ORIGINAL CONTRIBUTION

Does Stenting as a Bridge to Surgery in Left-Sided Colorectal Cancer Obstruction Really Worsen Oncological Outcomes?

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BACKGROUND: Although self-expandable metal stents are used as a bridge to surgery in patients with colorectal cancer obstruction, their long-term oncological outcomes are unclear.

OBJECTIVE: The aim of this study was to investigate long-term oncological outcomes of self-expandable metal stents as a bridge to surgery (stent group) compared with direct surgery (direct operation group) in patients with left-sided colorectal cancer obstruction.

DESIGN: This was a retrospective chart review.

SETTINGS: This study was conducted at a single tertiary academic center.

PATIENTS: Of 113 patients who underwent curative surgery for left-sided colorectal cancer obstruction at Asan Medical Center between 2005 and 2011, 42 underwent direct surgery and 71 underwent self-expandable metal stent insertion followed by elective surgery. After 1:1 propensity-score matching, 42 patients were enrolled in both groups, and their postsurgical outcomes were compared.

MAIN OUTCOME MEASURES: The primary outcomes of this study were long-term oncological outcomes, including overall survival and recurrence-free survival of patients in both groups.

RESULTS: Three- and 5-year overall survival rates were similar in the stent (87.0% and 71.0%) and direct operation (76.4% and 76.4%) groups ($p = 0.931$). Three- and 5-year recurrence-free survival rates were also similar in the stent (91.9% and 66.4%) and direct operation (81.2% and 71.2%) groups ($p = 0.581$), as were postsurgical complication rates (9.5% and 16.7%; $p = 0.344$). No patient in either group experienced a permanent stoma.

LIMITATIONS: This study was limited by its small patient numbers and retrospective nature.

CONCLUSIONS: The long-term oncological outcomes of self-expandable metal stents as a bridge to surgery may not be inferior to those of direct surgery for left-sided colorectal cancer obstruction.

KEY WORDS: Colorectal cancer; Intestinal obstruction; Stents.

The incidence rates of colorectal cancer (CRC) in both men and women are rapidly increasing worldwide.[1,2] CRC presents with various symptoms and signs, including obstruction. The incidence of acute malignant colorectal obstruction requiring urgent decompression has been reported to range from 8% to 13%.[3–5]

Self-expandable metal stents (SEMSs) for colonic decompression were first introduced for palliative purposes in patients with obstructing rectal cancer.[6] Thereafter, indications of SEMSs have been expanded to their use as a bridge to surgery, relieving colonic obstruction before surgical resection.[7] In addition to relieving obstructions, SEMS insertion as a bridge to surgery can allow preoperative bowel preparation and make elective single-stage

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surgical resection possible without the need for temporary stoma formation. Because improvements in stent technology have increased the technical and clinical success rates of SEMSs to as high as 90%, these stents are more widely used in clinical practice, both for palliation and as a bridge to surgery.[8–10] However, it is still unclear whether SEMSs as a bridge to surgery benefit patients with left-sided CRC obstruction.[11–18]

Some previous studies suggested that SEMSs as a bridge to surgery may provide many advantages to patients with left-sided CRC obstruction, including lower rates of stoma formation, morbidity, and mortality, when compared with emergency surgery.[8,9,16,19,20] More recent studies, however, found that SEMSs as a bridge to surgery did not have any clinical advantages when compared with emergency surgery; rather, SEMSs may be more dangerous because of additional morbidity and poorer long-term oncological outcomes, such as shorter overall survival.[13,14,21] These inconsistent findings indicated the need for additional research on the usefulness of SEMSs as a bridge to surgery in patients with left-sided CRC obstruction. Therefore, this study investigated whether SEMSs as a bridge to surgery, followed by curative surgical resection, had survival advantages, including recurrence-free and overall survival, compared with direct surgery in patients who presented with acute left-sided CRC obstruction in a tertiary referral center.

PATIENTS AND METHODS

Patients

Patients who underwent surgical colorectal resection for left-sided CRC obstruction at Asan Medical Center between January 2005 and December 2011 were eligible for inclusion. The electronic medical and surgical databases were reviewed to identify these patients. Analysis included patient presentation and clinical history, information about SEMS insertion, surgical management, and clinical outcomes. Patients were excluded if they had undergone palliative surgery, inherited cancer syndromes such as Lynch syndrome and familial adenomatous polyposis, synchronous colon cancer, IBD-associated colon cancer or cancer in other organs, or if the follow-up period was <6 months. Patient physiological status and postoperative mortality were assessed using the French Association for Surgery score[22] and the ASA score.[23]

Patients were classified into 2 groups based on whether they underwent SEMS insertion as a bridge to surgery. The SEMS group included patients who underwent emergency SEMS insertion to achieve colonic decompression before surgery, followed by elective surgical colorectal resection, whereas the OP group included patients who underwent direct surgery without SEMS insertion.

Figure 1 presents an inclusion flowchart of our study population. The institutional review board of the Asan Medical Center approved this study (No. 2015-0843). Patients provided informed consent for all of the procedures.

Definition of Variables

Colonic obstruction was defined as a failure of passage of the endoscope through the cancer and clinical evidence of a symptom of obstruction (eg, abdominal pain or distension or new-onset constipation) or radiological evidence of obstruction, including the results of plain abdominal x-rays and/or CT scans (gaseous distension of the large and/or small bowel with or without air-fluid levels). *Overall survival* was defined as the time from the date of surgery to either death or the last follow-up visit. *Recurrence-free survival* was defined as the time from the date of surgery to either cancer recurrence or the last follow-up without recurrence.[24] *Technical success* was defined as successful deployment of the SEMS through the obstructive lesion, with radiological confirmation of well expansion of the stent and visible stool passage. *Clinical success* was defined as significant colonic decompression on abdominal x-ray or CT and relief of obstructive symptoms within 72 hours of SEMS placement without additional interventions.

One-stage operation was defined as a surgical procedure that consists of resection of primary CRC with anastomosis in a single session. *Two-stage operation* was defined as a surgical procedure that consists of a colostomy or ileostomy to resolve the obstruction as the first step followed by closure of the stoma at the next session with resection of primary CRC during either the first or second session according to the condition of the patient.

SEMS Insertion and Surgery

All of the SEMS insertion procedures were performed by board-certified gastroenterologists who had experienced at least 20 cases of colonic SEMS insertion. SEMS was inserted using a through-the-scope technique under fluoroscopic guidance. Plain abdominal x-rays were taken after the procedure and the following day to check stent expansion and adequate positioning.

All of the surgeries were performed by board-certified, experienced colorectal surgeons. The type of surgery and the extent of resection were determined by the surgeon, according to tumor location and stage and the general condition of the patient. The surgeon attempted to perform a single-stage operation with a primary anastomosis whenever possible. However, if primary anastomosis was not feasible, a diversion method was used.

The usual follow-up and surveillance strategy after surgery for CRC in our center was as follows. Total colonoscopy was performed within 6 months after surgery for obstructive CRC. Next, surveillance colonoscopies were performed within 3 years after surgery. Abdominopelvic and chest CT scans and serum CEA levels were checked yearly after CRC surgery. These systematic follow-up schedules were recom-

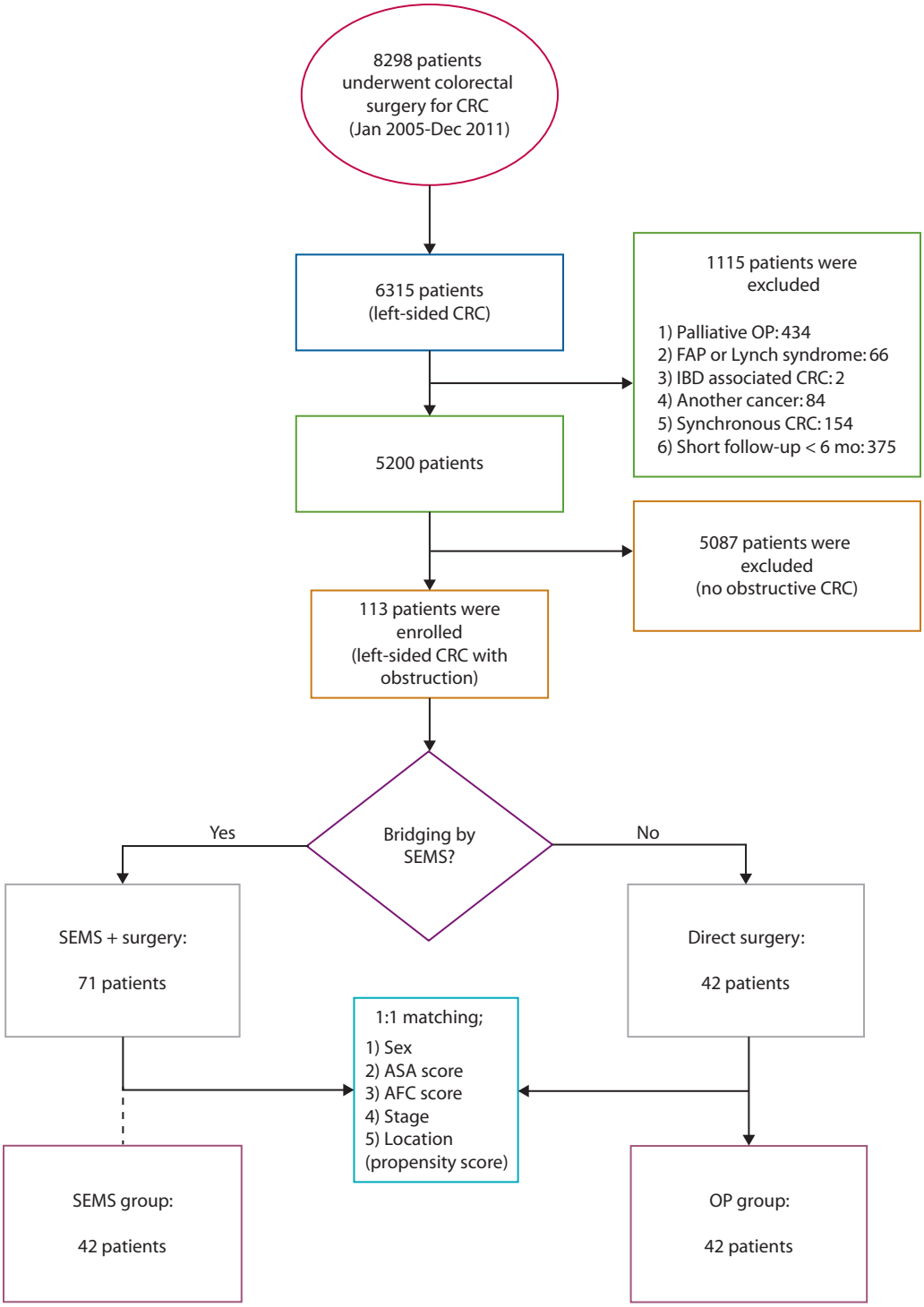

FIGURE 1. Patient selection flowchart. CRC = colorectal cancer; SEMS = self-expandable metal stent; AFC = French Association for Surgery; OP = emergency surgery; FAP = familial adenomatous polyposis.

mended in all of the CRC patients after surgery, although minor individualization could be permitted.

Outcome Measures

The primary outcomes of this study were long-term oncological outcomes, including overall survival and recurrence-free survival of the SEMS and OP groups. Secondary outcomes were short-term clinical outcomes, including overall periprocedural and postprocedural complication rates, temporary stoma creation rate at discharge, rates of 1-stage versus 2-stage operations for tumor resection, hospitalization period, and definitive stoma creation rate 1 year after diagnosis.

TABLE 1. Clinical characteristics of patients

Characteristics	Before propensity matching			After propensity matching		
	SEMS group (n = 71)	*OP group (n = 42)*	*p*	*SEMS group (n = 42)*	*OP group (n = 42)*	*p*
Age, median (IQR), y	66.0 (24.0)	60.0 (15.0)	0.104	62.0 (25.0)	60.0 (15.0)	0.232
Sex, n (%)			0.311			0.649
Men	37 (52.1)	26 (61.9)		28 (66.7)	26 (61.9)	
Women	34 (47.9)	16 (38.1)		14 (33.3)	16 (38.1)	
ASA fitness grade, n (%)			0.265			0.858
I	36 (50.7)	25 (59.5)		27 (64.3)	25 (59.5)	
II	28 (39.4)	15 (35.7)		12 (28.6)	15 (35.7)	
III	7 (9.9)	2 (4.8)		3 (7.1)	2 (4.8)	
AFC score, n (%)			0.178			0.647
0	29 (40.8)	23 (54.8)		23 (54.8)	23 (54.8)	
1	27 (38.0)	12 (28.5)		15 (35.7)	12 (28.5)	
2	13 (18.4)	7 (16.7)		4 (9.5)	7 (16.7)	
3	2 (2.8)	0 (0.0)		0 (0.0)	0 (0.0)	
4	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
TNM stage, n (%)			0.960			0.565
I	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
IIA	25 (35.2)	19 (45.2)		17 (40.5)	19 (45.2)	
IIB	3 (4.2)	3 (7.1)		1 (2.4)	3 (7.1)	
IIC	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
IIIA	23 (32.4)	5 (11.9)		16 (38.1)	5 (11.9)	
IIIB	13 (18.3)	5 (11.9)		5 (11.9)	5 (11.9)	
IIIC	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
IV	7 (9.9)	10 (23.9)		3 (7.1)	10 (23.9)	
Location of tumor, n (%)			0.008			0.369
Rectum	14 (19.7)	18 (42.9)		14 (33.3)	18 (42.9)	
Above rectum	57 (80.3)	24 (57.1)		28 (66.7)	24 (57.1)	
Primary tumor differentiation, n (%)			0.206			0.320
Poor	0 (0.0)	2 (4.8)		0 (0.0)	2 (4.8)	
Moderate	69 (97.2)	39 (92.9)		41 (97.6)	39 (92.9)	
Well	2 (2.8)	1 (2.4)		1 (2.4)	1 (2.4)	
Adjuvant chemotherapy, n (%)	43 (60.6)	31 (73.8)	0.152	24 (57.1)	31 (73.8)	0.108
Follow-up, median (IQR), mo	43.2 (30.0)	52.8 (35.1)	0.592	42.1 (24.8)	52.8 (35.1)	0.440

IQR = interquartile range; AFC = French Association for Surgery.

Statistical Analysis

Data analyses were performed with SPSS software (IBM SPSS Statistics for Windows, version 21.0. IBM Corp, Armonk, NY). Continuous variables were compared using 2-tailed Student *t* tests, and categorical variables were compared using 2-tailed χ^2 tests or Fisher exact tests. Survival outcomes were determined by the Kaplan–Meier method and compared using log-rank tests. *p* values <0.05 were considered statistically significant.

Propensity Score Matching

The distribution of baseline covariates between the SEMS and OP groups was not the same, making it difficult to compare the 2 groups. Comparability was improved by propensity score matching, using the following as variables: sex, tumor location (rectum vs above the rectum), and TNM stage according to the 7th American Joint Committee on Cancer and French Association for Surgery and ASA scores. After estimating propensity scores, participants were matched based on a 1:1 nearest-neighbor algorithm by SPSS software. This resulted in 42 matched pairs without large imbalances ($|d| > 0.25$) in the covariates used (Fig. 1).

RESULTS

Baseline Patient Characteristics

Of 8298 patients who underwent surgery for CRC at our center between January 2005 and December 2011, 113 fulfilled the eligibility criteria, including the strict definition of bowel obstruction. Of these 113 patients with left-sided CRC obstruction, 71 underwent SEMS as a bridge to surgery, followed by elective surgical resection, and 42 underwent direct surgery. After 1:1 propensity-score matching, 42 matched pairs were identified, with 42 patients each in the SEMS and OP groups (Fig. 1). The demographic characteristics of these 42 matched pairs are summarized in Table 1. After the propensity matching, pathological tumor stage, tumor differentiation, tumor location, and the percentage receiving adjuvant chemotherapy were comparable in the 2 groups, as was follow-up duration. The median follow-up period of the

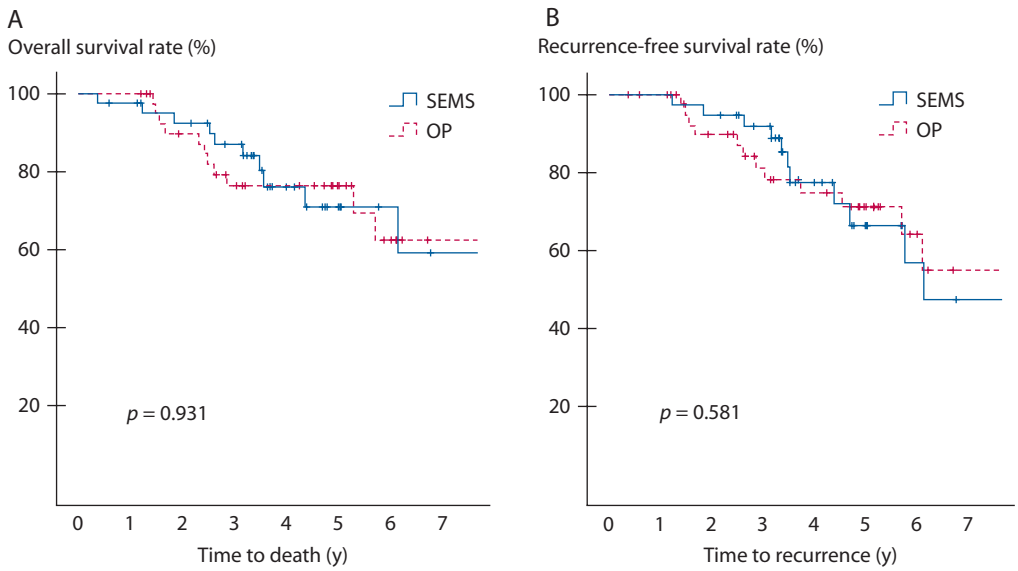

FIGURE 2. Kaplan–Meier curves of overall survival and recurrence-free survival in the self-expandable metal stent (SEMS) and emergency surgery (OP) groups.

84 patients was 44 months, and the follow-up duration of each group is presented in Table 1.

Oncological Outcomes

All of the patients enrolled in this study were included in the outcome analysis. Those who were not decompressed by SEMS and who developed perforation after SEMS were included in the SEMS group in intent-to-treat analyses. The 3- and 5-year overall survival rates were similar in the SEMS (87.0% and 71.0%) and OP (76.4% and 76.4%) groups ($p = 0.931$; Fig. 2A). Similarly, the 3- and 5-year recurrence-free survival rates were similar in the SEMS (91.9% and 66.4%) and OP (81.2% and 71.2%) groups ($p = 0.581$; Fig. 2B).

Procedure-Related Secondary Outcomes

Only 1 of the 42 patients in the SEMS group experienced a technical failure of the SEMS, making the technical success rate 97.6%. The clinical success rate of SEMS was 92.9%. SEMS-associated perforation occurred in 2 patients (4.8%). Elective surgery was performed a median 13.5 days (interquartile range, 11.0 days) after SEMS insertion.

Analysis of CRC surgery showed that 37 (88.1%) in the SEMS group and 41 (97.6%) in the OP group underwent open surgeries ($p = 0.090$; Table 2). Temporary stomas were created in 3 (7.1%) and 6 patients (14.3%) in the SEMS and OP groups ($p = 0.483$), because of dilated, insufficiently decompressed bowel. There were no difficulties in surgical procedures related to the inserted SEMS. Three patients in the SEMS group and 6 in the OP group required 2-stage operations, a difference that was not statistically significant ($p = 0.483$). No patient in either group required definite stoma formation (Table 2). Postsurgical complication rates were similar in the SEMS and OP groups (9.5% vs 16.7%; $p = 0.344$). The need for postoperative admission to the intensive care unit and the median length of hospital stay after surgery were similar in the 2 groups (Table 2). Of patients who received adjuvant chemotherapy, median time intervals between surgery and adjuvant chemotherapy were similarly 25 days in both groups ($p = 0.980$).

DISCUSSION

The management of acute malignant colonic obstruction is complicated and difficult because many patients are elderly and have multiple comorbidities. A dilated ischemic bowel with accumulated feces may increase the rates of postoperative morbidity, including stoma formation, and mortality. SEMS insertion as a bridge to surgery has been reported to reduce postoperative morbidity and postsurgical complication rates, suggesting that SEMSs be inserted before surgery in patients with left-sided CRC obstruction.[25–28] European Society of Gastrointestinal Endoscopy guidelines, however, do not recommend SEMS insertion as a bridge to surgery in patients with left-sided CRC obstruction unless they have an increased risk of postoperative mortality (ASA status ≥III and/or age >70 years),[29] because of poor long-term oncological outcomes. For example, a retrospective comparative study found that the 5-year overall survival rate was significantly lower (25% vs 62%; $p < 0.001$), and the 5-year cancer-specific mortality rate was significantly higher (48% vs 21%; $p = 0.02$), in the SEMS group than in the emergency surgery group.[21] Another randomized controlled trial found that the 5-year overall recurrence rate was higher in the SEMS group than in the emergency surgery group (42% vs 25%; $p = 0.027$).[29] A recent, Danish cohort analysis also showed that SEMSs

TABLE 2. Procedure-related outcomes

Variables	SEMS group (n = 42)	OP group (n = 42)	p
Technical success rate, n (%)	41 (97.6)	–	
Clinical success rate, n (%)	39 (92.9)	–	
Complication, n (%)			
Perforation	2 (4.8)	–	
Migration	0 (0.0)	–	
Stent to surgery, n (IQR), d	13.5 (11.0)	–	
CRC surgery-related outcomes			
Operation type, n (%)			0.090
Open	37 (88.1)	41 (97.6)	
Laparoscopic	5 (11.9)	1 (2.4)	
Operation method, n (%)			
1-stage operation	39 (92.9)	36 (85.7)	0.483
2-stage operation	3 (7.1)	6 (14.3)	0.483
Stoma, n (%)			
Temporary	3 (7.1)	6 (14.3)	0.483
Definite	0 (0.0)	0 (0.0)	1.000
Harvested lymph nodes, n (IQR)	28 (14.0)	20 (14.0)	0.017
Postoperative ICU care, n (%)	7 (16.7)	4 (9.5)	0.520
Complication, n (%)	4 (9.5)	7 (16.7)	0.344
Ileus	2 (4.8)	3 (7.1)	
Acute kidney injury	0 (0.0)	1 (2.4)	
Anastomosis site leak	1 (2.4)	0 (0.0)	
Postoperative bleeding	1 (2.4)	0 (0.0)	
Wound dehiscence	0 (0.0)	3 (7.1)	
Hospitalization period after surgery, n (IQR), d	8.0 (4.0)	10.0 (4.0)	0.513

SEMS = self-expandable metal stent; IQR = interquartile range; CRC = colorectal cancer; ICU = intensive care unit.

might be associated with an increased CRC recurrence, although long-term overall mortality was comparable between SEMS and urgent resection.[17]

Other studies, however, showed contrary results. For example, in a long-term follow-up analysis of a randomized trial, the 5-year overall survival (48% vs 27%; $p = 0.076$) and disease-free survival rates (52% vs 48%; $p = 0.63$) were similar in the SEMS and emergency surgery groups.[30] In another prospective comparative study, overall survival rates did not differ, with disease-free periods in the SEMS and emergency surgery groups of 25.5 and 27.1 months ($p = 0.096$).[31] Moreover, a prospective cohort study that enrolled 62 patients who underwent preoperative SEMS insertion and 43 who underwent emergency surgery and who were followed-up for a median 2.7 and 2.8 years found that the overall recurrence (32% vs 28%; $p = 0.824$), overall mortality (29% vs 44%; $p = 0.215$), and cancer-specific mortality rates (24% vs 37%; $p = 0.180$) were similar.[32] Finally, a recent meta-analysis also showed that both overall survival and recurrence did not differ between the SEMS and emergency surgery groups.[18] These findings suggest the importance of re-evaluating the clinical value of SEMSs as a bridge to surgery in various clinical situations.

The reasons for the discrepancies among studies are unclear. Follow-up analysis of patients who underwent SEMS insertion in the Stent-in 2 trial found that the recurrence rate was higher in patients with than without perforation (5/6 (83%) vs 8/20 (40%)).[33] In a study reporting that SEMSs as a bridge to surgery were associated with poor overall survival, perforation was an independent risk factor for poor overall survival.[21] In our study, all of the SEMSs were inserted by board-certified, experienced gastroenterologists. The technical and clinical success rates were 97.6% and 92.7%, higher than in previous studies of SEMS (64%–100% and 46%–100%).[8,9,16,34–36] Perforation occurred in only 2 patients (4.8%). These findings indirectly suggest that the SEMS insertion procedure in our center may be technically optimal and that careful SEMS insertion without perforation may avoid extra risks of cancer dissemination and achieve the same oncological outcomes as surgery without SEMS insertion. Regarding the relation between perforation and poor oncological outcomes, one may argue that late perforation after SEMS insertion may further deteriorate the oncological outcome.[15] However, surgical resection is followed usually 1 to 2 weeks after SEMS insertion and the late perforation may not be an important concern in the bridge-to-surgery setting.

In the era of contradictory data, which option should we choose regarding the management of left-sided CRC obstruction? The quality of individual centers may be the most important factor. For example, SEMS as a bridge to surgery may be a good option in centers with high-level endoscopists equipped with good-quality SEMS insertion devices. By contrast, emergency surgery may be a better option in centers optimized for colorectal surgery with a good postoperative care team. In addition, European Society of Gastrointestinal Endoscopy guidelines have suggested that patients at high surgical risk, including older patients and those with serious comorbidities, may benefit from SEMS because of the high risk of postoperative complications.[29]

In the present study, unlike previous meta-analyses, the SEMS group did not show superior short-term outcomes compared with the OP group, including in rates of 1-stage operation, stoma creation, and postsurgical complications.[8,9,16,34–36] This may be because of the small sample size and number of events or the highly specialized CRC surgical teams in our center. These teams, composed of board-certified, experienced colorectal surgeons, specialized nurses, anesthesiologists, and intensive care physicians, perform more than 1000 CRC surgeries per year. A specialized team approach with high-volume experience may improve surgical outcomes, even in patients who undergo emergency surgery without SEMS insertion. We suggest that the temporary stoma rate of the OP group in this study was only 14.3% for this reason, although other factors, such as the trial of natural decompression with or without cautious bowel preparation for several days in

some stable patients, might also contribute to the low temporary stoma rate. We believe that no creation of definite, permanent stoma in any patients was also related to the high quality of our surgical team, although earlier takedown of the temporary stoma in several months, which is a short time for disease progression, might be another reason. Anyhow, given the findings from the high-quality endoscopists and surgery team in our center, the generalization of our findings should be further evaluated by multicenter trials, which may minimize the bias related to the procedural quality.

This study had several limitations. First, it was a retrospective, nonrandomized study, which may be associated with difficulty in minimizing bias. For example, there could be a selection bias regarding how patients were selected for either the SEMS or OP group. In addition, despite the propensity matching, the 2 groups appeared to be numerically different in several respects, such as tumor stage and the frequency of adjuvant chemotherapy, although statistical significance was absent (Table 1). Second, the number of participants was small, which may have contributed to the absence of a statistically significant difference in survival rates between 2 groups. Finally, this study was conducted in a single, high-volume, experienced center. Some of these limitations could be overcome by propensity-score matching, thus minimizing the risk of selection bias. However, prospective, large-scale, multicenter studies are needed to assess and compare long-term oncological outcomes after SEMS as a bridge to surgery with emergency surgery more objectively and precisely.

CONCLUSION

These findings suggest that, if inserted cautiously by qualified endoscopists, an SEMS as a bridge to surgery does not have deleterious effects on long-term oncological outcomes in patients with left-sided CRC obstruction and can achieve similar outcomes to the direct surgery.

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