

Self-expanding metallic stent as a bridge to surgery versus emergency surgery for obstructive colorectal cancer: a meta-analysis

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Received: 10 March 2011 / Accepted: 22 June 2011
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Abstract

Background The use of a colonic stent as a bridge to surgery aims to provide patients with elective one-stage surgical resection while reducing stoma creation and postoperative complications. This study used meta-analytic techniques to compare the outcomes of stent use as a bridge to surgery and emergency surgery in the management of obstructive colorectal cancer.

Methods A literature search of Medline, Embase, Cochrane controlled trials registry, and the Chinese Biomedical Literature Database was performed on all studies comparing stent as a bridge to surgery and emergency surgery for obstructive colorectal cancer. A meta-analysis of the included studies was carried out to identify the differences in outcomes between the two procedures.

Results Eight studies matched the criteria for inclusion and reported on the outcomes of 601 patients, of whom 232 (38.6%) underwent stent insertion and 369 (61.4%) underwent emergency surgery. Fewer patients in the stent group needed intensive care (risk ratio [RR], 0.42; 95% confidence interval [CI], 0.19–0.93; $p = 0.03$) and stoma creation (RR, 0.70; 95% CI, 0.50–0.99; $p = 0.04$). The primary anastomosis rate in the stent group was higher (RR, 1.62; 95% CI, 1.21–2.16; $p = 0.001$). Overall complications (RR, 0.42; 95% CI, 0.24–0.71; $p = 0.001$), including anastomotic leakage (RR, 0.31; 95% CI, 0.14–0.69;

$p = 0.004$), were reduced by stent insertion. Stent placement before elective surgery did not adversely affect mortality and long-term survival.

Conclusions The use of a stent as a bridge to surgery for obstructive left-sided colorectal cancer could increase the chance of primary anastomosis and reduce the need for stoma creation and postprocedural complications. Stent insertion before subsequent surgery has no effect on perioperative mortality and long-term survival.

Keywords Stent · Large-bowel obstruction · Colorectal cancer · Bridge to surgery · Meta-analysis

Colorectal cancer is among the top three most common malignancies and the cause of cancer-related death in the United States [1], and the incidence of colorectal cancer has been increasing rapidly in Asia in the last few decades [2]. Around 8–29% of patients with colorectal malignancy present with acute colonic obstruction [3, 4], and 70% of all malignant large-bowel obstruction occurs in the left-sided colon [5, 6]. Conventionally, these patients are treated with emergency surgery, which includes a variety of procedures such as Hartmann's procedure and loop colostomy. These interventions are associated with a mortality rate of 15–20% and a morbidity rate of 40–50% [7, 8]. Moreover, the ostomies will never be reversed in a considerable number of patients [4, 9]. Patients with a permanent stoma have a significantly lower health-related quality of life than similar patients without colostomy [10–13].

Since Dohmoto et al. [14] first described the use of metallic stents in 1991, the self-expanding metallic stent (SEMS) has been widely applied as palliative treatment for malignant colorectal obstruction in patients with

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incurable disease. In the palliative setting, the use of SEMS significantly reduced the length of hospital stay, mortality, medical complications, and the need for stoma formation [15]. Tejero et al. [16] reported using SEMS as a bridge to surgery in two patients with colonic obstruction in 1994. Thereafter, a number of studies have shown that stent placement before elective surgery is a relatively simple and safe alternative to conventional surgical management of malignant obstruction of the left colon [9, 17]. Additionally, SEMS gives the physician the opportunity to perform medical resuscitation, optimization of comorbid disorders, bowel preparation, and tumor staging. Although preoperative stent insertion has such advantages, there are some noticeable stent-related complications such as perforation, stent migration, and reobstruction [18]. In theory, SEMS insertion is an endoscopic procedure that could have deleterious effects on both tumor development and metastasis, and thus the effect of SEMS on the long-term outcome of those patients whose disease is potentially curable is still unclear [19].

The aim of this meta-analysis is to compare the outcomes between SEMS as a bridge to surgery and emergency surgery for obstructive colorectal cancer in terms of treatment details, short-term adverse events, the proportions of patients with permanent stoma, and survival.

Materials and methods

Study selection

Relevant studies were identified and selected by searching Medline (1990–December 2010), Embase (1990–December 2010), Cochrane controlled trials registry (Cochrane Library Issue 4, 2010), and the Chinese Biomedical Literature Database (1990–December 2010) using the search words “stents,” “colorectal cancer,” “bridge to surgery,” “preoperative,” “intestinal obstruction,” and “large bowel obstruction.” We also did a full manual search of the bibliographies of each peer-reviewed paper selected. No language restrictions were applied.

Inclusion criteria

The following selection criteria were applied: (1) study design: randomized clinical trials (RCT) or other comparative studies comparing SEMS as a bridge to surgery and emergency surgery; (2) study population: patients with obstructive colorectal cancer; and (3) outcome measures: treatment details, short-term adverse events, and long-term outcomes.

Exclusion criteria

Studies were excluded if (1) the outcomes were not reported for the two techniques or it was impossible to calculate the outcomes from the published results; (2) a zero cell was displayed for the outcomes for both groups; or (3) they reported on a patient group undergoing palliative treatment (noncurative surgical intent).

Data extraction

Data were independently abstracted from each study by two researchers, and disagreement was resolved by consensus. Data were extracted from each study with a pre-designed review form. Data to be extracted were as follows: (1) treatment details: intensive care unit (ICU) usage, success rates for the colonic stent procedure, primary anastomosis rate, and the incidence of stoma creation; (2) short-term adverse events: perioperative mortality and complications; and (3) long-term outcomes: the proportions of patients with permanent stoma as well as 1-, 2-, and 3-year survival rates.

Quality of methodology

The quality of the randomized and nonrandomized studies was assessed by using the Newcastle-Ottawa Scale with some modifications to match the needs for this meta-analysis [20]. The quality of the studies was evaluated by examining three items: patient selection, comparability of study groups, and assessment of outcome. Studies achieving five or more stars were considered high quality.

Statistical analysis

Statistical analysis for dichotomous variables was performed by using the risk ratio (RR) with its 95% confidence interval (CI). In surgical research, each center has its own selection criteria for the patients, and these patients have varying risk profiles. Thus, taking into account the inherent heterogeneity of these studies, we assumed the presence of statistical heterogeneity and decided to use only a random effects model before pooling the data. The random effects model adjusts for variability of results among trials and provides a more conservative estimate of an effect by using a wider CI [21].

Graphic exploration with funnel plots was used to evaluate the publication bias [22, 23]. Sensitivity analysis was performed according to the following items: (1) studies published in English, (2) studies containing more than 40 patients, (3) studies including only open surgery, and (4) studies with patients matched for the site of tumor.

Analysis was performed by using Review Manager ver. 5.0 (The Cochrane Collaboration, Oxford, UK).

Results

Studies selected

The search strategy found 66 papers. From these we identified eight studies to include in this meta-analysis [24] (Fig. 1). The included studies reported on 601 patients overall, of whom 232 (38.6%) underwent attempted stent insertion and 369 (61.4%) underwent emergency surgery. In total, stents were successfully inserted in 202 patients (87.1%), with technical success rates of individual units ranging from 47 to 100%. There were 8 deaths in the SEMS as a bridge to surgery group (3.4%) and 15 deaths (4.1%) in the emergency surgery group. In one study, the subsequent surgery following SEMS decompression was laparoscopic surgery [29], and in two other studies, patients underwent either open or laparoscopic surgery after

stenting [26, 28]. There was one single-center RCT [29] and one multicenter RCT [31]. The remaining studies were all retrospective studies. Obstruction was in the left colon or rectum in all studies.

The characteristics of the eight studies are summarized in Table 1. All studies contained groups matched for age, sex, and diagnosis. Five studies had groups matched for site of tumor also [25, 27, 28, 30, 31]. Six studies were published in English [24–26, 28, 29, 31]. Six studies included more than 40 patients [24, 26, 28]. All studies scored more than five stars using the modified Newcastle-Ottawa scale. The outcomes of interest reported by each of the eight studies are summarized in Table 2.

Meta-analysis

Treatment details

Results of the meta-analysis of the studies are listed in Table 3. Figure 2 is a forest plot of the meta-analysis of permanent stoma and measures of treatment detail and

Fig. 1 Flowchart of selection of studies for inclusion in meta-analysis

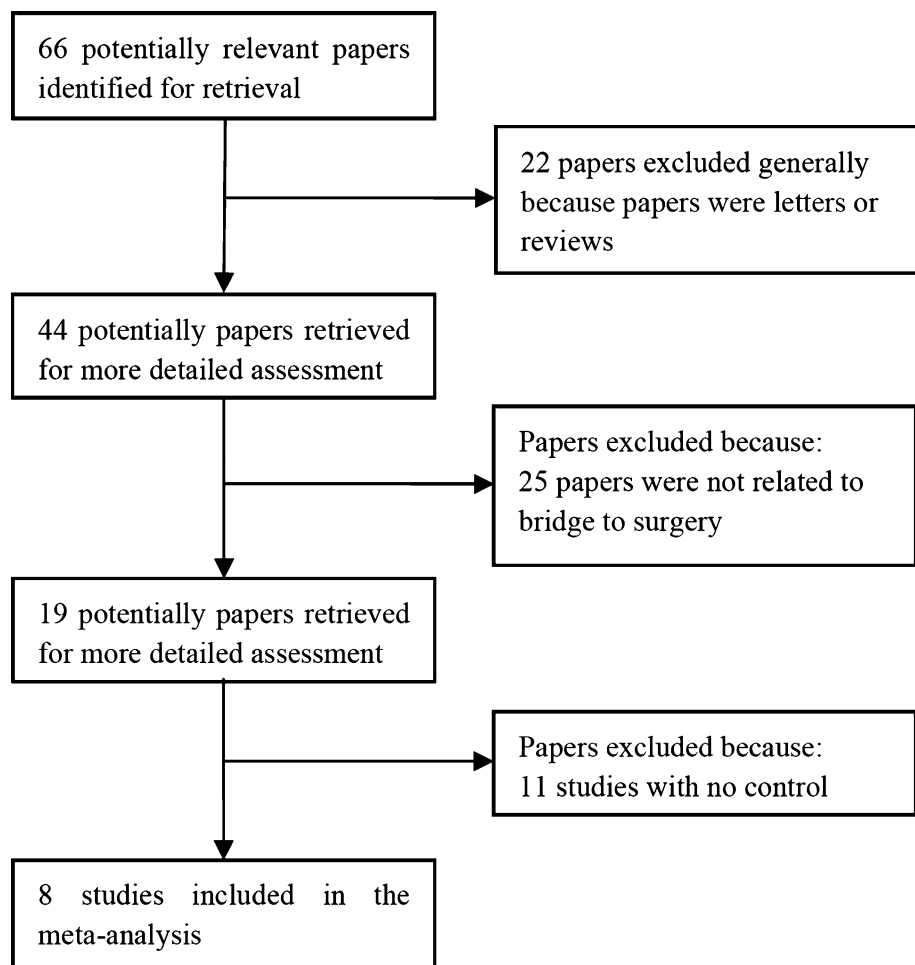


Table 1 Basic characteristics of included studies in meta-analysis

Study	Year	Design	SBTS	Stent success [n (%)]	ES	Types of surgery after stent insertion	Matching ^a	Female [n (%)]	Study quality (star rating) (max 11)
Saida [24]	2003	R	50	44 (88.0%)	40	O	1,2,3,6,8	39 (43.3%)	*****
Baik [25]	2006	R	18	18 (100%)	19	O	1,2,3,4	15 (40.5%)	*****
Ng [26]	2006	R	20	20 (100%)	40	O, L	1,2,3,5,6,8	14 (23.3%)	*****
Pessione [27]	2007	R	9	9 (100%)	7	O	1,2,3,4,5,8	5 (31.3%)	*****
Dastur [28]	2008	R	19	16 (84.2%)	23	O, L	1,2,3,4,5,6	18 (42.9%)	*****
Cheung [29]	2009	RCT	24	20 (83.3%)	24	L	1,2,3,5,7	22 (45.8%)	*****
Xu [30]	2010	R	62	61 (98.4%)	186	O	1,2,3,4,5	98 (39.5%)	*****
Pirlet [31]	2010	RCT	30	14 (47%)	30	O	1,2,3,4,7	31 (51.7%)	*****

R retrospective, RCT randomized controlled trial, O open, L laparoscopic, SBTS stent as bridge to surgery, ES emergency surgery

^a Matching: 1 = age, 2 = sex, 3 = diagnosis, 4 = tumor site, 5 = tumor stage, 6 = American Society of Anesthesiologists (ASA) score, 7 = body mass index (BMI), 8 = comorbidity

Table 2 Reported outcomes of the included studies

Outcomes	Saida [24]	Baik [25]	Ng [26]	Pessione [27]	Dastur [28]	Cheung [29]	Xu [30]	Pirlet [31]
Treatment details								
Length of hospital stay		✓	✓			✓		✓
ICU usage			✓		✓			
Primary anastomosis	✓		✓	✓	✓	✓	✓	✓
Stoma creation			✓	✓	✓	✓		✓
Short-term adverse events								
Mortality	✓	✓						
Medical complications	✓	✓	✓	✓		✓	✓	✓
Surgical complications	✓	✓	✓	✓	✓	✓	✓	✓
Stent-related complications	✓	✓	✓	✓	✓	✓	✓	✓
Long-term outcomes								
Permanent stoma						✓		✓
Survival	✓			✓	✓		✓	

short-term adverse events. Figure 3 is a forest plot of the meta-analysis of long-term survival.

Significantly fewer patients needed intensive care after treatment in the stent as a bridge to surgery group (RR, 0.42; 95% CI, 0.19–0.93; $p = 0.03$). The rate of primary anastomosis was significantly higher in the stent group (RR, 1.62; 95% CI, 1.21–2.16; $p = 0.001$), but this finding was associated with significant heterogeneity ($\chi^2 = 24.03$; $p = 0.0005$). The proportion of patients who underwent stoma creation was significantly lower in the stent group (RR, 0.70; 95% CI, 0.50–0.99; $p = 0.04$).

Meta-analysis of short-term adverse events

There was no significant difference in mortality between the two groups (RR, 0.73; 95% CI, 0.31–1.71; $p = 0.47$).

The overall complications were significantly lower in the stent group compared with the emergency surgery group (RR, 0.42; 95% CI, 0.24–0.71; $p = 0.001$), but this finding was associated with significant heterogeneity ($\chi^2 = 16.87$; $p = 0.010$). Anastomotic leakage rate was significantly lower in the stent group as well (RR, 0.31; 95% CI, 0.14–0.69; $p = 0.004$).

Meta-analysis of long-term outcomes

There was no difference between the two groups in regard to the chances of having a permanent stoma (RR, 0.39; 95% CI, 0.02–6.75; $p = 0.52$). However, this result should be interpreted with caution because studies that reported permanent stoma were poor. When overall survival was considered, no difference was observed between the two

Table 3 Meta-analysis of the included studies

	No. of studies	No. of patients	RR(95% CI)	<i>p</i> value
Treatment details				
ICU usage	2	102	0.42 (0.19, 0.93)	0.03
Primary anastomosis	7	558	1.62 (1.21, 2.16)	0.001
Stoma creation	5	226	0.70 (0.50, 0.99)	0.04
Short-term adverse events				
Mortality	5	426	0.73 (0.31, 1.71)	0.47
Overall complications	7	553	0.42 (0.24, 0.71)	0.001
Anastomotic leakage	6	303	0.31 (0.14, 0.69)	0.004
Long-term outcomes				
Permanent stoma	2	108	0.39 (0.02, 6.75)	0.52
1-year survival	4	390	1.07 (0.87, 1.31)	0.51
2-year survival	4	390	1.14 (0.98, 1.34)	0.10
3-year survival	3	374	1.08 (0.90, 1.31)	0.39

groups at 1 year (RR, 1.07; 95% CI, 0.87–1.31; $p = 0.51$), 2 years (RR, 1.14; 95% CI, 0.98–1.34; $p = 0.10$), and 3 years (RR, 1.08; 95% CI, 0.90–1.31; $p = 0.39$).

Publication bias

The funnel plots for the outcomes are shown in Fig. 4. These scatterplots were unequally distributed around the vertical axis, suggesting the possibility of publication bias.

Sensitivity analysis (Table 4)

Studies published in English

When the studies published in English were analyzed, the rate of primary anastomosis was significantly higher in the stent group (RR, 1.38; 95% CI, 1.18–1.61; $p < 0.0001$). There was no significant difference in mortality between the two groups. Although the overall complications were significantly reduced by stent insertion (RR, 0.38; 95% CI, 0.17–0.84; $p = 0.02$), the heterogeneity associated with this finding was significant ($\chi^2 = 15.88$; $p = 0.003$). The incidence of anastomotic leakage was lower in the stent group, but the difference did not reach statistical significance.

Studies containing more than 40 patients

In large studies, more patients underwent primary anastomosis in the stent group (RR, 1.56; 95% CI, 1.16–2.10;

$p = 0.004$), but this finding was associated with significant heterogeneity ($\chi^2 = 22.64$; $p = 0.0004$). The difference in mortality between the two groups did not reach statistical significance. Although the overall complications were significantly lower in the stent group (RR, 0.38; 95% CI, 0.19–0.75; $p = 0.005$), the heterogeneity associated with this finding was significant ($\chi^2 = 16.89$; $p = 0.002$). There were significantly fewer patients suffering anastomotic leakage in the stent group (RR, 0.31; 95% CI, 0.14–0.69; $p = 0.004$).

Studies that performed open surgery

In the studies that performed only open surgery in patients after stenting, the rate of primary anastomosis was significantly higher in the stent group (RR, 1.95; 95% CI, 1.36–2.80; $p = 0.0003$), but this finding was associated with significant heterogeneity ($\chi^2 = 8.44$; $p = 0.04$). There was no significant difference in mortality between the two groups. Although the overall complications were significantly lower in the stent group (RR, 0.46; 95% CI, 0.25–0.85; $p = 0.01$), the heterogeneity associated with this finding was significant ($\chi^2 = 11.59$; $p = 0.02$). The incidence of anastomotic leakage was significantly lower in the stent group (RR, 0.34; 95% CI, 0.14–0.85; $p = 0.02$).

Studies with patients matched for tumor site

In the studies that matched groups with respect to tumor location, significant benefits for patients who underwent stent insertion were found in terms of primary anastomosis (RR, 1.73; 95% CI, 1.01–2.95; $p = 0.04$), overall complications (RR, 0.56; 95% CI, 0.33–0.97; $p = 0.04$), and anastomotic leakage (RR, 0.36; 95% CI, 0.14–0.93; $p = 0.03$). There was no significant difference in mortality between the two groups. Only for primary anastomosis was there significant heterogeneity between the studies ($\chi^2 = 12.93$; $p = 0.005$).

Discussion

The conventional treatment for left-sided colorectal cancer with acute obstruction is Hartmann's procedure. However, stoma creation could induce discomfort, lifestyle change, increased health-care costs, and poor quality of life [10, 11]. In addition, bowel continuity is never restored in a substantial number of patients [4]. Although primary anastomosis could be performed as part of the emergency operation, the cases are often highly selected [32]. Therefore, most patients undergo Hartmann's procedure instead of primary anastomosis in the emergency setting.

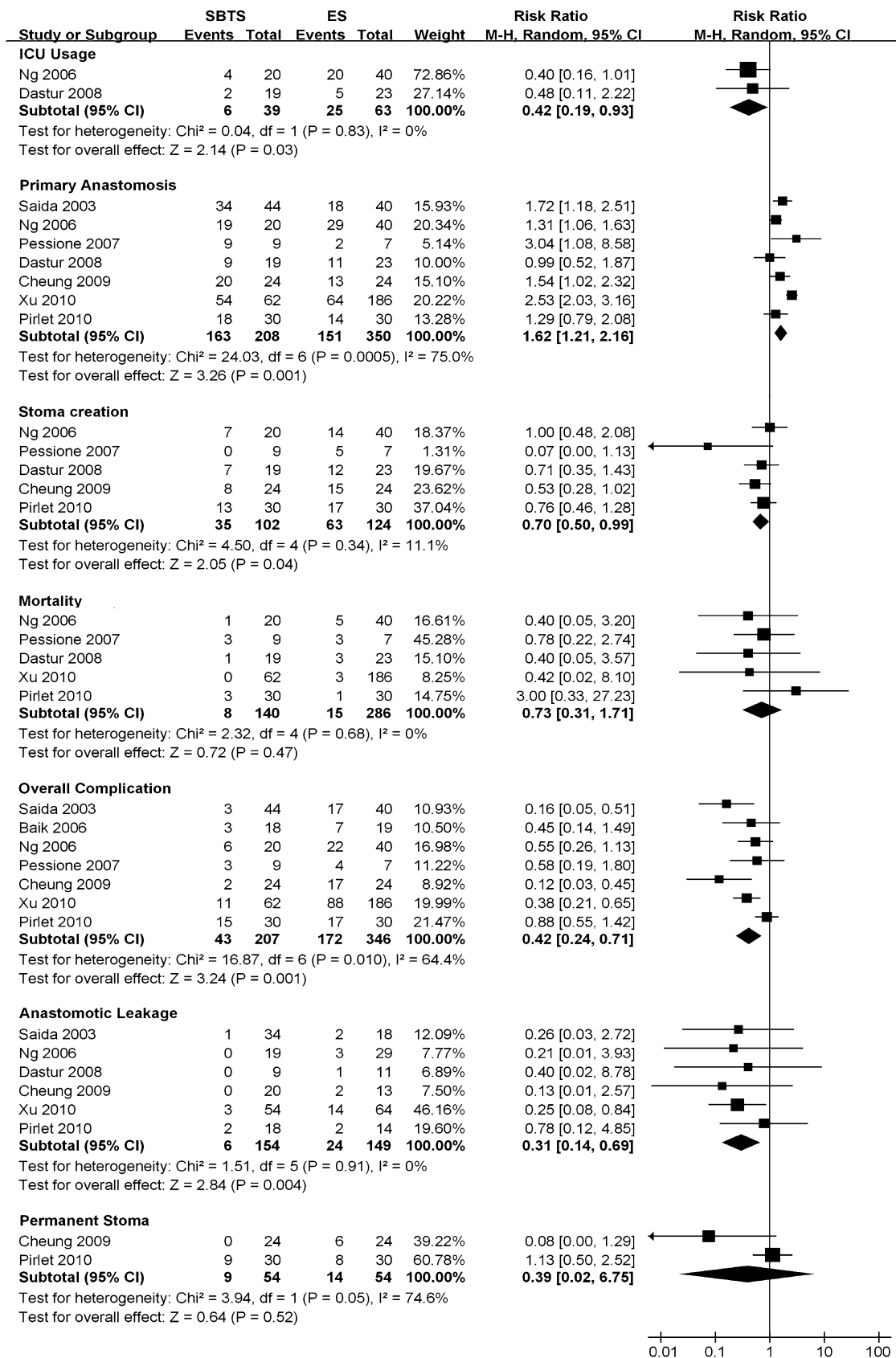


Fig. 2 Meta-analysis of permanent stoma and measures of treatment details and short-term adverse events

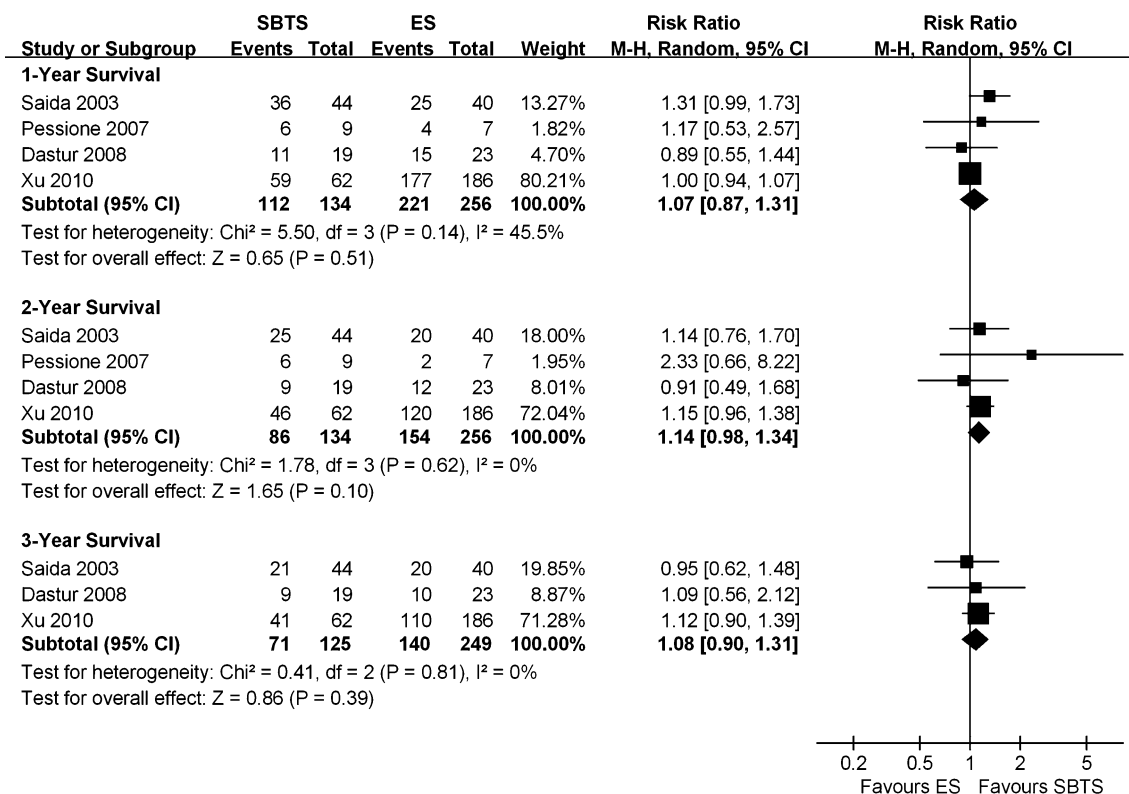


Fig. 3 Forest plot of the meta-analysis of long-term survival

As an alternative to urgent surgical decompression, SEMS could relieve the obstruction and enable elective resection to be performed with optimal bowel preparation. The results of this meta-analysis showed that using SEMS as a bridge to surgery for obstructive colorectal cancer could significantly increase the primary anastomosis rate and reduce the stoma creation rate. However, most of the included studies did not describe whether the stomas created in the emergency setting were reversed, and only two studies reported permanent stoma [29, 31]. Thus, the current evidence might be not strong enough to decide whether the SEMS could reduce the need for permanent stoma.

The results of the present analysis illustrated that SEMS placement significantly decreased the overall complications compared with urgent surgery. Performing an emergency surgery on an obstructed colon is more difficult than an elective one, and usually associated with increased morbidity [33]. The conversion of an emergency operation to an elective one can be achieved by the insertion of a SEMS. The relief of symptoms provided by SEMS placement gives extra time to stabilize the patient, address underlying comorbid medical illnesses, and carry out a thorough tumor staging [34]. Consequently, patients could undergo subsequent surgery with adequate bowel preparation and in better physical condition, and recover from surgery with fewer short-term adverse events.

As one of the most serious postoperative complications, anastomotic leakage could increase postoperative mortality. Moreover, it has a negative influence on local tumor recurrence and long-term survival [35, 36]. The results of this meta-analysis of 303 patients who underwent primary anastomosis revealed that fewer patients suffered anastomotic leakage in the stent group.

Potential complications following attempted SEMS insertion include perforation, malposition, stent migration, reobstruction, bleeding, and tenesmus [37]. Perforation is the most severe complication because it could lead to postprocedural death and tumor dissemination. Seven perforations (1.2%) occurred in 232 patients in the included studies [25, 26, 28, 30, 31]. Balloon dilation was considered the most important factor associated with stent-related perforation and should be avoided [17]. However, a recent study found that histopathological and morphological items associated with a decrease in elastic compliance were more important as predictors of perforation than dilation procedure parameters [38].

In regard to perioperative mortality, this analysis did not reveal any significant difference between the two groups. The fact that preoperative SEMS insertion did not significantly reduce mortality is interesting to note because it is often considered to be one of the potential benefits of using SEMS as a bridge to surgery. However, it is difficult to comment on mortality for it is rarer than other short-term

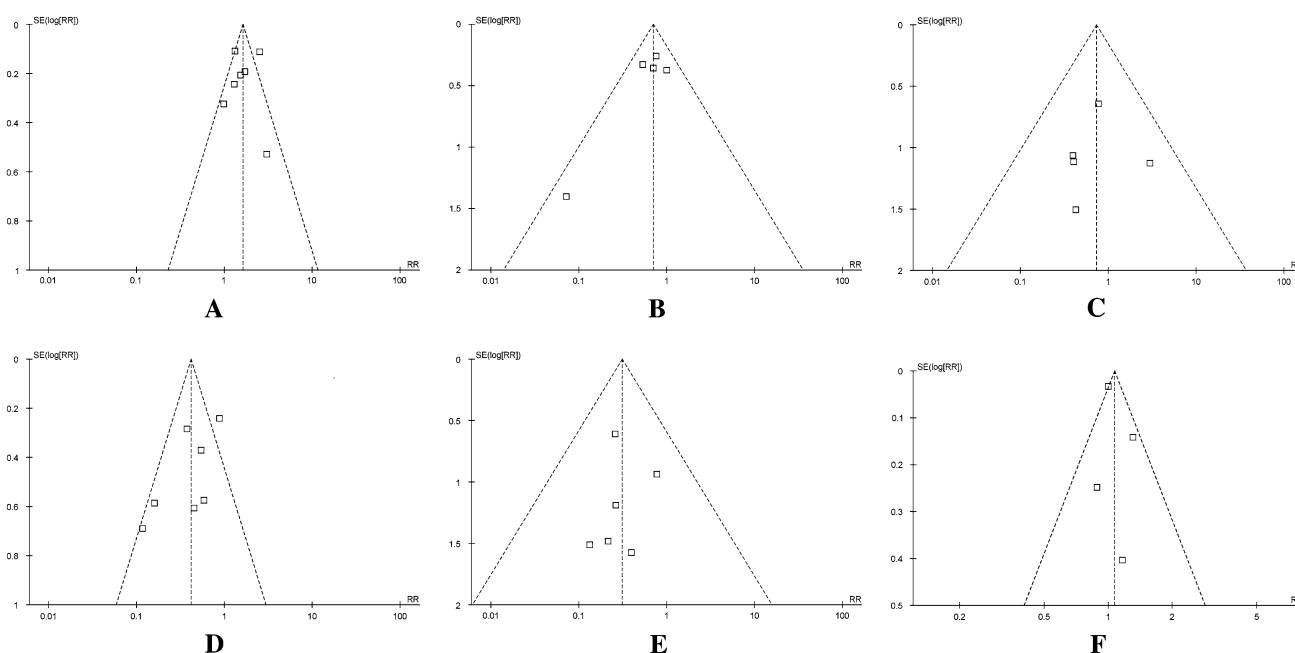


Fig. 4 Funnel plots of the included trials: **A** Primary anastomosis. **B** Stoma creation. **C** Mortality. **D** Overall complications. **E** Anastomotic leakage. **F** 1-year survival

Table 4 Sensitivity analysis of the included studies

	No. of studies	No. of patients	RR (95% CI)	<i>p</i> value
Studies published in English				
Primary anastomosis	5	294	1.38 (1.18, 1.61)	<0.0001
Mortality	3	162	0.76 (0.21, 2.79)	0.68
Overall complications	5	289	0.38 (0.17, 0.84)	0.02
Anastomotic leakage	5	185	0.36 (0.12, 1.10)	0.07
Studies containing more than 40 patients				
Primary anastomosis	6	542	1.56 (1.16, 2.10)	0.004
Mortality	4	410	0.70 (0.22, 2.19)	0.54
Overall complications	5	500	0.38 (0.19, 0.75)	0.005
Anastomotic leakage	6	303	0.31 (0.14, 0.69)	0.004
Studies including only open surgery				
Primary anastomosis	4	408	1.95 (1.36, 2.80)	0.0003
Mortality	3	324	0.97 (0.35, 2.70)	0.95
Overall complications	5	445	0.46 (0.25, 0.85)	0.01
Anastomotic leakage	3	202	0.34 (0.14, 0.85)	0.02
Studies with patients matched for site of tumor				
Primary anastomosis	4	366	1.73 (1.01, 2.95)	0.04
Mortality	4	366	0.83 (0.33, 2.09)	0.69
Overall complications	4	361	0.56 (0.33, 0.97)	0.04
Anastomotic leakage	3	170	0.36 (0.14, 0.93)	0.03

adverse events, and the sample size of the current analysis might be too small to detect the difference. This issue requires further large-size prospective randomized studies such as the Stent-in 2 study in process [39].

In the studies included in this meta-analysis, 30 patients underwent laparoscopic surgery after insertion of the stent, and only two of them required conversion to open surgery [26, 28, 29]. Apparently, laparoscopy-assisted colectomy is

associated with more favorable short-term outcomes and earlier postoperative recovery [40]. However, it is impossible to carry out such a procedure on patients with malignant left-sided colonic obstruction because of poor exposure and potential injury to the distended bowel. The successful decompression provided by SEMS insertion makes it possible to perform laparoscopic resection on patients with obstructive colorectal cancer. Although this minimally invasive surgery has an advantage with respect to short-term outcomes, its effect on long-term outcomes is uncertain and requires further study.

When s SEMS is used as a bridge to surgery, concern is raised 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 [41]. The results of the present analysis showed no significant difference in long-term survival between the patients who underwent preoperative stent insertion and those who had emergency surgery. These findings were consistent when subgroups of patients with Dukes B and C cancers were assessed [24].

Meta-analytic research such as this study has several limitations that must be taken into account. First, six of the eight studies included in this meta-analysis were retrospective and based on non-intention-to-treat analysis. Second, the two groups were not matched for all the factors, which might affect the results. Third, the included studies varied in selection criteria, treatment protocols, and operative techniques. 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 present meta-analysis illustrated that using SEMS as a bridge to surgery for obstructive colorectal cancer could increase the chance of primary anastomosis and reduce the need for stoma creation and overall complications. The insertion of SEMS followed by subsequent surgery has no effect on perioperative mortality and long-term survival.

Disclosure Yi Zhang, Jian Shi, Bin Shi, Chun-Yan Song, Wei-Fen Xie and Yue-Xiang Chen have no conflicts of interest or financial ties to disclose.

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