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REVIEW ARTICLE

Customized bariatric stents for sleeve gastrectomy leak: are they superior to conventional esophageal stents? A systematic review and proportion meta-analysis

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Abstract

Objective Recently, there has been a burgeoning interest in the utilization of customized bariatric stents (CBS) for management of sleeve gastrectomy leak (SGL). We aimed to conduct a proportion meta-analysis to evaluate the cumulative efficacy and safety of these new stents and to compare them with the conventional esophageal stents (CES).

Methods A systematic literature search of the PubMed, Cochrane Library, Scopus, Web of Science and Google Scholar databases was conducted through May 1, 2020. Primary outcomes were technical and clinical success and post-procedure adverse events of CBS and CES. Secondary outcomes were number of stents and endoscopic sessions per patient, and time to leak closure. A proportion meta-analysis was performed on outcomes using a random-effects model, and the weighted pooled rates (WPRs) or mean difference with 95% confidence interval (CI) were calculated.

Results The WPR with 95% CI of technical success, clinical success, and stent migration for CBS were 99% (93–100%) $I^2 = 34\%$, 82% (69–93%) $I^2 = 58\%$, and 32% (17–49%), $I^2 = 69\%$, respectively. For CES, the WPR (95% CI) for technical success, clinical success, and stent migration were 100% (97–100%) $I^2 = 19\%$, 93% (85–98%) $I^2 = 30\%$, and 15% (7–25%), $I^2 = 41\%$, respectively. Adverse events other than migration were very low with both types of stents. On proportionate difference, CBS had lower clinical success (11%) and higher migration rate (17%) in comparison to CES. In successfully treated patients, CBS was associated with lower mean number of stents and endoscopic sessions, and shorter time to leak closure compared to CES. The overall quality of evidence was very low.

Conclusions In treatment of SGL, there is very low level evidence that CES are superior to CBS in terms of clinical success and migration rate, though may require more stent insertions and endoscopic procedures. The evidence however remains very uncertain. Perhaps relevant to some types of stents, CBS are promising; however design modification is strongly recommended to improve outcomes.

Keywords Bariatric stents · Endoscopic · Leak · Obesity · Sleeve gastrectomy

Staple line leak is a rare yet potentially life threatening complication of laparoscopic sleeve gastrectomy. The reported mean incidence rate is 2.1% (1.1–5.3%), and the mortality rate runs between 0.4 and 3.7% [1–3]. A multitude of treatment options are available for management of sleeve gastrectomy leak (SGL) including surgery, percutaneous drainage, and a wide range of endoscopic approaches. The latter include over-the-scope-clips (OTSC), transmural internal drainage with double-pigtail stents, septotomy, endoscopic vacuum therapy, placement of endoluminal stents, and biological glue; these modalities may be used alone or in combination [4]. Among these, endoluminal stenting is considered an effective treatment of SGL, which offers several advantages. In addition to sealing the anatomical area of leakage, it may aid in the correction of the sleeve axis in

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cases of gastric twist, and allows treatment of concomitant strictures and oral intake during the healing process [5].

The most widely used stents in the current practice are conventional esophageal stents (CES) including partially and fully covered self-expandable metallic stents and self-expandable plastic stents. Recently, customized bariatric stents (CBS) with a longer length and larger diameter have been specifically designed for treatment of SGL. These stents have anti-migration system and confer the advantage of reducing the overpressure in the proximal part of the gastric tube [6]. Nonetheless, due to the scarcity of publications on this topic, it is difficult to determine the superiority of one stent type over the other. We therefore conducted this systematic review and proportion meta-analysis to compare the efficacy and safety of CBS with CES in management of SGL.

Methods

Literature search

A systematic review was performed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [7]. A systematic literature search of the PubMed (Medline), Cochrane Library, Scopus, Web of Science, and Google Scholar databases was undertaken to identify relevant studies published before May 1, 2020. Search terms used were based on the type of surgery (eg, ‘‘sleeve gastrectomy’’), endoscopic treatment (eg, "stent"), and complication (eg, ‘‘leak’’). No language restriction was applied. Based on the preliminary searches, the bibliography of the studies that met the inclusion criteria were manually searched for additional articles relevant to this systematic review. A detailed overview of the literature search is shown in Appendix S1 (Supplementary Material).

Selection of articles

Titles and abstracts screening as well as assessment of full-text articles were performed by two independent reviewers (H.K.S.H and S.H.E) and discrepancies were discussed and resolved through adjudication by a third reviewer (A.A.S). Articles were included if (1) original data of SGL were reported, (2) they described endoscopic therapy with endoluminal stents whether used as a first-line or second-line treatment.

Studies were excluded if one of the following factors existed: combined treatment (defined as treatment with stents in association with other endoscopic treatment modalities), treatment of SGL with a predefined pathway using multiple endoscopic treatment modalities or with concurrent use of CES and CBS; lack of useful information regarding outcomes; stent type not described; small-sampled studies (< 5 patients) or case reports. Letters, conference abstracts, and reviews were also excluded. To prevent inclusions of duplicate cases, articles published by identical authors or institutions were evaluated, and data from the most recent comprehensive report were included.

Quality assessment

Two reviewers (H.K.S.H and S.H.E) independently assessed the methodological quality of each study, and any disagreement was resolved by joint discussion. The checklist for the quality of case series of the National Institute for Health and Clinical Excellence (NICE) was used for the assessment of the included studies and each study was given a score [8]. Quality of the studies was defined as good (score = 7–8), fair (score = 4–6), and poor (score = 0–3).

Data extraction

Two independent reviewers (H.K.S.H and S.H.E) analyzed the included articles and extracted the data using a predefined form. Data were collected on study design, year of publication, country, sample size, patient demographics, site, number, and time to diagnosis of SGL, previous leak treatment, type of stents, use of drainage procedure, stent fixation, duration of stenting, number of stents and endoscopic sessions per patient, time to leak closure, technical and clinical success rates, adverse events, hospital stay and follow-up. For patients with failed stenting treatment, additional treatment was recorded. Time to diagnosis of SGL was categorically defined according to Rosenthal's classification [9].

Outcomes

The primary outcomes were the pooled technical and clinical success rates, and adverse events. Secondary outcomes included mean number of stents and endoscopic sessions per patient, and time to leak closure. Definitions of outcomes are provided in Appendix S2 (Supplementary Material).

Statistical analysis

All analyses were performed using STATA software (version 16, StataCorp, College Station, TX) and Excel 2010 software (Microsoft Corp, Redmond, WA). Weighted pooled rates (WPR) were calculated for dichotomous outcomes. We estimated the related Wilson confidence intervals (CIs) and transformed the proportion using the Freeman-Tukey double arcsine transformation [10]. For continuous outcomes, the pooled effect size with 95% CI was estimated. Because of anticipated heterogeneity, the DerSimonian and Laird random-effects model [11] was used to pool estimates from the included studies. The I^2 statistic was used to estimate heterogeneity, where I^2 values of 0–40%, 30–60%, 50–90%, and 75–100% were reflective of low, moderate, substantial, and considerable heterogeneity, respectively [12]. Leave-one-out sensitivity analysis and meta-regression were performed to explore significant heterogeneity, to estimate the proportion of the total variance explained by the covariates (R^2), and to evaluate a possible association between baseline characteristics and the effect size on evaluated outcomes. The following variables were considered as moderators in the meta-regression analyses of stent migration and clinical failure: the age, body mass index (BMI), type of leak (acute/early vs. late/chronic), location of leak (proximal vs. mid-distal), type of treatment (first-line vs. second-line), presence of sleeve stenosis, use of drainage procedure, number and type of stent (Niti-S Mega vs. non-Niti-S Mega), stent position (prepyloric vs. postpyloric), duration of stenting, stent fexation and migration. Publication bias was assessed through funnel plots and Egger's regression test. Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used to rate the quality of evidence [13].

In patients treated with CBS placement, a subgroup analysis was done based on the type of stent used, that is, Niti-S Mega stents or non-Niti-S Mega stents, including Niti-S Beta, Hanaro GastroSeal, and Hanaro ECBB. We also calculated the proportion difference of WPRs for technical and clinical success, and stent migration in CBS and CES procedures [14].

Results

Search results

The literature search yielded a total of 752 unique articles. After title and abstract screening, 128 full-text articles were evaluated for eligibility. Finally, 23 studies [5, 6, 15–35] were included in the quantitative synthesis. Details of the study selection process are shown in Fig. 1.

Characteristics of the studies and patients

The characteristics and methodologic quality evaluation of 23 eligible studies are shown in Table S1 (Supplementary Material). These studies were published between 2011 and 2019, and involved 308 patients with SGL. Of these, 303 patients had laparoscopic procedures and 5 patients had open surgery. The sample size of the studies ranged from 5 to 64. Two studies were multi-centre based [15, 21], and 21 were from single centre; all were case-series or cohort studies. The majority of studies were conducted in Europe ($n = 10$), followed by Asia ($n = 5$), North America ($n = 3$), Latin America ($n = 3$), and Africa ($n = 2$). Data were collected prospectively in 12 studies [15–22, 26–29] and retrospectively in 11 studies. Availability of the studied variables in the analyzed articles is reported in Table S2 (Supplementary Material). All studies had clear information reported on the technical and clinical success, adverse events, and number of stents and endoscopic sessions per patient. Leak closure was always confirmed by absence of contrast extravasation on upper gastrointestinal studies or oral contrast computed tomography scan, with or without endoscopic confirmation. On quality assessment, 21 studies were of fair quality [5, 6, 17–35], and 2 were of good quality [15, 16]. None were of poor quality.

In total, 12 studies (141 patients) used CBS [6, 15–25], and 11 studies (167 patients) used CES [5, 26–35]. Baseline characteristics of the CBS and CES group are summarized in Table 1. The CES group had more frequent use of stent fixation ($P < 0.001$), and longer duration of stenting ($P < 0.001$) and length of hospital stay ($P = 0.004$). Sleeve stenosis was observed only in the CBS group ($P < 0.001$), in three studies [6, 17, 20]. There were no significant differences in demographics, leak characteristics, previous treatment, and use of drainage procedures among the groups. Four types of CBS were used including Niti-S Mega, Niti-S Beta, Hanaro Gastroseal, and Hanaro ECBB (Supplementary Material, Table S3); all were fully-covered with stent length of 18–24 cm. In the CES group, the type of stent varied widely and often with more than one stent type being used per study; the stent length ranged from 7 to 17 cm (Supplementary Material, Table S1), and almost 50% of patients received partially-covered stents.

Primary outcomes

Technical success

Technical success was achieved in 135 (95.7%) and 163 (97.6%) patients in the CBS and CES group, respectively. The WPR for technical success of CBS was 99% (95% CI 93–100%, $I^2 = 34\%$, $P = 0.11$), and for technical success of CES was 100% (95% CI 97–100%, $I^2 = 19\%$, $P = 0.27$) (Supplementary Material, Figures S1). The proportion difference of WPR for technical success between CBS and CES was 1% (95% CI − 0.6 to 2.6%, $P = 0.46$).

Clinical success

A total of 105 (74.5%) and 150 (89.8%) patients achieved clinical success (per-protocol) after treatment with CBS and CES, respectively. The WPR for clinical success in procedures with CBS was 82% with 95% CI 69–93% (Fig. 2). Heterogeneity was substantial ($I^2 = 58\%$, $P = 0.01$) and

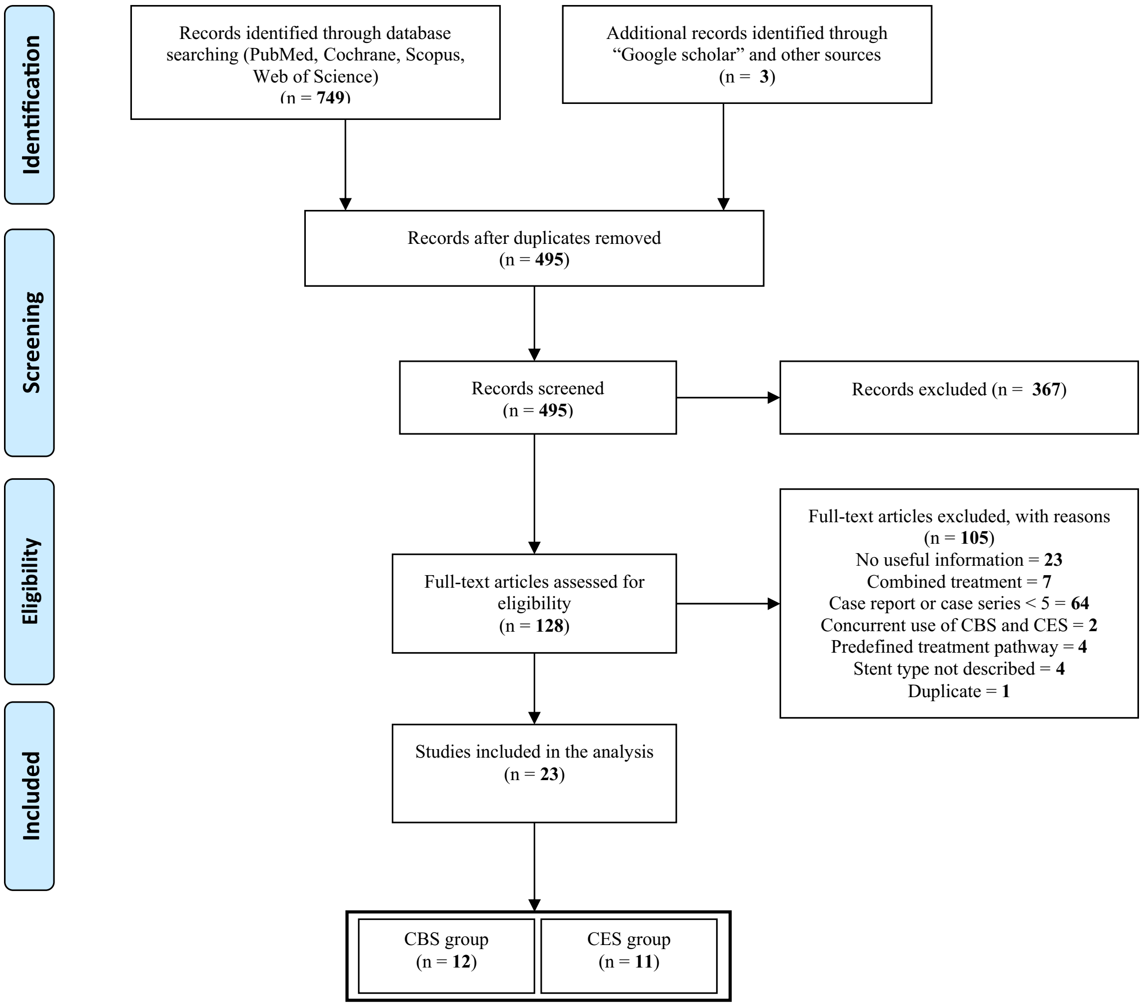


Fig. 1 PRISMA flowchart

56% of the total variance could be explained by the studies using Niti-S Mega stents. The WPR for clinical success for non-Niti-S Mega stents (89%, 95% CI 80–96%) trended to be higher than the rate for Niti-S Mega stents (66%, 95% CI 45–85%), but with confidence intervals overlap (Fig. 2). One study [6] appeared to be an outlier in the effect estimate; therefore, a sensitivity analysis was done, after which WPR for clinical success of all CBS and Niti-S Mega stents was 85% (95% CI 77–92%) and 76% (95% CI 60–90%), respectively. The WPR for clinical success when CES were placed was 93% (95% CI 85–98%, $I^2=30\%$, $P=0.16$) (Fig. 3). The proportion difference of WPR for clinical success between CBS and CES was 11% (95% CI 3.6–18.4%, $P=0.008$).

Adverse events

Overall, 43 (30.5%) and 28 (16.8%) patients in the CBS and CES group, respectively, had at least one episode of stent migration. Serious migration requiring surgical stent extraction occurred only with CBS placement (2.1%) [15, 24]; treatment of these cases included laparoscopic enterectomy with primary anastomosis with no reported device-related mortality. The WPR for migration of CBS was 32% with 95% CI 17–49% (Fig. 4). Heterogeneity was substantial ($I^2=69\%$, $P<0.001$) and 47% of the total variance could be explained by removal of the study by Tsai et al. [23] The WPR for migration for non-Niti-S Mega stents (41%, 95% CI 15–71%) was higher than the rate for Niti-S Mega stents (24%, 95% CI 11–40%), with confidence intervals overlap (Fig. 4). For the CES group, the WPR (95% CI) for migration was 15% (95% CI 7–25%, $I^2=41\%$, $P=0.07$) (Fig. 5). A metaregression analysis did not identify an association between stent fixation and migration (slope coefficient (s.e.) $=-0.0879$, $P=0.599$). The proportion difference of WPR for migration between CBS and CES was 17% (95% CI 7.6–26.4%, $P<0.001$).

Esophageal stenosis occurred only with CBS placement (1.4%) [15, 21]. Other adverse events including

Table 1 Baseline characteristics of 308 SGL patients treated with endoluminal stenting

Characteristic	CBS (*N* = 141), No. (%) or Mean ± SD	CES (*N* = 167), No. (%) or Mean ± SD	*P* value
Age, years	38.3 ± 10.2	37.5 ± 12.4	0.55
Gender, % female	91 (65.9)	87 (56.1)	0.11
Body mass index, kg/m^2	43 ± 6.7	41.7 ± 7.8	0.17
Number of defects			
Single	140 (99.3)	164 (98.2)	0.63
Multiple	1 (0.7)	3 (1.8)	
Leak/fistula location			
Proximal	135 (95.7)	159 (98.8)	0.15
Middle-distal	6 (4.3)	2 (1.2)	
Time to diagnosis			
Acute/early	124 (87.9)	145 (90.6)	0.30
Late/chronic	17 (12.1)	15 (9.4)	
Sleeve stenosis	15 (10.6)	0	**< 0.001**
First-line treatment	121 (85.8)	137 (82)	0.46
Drainage procedure	114 (80.9)	129 (77.2)	0.53
Nutritional support			
Enteral[a]	99 (71.7)	118 (79.2)	0.18
TPN	35 (25.4)	30 (20.1)	
Jejunostomy tube	4 (2.9)	1 (0.7)	
Stent type			
Fully-covered	141 (100)	89 (53.3)[b]	–
Partially-covered	0	83 (49.7)[b]	
Stent fixation	2 (1.4)	41 (24.6)	**< 0.001**
Duration of stenting, weeks	4.9 ± 2.3	8.3 ± 6	**< 0.001**
Hospital stay, days	14.3 ± 15.6	22.7 ± 23.1	**0.004**
Follow-up, months	8.4 ± 8.7	8.4 ± 5.4	1.00

CES conventional esophageal stent, *CBS* customized bariatric stent, *TPN* total parenteral nutrition

[a]Enteral feeding includes oral and nasojejunal feeding

[b]Some patients treated with both fully-covered and partially-covered stents

Bold values indicate statistical significance

perforation, bleeding, intractable symptoms, stent malfunction, and device-related and overall mortality were very low and not different between the CBS and CES groups (Supplementary Material, Table S4).

Secondary outcomes

In patients who achieved clinical success, 96 (91.4%) in the CBS group and 54 (36%) in the CES group required one stent ($P < 0.001$) (Table 2). The CBS group had a significantly lower mean number of stents per patient (1 vs. 1.74 stents, $P < 0.001$), mean number of endoscopy sessions per patient (2.1 vs. 2.9 sessions, $P < 0.001$), and shorter time to leak closure (4.57 vs. 6.88 weeks, $P < 0.001$) compared to the CES group. Additional interventions in patients with clinical failure are summarized in Table S5 (Supplementary Material).

Predictors of clinical failure and migration in the CBS group

Metaregression results of factors associated with clinical failure and migration of CBS are summarized in Tables S6 (Supplementary Material). Sleeve stenosis (s.e. = 0.009, $P < 0.001$) and use of Niti-S Mega stents (s.e. = 0.003, $P < 0.001$) were significantly associated with clinical failure of CBS. Age, BMI, timing and location of leak, type of treatment (first-line vs. second-line), stent migration, use of drainage procedure, duration of stenting, and number and position of stents (prepyloric vs. postpyloric) were not significantly associated with treatment failure. Likewise, none of the assessed variables, including age, BMI,

Fig. 2 Weighted pooled rate for clinical success of customized bariatric stents

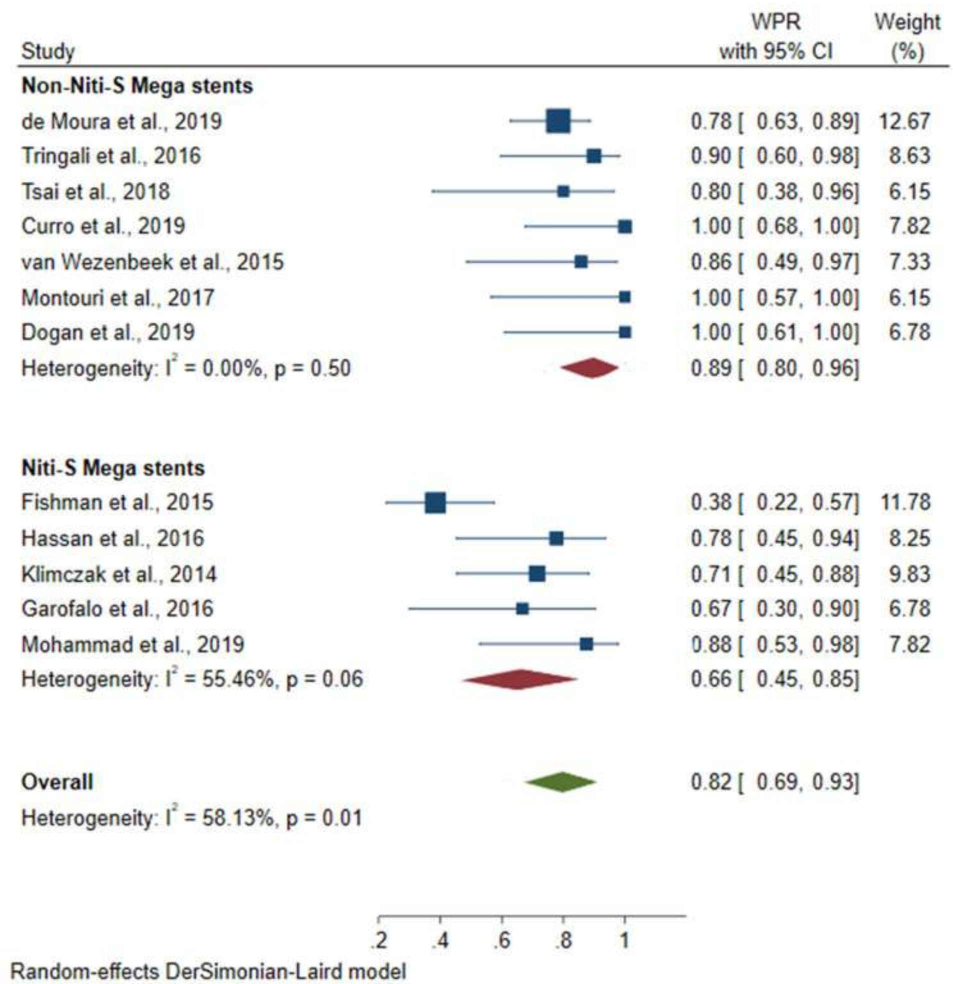
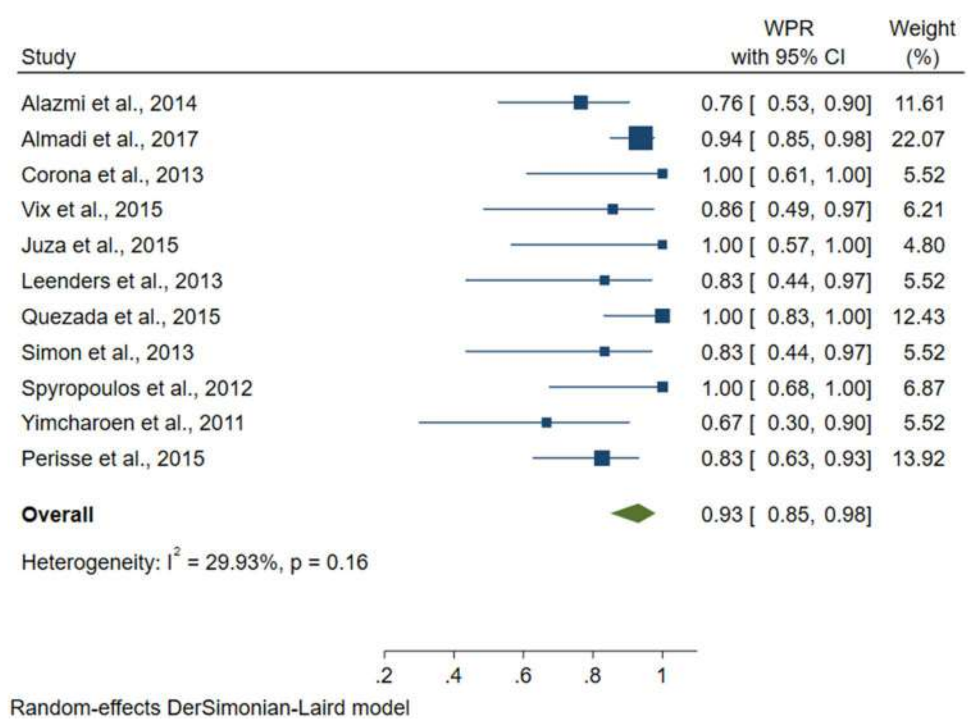


Fig. 3 Weighted pooled rate for clinical success of conventional esophageal stents



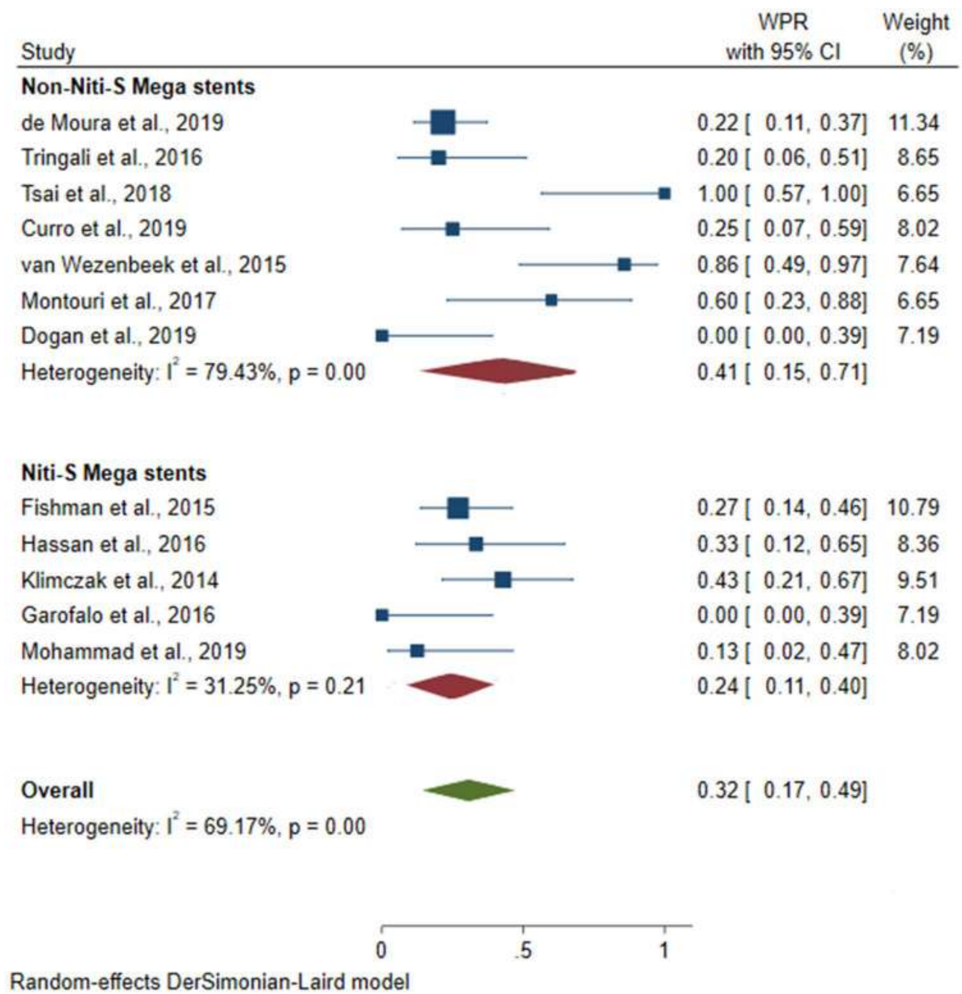


Fig. 4 Weighted pooled rate for migration of customized bariatric stents

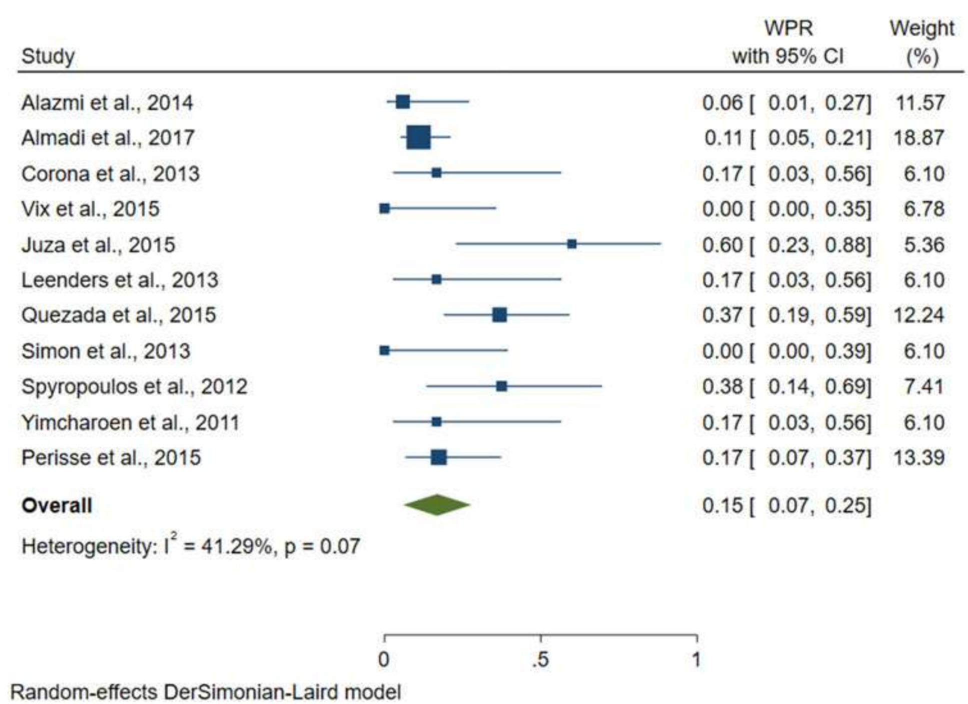


Fig. 5 Weighted pooled rate for migration of conventional esophageal stents

Table 2 Secondary outcomes in 255 patients with clinical success

Outcome	CBS (*N* = 105) No. (%) or weighed mean (95% CI)	CES (*N* = 150) No. (%) or weighed mean (95% CI)	*P* value
No. of stents used			
1	96 (91.4)	54 (36)	< 0.001
2	9 (8.6)	79 (52.7)*	
≥ 3	0	17 (11.3)	
Mean no. of stents	1 (0.99–1.01)	1.74 (1.30–2.19)	< 0.001
Mean no. of endoscopy sessions	2.07 (2.03–2.11)	2.90 (2.63–3.17)	< 0.001
Time to leak closure, weeks	4.57 (4.42–4.73)	6.88 (6.34–7.42)	< 0.001

CES conventional esophageal stent, *CBS* customized bariatric stent

*In 62 patients, an additional stent was required for removal of a partially-covered stent (stent in stent technique)

timing of leak, stent type and position were associated with migration of CBS.

Publication bias and GRADE quality assessment

Results of publication bias assessment for primary outcomes are available in Appendix S3 and Figures S2–S7 (Supplementary Material). According to the GRADE system, the quality of evidence for the primary and secondary outcomes was very low (Table 3).

Discussion

This proportion meta-analysis supports the efficacy and safety of CBS and CES for treatment of patients with acute and early SGL. Treatment with CBS was associated with similar technical success rate, fewer stent insertions and endoscopic interventions, and shorter time to leak closure compared to CES. Moreover, non-Niti-S Mega stents had a higher clinical success rate (89%) than Niti-S Mega stents (66%), and a similar clinical success rate to CES (93%). On the other hand, non-Niti-S Mega stents had the highest migration rate (41%) compared to other types of stents, including CES and Niti-S Mega stents (15–24%). Following the GRADE system, the overall level of evidence was very low.

Unexpectedly, our results showed a lower clinical success rate for CBS compared to CES (82% vs. 93%). This could partially be ascribed to the presence of sleeve stenosis in nearly 11% of patients treated with CBS and none of those treated with CES. Combined sleeve leakage and stenosis is known to be associated with a lower clinical success [36, 37], and was significantly associated with clinical failure of CBS in our study. Of note, all cases with combined sleeve leakage and stenosis were reported in the studies using Niti-S Mega stents [6, 17, 20] which may have accounted for the low clinical success rate (66%) associated with these stents. Although late and chronic SGLs were reportedly associated with clinical failure of endoluminal stenting [9], we could not demonstrate such an association. The small number of late/chronic leaks in the present study could be a simple explanation as it did not allow the exposure of statistical significance.

One option to improve the clinical success of CBS is the selective use of adjunctive treatment depending on the leak size, and presence of infection and stenosis. Shehab et al. [38] recently reported the combined use of Niti-S Mega stents and OTSC for treatment of SGL with clinical success rate of 86%. Similarly, Nedelcu et al. [39] described a combined approach employing CBS and endoscopic internal drainage (EID) with double-pigtail stents (DPS), and achieved successful leak closure in all patients.

The hypothesis behind using CBS is that they have flexible body structure to enable conformity to sleeve anatomy, and large diameters which provide better coaptation and compression against the lumen wall, and therefore less risk of migration. Furthermore, the long length of these stents with the distal edge often abutting against the duodenum would prevent distal migration. Despite these designs, we found higher migration rate for CBS compared to CES (32% vs. 15%). Moreover, although rare, serious migration requiring surgical extraction occurred only with CBS placement. These findings support previous observations that longer stents may have higher risk of migration, possibly due to the pronounced effect of peristaltic movements [32]. Another possible explanation is that all CBS used in this study were fully-covered stents, whereas almost 50% of patients in the CES group were treated using partially-covered stents. The latter significantly migrate less than fully-covered stents [40]. On the other hand and in line with previous studies [32, 41], our analysis showed no association between stent fixation and CES migration, indicating that the more frequent

Table 3 GRADE quality assessment of primary and secondary outcomes

Certainty assessment							Impact	Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Technical success									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The pooled technical success rate for CBS (WPR 99% [95% CI 93–100%]) and CES (WPR 100% [95% 97–100%]) were similar, with a proportion difference of WPR of 1% (95% CI − 0.6 to 2.6%, $P=0.46$)	⊕◯◯◯ Very low	Important
Clinical success									
23	observational studies	Serious[d]	Not serious	Serious[a,b,c]	Not serious	Strong association	The pooled clinical success rate for CBS (WPR 82% [95% CI 69–93%]) was lower than that for CES (WPR 93% [95% CI 85–98%]), with a proportion difference of WPR of 11% (95% CI 3.6–18.4%, $P=0.008$)	⊕◯◯◯ Very low	Critical
Stent migration									
23	observational studies	Serious[d]	Not serious	Serious[a,b,c]	Not serious	Strong association	The pooled migration rate for CBS (WPR 32% [95% CI 17–49%]) was higher than that for CES (WPR 15% [95% CI 7–25%]), with a proportion difference of WPR of 17 (95% CI 7.6–26.4%, $P<0.001$)	⊕◯◯◯ Very low	Important
Esophageal stenosis									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The pooled rates of esophageal stenosis for CBS (WPR 0% [95% CI 0–2%]) and CES (WPR 0% [95% CI 0–0%]) were similar and very low	⊕◯◯◯ Very low	Important
Perforation									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The pooled rates of perforation for CBS (WPR 0% [95% CI 0–3%]) and CES (WPR 0% [95% CI 0–1%]) were similar and very low	⊕◯◯◯ Very low	Important
Bleeding									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The pooled rates of bleeding for CBS (WPR 0% [95% CI 0–2%]) and CES (WPR 0% [95% CI 0–1%]) were similar and very low	⊕◯◯◯ Very low	Important
Intractable symptoms									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The pooled rates of intractable symptoms for CBS (WPR 0% [95% CI 0–5%]) and CES (WPR 0% [95% CI 0–3%]) were similar and very low	⊕◯◯◯ Very low	Important
Device malfunction									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The pooled rates of device malfunction for CBS (WPR 0% [95% CI 0–2%]) and CES (WPR 0% [95% CI 0–3%]) were similar and very low	⊕◯◯◯ Very low	Important

Table 3 (continued)

Certainty assessment							Impact	Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Device-related mortality									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The pooled device-related mortality rates for CBS (WPR 0% [95% CI 0–1%]) and CES (WPR 0% [95% CI 0–1%]) were similar and very low	⊕◯◯◯ Very low	Important
Overall mortality									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The pooled overall mortality rates for CBS (WPR 0% [95% CI 0–3%]) and CES (WPR 0% [95% CI 0–3%]) were similar and very low	⊕◯◯◯ Very low	Not important
No. of stents									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The weighted mean number of stents for CBS was lower than that for CES (1 stent [95% CI 0.99–1.01] vs. 1.74 stents [95% CI 1.30–2.19], $P<0.001$)	⊕◯◯◯ Very low	Not important
No. of endoscopy sessions									
23	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The weighted mean number of endoscopy sessions for CBS was lower than that for CES (2.07 sessions [95% CI 2.03–2.11] vs. 2.90 sessions [95% CI 2.63–3.17], $P<0.001$)	⊕◯◯◯ Very low	Not important
Time to leak closure									
22	Observational studies	Not serious	Not serious	Serious[a,b,c]	Not serious	None	The weighted mean time to leak closure for CBS was lower than that for CES (4.57 weeks [95% CI 4.42–4.73] vs. 6.88 weeks [95% CI 6.34–7.42], $P<0.001$)	⊕◯◯◯ Very low	Important

CBS customized bariatric stents, *CES* conventional esophageal stents, *WPR* weighted pooled rate, *CI* Confidence interval

[a]Data were derived from case-series, and not comparative studies

[b]Heterogeneity in study characteristics (sample size, baseline characteristics of patient, and treatment strategies..)

[c]Few clinical information on patients

[d]Asymmetrical funnel plot

use of antimigration measures with CES would not explain the difference in migration rate.

In order to reduce the migration rate of CBS, we recently demonstrated a significantly lower migration rate with prepyloric stent positioning, and advocated placement of the distal edge of CBS proximal to the pylorus [15]. Nevertheless, the present analysis did not show an association between the position of CBS in relation to the pylorus and stent migration. Despite this, we still believe that prepyloric CBS placement may lower the rate of migration. Development of partially-covered CBS may also reduce the migration rate; albeit this may come at the expense of a potentially increased risk of tissue adherence and esophageal stenosis which was only reported with CBS placement in our study. Southwell et al. [42] recently described a modification of the Niti-S Beta stent (Ogra stent) with uncovered proximal flare to allow a small area of tissue seal. This design provides an additional anti-migratory mechanism and ensures easy stent removal without the need for overlapping stents for disimpaction. Another possible modification is the double-type metallic stent with an outer uncovered part and inner covered part in order to prevent a mucosal ingrowth [43]. This design combines the advantages of non-covered and fully-covered stents in terms of migration and removability. Importantly, the relatively high migration rate of CBS did not seem to adversely impact the clinical success rate of these stents, and did not lead to higher number of repeat endoscopies compared to CES.

Overall, apart from stent migration, our meta-analysis showed a very low incidence of complications for both CBS and CES placement including bleeding, perforation, stent malfunction, and device-related mortality. Further, although symptoms such as abdominal pain, nausea, vomiting, and reflux were reported in the majority of patients receiving endoluminal stenting, particularly CBS [6, 15, 16], these symptoms are often mild, fairly tolerated, and did not require premature stent removal. Our results are in accordance with previous meta-analyses and confirm the safety of endoluminal stenting [44, 45].

An important advantage provided by CBS compared to the commonly used EID is the shorter time to leak closure (4.6 vs. 17 weeks) with a similar overall clinical success rate (82% vs. 83%, respectively) [46]. Additionally, CBS treatment required a fewer mean number of endoscopic interventions of 2 sessions compared with 2.5–3.1 sessions reported for EID therapy [47, 48]. Yet, it is noteworthy to mention that almost 80% of patients treated with CBS required radiological and/or surgical drainage procedures which may increase morbidity. Regarding cost-effectiveness, Cosse et al. [48] concluded the mean cost for treatment with CES to be 1.25 times that for EID therapy, with the duration of hospital stay per procedure being the key driver of the incremental cost-effectiveness ratio. We demonstrated a significantly shorter length of hospital stay and lower number of endoscopic procedures for CBS compared to CES. Based on these results, it seems that CES may be as cost-effective as EID.

Based on the available evidence, we believe that CES can be used as a first-line treatment for acute and early SGL, whereas the use of a complementary treatment such as glue and OTSC may help reducing time to leak closure [42, 49]. Non-Niti-S Mega stents remain reasonable alternatives, given they are positioned proximal to the pylorus. Adequate percutaneous or surgical drainage of any collection is crucial in all patients undergoing endoluminal stenting to attain a satisfactory outcome. In late and chronic SGL, DPS and cardiac septal occluders appear to be more effective than stenting [50, 51]. Combination of endoluminal stents and DPS may be more appropriate for treatment of SGL with stenosis, allowing fewer endoscopic insertions and shorter treatment duration [37, 39]. Reconstructive surgery can be used as the last resort in patients with failed endoscopic treatment.

To the best of our knowledge, this is the first meta-analysis to evaluate not only the efficacy and safety of CBS, but also the first to compare CBS with CES in treatment of SGL. We conducted a comprehensive literature search, not restricted to English language, to include all relevant studies; to minimize bias small case-series were excluded. We also successfully obtained additional unpublished data for several of the included studies. This allowed us to provide a larger estimate of effects and more generalizable results. Two recent meta-analyses culling data of 24 and 37 studies revealed 73% and 92% clinical success rate, respectively, for treatment of SGL with endoluminal stenting, though types of stents were not looked at individually [44, 52]. In addition, almost 40–50% of the included studies in these meta-analyses were small case-series (< 5 cases) which have the tendency towards publication bias, only reporting successful cases [53].

This meta-analysis has some limitations. First, none of the included studies were randomized or case–control studies comparing CBS with CES, and most studies included a limited number of subjects. Therefore, the results should be cautiously interpreted. Second, although previous studies suggested that the efficiency of endoscopic treatment is related to operator experience [54], we could not evaluate the presence of a learning curve for CBS as a potential predictor of clinical success, because the data were not reported for this evaluation. Finally, although previous studies have shown that leak size is an important determinant of clinical success of endoluminal stenting, this factor was not reported in most studies precluding any conclusion regarding the impact of leak size on clinical success of CBS.

Conclusion

The evidence is very uncertain about the advantages and disadvantages of CBS compared to CES in treatment of SGL. CES may be superior to CBS with respect to clinical success and migration rate, meanwhile, CBS may offer the advantages of a lower number of stent insertions and endoscopic interventions, and shorter time to leak closure compared to CES. Further studies, perhaps randomized trials, are warranted including large number of patients and new designs to directly compare outcomes between CBS and CES in treatment of different sizes of SGL, as well as outcomes between different stent positions for each CBS design.

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Compliance with ethical standards

Disclosures Hytham K. S. Hamid, Sameh H. Emile, Alan A. Saber, Mürşit Dincer, Diogo T. H. de Moura, Lennard P. L. Gilissen, Majid A. Almadi, Mauro Montuori, Michel Vix, Luis G. S. Perisse, Nicolás Quezada, Fabio Garofalo, and Radu Pescarus have no conflicts of interest or financial ties to disclose.

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