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Comparison of treatment outcomes of endoscopic stenting for colonic and extracolonic malignant obstruction

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Abstract
Background Self-expandable metal stents (SEMS) have been used as a bridging or palliative treatment for malignant colorectal obstruction. Colonic obstruction also may arise from advanced extracolonic malignancy, but the clinical outcomes of stent placement for extracolonic malignancy are unclear. This study compared the clinical outcomes of SEMS between patients with colorectal cancer and those with extracolonic malignancy.
Methods Patients who underwent endoscopic SEMS placement for a malignant colorectal obstruction were enrolled at Seoul National University Hospital from April 2005 and August 2011. Their medical records were retrospectively reviewed in terms of success rate, complications, and duration of stent patency.
Results Endoscopic SEMS placements were performed for colorectal cancer in 149 patients and for extracolonic malignancy in 60 patients. The causes of obstruction in extracolonic malignancy were advanced gastric cancer in 39 patients (65 %), pancreatic cancer in nine patients (15 %), ovarian cancer in three patients (5 %) and other causes in nine patients (15 %). The clinical success rates were similar between the two groups (92.6 vs 86.7 %; $p = 0.688$), and multivariate analysis showed no significant risk factor for unsuccessful endoscopic SEMS placement. Reobstruction in palliative endoscopic SEMS placement occurred for 16 patients with colorectal cancer (21.9 %) and 18 patients with extracolonic malignancy (30 %) during a median follow-up period of 90 days ($p = 0.288$). The rates did not differ significantly between the two groups (4.1 vs 8.3 %; $p = 0.467$). The median duration of stent patency was 193 ± 42 days for the patients with colorectal cancer and 186 ± 31 days for the patients with extracolonic malignancy ($p = 0.253$). The duration of stent patency was not affected by underlying malignancy, previous surgery, or palliative chemotherapy.
Conclusions Endoscopic SEMS placement is highly effective and comparable for palliation of obstruction in extracolonic malignancy and colorectal cancer in terms of clinical success, complications, and duration of patency.

Keywords Extracolonic malignancy · Malignant colonic obstruction · Outcomes · Self-expandable metal stents · SEMS

Acute colorectal obstruction usually requires rapid bowel decompression for prevention of strangulation or perforation. However, emergent surgery is associated with relatively high morbidity and mortality rates [1–4]. Since the introduction of a self-expandable metallic stent (SEMS) for the treatment of malignant colorectal obstruction [5], SEMS has been used as an alternative option for the treatment of acute colorectal obstruction in place of emergent surgery.

To date, SEMS usually has been used as a bridge therapy for a single-stage surgical resection or as a palliative measure for patients with advanced obstructions [6]. Colonic obstructions also occur due to direct tumor invasion, peritoneal seeding, or extraluminal compression resulting from advanced extracolonic malignancy (ECM).

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Because the characteristics of malignancy and the patterns of obstruction differ in many ways between colorectal cancer (CRC) and ECM [7, 8], the clinical results of SEMS insertion may differ between CRC and ECM. Patients with advanced ECM often have complex strictures of the gut, potentially at more than one location. They also may have simple or complex adhesions because of prior debulking surgery, radiotherapy, or both. In addition, it may be difficult to fix a stent to the wall of the lumen in extrinsic compression.

However, few data have been reported to date on the outcomes of SEMS used to treat colorectal obstruction by ECM. This study aimed to compare the clinical outcomes including clinical success rates, complications, and stent patency duration of colorectal stenting between patients with CRC and those with ECM.

Materials and methods

Patients

The endoscopy database at Seoul National University Hospital was used between April 2005 and August 2011 for procedures in which SEMS was placed for malignant colonic obstruction. Placement of SEMS was considered for preoperative colonic decompression in cases of potentially resectable colon cancer and for palliation of one-point symptomatic malignant colonic obstruction in cases of unresectable or inoperable disease.

We retrospectively reviewed the pathologic, surgical, and colonoscopic reports as well as the medical records of 209 consecutive patients. The current study was approved by the ethics committee of the Seoul National University Hospital (IRB no. H-1108-042-372) and performed in accordance with the Declaration of Helsinki.

Procedure details

Before SEMS placement, the site, degree, and length of obstruction were assessed by conventional computed tomography (CT), three-dimensional CT colonography, colonoscopy, and/or water-soluble contrast enema. Stent size (diameter, 18–25 mm) and length (80–170 mm) were chosen according to the measured lengths of obstructions (M.I. Tech, Seoul, Korea). The length of the stent was chosen to be at least an additional 3 cm on each side of the obstruction to allow for adequate margins.

Generally, patients underwent cleansing enemas for bowel preparation and were maintained under conscious sedation with intravenous 0.05 mg/kg midazolam. All procedures were performed under endoscopic guidance using a conventional endoscope (CF-H260; Olympus, Tokyo, Japan) with or without fluoroscopic guidance. After SEMS placement, adequate positioning and expansion of the stent were confirmed by simple abdomen radiography [9].

Clinical outcomes

Technical success was defined as successful deployment of the stent across the stricture. Clinical success was defined as the relief of obstructive symptoms and the recovery of normal bowel function without complication. Immediate mortality was defined as death within 10 days, and procedure-related death was defined as death directly related to complications from the procedure. Duration of stent patency was defined as the period between stent placement and recurrence of obstructive symptoms caused by tumor overgrowth, ingrowth, or stent migration, confirmed either endoscopically or radiologically.

Statistical analysis

Statistical analysis was performed using the SPSS 16.0 statistical package (SPSS, Chicago, IL, USA). Patient demographics and clinical characteristics were described by means and ranges. Comparisons of means for continuous variables between the CRC and ECM groups were performed by using Student's t test or nonparametric tests when appropriate. Differences in outcomes between the patient groups were compared using the chi-square test or Fisher's exact test. To identify independent influential factors of clinical success rates and complications, multivariate logistic regression models were fitted. The Kaplan-Meier method was used to compare durations of stent patency. All p values <0.05 were considered statistically significant.

Results

Baseline characteristics

In 209 patients, malignant colorectal obstruction had been treated with 211 SEMS placements, and two patients with long-segment obstruction had received two stents. Endoscopic SEMS placement was performed for CRC in 149 patients (71.3 %) and for ECM in 60 patients (28.7 %). It was offered as a bridging therapy before a curative operation for 76 patients and as an alternative therapy to surgery for the remaining patients. The mean follow-up period for the palliative treatment group was 206.86 days, and the median follow-up period was 90 days (range, 0–1,621 days) (Table 1).

Table 1 Baseline characteristics

	CRC ($n = 149$)	ECM ($n = 60$)	p Value
Patient demographics			
Mean age (years)	65.66 ± 12.57	58.08 ± 12.22	0.000
Women: n (%)	48 (32.2)	29 (48.3)	0.029
Coexisting medical morbidities			
Hypertension	57	7	0.000
Pulmonary disease	4	1	1.000
Diabetes	30	8	0.249
Renal disease	4	1	1.000
Cardiovascular disease	14	0	0.012
Purpose of procedure			
Bridge to surgical resection	76	0	
Palliation	73	60	
Treatment history			
Prior chemotherapy	23	45	0.000
Prior radiotherapy	5	2	1.000
Prior major abdominal surgery	25	41	0.000
Post chemotherapy	38/73[a]	32/60[a]	0.883
Stricture location			0.000
Rectum	38	15	
RS junction/sigmoid colon	19/61	2/6	
SD junction/ descending colon	9/7	2/7	
Splenic flexure/ transverse colon	3/5	17/7	
Hepatic flexure/ ascending colon	6/1	3/1	
Stent diameter (mm)			0.344
18	1	0	
20	0	1	
22	113	48	
24	30	11	
25	5	0	
Stent length (mm)			0.810
80	4	2	
100	6	2	
120	27	8	
140	15	7	
150	5	0	
160	91	41	
170	1	0	

CRC colorectal cancer, *ECM* extracolonic malignancy, *RS* rectosigmoid, *SD* sigmoid-descending

[a] Palliative only

The CRC group was significantly older than the ECM group ($p < 0.001$) and had significantly fewer women ($p = 0.029$). The coexisting medical comorbidities were similar between the two groups except for hypertension and cardiovascular disease. Prior abdominal surgery and chemotherapy were more frequent in the ECM group. The proportion of patients who had undergone prior radiation therapy did not differ between the two groups.

The obstruction sites were the rectum in 53 patients (25.4 %), the rectosigmoid junction or sigmoid colon in 88 patients (42.1 %), the descending colon in 25 patients (12 %), the splenic flexure or transverse colon in 32 patients (15.3 %), and the hepatic flexure or ascending colon in 11 patients (5.3 %). Strictures in the rectosigmoid junction and sigmoid colon were more common in the CRC group, whereas strictures in the splenic flexure and transverse colon were more common in ECM group. Stricture length, estimated from stent length, was similar in the two groups. In most cases, uncovered stents (diameter, 18, 20, 22, 24, or 25 mm) were used except in only one patient with an advanced rectal cancer. The causes of obstruction in ECM were advanced gastric cancer in 39 patients (65 %), pancreatic cancer in nine patients (15 %), ovarian cancer in three patients (5 %), and other causes in nine patients (15 %) (Table 2).

Procedure outcomes and complications

The CRC group had one technical failure of stent deployment compared with three failures in the ECM group. The clinical success rates were similar in the two groups (92.6 vs 86.7 %; $p = 0.688$) (Table 3). The most common complication was reobstruction, which occurred in 16 CRC cases (21.9 %) and 18 ECM cases (30 %). Three of four cases of migration in the CRC group were spontaneous removal due to tumor regression after chemotherapy.

Perforation occurred in three CRC cases and five ECM cases. Only one case of procedure-related perforation occurred in the ECM group. In the remaining cases,

Table 2 Extracolonic malignancy ($n = 60$)

	n (%)
Advanced gastric cancer	39 (65.0)
Pancreatic cancer	9 (15.0)
Ovarian cancer	3 (5.0)
Bladder cancer	2 (3.3)
Breast cancer	2 (3.3)
Duodenal cancer	1 (1.7)
Klatskin tumor	1 (1.7)
Endometrial cancer	1 (1.7)
ACUP	1 (1.7)
Prostate cancer	1 (1.7)

ACUP adenocarcinoma of unknown primary

Table 3 Clinical outcomes and complications

Clinical outcomes	CRC ($n = 149$) n (%)	ECM ($n = 60$) n (%)	p Value
Technical success	149/150[a] (99.3)	60/63[a] (95.2)	0.079
Clinical success	138 (92.6)	52 (86.7)	0.688
Complication	**Stage 4 CRC ($n = 73$)**	**ECM ($n = 60$)**	
Reobstruction	16 (21.9)	18 (30.0)	0.288
Migration	4 (5.5)[b]	1 (1.7)	0.378
Perforation	3 (4.1)	5 (8.3)	0.467
Immediate mortality (<10 days)	2 (2.7)	2 (3.3)	1.000

CRC colorectal cancer, *ECM* extracolonic malignancy

[a] Location of stricture in technical failure: sigmoid-descending junction in the CRC group; sigmoid-descending junction, splenic flexure, and midtransverse colon in the ECM group

[b] Three cases had spontaneous removal due to tumor regression after chemotherapy

perforation was caused by disease progression or tumor regression after chemotherapy.

Two patients in each group died of septic shock within 10 days after the procedure, but no death was directly related to the endoscopic procedure. The rate for complications from SEMS placement did not differ statistically between the two groups (Table 3).

According to univariate analysis, the significant risk factors for unsuccessful endoscopic SEMS placement were purpose of the procedure, peritoneal carcinomatosis, and history of prior major abdominal surgery ($p < 0.05$). But multivariate analysis showed no significant risk factor for failed endoscopic SEMS placement (Table 4). However, multivariate analysis showed that a history of prior radiotherapy and a history of postchemotherapy and stenting for the right colon (proximal to splenic flexure) were significant risk factors for complications (Table 5).

Duration of stent patency

The median duration of stent patency was 193 ± 42 days (range, 110–276 days) in the CRC group and 186 ± 32 days (range, 124–248 days) in the ECM group.

Table 4 Multivariate analysis of risk factors for unsuccessful endoscopic stenting

Risk factor	Hazard ratio (95 % CI)	p Value
Age ≥ 65 years	0.353 (0.480–4.218)	0.524
Extracolonic malignancy	0.000 (0.268–3.733)	0.999
Prior chemotherapy	0.089 (0.301–3.964)	0.893

CI confidence interval

Table 5 Multivariate analysis of risk factors for complications

Risk factor	Hazard ratio (95 % CI)	p Value
Extracolonic malignancy	0.113 (0.467–2.683)	0.800
Prior radiotherapy	1.853 (1.008–40.390)	0.049
Postchemotherapy	0.888 (1.090–5.421)	0.030
Stenting for right colon	1.168 (1.254–8.244)	0.015

CI confidence interval

Survival analysis did not show a significant difference in duration of stent patency between the two groups ($p = 0.253$) (Fig. 1) nor a significant effect by previous surgery or palliative chemotherapy. Survival analysis for advanced gastric cancer to determine the effect of underlying malignancy on duration of stent patency also did not show a significant difference between advanced gastric cancer and the remaining cases ($p = 0.327$) (Fig. 2).

Discussion

Endoscopic SEMS placement has been an established, safe, and effective method to palliate acute large bowel obstruction from CRC or to allow bowel decompression for a subsequent elective surgical resection [10, 11]. However, the clinical outcomes of SEMS in the treatment of colorectal obstruction by ECM have not been fully clarified compared with CRC [12–14].

In a metanalysis of palliative colonic SEMS placement, the clinical success rate was 91 % [15], and in a prospective multicenter study of palliative colonic SEMS placement, the success rate reached 95 % [16]. However, the clinical success rates for colorectal SEMS placement in

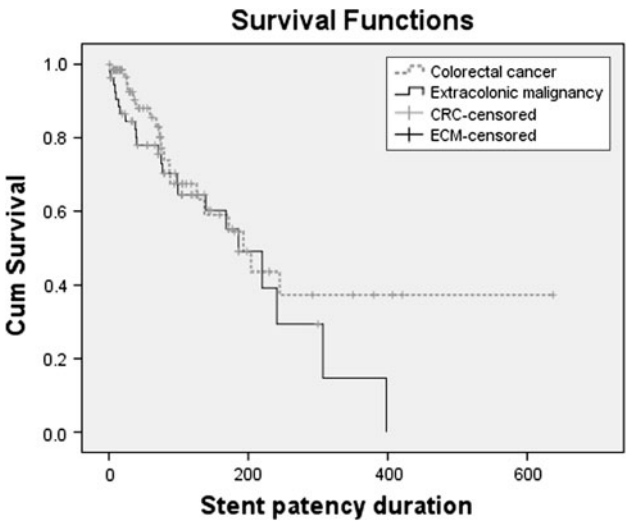

Fig. 1 Kaplan-Meier curve of stent patency according to underlying malignancy: colorectal cancer versus extracolonic malignancy

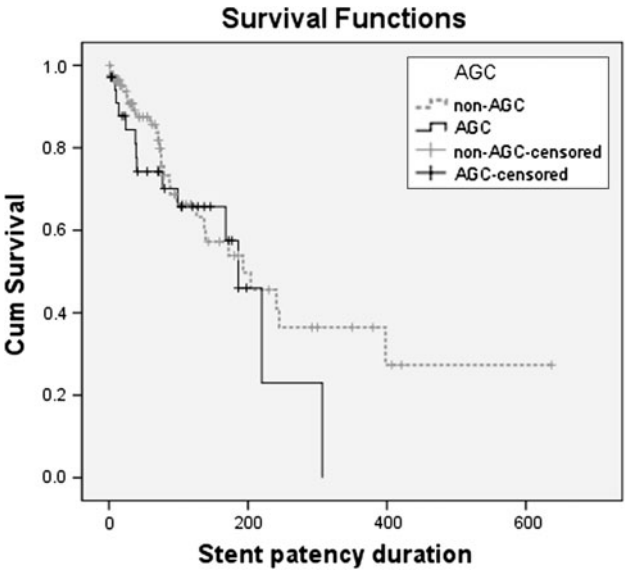

Fig. 2 Kaplan-Meier curve of stent patency according to underlying malignancy: advanced gastric cancer versus other malignancy except advanced gastric cancer

ECM have varied greatly. Whereas a previous study reported a clinical success rate of 82.1 % in SEMS placement for ECM [13], another study reported a success rate of 20 % for ECM compared with 88.6 % for CRC [14].

In our study, the clinical success rate for ECM (86.7 %) was comparable with that for CRC (92.6 %) ($p = 0.688$). Although previous radiation therapy, peritoneal carcinomatosis, or ECM itself rather than CRC might contribute to a decreased success rate and increased complication rate for SEMS placement in patients with ECM, the multivariate analysis found no significant predictor of unsuccessful SEMS placement.

Among the complications of SEMS in colorectal obstruction, perforation rate is reported to be 2–10 %, the migration rate 8–36 %, and the reobstruction rate 4–28 % [3, 7, 17]. In the current study, the complication rates were similar to those of previous studies and not significantly different between the two groups. The multivariate analysis showed history of prior radiotherapy, post-SEMS chemotherapy, and stenting proximal to splenic flexure to be significant risk factors for complications. Because radiotherapy or chemotherapy can result in luminal fibrosis/stricture or tumor regression, the risk of complications may be heightened by multidisciplinary treatment. Also, the proximal site of obstruction may have a higher risk for complications because of relative technical difficulty in SEMS placement.

Although the clinical success rate for SEMS is high and the complication rate is low, the long-term efficacy of SEMS still is doubtful. As new chemotherapeutic agents have been developed, patients' survival has been on the increase. Therefore, the long-term efficacy of SEMS has been important as well as clinical success and complications in deciding how to manage malignant colon obstruction.

The median patency duration of previous studies conducted with palliative populations has ranged from 68 to 288 days [6, 18–21]. These variations in duration of stent patency may be due to different demographic factors, underlying malignancies, or stent types. In the current study, the median duration of stent patency was 193 days with CRC and 186 days with ECM ($p = 0.253$, nonsignificant difference) and not affected by previous surgery, palliative chemotherapy, or underlying malignancy. Considering the life expectancy associated with metastatic ECM, including advanced gastric cancer and pancreatic cancer, SEMS is a highly effective treatment method for malignant obstruction due to ECM.

In our study, among 77 patients, except patients still alive and those who failed the follow-up assessment, the proportion of patients whose stent had been patent until their death reached 71.1 % in CRC group and 71.8 % in ECM group, with no significant difference between the two groups ($p = 0.943$).

The strength of this study comparing the clinical outcomes of SEMS between CRC and ECM was the relatively large sample. However, the patient demographics, coexisting medical morbidities, treatment histories, and stricture locations were not sufficiently controlled between the two groups because the data were collected retrospectively. The role of endoscopic SEMS placement for large bowel obstruction from ECM should be studied further in a randomized, prospective manner.

In conclusion, endoscopic SEMS placement is highly effective and comparable for palliation of obstruction in both extracolonic malignancy and colorectal cancer. Palliative SEMS insertions could be a good alternative for the treatment of colorectal obstruction by both ECM and CRC.

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