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BRIEF ARTICLE

Colonic stenting *vs* emergent surgery for acute left-sided malignant colonic obstruction: A systematic review and meta-analysis

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Abstract

AIM: To investigate the effects of emergent preoperative self-expandable metallic stent (SEMS) *vs* emergent surgery for acute left-sided malignant colonic obstruction.

METHODS: Two investigators independently searched the MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials, as well as references of included studies to identify randomized controlled trials (RCTs) that compared two or more surgical approaches for acute colonic obstruction. Summary risk ratios (RR) and 95% CI for colonic stenting and emergent surgery were calculated.

RESULTS: Eight studies met the selection criteria, involving 444 patients, of whom 219 underwent SEMS and 225 underwent emergent surgery. Seven studies reported difference of the one-stage stoma rates between the two groups (RR, 0.60; 95% CI: 0.48-0.76; $P < 0.0001$). Only three RCTs described the follow-up stoma rates, which showed no significant difference between the two groups (RR, 0.80; 95% CI: 0.59-1.08; $P = 0.14$). Difference was not significant in the mortality between the two groups (RR, 0.91; 95% CI: 0.50-1.66; $P = 0.77$), but there was significant difference (RR, 0.57; 95% CI: 0.44-0.74; $P < 0.0001$) in the overall morbidity. There were no significant differences between the two groups in the anastomotic leak rate (RR, 0.60; 95% CI: 0.28-1.28; $P = 0.19$), occurrence of abscesses, including peristomal abscess, intraperitoneal abscess and parietal abscess (RR, 0.83; 95% CI: 0.36-1.95; $P = 0.68$), and other abdominal complications (RR: 0.67; 95% CI: 0.40-1.12; $P = 0.13$).

CONCLUSION: SEMS is not obviously more advantageous than emergent surgery for patients with acute left-sided malignant colonic obstruction.

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Key words: Acute obstruction; Colonic cancer; Self-expandable metallic stent; Stoma placement; Meta-analysis; Systematic review

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INTRODUCTION

Colorectal cancer is the fourth most common malignancy worldwide, with an estimated number of 1 023 000 new cases and 529 000 deaths each year[1]. The incidence of colorectal cancer has been increasing rapidly in Asia over the past few decades[2]. About 7%-29% of the patients with colorectal cancer present with bowel obstruction[3,4]. And benefit of surgical management of malignant large bowel obstruction remains controversial, especially for left-sided colonic obstruction. Emergent colorectal surgery for acute obstruction is associated with a mortality rate of 15%-20% and a morbidity rate of 15%-20%, both significantly higher than that in the elective situation[5-7]. Emergent surgery is an independent factor of mortality and morbidity, and about two-thirds of patients end up with a permanent stoma[3,6,8,9].

In 1991, colonic stenting was introduced to restore luminal patency in patients with malignant obstruction of the left side colon[10]. Tejero *et al*[11] used self-expandable metallic stent (SEMS) as a bridge to surgery in two patients with colonic obstruction in 1994. Stent placement before elective surgery, also known as a bridge to surgery, improved the clinical condition of the patient and seemed to decrease the mortality, morbidity, and number of colostomies in uncontrolled studies[12-15]. Although preoperative SEMS insertion has such advantages, it may result in the related complications such as perforation, stent migration, and reobstruction. As shown in the recent randomized controlled trials (RCTs), whether preoperative SEMS can reduce mortality, complication rate and stoma rate is still a big controversy[16-18]. Thus, this meta-analysis was performed to evaluate the effects of preoperative SEMS *vs* emergent surgery for acute left-sided malignant colonic obstruction.

MATERIALS AND METHODS

Search strategy

SEMS was first used in 1991. We therefore, searched the databases, including the Cochrane Central Register of Controlled Trials (1991-April 2011), MEDLINE (1991-September 2011), EMBASE (1991-September 2008), Elsevier ScienceDirect (1998-September 2008), SpringLink (up to September 2011), Ovid LWW (1991-September 2011) and BMJ Journals Online (up to September 2008). The following keywords were used: "intestinal obstruction", "colon", "rectum", "left-sided colon", "surgery", "resection", "stents", "randomized" and "controlled study". The detailed search strategy is available from the authors. All included studies also had access to the PubMed "related articles" function and the Science Citation Index. In addition, the reference lists of included studies were scrutinized. No language restrictions were applied.

Data extraction

Data were independently abstracted from each study by two researchers, and disagreement was resolved by consensus. Data were extracted from each study using a pre-designed review form. Data to be extracted were as follows: (1) treatment details: primary anastomosis rate, and the incidence of stoma creation; (2) short-term adverse events: mortality and morbidity such as anastomotic leak rate, abscess and extra abdominal complications; and (3) long-term outcomes: follow-up stoma rate.

Inclusion and exclusion criteria

Studies fulfilling the following criteria were included in the meta-analysis: (1) RCTs or other comparative studies comparing SEMS as a bridge to surgery and emergent surgery; (2) reports on at least one of the outcome measures mentioned below; and (3) studies reporting patients with malignant acute left-sided colonic obstruction.

Quality of methodology

The quality of nonrandomized studies was assessed using the Newcastle-Ottawa Scale with some modifications to meet the needs for this meta-analysis[19], and the quality of randomized studies was evaluated by means of the modified Jadad score[20]. The quality of the studies was evaluated based on three items: patient selection, comparability of study groups, and assessment of outcome. Studies achieving five or more stars were considered high quality. The quality of randomized studies was evaluated by means of the modified Jadad score including the following four areas: (1) randomization method; (2) hidden subgroups; (3) blinding; and (4) the description of the loss to follow-up and drop-out and the intention-to-treat. The total score of 1 to 3 points were ascribed to low-quality studies, whereas a total score of 4 to 7 points to high-quality researches.

Statistical analysis

Using the Cochrane Collaboration's RevMan 5.1 software provided by meta-analysis, the results of included measurement of indicators were all count data, and 95% CI was used for the efficacy analysis. The heterogeneity between studies was tested. When there was homogeneity among studies ($P > 0.1$, $I^2 < 50\%$), a fixed effects model was used for meta-analysis; if there is significant heterogeneity among studies ($P < 0.1$, $I^2 > 50\%$), the random effects model was used. We also analyzed the different quality of the possible causes, and conducted subgroup analysis. If the heterogeneity among the studies was too large, descriptive analysis was performed.

RESULTS

Selection of trials

The initial search strategy retrieved 88 articles after screening all titles, abstracts and full texts. Twenty-two articles were excluded due to lack of comparison with other surgical strategies in most of the cohort studies, 45 articles were excluded because of comparison stenting *vs* surgery without a bridge to the surgery, and 13 studies were excluded because there was no control. Finally, 8 trials with 444 patients were included, of whom 219

Table 1 Randomized controlled trials involved in the meta-analysis

Year	Author	Region	Total	SEMS	Surgery	Concealment of allocation	Jaded score	Quality
2009	Cheung	Hongkong	60	30	30	Appropriant	5	High
2010	Pirlet	France	48	24	24	Appropriant	5	High
2011	Van Hooft	Holland	98	47	51	Appropriant	5	High

SEMS: Self-expandable metallic stent.

Table 2 Basic characteristics of included nonrandomized controlled studies in the meta-analysis

Year	Author	Design	Total	SEMS	Surgery	Match	Study quality (rate, max 11)
2008	Dastur	R	43	19	23	1,2,3,4,5,6	8
2002	Martin	R	52	26	26	1,2,3,4,5,8	7
2006	Ng	R	60	20	40	1,2,3,5,6,8	8
2007	Pessione	R	16	9	7	1,2,3,4,5,8	7

Matching: 1 = age, 2 = sex, 3 = diagnosis, 4 = tumor site, 5 = tumor stage, 6 = American Society of Anesthesiologists score, 7 = body mass index, 8 = comorbidity. SEMS: Self-expandable metallic stent. "R" represents that the study was a randomized clinical trail.

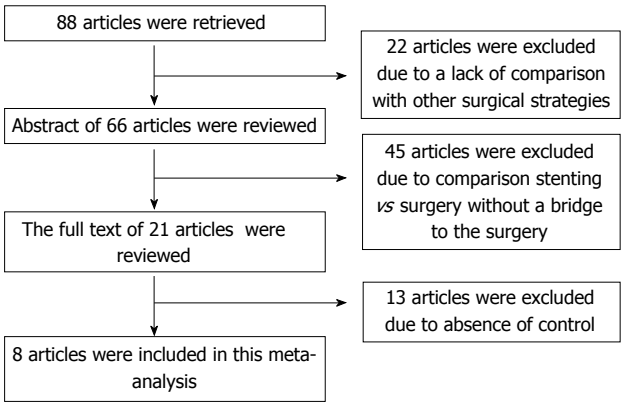


Figure 1 Flow chart of selection of studies and reasons for exclusion from the meta-analysis.

(49.3%) successfully underwent stent insertion and 225 (50.7%) underwent emergent surgery. There were 17 (7.8%) deaths in the SEMS as a bridge to surgery group and 21 (9.3%) deaths in the emergent surgery group. There were only three RCTs[16-18] and five nonrandomized controlled studies (NRCTs)[12-14,21,22]. The flow chart of selection of studies and reasons for exclusion is presented in Figure 1. Characteristics of studies included in the meta-analysis are presented in Tables 1 and 2.

Quality of studies

Three RCTs were of moderate to good methodological quality evaluated by the modified Jadad score[20]. Because of the special strategies under assessment, no blind method was used in all the RCTs. All five NRCTs contained groups matched for age, sex, and diagnosis; five articles contained information on tumor site, tumor stage, American Society of Anesthesiologists score, or body mass index, respectively. All studies were scored more than five stars using the modified Newcastle-Ottawa scale[19].

Meta-analysis of treatment details and long-term outcomes

Our meta-analysis showed statistically significant difference between the SEMS group (175 patients) and the emergent surgery group (201 patients) in seven studies with regard to the one-stage stoma rate [risk ratios (RR): 0.60, 95% CI: 0.48-0.76; $P < 0.0001$]. There was no significant heterogeneity between the studies ($P = 0.14$, $I^2 = 37\%$) (Figure 2A). Only three RCTs compared the two groups (101 patients in the SEMS group and 105 in the emergent surgery group) and described the follow-up stoma rates. There was neither significant difference in follow-up stoma rates (RR: 0.80; 95% CI: 0.59-1.08; $P = 0.14$), nor heterogeneity ($P = 0.17$, $I^2 = 44\%$) between the two groups (Figure 2B).

Anastomosis rates were reported by all eight trials involving 219 patients in the SEMS group and 225 in the emergent surgery group. There was a significant difference between the two groups, with a pooled RR of 1.64 (95% CI: 1.39-1.94; $P < 0.00001$) (Figure 2C).

Meta-analysis of short-term adverse events: Mortality and morbidity such as anastomotic leak rate, abscess and extra abdominal complications

Six trials reported mortality in 149 patients in the SEMS group and 175 patients in the emergent surgery group. There was no significant difference (RR: 0.91; 95% CI: 0.50-1.66; $P = 0.77$) and heterogeneity ($P = 0.65$, $I^2 = 0\%$) between the two groups (Figure 2D).

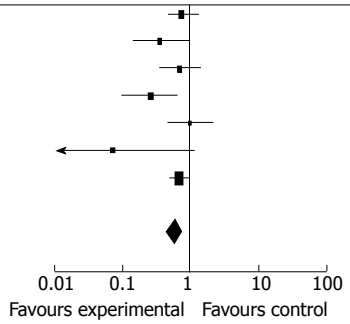
Seven trials with 200 patients in the SEMS group and 218 patients in the emergent surgery group reported the overall morbidity. There was no significant difference between the two groups with a pooled RR of 0.57(95% CI; 0.44-0.74; $P < 0.0001$). However, significant heterogeneity was observed ($P = 0.0001$, $I^2 = 78\%$) (Figure 2E).

Further complication analysis was also performed, such as anastomotic leak, abscess and extra abdominal complications. The incidence of anastomotic leakage in

A

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk ratio M-H, fixed, 95% CI
Pirlet 2010	13	30	17	30	16.1%	0.76 [0.46, 1.28]
Cheung 2009	4	24	11	24	10.4%	0.36 [0.13, 0.98]
Dastur 2008	7	19	12	23	10.3%	0.71 [0.35, 1.43]
Martinez-Santos 2002	4	26	15	26	14.2%	0.27 [0.10, 0.70]
Ng 2006	7	20	14	40	8.8%	1.00 [0.48, 2.08]
Pessione 2007	0	9	5	7	5.8%	0.07 [0.00, 1.13]
van Hooft 2011	24	47	38	51	34.5%	0.69 [0.50, 0.95]
Total (95% CI)		175		201	100.0%	0.60 [0.48, 0.76]
Total events	59		112			

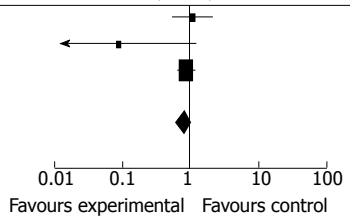
Heterogeneity: Chi^2 = 9.58, df = 6 (P = 0.14); I^2 = 37%
Test for overall effect: Z = 4.32 (P < 0.0001)



B

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk ratio M-H, fixed, 95% CI
Pirlet 2010	9	30	8	30	17.0%	1.13 [0.50, 2.52]
Cheung 2009	0	24	6	24	13.8%	0.08 [0.00, 1.29]
van Hooft 2011	27	47	34	51	69.2%	0.86 [0.63, 1.18]
Total (95% CI)		101		105	100.0%	0.80 [0.59, 1.08]
Total events	36		48			

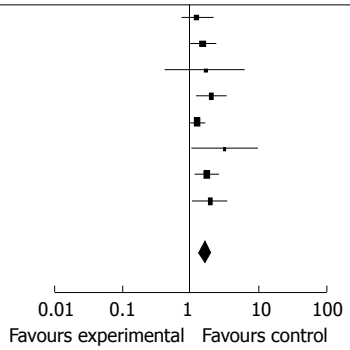
Heterogeneity: Chi^2 = 3.56, df = 2 (P = 0.17); I^2 = 44%
Test for overall effect: Z = 1.46 (P = 0.14)



C

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk ratio M-H, fixed, 95% CI
Pirlet 2010	18	30	14	30	14.8%	1.29 [0.79, 2.08]
Cheung 2009	20	24	13	24	13.8%	1.54 [1.02, 2.32]
Dastur 2008	9	19	2	7	3.1%	1.66 [0.47, 5.87]
Martinez-Santos 2002	22	26	11	26	11.7%	2.00 [1.24, 3.23]
Ng 2006	19	20	29	40	20.5%	1.31 [1.06, 1.63]
Pessione 2007	9	9	2	7	2.9%	3.04 [1.08, 8.58]
Saida 2003	34	44	18	40	20.0%	1.72 [1.18, 2.51]
van Hooft 2011	23	47	13	51	13.2%	1.92 [1.10, 3.34]
Total (95% CI)		219		225	100.0%	1.64 [1.39, 1.94]
Total events	154		102			

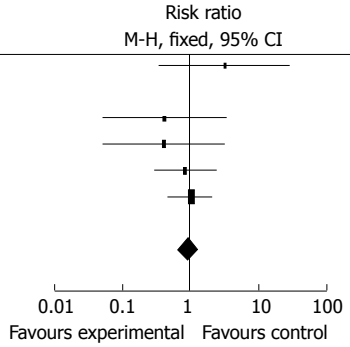
Heterogeneity: Chi^2 = 7.66, df = 7 (P = 0.36); I^2 = 9%
Test for overall effect: Z = 5.83 (P < 0.00001)



D

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk ratio M-H, fixed, 95% CI
Pirlet 2010	3	30	1	30	5.2%	3.00 [0.33, 27.23]
Cheung 2009	0	24	0	24		Not estimable
Dastur 2008	1	19	3	23	14.2%	0.40 [0.05, 3.57]
Ng 2006	1	20	5	40	17.5%	0.40 [0.05, 3.20]
Pessione 2007	3	9	3	7	17.7%	0.78 [0.22, 2.74]
van Hooft 2011	9	47	9	51	45.3%	1.09 [0.47, 2.50]
Total (95% CI)		149		175	100.0%	0.91 [0.50, 1.66]
Total events	17		21			

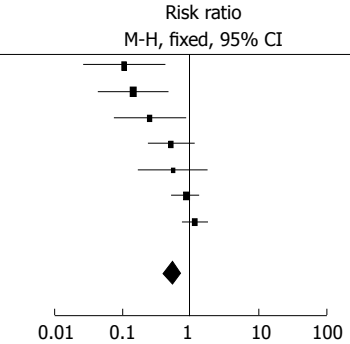
Heterogeneity: Chi^2 = 2.49, df = 4 (P = 0.65); I^2 = 0%
Test for overall effect: Z = 0.29 (P = 0.77)



E

Study or subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk ratio M-H, fixed, 95% CI
Cheung 2009	2	24	17	24	16.3%	0.12 [0.03, 0.45]
Saida 2003	3	44	17	40	17.1%	0.16 [0.05, 0.51]
Martinez-Santos 2002	3	26	11	26	10.6%	0.27 [0.09, 0.87]
Ng 2006	6	20	22	40	14.1%	0.55 [0.26, 1.13]
Pessione 2007	3	9	4	7	4.3%	0.58 [0.19, 1.80]
Pirlet 2010	15	30	17	30	16.3%	0.88 [0.55, 1.42]
van Hooft 2011	25	47	23	51	21.2%	1.18 [0.79, 1.77]
Total (95% CI)		200		218	100.0%	0.57 [0.44, 0.74]
Total events	57		111			

Heterogeneity: Chi^2 = 27.04, df = 6 (P = 0.0001); I^2 = 78%
Test for overall effect: Z = 4.30 (P < 0.0001)



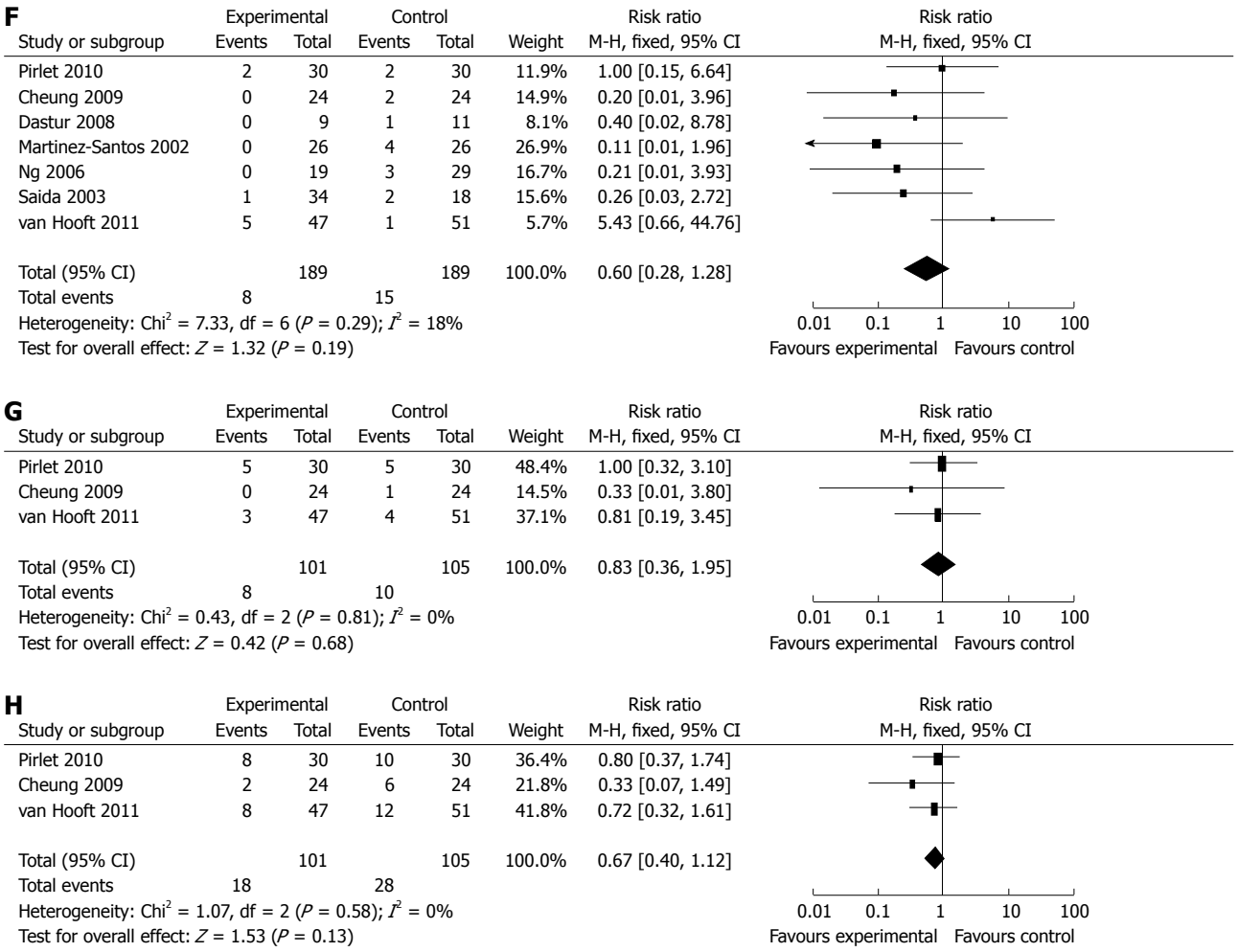


Figure 2 Colonic stenting *vs* emergent surgery. A: One-stage stoma rates; B: Follow-up stoma rates; C: Anastomosis rates; D: Mortality; E: Morbidity; F: Anastomotic leak; G: Abscesses; H: Extra abdominal complication. M-H: Mantel Haenszel.

the two groups was reported in seven studies. SEMS did not reduce the incidence of anastomotic leakage in patients treated with emergent surgery (RR: 0.60; 95% CI: 0.28-1.28; $P = 0.19$). No significant heterogeneity was observed between the two groups ($P = 0.29$, $I^2 = 18\%$) (Figure 2F).

Three studies compared the rates of abscesses, including peristomal abscess, intraperitoneal abscess and parietal abscess and extra abdominal complication. The analyses showed no significant difference in occurrence of abscess (RR: 0.83, 95% CI: 0.36-1.95; $P = 0.68$) and extra abdominal complications (RR: 0.67, 95% CI: 0.40-1.12; $P = 0.13$). No significant heterogeneity was found in abscess ($P = 0.81$, $I^2 = 0\%$) (Figure 2G) and extra abdominal complications ($P = 0.58$, $I^2 = 0\%$) (Figure 2H).

RCTs vs NRCTs

We also compared three RCTs with other NRCTs. There were significant differences in the morbidity (RCT group, RR 1.18; 95% CI: 0.79-1.77; $P = 0.08$ *vs* NRCTs group, RR 0.34; 95% CI: 0.21-0.56; $P < 0.0001$), anastomotic leak rate (RCT group, RR 5.43; 95% CI: 0.66-44.76; $P = 0.53$, *vs* NRCT group, RR 0.21; 95% CI: 0.05-0.82; $P = 0.02$), and anastomosis rates (RCT group, RR 1.57; 95% CI: 1.10-2.08; $P = 0.002$, *vs* NRCT group, RR 1.69; 95% CI: 1.38-2.08; $P < 0.00001$). There were no differences in the stoma rates (RCT group, RR 0.65; 95% CI: 0.50-0.85; $P = 0.002$, *vs* NRCT group, RR 0.52; 95% CI: 0.34-0.08; $P = 0.003$) and mortality (RCT group, RR 1.09; 95% CI: 0.47-2.50; P=0.53, *vs* NRCT group, RR 0.54; 95% CI: 0.2-1.45; $P = 0.22$).

DISCUSSION

Meta-analysis can be used to evaluate the existing literature both qualitatively and quantitatively by comparing and integrating the results of different studies and taking into account the variations in characteristics that could influence the overall estimate of the outcome of interest[23]. Although meta-analysis is traditionally applied and best confined to RCTs, meta-analytical techniques using NRCTs might be a good method in some clinical settings in which either the number or the sample size of RCTs was insufficient[24].

The concept of colonic stenting as a bridge to elective surgery in patients with acute left-sided malignant

colonic obstruction has been established to reduce the morbidity, mortality and number of colostomies. The nonrandomized or retrospective studies showed a significant reduction of morbidity and mortality, and need for stoma placement when SEMS was inserted before surgery with palliative intent. In contrast to these studies, two RCTs failed to confirm the findings.

Our meta-analysis illustrated that SEMS placement significantly decreased the one-stage stoma rates (RR: 0.60; 95% CI: 0.48-0.76; $P < 0.0001$) and increased anastomosis rates (RR: 1.64; 95% CI: 1.39-1.94; $P < 0.00001$), but no difference was found by the end of follow-up. The results of 206 patients in three RCTs which reported follow-up stoma rates demonstrated no difference. The difference of the stoma rate in the follow-up was partly caused by the high leakage rate of primary anastomosis in one stent group[16], probably because bowel decompression and improvement of the patients' clinical condition were insignificant at the time of elective operation. Another reason might be that more patients with complete obstruction had been selected in a Holland study[16]. In a retrospective study from a renowned tertiary referral centre, complete obstruction has been identified as a risk factor for complications[25]. Additionally, the elective nature of the operation and the surgeons' faith in the idea of bridge to surgery might have made the surgeons less conservative than the emergent surgery group.

The perioperative mortality is frequently used to evaluate the outcome of SEMS. Our study failed to reveal the difference between the two groups. Six studies including 324 patients came to a conclusion that there was no difference (RR: 0.91; 95% CI: 0.50-1.66; $P = 0.77$) between SEMS group and emergent surgery group. These outcomes might imply the potential benefits for preoperative SEMS as a bridge to surgery. It is hard to evaluate this outcome as the patients picked up did not match with the clinical stages. Clinical stage is considered as one of independent factors for prognosis. When SEMS is used as a bridge to surgery, there is concern about the oncologic outcome of those patients whose disease is potentially curable, because theoretically SEMS placement could induce tumor dissemination and worsen long-term survival[26]. More subgroup analyses should be performed to obtain a more accurate assessment.

In acute colonic obstruction, doctors and patients both want to remove the tumor with primary anastomosis with a shorter hospital stay. But the major concern is how to avoid complications. In right-sided bowel obstruction, a resection with primary anastomosis has been generally accepted by surgeons, but it is controversial in left-sided bowel obstruction. It is believed that the left colon obstruction has a high risk of radical resection and anastomosis with a high incidence of complications. Even with modern enema techniques and nutritional support, the rates of postoperative complications are still as high as 40%-50% (both significantly higher than in the elective situation with a < 14.0% anastomotic leakage rate and 10.0% operative mortality)[5,6,15,17,21-23,27,28] because of the long procedure time, peritoneal contamination, thin proximal wall of obstruction bowel, inflammatory edema, and poor blood supply. Although preoperative SEMS can potentially ameliorate bowel edema, there was no improvement in the overall situation. There was a significant difference between the two groups in the overall complications in seven studies with 418 patients, (RR: 0.57; 95% CI: 0.44-0.74; $P < 0.0001$). We found that SEMS, as a bridge to elective surgery, could decrease the incidence of anastomotic leakage. Leakage occurred in eight patients in the stenting group as compared with 15 patients in the control group. Anastomotic leakage could increase local recurrence and postoperative mortality. SEMS as a bridge to surgery can provide abundant bowel preparation to decrease tissue edema. But, there was no difference in the operation-related complications as shown in three studies involving 206 patients with abscess (RR: 0.83; 95% CI: 0.36-1.95; $P = 0.68$) and extra abdominal complications (RR: 0.67; 95% CI: 0.4-1.12; $P = 0.13$). Abscess was found as the main complication and pneumonia as the most common adverse event.

The major adverse events occurring in the SEMS group was bowel perforation during the stent placement procedure. Procedure- and stent-related complications were found in 5%-23.1% of patients, with an average rate of stent-related perforations of 5%[29,30]. The oncological consequences of potential tumor dissemination caused by perforations are unclear[15]. The data from NRCTs are inconsistent, ranging from no difference between colonic stenting and emergent surgery to a significantly reduced 5-year survival rate for patients treated with colonic stenting before elective surgery[27]. But the possibility of dissemination should be taken into account and the silent perforations should not be disregarded.

A cost-effectiveness analysis, including cost per quality-adjusted life-year as an outcome measure, was also performed in the meta-analysis. As a result, mortality, morbidity, quality-of-life dimensions, and stoma rates between treatment groups suggest that the probability of colonic stenting which could become more effective than emergent surgery is negligible. As only two authors have evaluated the cost-effectiveness, the results may have limitations, and a large sample would be gathered and assessed.

As this meta-analysis has a few limitations, there might be bias in the results. First, only three studies were RCTs, and confounding factors such as age and gender inevitably existed. Second, there was difference in the selection criteria, such as different protocols, method of procedures and so on. Finally, publication bias might exist when the meta-analysis was based on published studies, because positive results are more likely to be published than negative results.

In summary, the current meta-analysis demonstrated that SEMS as a bridge to surgery for obstructed left-sided colon cancer decreased the incidence of primary stoma rates and anastomotic leakage. But the consequence

failed to show the effect on mortality and complications related to surgery. Therefore, preoperative SEMS can be used as an alternative approach for emergent surgery, but should be used with caution, mainly because of concerns of overt and silent perforations. Future studies are needed to further investigate the oncological outcomes and establish whether specific groups of patients could benefit more from either colonic stenting or emergent surgery.

COMMENTS

Background

Colorectal cancer is one of the most commonly diagnosed malignancies worldwide. And many patients with colorectal cancer present with an acute left-sided colonic obstruction. The benefit of surgical management of malignant large bowel obstruction remains controversial. Stent placement before elective surgery as a bridge to surgery is an alternative for emergent surgery in patients with acute left-sided malignant colonic obstruction. Its benefits are uncertain.

Research frontiers

The authors performed a systematic review of the literature and meta-analysis of the one-stage stoma rates, follow-up stoma rates, anastomotic leakage rates, abscess, extra abdominal complications, morbidity and mortality of SEMS compared with emergent surgery.

Innovations and breakthroughs

The current meta-analysis demonstrated the advantage of SEMS as a bridge to surgery for obstructed left-sided colon cancer in term of decreasing the incidence of primary stoma rates and anastomotic leakage. But the consequence failed to show the effect on mortality and complications related to surgery.

Applications

The analysis has shown that preoperative SEMS can be used as an alternative approach for emergent surgery, but should be used with caution, mainly because of the concerns of overt and silent perforations. Future studies are needed to further investigate oncological outcomes and establish whether specific groups of patients could benefit more from either colonic stenting or emergent surgery.

Terminology

SEMS: SEMS is a metallic tube or stent, used to hold a structure in the gastrointestinal tract in order to allow the passage of food, stool, or other secretions required for digestion; Systematic review: A literature review focused on a research question that tries to identify, appraise, select and synthesize all high quality research evidence relevant to that question; Meta-analysis: A combination of the results of several studies that address a set of related research hypotheses.

Peer review

Overall, this is a nice review with good metrics and appropriate analysis.

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