The Role of Stents as Bridge to Surgery for Acute Left-Sided Obstructive Colorectal Cancer: Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

Background: The role of self-expanding metallic stents (SEMS) as a bridge to surgery for acute left-sided obstructive colorectal cancer has remained controversial. Objective: To study the efficacy of this approach, we performed a meta-analysis at the gastrointestinal surgery center of Sichuan Academy of Medical Sciences and Sichuan Provincial People’s Hospital (Eastern Hospital). Methods: Two PubMed and science-direct electronic databases were searched up to December 30, 2017. Eligible studies were randomized controlled trials (RCTs). Results: We selected 8 RCTs articles, which included 497 cases. The directly stoma rates were significantly lower in the stent group (odds ratio [OR] = 0.46, 95% confidence intervals [CIs] = 0.30–0.70, \( p = 0.0003 \)). The successful primary anastomosis rates were significantly higher in the stent group (OR = 2.29, 95% CI = 1.52–3.45, \( p < 0.0001 \)). The post-procedural complication rates were significantly lower in the stent group (OR = 0.39, 95% CI = 0.18–0.82, \( p = 0.01 \)). However, tumor recurrence rates were significantly higher in the stent group (OR = 1.79, 95% CI = 1.09–2.93, \( p = 0.02 \)). Conclusions This meta-analysis confirms that SEMS placement could reduce direct stoma rate and increases the successful primary anastomosis rate; however, it was associated with a seemingly higher incidence of tumor recurrence. (REV INVEST CLIN. 2018;70:269-78)

Key words: Colorectal cancer. Stent. Intestinal obstruction. Meta-analysis.

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INTRODUCTION

Colorectal cancer is a major problem worldwide with high incidence and mortality rates. In China, in 2015 the estimated incidence rate was 376.3/100,000 and mortality rate was 191.0/100,000. Left-sided colonic tumors are the most common, accounting for more than 50%. Tumors at the splenic flexure were associated with the highest risk of obstruction (in 8.4% of cases, there was complete obstruction). Published literature reported that 7-29% of patients present with acute colonic obstruction at the time of diagnosis.

Patients with acute left-sided colonic obstruction have traditionally undergone emergency surgery that often leads to the formation of a stoma, and about 40% of them will never have their stoma reversed. Those with a permanent colostomy have a lower health-related quality of life. Moreover, emergency surgery for acute colonic obstruction has a high mortality rate, of 8.2-19%, and a morbidity rate of 22.3-38%.

At present, numerous studies have shown that self-expandable metal stent (SEMS) placement is an effective treatment for patients stented as a bridge to surgery or as palliation due to acute obstructive colorectal cancer. The literature has reported colonic stent success rates ranging from 47% to 100%, and the overall stenting complication rate ranging from 7.8% to 19%. A recent meta-analysis showed a reduction on the rate of stoma and a higher primary anastomosis rate in the colonic stent as a bridge to surgery group compared with the emergency surgery group. However, the study included only three randomized trials, which led to significant publication bias. Since some new reports have been published updating this meta-analysis, we performed a revised meta-analysis, including only randomized controlled trials (RCTs).

METHODS

Literature search strategy

Search was conducted in two electronic databases, PubMed, and science direct (the last search was updated on December 30, 2017). The following terms were used: colorectal neoplasm, stents, and intestinal obstruction. The search was done on studies conducted in human subjects, without restriction of language. We did not consider abstracts or unpublished studies. The reference lists of reviews and retrieved articles were hand-searched at the same time. We performed this meta-analysis according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis guidelines.

Inclusion and exclusion criteria

We reviewed abstracts of all citations and retrieved studies. The following criteria were used to include published studies: (a) they had to be RCTs; (b) studies should include patients ≥ 18 years old, of either sex, who had left-sided colonic obstruction due to colorectal cancer confirmed by abdominal computed tomography (CT) scan; (c) studies should compare patient’s stenting as a bridge to surgery with emergency surgery due to acute left-sided obstructive colorectal cancer; and (d) studies should contain sufficient raw data for estimating odds ratio (OR) with 95% confidence intervals (CI). The major reasons for exclusion of studies were: (1) studies without raw data available; (2) duplicates; and (3) no usable data reported.

Data extraction

Data were extracted from each study by two reviewers (Yang P and Lin Xiu-Feng) independently according to the per specified selection criteria. Any disagreements during screening and quality assessment were resolved by discussion.

Main and secondary outcomes

We considered the following main outcomes for the two different treatment groups: successful primary anastomosis rates, directly stoma rate, and postoperative complications. The rate of tumor recurrence was recorded as a secondary outcome for the current meta-analysis. Furthermore, within the SEMS group, we considered data regarding technical success, clinical success, and stent-related complications.

Statistical analysis

Statistical analysis was performed by RevMan5.3 software, which was provided by the Cochrane...
Collaboration. Heterogeneity was checked by chi-square test. If the results from the trials had heterogeneity, random effects model was used for meta-analysis. Otherwise, fixed effects model was used. \( p < 0.05 \) was considered statistically significant. The result was expressed with OR for the dichotomous variables with 95% CI.

**Assessment of study quality**

Included studies were reviewed and appraised for methodological quality using the Jadad composite scale\(^\text{18}\). High-quality trials scored more than 2 of a maximum possible score of 8\(^\text{19}\).

**RESULTS**

**Study characteristics**

There were 774 articles relevant to the searching words (Fig. 1). Through the steps of filtering the title, abstracts, and the full text, 8 papers were finally found to conform to our inclusion criteria\(^\text{20-27}\). From the 8 RCTs articles, which included 497 cases, 251 were randomly divided into the emergency SEMS as a bridge to surgery group, and 246 to the emergency surgery group. Technical and clinical success rates for stenting were 46.7-100% and 78.6-100%, respectively.

The clinical perforation rate was 5.6% (14 of 251) and the silent perforation rate, 14.3% (11 of 77). Two studies included rectal cancer cases\(^\text{21,23}\). One study\(^\text{21}\) included one case in the stent as a bridge to surgery group only, and the other\(^\text{23}\) did not report the number of rectal cancer cases.

The median time between stent placement and elective surgery varied in the included studies, from 3 to 10 days. Regarding the surgical approach, four studies\(^\text{21,22,23,26}\) used laparotomy, three\(^\text{20,25,27}\) used laparotomy and laparoscopic surgery, and one\(^\text{24}\) used laparoscopic surgery. Characteristics of studies included in this meta-analysis are presented in Table 1.
Quality of included studies

All the eight studies were randomized, non-blinded controlled trials and all of them had a detailed description of methods for randomization, six with a computer-generated list’s allocation, and two with a random envelope method. The mean Jadad score of the included studies was 3 (Table 2). The main study limitations pertained to the justification of sample size, allocation concealment, and double-blinding.

Quantitative data synthesis

Directly stoma rates

All the eight studies reported directly stoma rates. The combined results showed that the directly stoma rates were significantly lower in the stent group (OR = 0.46, 95% CI = 0.30–0.70, p = 0.002). Heterogeneity was not observed between the eight studies (χ² = 4.07, p = 0.77, I² = 0%), so the fixed effects model was used (Fig. 2).
Successful primary anastomosis rates

All the eight studies reported successful primary anastomosis rates. The meta-analysis showed that the successful primary anastomosis rates were significantly higher in the stent group (OR = 2.29, 95% CI = 1.52–3.45, p < 0.0001), the finding not associated with significant heterogeneity ($\chi^2 = 2.19$, $p = 0.95$, $I^2 = 0\%$) (Fig. 3).

Post-operative complications

The overall complications were lower for the stent group (OR = 0.39, 95% CI = 0.18–0.82, $p = 0.01$), but this finding was associated with significant heterogeneity ($\chi^2 = 4.07$, df = 7 ($p = 0.77$); $I^2 = 0\%$) (Fig. 4). This advantage has also been found in wound infections and permanent stoma. However, there was no statistically difference in mortality, anastomotic leak, intraperitoneal abscess, post-operative ileus, pulmonary infection,
Figure 3. Forest plot of successful primary anastomosis rates (SEMS vs. ES).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>SEMS Events</th>
<th>SEMS Total</th>
<th>ES Events</th>
<th>ES Total</th>
<th>Weight</th>
<th>M-H. Fixed. 95% CI</th>
<th>M-H. Fixed. 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcantara (2011)</td>
<td>14</td>
<td>15</td>
<td>9</td>
<td>13</td>
<td>2.1%</td>
<td>6.22 [0.60, 64.97]</td>
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<tr>
<td>Arezzo (2017)</td>
<td>43</td>
<td>56</td>
<td>36</td>
<td>59</td>
<td>26.7%</td>
<td>2.11 [0.94, 4.76]</td>
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</tr>
<tr>
<td>Cheung (2009)</td>
<td>16</td>
<td>24</td>
<td>9</td>
<td>24</td>
<td>9.9%</td>
<td>3.33 [1.02, 10.90]</td>
<td></td>
</tr>
<tr>
<td>Cui (2011)</td>
<td>18</td>
<td>29</td>
<td>7</td>
<td>20</td>
<td>10.3%</td>
<td>3.04 [0.93, 9.95]</td>
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</tr>
<tr>
<td>Ghazal (2013)</td>
<td>29</td>
<td>30</td>
<td>29</td>
<td>30</td>
<td>3.2%</td>
<td>1.00 [0.06, 16.76]</td>
<td></td>
</tr>
<tr>
<td>Ho KS (2012)</td>
<td>17</td>
<td>20</td>
<td>13</td>
<td>19</td>
<td>6.6%</td>
<td>2.62 [0.55, 12.48]</td>
<td></td>
</tr>
<tr>
<td>Pirlet (2011)</td>
<td>16</td>
<td>30</td>
<td>12</td>
<td>30</td>
<td>18.4%</td>
<td>1.71 [0.62, 4.77]</td>
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</tr>
<tr>
<td>van Hooft (2011)</td>
<td>16</td>
<td>47</td>
<td>11</td>
<td>51</td>
<td>22.9%</td>
<td>1.88 [0.76, 4.61]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 251 246 100.0% 2.29 [1.52, 3.45]

Total events 169 126
Heterogeneity: Chi² = 2.19, df = 7 (P = 0.95); I² = 0%
Test for overall effect: Z = 3.95 (P < 0.0001)

SEMS: Self-expandable metallic stent; ES: Emergency surgery.

Figure 4. Forest plot of overall complications (SEMS vs. ES).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>SEMS Events</th>
<th>SEMS Total</th>
<th>ES Events</th>
<th>ES Total</th>
<th>Weight</th>
<th>M-H. Fixed. 95% CI</th>
<th>M-H. Fixed. 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcantara (2011)</td>
<td>2</td>
<td>15</td>
<td>7</td>
<td>13</td>
<td>8.9%</td>
<td>0.13 [0.02, 0.83]</td>
<td></td>
</tr>
<tr>
<td>Arezzo (2017)</td>
<td>29</td>
<td>56</td>
<td>34</td>
<td>59</td>
<td>16.4%</td>
<td>0.79 [0.38, 1.65]</td>
<td></td>
</tr>
<tr>
<td>Cheung (2009)</td>
<td>2</td>
<td>24</td>
<td>17</td>
<td>24</td>
<td>9.7%</td>
<td>0.04 [0.01, 0.20]</td>
<td></td>
</tr>
<tr>
<td>Cui (2011)</td>
<td>3</td>
<td>29</td>
<td>4</td>
<td>20</td>
<td>10.1%</td>
<td>0.46 [0.09, 2.34]</td>
<td></td>
</tr>
<tr>
<td>Ghazal (2013)</td>
<td>4</td>
<td>29</td>
<td>15</td>
<td>30</td>
<td>12.4%</td>
<td>0.16 [0.04, 0.57]</td>
<td></td>
</tr>
<tr>
<td>Ho KS (2012)</td>
<td>7</td>
<td>20</td>
<td>11</td>
<td>19</td>
<td>12.3%</td>
<td>0.39 [0.11, 1.43]</td>
<td></td>
</tr>
<tr>
<td>Pirlet (2011)</td>
<td>15</td>
<td>30</td>
<td>17</td>
<td>30</td>
<td>14.3%</td>
<td>0.76 [0.28, 2.11]</td>
<td></td>
</tr>
<tr>
<td>van Hooft (2011)</td>
<td>25</td>
<td>47</td>
<td>23</td>
<td>51</td>
<td>15.9%</td>
<td>1.38 [0.62, 0.03]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 250 246 100.0% 0.39 [0.18, 0.82]

Total events 87 128
Heterogeneity: Tau² = 0.74; Chi² = 22.53, df = 7 (P = 0.002); I² = 69%
Test for overall effect: Z = 2.08 (P = 0.01)

SEMS: Self-expandable metallic stent; ES: Emergency surgery.

Figure 5. Forest plot of tumor recurrence rate (SEMS vs. ES).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>SEMS Events</th>
<th>SEMS Total</th>
<th>ES Events</th>
<th>ES Total</th>
<th>Weight</th>
<th>M-H. Fixed. 95% CI</th>
<th>M-H. Fixed. 95% CI</th>
</tr>
</thead>
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<tr>
<td>Alcantara (2011)</td>
<td>8</td>
<td>15</td>
<td>2</td>
<td>13</td>
<td>4.2%</td>
<td>6.29 [1.02, 38.65]</td>
<td></td>
</tr>
<tr>
<td>Arezzo (2017)</td>
<td>17</td>
<td>56</td>
<td>20</td>
<td>59</td>
<td>57.6%</td>
<td>0.85 [0.39, 1.86]</td>
<td></td>
</tr>
<tr>
<td>Ghazal (2013)</td>
<td>5</td>
<td>30</td>
<td>4</td>
<td>30</td>
<td>14.1%</td>
<td>1.30 [0.31, 5.40]</td>
<td></td>
</tr>
<tr>
<td>van Hooft (2011)</td>
<td>13</td>
<td>26</td>
<td>9</td>
<td>32</td>
<td>17.1%</td>
<td>2.56 [0.86, 7.59]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 151 158 100.0% 1.79 [1.09, 2.93]

Total events 54 38
Heterogeneity: Chi² = 8.51, df = 4 (P = 0.07); I² = 53%
Test for overall effect: Z = 2.30 (P < 0.02)

SEMS: Self-expandable metallic stent; ES: Emergency surgery.
Tumor recurrence rate

Tumor recurrence was reported in five studies, with a median follow-up period of 18-65 months. The tumor recurrence rates were 35.8% (54/151) in the stent group and 24.1% (38/158) in the emergency surgery group. The meta-analysis showed that the rate was significantly higher in the stent group compared to the emergency surgery group (OR = 1.79, 95% CI = 1.09–2.93, \( p = 0.02 \)), the finding not associated with significant heterogeneity (Chi \( \chi^2 = 8.51, \ I^2 = 53\% \) (Fig. 5).
and the funnel plots’ shapes of successful primary anastomosis rates were the same as those in figures 6 and 7.

DISCUSSION

Since colorectal SEMS introduction in the early 1990s, the SEMS as a bridge to surgery for acute left-sided obstructive colorectal cancer is a recent and appealing option. Some prior uncontrolled studies reported that it would improve the clinical condition of the patient and seemed to decrease mortality and morbidity. This meta-analysis showed that using SEMS as a bridge to surgery for acute left-sided obstructive colorectal cancer did not have advantaged benefits for post-procedural overall complications and mortality. This result was different from the prior meta-analysis study.

The successful primary anastomosis rate and directly stoma creation rate have been frequently used to assess different treatments for acute left-sided obstructive colorectal cancer. In our meta-analysis, directly stoma rate, permanent stoma rate, and wound infection rate were significantly lower in the colonic stenting group than in the emergency surgery group. Moreover, the successful primary anastomosis rates were significantly higher for the stent group. However, this advantage was not obtained in the anastomotic leak. The reasons probably were insufficient bowel decompression so that there was no improvement in the patients’ clinical condition. In addition, the emergency surgery nature and the surgeons’ faith may have made the surgeons more conservative than in the SEMS as a bridge to surgery group.

Major post-procedural stent-related complications include perforation, stent migration, bleeding, and persistent obstruction. In this meta-analysis, four studies reported stent-related and procedure-related complications, and the other four studies did not report the complications with stent placement. Pirlet et al. reported 2 (6.6%) stent-related perforations and 8 silent perforations in 30 patients randomized to colonic stenting as a bridge to surgery. However, if the number of silent perforations is counted, the total perforation rate was as high as 33.3%. van Hooft et al. reported 6 (12.8%) stent-related and post-procedural perforations. The total perforation rate was 19.1% (9 perforations in 47 patients) if the number of silent colonic perforations is added. This matter of concern from an oncological aspect raises the question of tumor dissemination after stenting. However, the consequences of dissemination are inconsistent if this information derived from survival data at present, ranging from no difference between colonic stenting and emergency surgery to a significantly reduced 5-year survival for patients treated with colonic stenting before elective surgery. In our meta-analysis, the tumor recurrence rate was higher in the stent group. Due to the lack of raw data, we did not make Kaplan–Meier curves in this meta-analysis. Although stent placement was associated with a higher risk of recurrence, the numbers were too small to draw a definitive conclusion from this meta-analysis. The main reason for this difference was a stent-related perforation. The clinical perforation rate was 5.6% (14 of 251) and the silent perforation rate, 14.3% (11 of 77) in our meta-analysis. The safe use of stents already was shown by Saito et al. in a recent study, with only 1.6% risk of perforation and 1.3% risk of silent perforation. Hence, the weaknesses of this meta-analysis were the variation in operator experience with stenting in the included studies. As a result, surgeons must demonstrate sufficient expertise in colonic stenting before they can perform these procedures.

The technical success rate ranged from 46.7% to 100% in the 8 articles included in this meta-analysis. Four studies described the reasons for technical failure. The main reason was inability to pass the stricture with the guide-wire (13 of 16 in the study by Pirlet et al., 12 of 14 in the study by van Hooft et al., 4 of 5 in Ho et al.’s study, and 1 of 1 in the study by Ghazal et al.). In patients with complete obstruction, stent placement is more difficult, and the bowel might be less easily decompressed than in patients with incomplete obstruction. Due to insufficient bowel decompression at the time of surgery, there was a fairly high leak rate in primary anastomosis without a stoma. A study reported that complete obstruction was an identified risk factor for complications. However, our meta-analysis did not find the difference in anastomotic leakage between the two groups.
In this meta-analysis, only one study\textsuperscript{23} reported the overall health status and quality of life between the two groups. Since there was no raw data, we could not do data synthesis. In their study\textsuperscript{23}, van Hooft et al. did not record any significant differences in overall health status, cancer-specific quality of life, or tumor-specific quality of life between the treatment groups, except for more stoma-related problems in the colonic stenting group than in the emergency surgery group. Two studies reported the cost-benefit analysis\textsuperscript{21,24}. However, the two articles have reached the opposite conclusion. Alcántara et al. reported in their study that the cost was significantly higher for the colonic stenting group when the cost of material used was added\textsuperscript{21}.

As in most meta-analysis, these results should be interpreted with caution. There are several limitations, although the research includes eight high-quality studies. First, all the eight studies included lack allocation concealment and double-blinding. Due to the obvious difference between the two methods, a completely double-blind randomized control is not possible. Therefore, there may be selection bias, implementation bias, and measurement bias. For example, the selection bias was very easy to choose in this colonic stenting group of stoma and primary anastomosis. Second, all of the eight studies included small numbers of patients; the largest number included was only 115 cases\textsuperscript{27}. Third, differences in technical success rates, colonic stent designs, and operative techniques were associated with the confounding bias. Finally, this study did not perform an economic data synthesis due to the lack of relevant raw data on economics, as well as overall survival, progression-free survival, and quality of life.

In conclusion, this meta-analysis confirms that SEMS placement seems to reduce directly stoma rate and increases the successful primary anastomosis rate and is associated with a lower rate of overall complications, permanent stoma, and wound infection. However, it was seemingly associated with a high tumor recurrence incidence. Further large-scale studies are necessary to compare with the overall survival rate, progression-free survival rate, and quality of life in the two strategies.

REFERENCES


