Short-Term and Long-Term Outcomes of Self-Expanding Metallic Stent Versus Decompressing Stoma as the Bridge of Elective Surgery for Left-Sided Obstructive Colon Cancer: A Meta-Analysis

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Background: Compared to emergency resection, elective surgery is a better choice for the people suffering from left-sided obstructive colon cancer (LOSCC). Both are considered as self-expanding decompressing stoma (DS) construction and metallic stent (SEMS) placement are accessible bridges for elective surgery (BTS). We aimed to perform meta-analysis of LOSCC databases to comparethe pros and cons of the two options.

Method: LOSCC patients with curative intent were searched in medical databases, including PUBMED, MEDLINE, and the Cochrane Library. Results were expressed as risk ratios. The meta-analysis was performed by Revman5.3.

Result: Three comparative studies were selected, including 847 LOSCC patients. The complete analysis showed that there is no statistically significant difference regarding primary anastomosis (OR=1.15, 95% CI 0.30-4.41, P=0.84), There was no significant difference in 90-day recurrence rate post resection (OR=0.90, 95% CI 0.68-1.20, P=0.47), and major complication (OR=1.86, 95% CI 0.98-3.54, P=0.06) between SEMS and DS group. In addition, the permanent stomas (OR=0.82; 95% CI 0.60-1.13, P=0.23), overall recurrence (OR=0.82, 95% CI 0.48-1.40, P=0.46), and overall survival of 3-years (OR=1.24, 95% CI 0.69-2.25, P=0.48) showed no statistical difference between SEMS and DS group.

Conclusion: The after-effects of both short-term and long-term in patients who were treated by SEMS or DS as BTS for LSOCC were not statistically significant. Considering of the even complicated surgical interventions, prolonged hospital stays, and worse body image of DS

construction, SEMS placement seems to be the preferred option in treating LSOCC patients.

Keywords: Decomposing stoma, self-expanding metallic stent; decompressing stoma; a link to surgery and, left-sided obstructive colon cancer.

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1. Introduction

It is observed from the recent research that colorectal cancer is the major cause of malignant colorectal obstruction, among which the left-sided obstructive colon cancer (LSOCC) was the most common type in clinical practice[1]. LSOCC patients are often elderly and fragile because of intake induction. To relieve the obstruction, oncologic resection is usually required. Traditionally, patients with LSOCC aretreated with emergency resection, which leads to60%morbidity and 20%mortality [2].Compared to emergency resection, elective surgery after colonic decompression seems to be a better choice considering of its adequate oncological staging, optimization of the patient's condition and lower postoperative morbidity.

Nowadays, elective surgery can be done by implementing self-expandable decompressing stoma (DS) construction or metal stent (SEMS) placement as bridge to surgery (BTS) in routine practice[3].Both approaches can effectively eliminate acute colonic obstruction. There are very few Meta-analysis studies that showed that SEMS placement as BTS was more safe than emergency resection, while its short-term outcome and long-term survival resultswere equivalent to those of emergent surgery[4-6]. DS construction exhibited highly successful colonic decompression and showed primary anastomoses and fewer permanent stomas more than that of emergency resection[7]. These evidences have led to the formation of international guidelines for the application of BTS approach in elderly and frail patients with LSOCC[8]. Nevertheless, there is no consensus on which BTS approach is preferable. Therefore, this meta-analysis has been performed to compare the after-effects (short-term and long term) of SEMS placement as BTS and DS construction as a surgical transition in patients with LSOCC.

2. Methods

The methodology, literature retrieval strategy and inclusion criteria of this study have been based on the Meta-Analyses Statement and Reporting Items for Systematic Reviews (PRISMA) recommendations.

2.1 Search strategy

Studies comparing the efficiency of DS construction and SEMS placement as a link to surgery for LSOCC were included according to the inclusion criterion. The eligible studies were screened bythe object of study, intervention, control measures, outcome indicators,(PICOS) principles of research design. The research strategy was synonyms for bridge to surgery, stoma, stent and left-side obstructive colon cancer in database including PUBMED, MEDLINE, and Cochrane Library.

2.2. Inclusion/exclusion criteria

The study sources were considered credible when they followed the below mentioned criteria: 1) the subject was restricted to LSOCC patient treated with curative intent, 2) comparison analysis between SEMS placement and DS construction as BTS 3) the studies reported at least one short-term

and long-term effect measure respectively; primary anastomosis or complication after complete survival; without disease survival and/or local recurrence; resection. Studies were excluded if exact number for outcome measures were not accessible.

2.3. Data collection and study results

Two reviewers extracted all the data independently by using an extraction technique form predesigned criteria. The information collected from each study included: country, the main author and his credentials, design, year of publication and time spent on the study, intervention, primary characteristic of subject, and outcome measures.

Primary outcomes included short-term and long-term after-effects. And the short-term after-effects included primary anastomosis and total complication after resection, and long-term after-effects included permanent anastomosis, overall recurrence and 3-year overall survival.

2.4. Assessment of the quality

As all the included studies were retrospective and comparative cohort studies, the quality and the risk of bias of these studies have been calculated using the MINORS score[9].

2.5. Statistical analysis

The detailed analysis of the data has been done using Review Manager Software. Odds ratios (OR) with 95% confidence intervals for primary anastomosis, total complication after resection, permanent stoma, and local recurrence, were assessed using a fixed model or random effects. The OR suggested the cons of a negative event (i.e. complication) present in the SEMS group versus the DS group. An OR < 1 favored the better benefits of SEMS placement than DS construction. The point estimate OR has been estimated as significant. The heterogeneity among the included researches was calculated using graphical representation of funnel plots, the Cochrane Q-statistic and the I^2statistic.

3. Results

3.1. Selection of the Study

The firstly done research included 477 relevant literature reviews. After the duplications have been removed, 387 studies were left, of which 376 studies have been excluded because their abstract were irrelevant (Fig. 1). Finally, the complete 10 articles were carefully evaluated, with seven studies being excluded. The reasons for omitting included non-comparative study or comparative study regarding to emergency resection and other interventions, SEMS or DS were used for palliative therapy, and subject were not restricted to LSOCC patients treated with curative intent.

All the included studies were retrospective cohort study. Totally, 847 patients were reported, among which 362 and 485 LSOCC patients were respectively included in SEMS group and DS group. The basic properties of the studies being included are shown in Table 1.

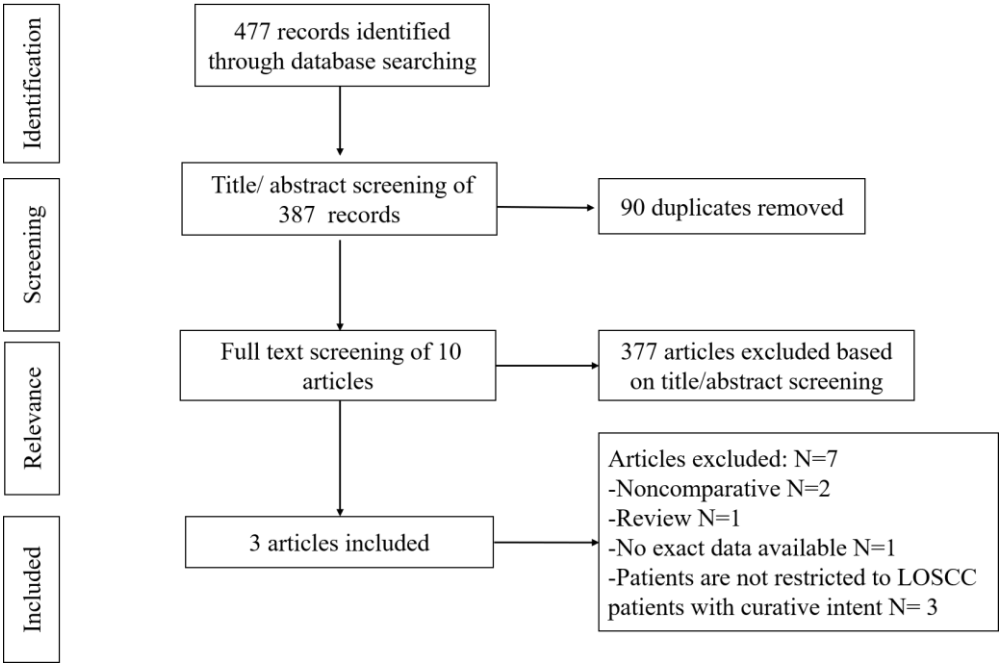

Fig.1: A Flowchart of searched literatures on March 19th 2020.

Table 1 Study characteristics of the included studies

Study	Methods	Study time	Country	Participants	Interventions	Outcomes	Total hospital stay	MINORS scores
Amelung -2016	retrospective multi-institutional cohort study	2004.01—2013.12	The Netherlands	LSCO patients treated with curative intent	Endoscopic Stent as a Bridge to Surgery	1.30-day morbidity and mortality; 2.Major morbidity; 3.Success rates of stent placement; 4.Primary anastomosis rate;	SEMS: 14 (11–17) DS:14 (11–17)	17

						5.Temporary colostomy rate, 6.Permanent colostomy rate, 7.total hospital stay		
Mege -2019	retrospective multi-institutional cohort study	2001.01—2015.12	France	patients treated for OLCC by PDC or ES in a curative intent	Diverting stoma or endoscopic stent as a bridge to surgery	1.Primary anastomosis rate; 2.Permanent colostomy rate, 3.the overall postoperative morbidity, mortality 4.length of stay	SEMS: 17 ± 20 DS:29 ± 37	20
Veld	retrospective cohort study	2009.01—	The Netherlands	LSCO patients treated with curative intent	Decompressing stoma vs SEMS as a bridge to surgery	1.Primary anastomoses rate, 2.90-day mortality, complications, additional interventions, hospital stay,	SEMS: 30.0 (19.0-47.0) DS:18.0 (8.0-30.8)	20

-2020	2017.12	3.Postresection presence of a stoma, 4.SEMS-related perforations, 5. 3-year locoregional recurrence, 6. 3-year disease-free survival (DFS), 7.3-year overall survival (OS), 8.Total hospital stay, 9. Permanent stoma rate

3.2. Primary anastomosis

All the 3 studies included the information of primary anastomosis after curative resection. There are 208 patients in the SEMS group, and 304 patients in the DS group. High evidence of heterogeneity was found (P<0.0001, I^2=93%), and the random effect model analysis was performed to demonstrate that the primary anastomosis rate between two group is not significant (OR=1.15, 95% CI 0.30-4.41, P=0.84; Fig. 2).

3.3. Complications (after BTS) and resection (less than 90 days after it)

The total complications and 90-day recurrence rate after BTS in SEMS group and DS group were 40.17% (143/356) and 43.57% (210/482) respectively. The heterogeneity between SEMS group and DS group was found (P=0.07, I2=63%), while the random effect model showed that the total complications rate was not significant between two group (OR=0.90, 95% CI 0.68-1.20, P=0.47;

Fig. 3). In addition, the major complication rate in the SEMS and DS group were 21.67% and 16.29% respectively (OR=1.86, 95% CI 0.98-3.54, P=0.06), indicating between the 2 groups (the comparable major complication rate).

3.4. SEMS-related perforation

Pooled SEMS-related perforation rate of three studies was 7% (1/14), 95%CI 1%-12%, demonstrating the heterogeneity as statistically significant in perforation among three studies. (P=0.008, I2=79%; Fig. 5).

3.5. Permanent stoma

All the studies included provided data on permanent stomas: there were 85 out of 362 (23.48%) patients in the SEMS group and in 137 out of 485 (28.24%) patients in the DS group were included for analysis. Pooled analysis also have not showed any significant difference between the two groups (OR=0.82; 95% CI 0.60-1.13, P=0.23; Fig. 6). Therefore, the heterogeneity of permanent stoma was not statistically significant among three studies. (P=0.39, I2=0%).

3.6. Overall recurrence

All three studies reported on overall recurrence rates indexes: including local recurrence and distant metastases. The overall recurrence rate was 40.22% (144/358) and 48.76% (235/482) respectively in the SEMS group and the DS group. Therefore, the heterogeneity of recurrence rates among three studies were found (P=0.08, I2=63%), while the random effect model showed that the overall recurrence rate was not significant between SEMS and DS group.

3.7. 3-year overall survival

There were two studies that listed information about the overall survival of 3 years. These studies showed that the 3-year overall survival in two group was not significant (OR=1.24, 95% CI 0.69-2.25, P=0.48). The 3-year overall survival heterogeneity among the two studies was not significant (i.e. P=0.53, I2=0%, Fig. 8).

3.8. Publication bias and sensitivity analysis

As there are only three studies included, we did not estimate the publication bias and conduct sensitivity analysis.

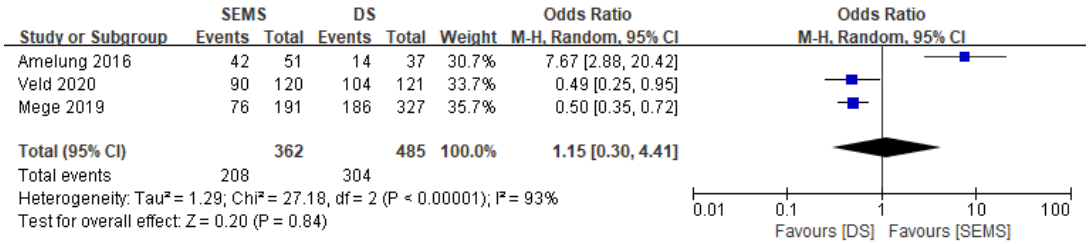

Fig. 2 Forest plot of primary anastomosis rate between SEMS and DSgroup.

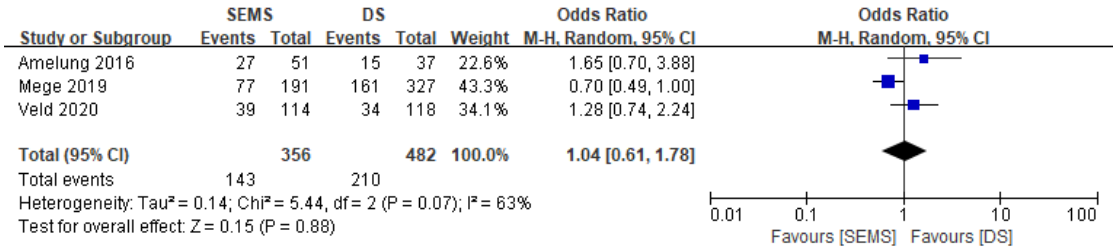

Fig. 3 Forest plot of Combination of complications after BTS and less than 90-day recurrence rate post resectionbetween SEMS and DSgroup.

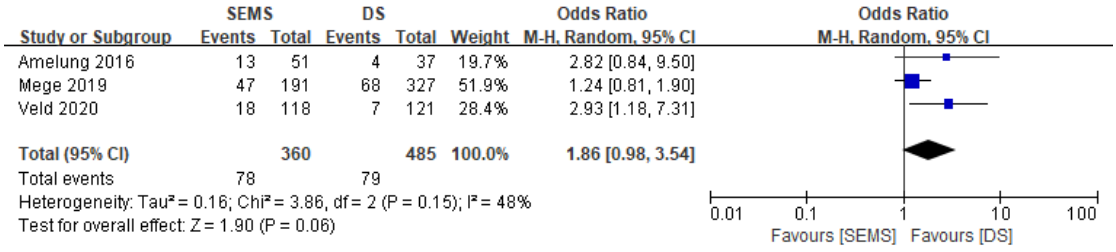

Fig. 4 Forest plot of major complication rate between SEMS and DSgroup.

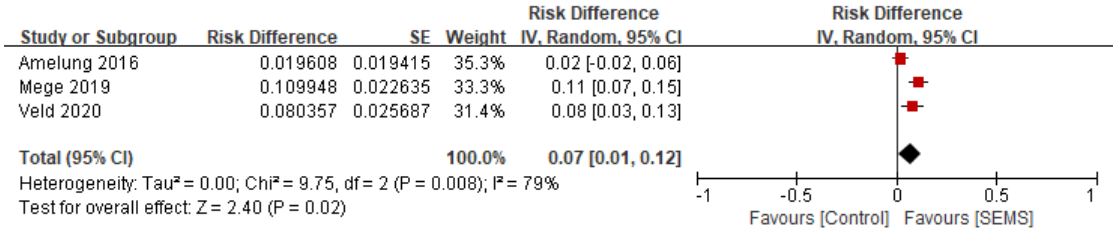

Fig. 5 Forest of perforation rate in SEMS

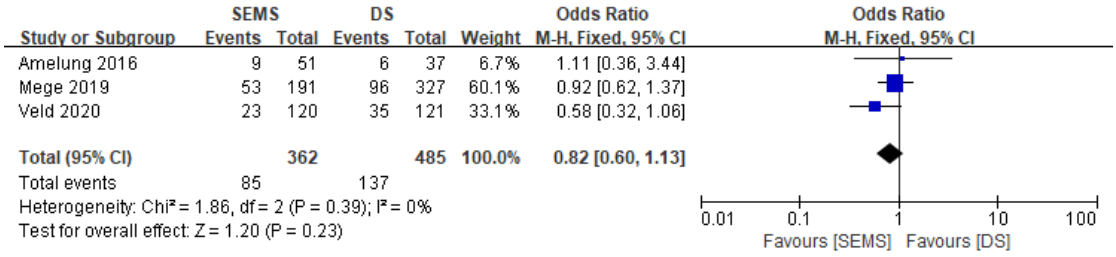

Fig. 6 Forest of permanent stoma between SEMS and DSgroup.

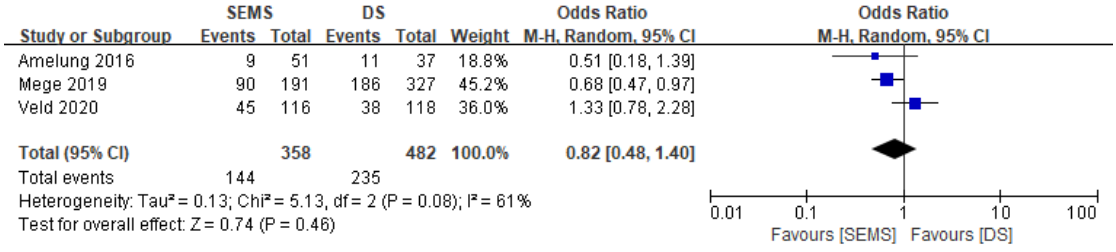

Fig. 7 Forest of overall recurrence rate between SEMS and DSgroup.

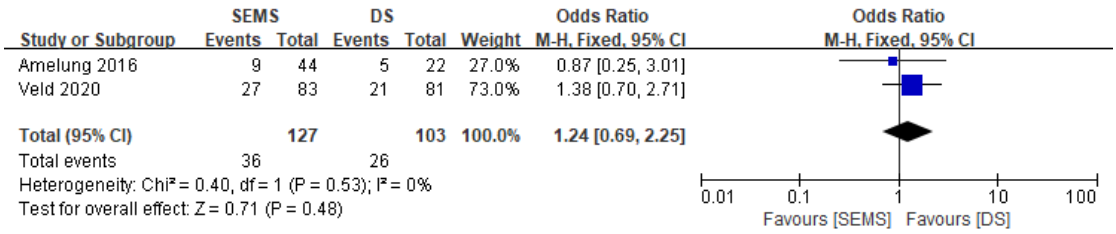

Fig. 8 Forest of 3-year overall survival rate between SEMS and DS group.

4. Discussion

After being studied all the relevant material, it is seen that the SEMS placement and DS construction are both effective decompression approaches as a link to elective surgery for LSOCC patients with curative intent. This meta-analysis compared the short and long-term after-effects in LSOCC patients who were treated by SEMS or DS as BTS. Short-term outcomes including Primary anastomosis, total and major complications after BTS and 90-day recurrence rate post resection did not significantly differ between SEMS and DS group. In addition, long-term outcomes, comprising of permanent stoma, overall recurrence and 3-year overall survival have not showed statistically significant difference between two groups. The results were concordant with two randomize studies which observed that there is no difference in morbidity and mortality rates between SEMS and DS group[10]

Both SEMS placement and DS construction have its pros and cons. The building of DS is comparably fast and easy to control, which could be operated in almost every patient and achieve 100% success rate. In addition, colostomy construction was hypothesized not to be associated with an increased oncologic risk. However, numerous surgical interventions were required due to colostomy reversal and incisional hernias repair, which prolonged the hospital stay and increased the cost[11]. Finally, although the *in situ* stoma after DS procedure will be reversed, the temporary stoma will lead to side effects on patients. For example, Song Letal revealed that the patients with temporary stoma exhibited worst body shape and lots of anxiety and depression than the non-stoma patients[12]. In contrast, SEMS insertion needed experienced clinicians and was technically difficult, which was not suitable for every patient. Patients needed to be screened according to the characteristics of the tumor and there was a risk of perforation and the failure of decompression. Dutch stent-in II randomized trial suffered early termination owning to as high as 19.1% perforation rate [13], while the pooled perforation rate is 7% (95% CI 1%-12%) in our meta-analysis. Concerns also included a high risk of tumor cell transmission due to the operation of the SEMS insertion, the pressure of expansion, and tumor recurrence after perforation. However, meta-analysis[4-6] did not show coalition with deceased survival and SEMS insertion. In brief, patients underwent SEMS have lower level of surgical interventions and shorter stay at hospital during the bridging interval than patients treated with DS construction. Compared with patients underwent SEMS, patients treated with DS suffered more postoperative pain, negative body image and tedious stoma care, which also caused

additional psychological burden to not only patients themselves but also their family members. Therefore, SEMSinsertionwasadvisable as BTS for LOSCC patients ifthe tumor characteristic met the requirements of colonic stent and the accessibility of experienced physician.

This meta-analysis first explored the short-term and long-term after-effects of SEMS placement and DS construction as BTS for LOSCC patients with curative intent. However, our study hadsome limitations. Firstly, although we made great effort to retrieve relevant articles in multiple databases, there were only three studies eligiblestudies in line with our specific study subjects interventions. Among initially retrieved 477 relevant literatures, the majority of them are studies regarding SEMS or DS as BTS versus emergency for LOSCC patients with curative intent respectively or studies SEMS versus DS for colonic cancer patients with palliative intent and studies of comparing trans-anal drainage tube (TDT) with metallic stent for LOSCC[17], indicatingthe rare of studies comparing SEMS and DS as BTS for LOSCC patients.

Secondly, the total number of LOSCC case was relatively small in meta-analysis, which may lead to low statistical efficiency. A potential explanation wasthat the specifics of our subject and the strict inclusion and exclusion criteria. And one out of three studies had relatively small sample size, including 51 patients in SEMS group and 37 patients in DS group, which may cause potential selectionbias[18].Regarding of the rest of two studies, the heterogeneity within study was balanced by using propensity score matching, which wasaimed to mimic RCT[19, 20].Given the less number of studies being included in this analysis, the finding of our meta-analysis should be confirmed in future research.

Another limitation of this study is that, it assessed only a part of short-term and long-term after-effects of LOSCC patients with curative intent underwent SEMS or DS as BTS. The role of quality of life, and treatment costs of patients in both groups are not the endpoint of this study, which were also important factors for decision making.

Therefore, the researchers need to do the future research in order to overcome the aforesaid limitations. For example, the database including information about demographic and tumor characteristics of patients, physician's reasons for SEMS or DS as BTS, physician's experience for SEMS placement, postoperative adjuvant chemotherapy and so on may be developed, which may help researchers to enroll homogeneous populations in retrospective studies. In addition, we found no RCT evidence-supportive or otherwise for the implement of SEMS and DS as BTS for patients with LOSCC.It is advisable that the future RCT trials canbe conducted to clarify the role of SEMS placement and DS construction as BTS in those LOSCC patients with curative intent.

5. Conclusion

Hence, if the tumor characteristicsare manageable for SEMS insertion and the experiencedphysician is accessible, SEMS placement seems to be the preferred BTS approach for LSOCC patients with curative intent.In addition, we concluded that there is an urgent need for well conducted RCTs in this area.

6.Conflicts of Interest

the authors declare that they have no conflicts of interest.

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