Figure 1. Search process for trials included in this meta-analysis.

radial dilation of a stricture equivalent to that of six or seven 10-Fr plastic stents.[6–9] Some studies have reported that the use of cSEMS could achieve comparable effects with fewer ERCP procedures.[10–12] However, because of small sample sizes, the results were not convincing. Thus, we conducted this meta-analysis to compare the effect of cSEMS with MPS on BBS resolution.

2. Methods

2.1. Search strategy

We searched for relevant articles published between January 1, 1990 and April 12, 2017. Computerized searches in the PubMed, Embase, and Cochrane library electronic databases were performed by using the terms "benign biliary stricture" or "bile duct stenosis" or "biliary anastomotic strictures" and "plastic stent" and "metal stent" or "metallic stent." Relevant reviews and meta-analyses focusing on BBS treatment were manually examined to identify additional eligible studies.

2.2. Inclusion criteria

Studies meeting the following criteria were included: the enrolled patients had BBS, and strictures resulting from malignant disease were excluded; the study design was a prospective randomized controlled trial (RCT); the study compared the treatment efficacy of plastic stents and cSEMS for BBS, and studies using uncovered SEMS were excluded; and the study should clearly report primary endpoint outcomes, as defined herein.

2.3. Endpoint outcomes defined

The primary endpoint outcome was stricture resolution, and the secondary endpoint outcomes included stricture recurrence, number of ERCP sessions, stent migration, and complications, such as pancreatitis, cholangitis, perforation, hemorrhage, pain, infection, and stent occlusion.

2.4. Data extraction and quality assessment of included studies

Two authors (XZ and XW) independently extracted and recorded data from the studies. The data included the publication year, study period, etiology of stricture, stent design, follow-up time, number of ERCP sessions, success rate, and recurrence rate. Disagreements would be settled through discussion. The risk of bias for RCTs was assessed using the Jadad score.[13]

2.5. Ethics approval

As all analyses were based on previously published studies, no ethics approval or patient consent was required.

Table 1

The characteristics of studies included.

Study ID	Publication year	Study period	Country	Arm	No. of patients	Sex (M/F)	Age median (range)	Etiology of BBS (anastomosis stricture/ chronic pancreatitis/ biliary injury)	Follow-up time, mo	Session of ERCP median (range)	Success rate	Recurrence rate	Stent migration	Jadad score
Tal et al	2017	2012–2015	Germany/Italy/ Finland	MPS	24	18/6	58.5(32–72)	48/0/0	16.9 (2–39.4)	4 (3–12)	23/24 (95.8%)	5/23 (21.7%)	NA	2
				cSEMS	24	14/10	57 (32–69)		13.3 (6.3–34.9)	2 (2–2)	24/24 (100%)	5/24 (20.8%)		
Martins et al	2017	October 2009 to January 2014	Brazil	MPS	29	20/9	50 (28–71)	64/0/0	32.9	5 (4–6)	28/29 (96.6%)	0/28 (0%)	4/141 (2.8%)	4
				cSEMS	30	22/8	54 (23–73)		36.4	2	25/30 (83.3%)	8/25 (32%)	3/30 (10%)	
Coté et al	2016	April 2011 to September 2014	USA	MPS	55	38/17	56.7 (11)	73/35/4	NA	3.24 (1.1)*	41/48 (85.4%)	2/41 (4.9%)	10/55 (18.2%)	3
				cSEMS	57	38/19	54.5 (10.4)			2	50/54 (92.6%)	7/50 (14%)	16/57 (28.1%)	
Haapamäki et al	2014	April 2008 to September 2012	Finland	MPS	30	29/1	49.5 (30–69)	0/60/0	37 (3–61)	4	22/30 (73.3%)	3/22 (13.6%)	3/30 (10%)	3
				cSEMS	30	25/5	54.5 (30–78)		41 (1–66)	4	20/30 (66.7%)	2/20 (10%)	2/30 (6.7%)	
Kaffes et al	2014	August 2008 to July 2011	Australia	MPS	10	5/5	49.5 (23–69)	10/0/0	25.5 (3–44)	4 (2–6)	8/10 (80%)	3/8 (37.5%)	NA	3
				cSEMS	10	5/5	56.5 (38–67)		26 (6–40)	2 (2–2)	10/10 (100%)	3/10 (30%)		
Artifon et al	2012	2002–2006	Brazil	MPS	16	6/10	45.19	0/0/16	72	NA	16/16 (100%)	5/16 (31.3%)	NA	3
				cSEMS	15	5/10	45.53	0/0/15	72		15/15 (100%)	3/15 (20%)		

BBS = benign biliary stricture, cSEMS = covered self-expanding metal stent, ERCP = endoscopic retrograde cholangiopancreatography, MPS = multiple plastic stents, NA = not available.
* The data were reported in mean ± standard deviation.

2.6. Statistical analysis

Statistical analyses were performed using Stata 14.0 software. For the analysis of stricture resolution rate, stricture recurrence rate, and stent migration rate, pooled odds ratios (ORs) with 95% confidence intervals (CIs) were used (OR > 1 favored the MPS group and OR < 1 favored the cSEMS group). Heterogeneity across studies was evaluated using the I^2 statistic, an $I^2 > 50\%$ was regarded as indicating significant heterogeneity and a random-effects model was used; otherwise, a fixed-effects model was used. Potential publication bias was assessed using Egger linear regression test. A P value < .05 indicated statistical significance.

3. Results

3.1. Characteristic of studies included

Based on the inclusion and exclusion criteria, 6 RCTs with 330 patients were included in the present meta-analysis (Fig. 1).[10–12,14–16] The characteristics of included studies are shown in Table 1. Cochrane bias risk assessment was performed, and the results are shown in Table 2.

3.2. Stricture resolution

All 6 RCTs reported stricture resolution. As shown in Fig. 2, the stricture resolution rate in the cSEMS and MPS groups was comparable (OR = 1.05, 95% CI = 0.53–2.07, $I^2 = 29\%$, $P = .23$, $Z = 0.13$, $P = .90$).

Egger test showed no indication of publication bias (2-sided $P = .887$) in stricture resolution rates (Fig. 3).

3.3. Recurrence rate

All 6 RCTs reported stricture recurrence. The recurrence rate was similar in cSEMS and MPS groups (OR = 1.39, 95% CI = 0.69–2.81, $I^2 = 38\%$, $P = .17$, $Z = 0.91$, $P = .36$) (Fig. 4).

3.4. ERCP session

As shown in Table 1, there were significantly fewer ERCP sessions in the cSEMS group than in the MPS group. In a study by Martins et al, patients receiving MPS treatment underwent an average of 5 (4–6) ERCP procedures, whereas the cSEMS group underwent an average of 2 sessions until anastomotic biliary stricture resolution ($P < .001$). Similarly, in a study by Tal et al, the MPS group underwent an average of 4 (3–12) ERCP sessions, while the cSEMS group underwent an average of 2 ($P < .001$). In a study by Coté et al, fewer ERCP sessions were required to achieve resolution in the cSEMS (2.14) versus MPS group (3.24; mean difference, 1.10; 95% CI = 0.74–1.46; $P < .001$). A study by Kaffes et al showed similar results (MPS vs cSEMS, 4 [2–6] vs 2 [2–2], $P = .001$). Thus, the use of cSEMS can decrease the number of ERCP procedures.

3.5. Stent migration

Three studies reported the complication of stent migration. Migration was more common in the cSEMS group than in the MPS group. (OR = 1.71, 95% CI = 0.84–3.50, $I^2 = 4\%$, $P = .241$, $Z = 1.47$, $P = .14$) (Fig. 5).

4. Discussion

Numerous studies have evaluated cSEMS as salvage and first-line treatment for BBS. It has been reported that cSEMS were

Table 2

The risk of bias for the studies included.

	Random sequence generation	Allocation concealment	Blinding of participant and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective r eporting	Other source of bias
Tal et al	Unclear	Unclear	Low	Low	Low	Low	Unclear
Martins et al	Low	Low	Low	Low	Low	Low	Unclear
Coté et al	Low	Low	Low	Low	Low	Low	Unclear
Haapamäki et al	Unclear	Unclear	Low	Low	Low	Low	Unclear
Kaffes et al	Low	Low	Low	Low	Low	Low	Unclear
Artifon et al	Unclear	Unclear	Low	Low	Low	Low	Unclear

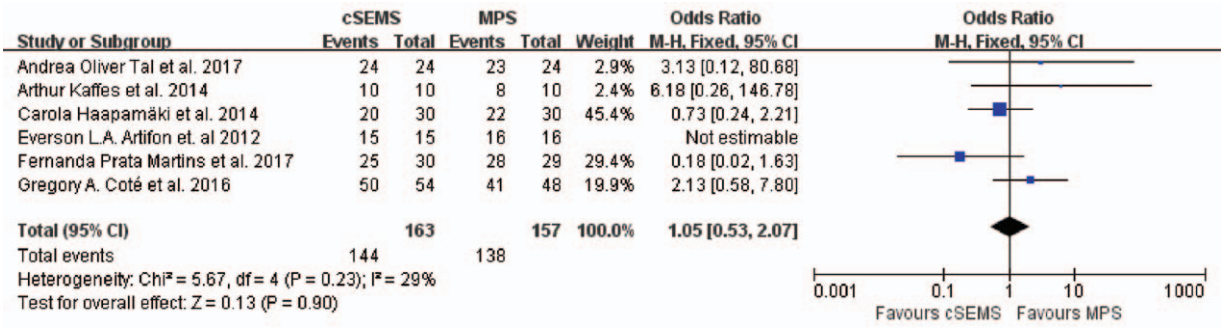

Figure 2. Meta-analysis of data on stricture resolution in patients with BBS following either cSEMS or MPS treatment. BBS = benign biliary stricture, cSEMS = covered self-expanding metal stent, MPS = multiple plastic stents.

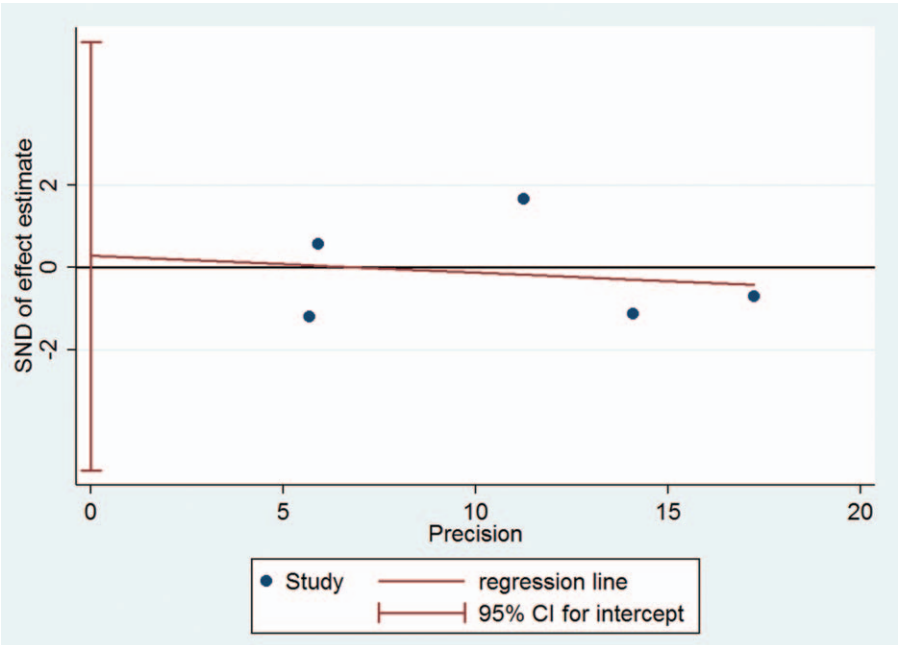

Figure 3. Egger test of publication bias for stricture resolution rates.

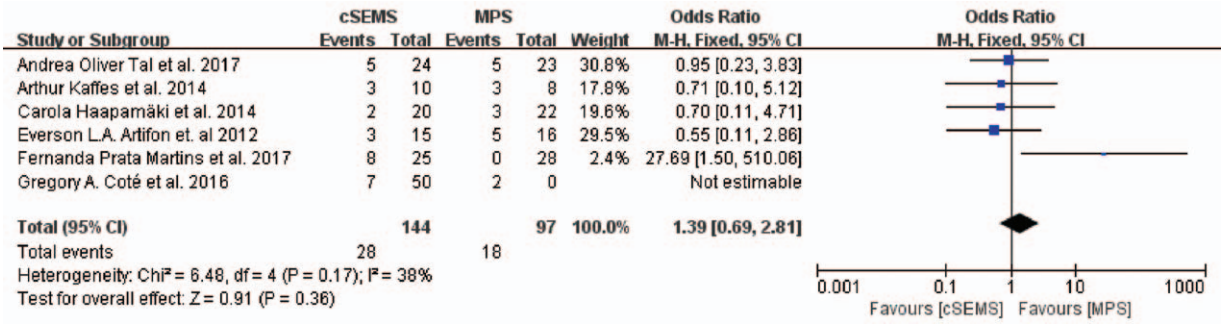

Figure 4. Meta-analysis of data on stricture recurrence rates in patients with BBS following either cSEMS or MPS treatment. BBS = benign biliary stricture, cSEMS = covered self-expanding metal stent, MPS = multiple plastic stents.

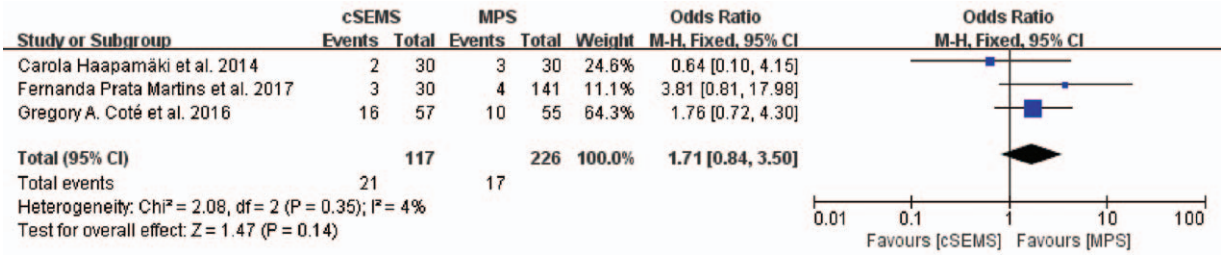

Figure 5. Meta-analysis of data on stent migration in patients with BBS following either cSEMS or MPS treatment. BBS = benign biliary stricture, cSEMS = covered self-expanding metal stent, MPS = multiple plastic stents.

comparable to MPS when used for initial treatment, but achieved resolution with significantly fewer ERCP procedures.[10–12,17] This meta-analysis further confirms the treatment benefit of cSEMS for BBS.

Stricture recurrence after endoscopic treatment occurs in about 10% to 30% of cases.[18–21] However, it has been unclear as to which type of stent could decrease the recurrence rate. This meta-analysis showed that the recurrence rate was similar between cSEMS and MPS groups.

Stent migration remains an important limitation of currently available cSEMS.[22,23] However, this study found that the stent migration rate was similar in cSEMS and MPS groups. This is most likely attributable to the improvement of cSEMS with antimigration features. There remains a need to develop novel, expandable stents that can be used in smaller-diameter ducts, without the need for routine follow-up ERCP for retrieval. Similarly, stent migration is also an issue with MPS, because of the sphincterotomy procedure used to facilitate side-by-side stent placement.

Because of lacking of RCTs, the previous meta-analysis was focusing on 1 method (MPS alone or cSEMS alone) in the management of BBS,[24,25] leading to less convincible result. In this meta-analysis, the including studies was all RCTs, resulting in the result more credible.

This meta-analysis had some limitations. First, few RCTs focused on the treatment of BBS using either cSEMS or MPS, limiting the robustness of the meta-analysis. Second, as the etiology of BBS was mixed, subgroup analysis was difficult. Third, the pooled results for stent migration were less valid because of high heterogeneity.

cSEMS were comparable to MPS in achieving stricture resolution in patients with BBS, using fewer ERCP procedures. Further randomized studies are required to improve the treatment of BBS.

Author contributions

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Formal analysis: Xinjing Zhang.
Funding acquisition: Jiahong Dong.
Investigation: Xinjing Zhang.
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Software: Xinjing Zhang, Xuedong Wang, Rui Tang.
Supervision: Jiahong Dong.
Validation: Liang Wang.
Writing – original draft: Xinjing Zhang, Rui Tang.
Writing – review & editing: Jiahong Dong.

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