



# Which prognostic factors are important for long-term outcomes in symptomatic obstructive colon cancer? A multi-institutional retrospective cohort study

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**Purpose:** The prognostic factors in obstructive colon cancer have not been clearly identified. We aimed to identify the prognostic factor to establish optimal treatment strategy in obstructive colon cancer.

**Methods:** Patients who underwent surgery for primary colon cancer in stages II and III with symptomatic obstruction from 2004 to 2010 in six hospitals were retrospectively collected. Clinicopathological and surgical outcomes were compared between stent insertion and emergent surgery group. Multiple regression analysis and survival curve analysis were used to identify the prognostic factors in symptomatic obstructive colon cancer.

**Results:** Among 210 patients, 168 patients (80.0%) underwent stent insertion followed by surgery and 42 patients (20.0%) underwent emergent surgery. Laparoscopic approach (55.4% vs. 23.8%,  $p < 0.001$ ) and adequate lymph node (LN) harvest ( $\geq 12$ ) (93.5% vs. 69.0%,  $p < 0.001$ ) were significantly higher in stent insertion group. In multiple regression analysis, emergent surgery (hazard ratio [HR], 2.153; 95% confidence interval [CI], 1.031–4.495), vascular invasion (HR, 6.257; 95% CI, 2.784–14.061), and omitting adjuvant chemotherapy (HR, 3.107; 95% CI, 1.394–6.925) were independent poor prognostic factors in 5-year overall survival, and N stage (N1: HR, 3.095; 95% CI, 1.316–7.284; N2: HR, 4.156; 95% CI, 1.671–10.333) was the only poor prognostic factor in 5-year disease-free survival.

**Conclusion:** In symptomatic obstructive colon cancer, emergent surgery, N stage, vascular invasion, and omission of adjuvant chemotherapy were independent poor prognostic factors. Stent insertion is suggested as the initial treatment for symptomatic obstructive colon cancer, and adjuvant chemotherapy is recommended, especially when vascular invasion or LN metastasis is confirmed.

**Keywords:** Colonic neoplasms, Intestinal obstruction, Self expandable metallic stents, Laparoscopy, Prognosis

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## INTRODUCTION

Obstruction is one of the complications occurring in colon cancer, and up to 29% of colon cancers present with symptomatic obstruction, resulting in poor prognosis [1]. Symptomatic obstruction needs emergent management because of the risk of bowel perforation or peritonitis. In general, there are two treatment options for obstructive colon cancer; emergent surgical procedure with or without anastomosis and bridge-to-surgery following self-expanding metallic stent (SEMS) insertion [2,3].

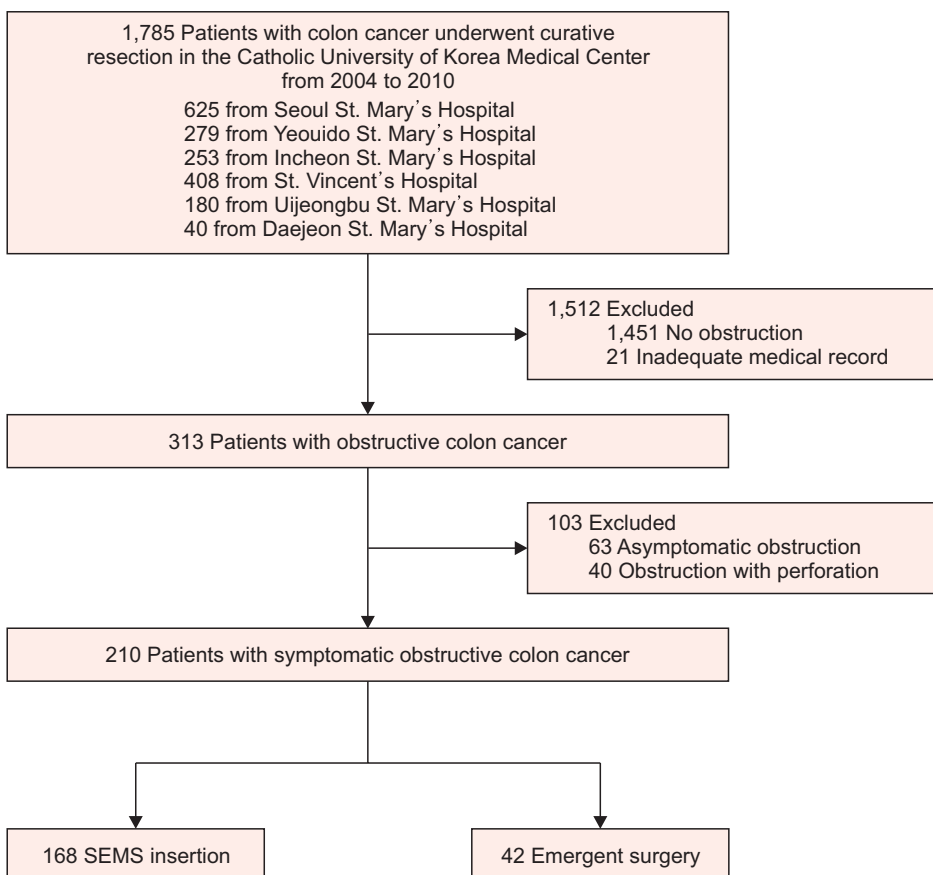
Although some guidelines have recently been established for obstructive colon cancer, whether to perform SEMS insertion or emergent surgery remains controversial [4–7]. Recently, several studies have shown that the long-term outcome in SEMS insertion is comparable to that of emergent surgery, but the choice of treatment is still not clear because the prognostic factors of obstructive colon cancer have not been verified yet [8–12]. Identifying the prognostic factors is required to predict the long-term outcome and determine the treatment strategy. However, there are relatively few studies about prognostic risk evaluation including treatment strategies for obstructive colon cancer. The present study aimed to analyze the poor prognostic factors including both pathologic outcomes and treatment strategies in symptomatic

obstructive colon cancer.

## MATERIALS AND METHODS

### Patient selection and study design

Flow diagram of patient selection is demonstrated in (Fig. 1). Patients who underwent curative resection for stage II, III colon cancer from January 2004 to December 2010 in the Catholic University of Korea Medical Center (Seoul St. Mary's Hospital, Yeouido St. Mary's Hospital, Incheon St. Mary's Hospital, St. Vincent's Hospital, Uijeongbu St. Mary's Hospital, and Daejeon St. Mary's Hospital) were retrospectively reviewed with medical records. A total of 1,785 patients were identified. We excluded 1,451 patients without colonic obstruction, 63 patients who had colonic obstruction without clinical symptom, 40 patients with evidence of perforation, and 21 patients with inadequate medical information were excluded. In final, 210 patients with symptomatic obstructive colon cancer were finally enrolled in the study. All patients were followed up with routine laboratory tests, imaging evaluation including chest and abdomen computed tomography (CT), and annual colonoscopy. The follow-up was completed in December 2015.



**Fig. 1.** Flow chart of patient's selection in symptomatic obstructive colon cancer. SEMS, self-expanding metallic stent.

**Table 1.** Clinicopathological characteristics and surgical outcomes of symptomatic obstructive colon cancer

Variable	Total	SEMS insertion	Emergent surgery	p value
Patient	210 (100)	168 (80.0)	42 (20.0)	
Age (yr)				0.010
≤65	92 (43.8)	81 (48.2)	11 (26.2)	
>65	118 (56.2)	87 (51.8)	31 (73.8)	
Sex				0.534
Male	111 (52.9)	87 (51.8)	24 (57.1)	
Female	99 (47.1)	81 (48.2)	18 (42.9)	
Comorbidity				0.622
No	180 (85.7)	145 (86.3)	35 (83.3)	
Yes	30 (14.3)	23 (13.7)	7 (16.7)	
Tumor location				<0.001
Right sided	46 (21.9)	27 (16.1)	19 (45.2)	
Left sided	164 (78.1)	141 (83.9)	23 (54.8)	
Stent procedure				
Clinical success		155 (92.3)		
Clinical failure		13 (7.7)		
Surgical approach				<0.001
Laparoscopic	103 (49.0)	93 (55.4)	10 (23.8)	
Conventional	107 (51.0)	75 (44.6)	32 (76.2)	
Combined resection				0.303
No	176 (83.8)	143 (85.1)	33 (78.6)	
Yes	34 (16.2)	25 (14.9)	9 (21.4)	
Stoma formation				0.240
No	190 (90.5)	154 (91.7)	36 (85.7)	
Yes	20 (9.5)	14 (8.3)	6 (14.3)	
T stage <sup>a)</sup>				0.643
3	175 (83.3)	141 (83.9)	34 (81.0)	
4	35 (16.7)	27 (16.1)	8 (19.0)	
N stage				0.046
0	95 (45.2)	70 (41.7)	25 (59.5)	
1	63 (30.0)	53 (31.5)	10 (23.8)	
2	52 (24.8)	45 (26.8)	7 (16.7)	
TNM stage <sup>b)</sup>				0.038
II	95 (45.2)	70 (41.7)	25 (59.5)	
III	115 (54.8)	98 (58.3)	17 (40.5)	
LN harvest				<0.001
≥12	186 (88.6)	157 (93.5)	29 (69.0)	
<12	24 (11.4)	11 (6.5)	13 (31.0)	

Table 1. Continued

Variable	Total	SEMS insertion	Emergent surgery	p value
Histologic type				0.190
Well/moderate	176 (83.8)	138 (82.1)	38 (90.5)	
Poor/Muc/Sig	34 (16.2)	30 (17.9)	4 (9.5)	
Vascular invasion				0.630
No	191 (91.0)	152 (90.5)	39 (92.9)	
Yes	19 (9.0)	16 (9.5)	3 (7.1)	
Lymphatic invasion				0.188
No	96 (45.7)	73 (43.5)	23 (18.1)	
Yes	114 (54.3)	95 (56.5)	19 (45.2)	
Perineural invasion				0.143
No	140 (66.7)	108 (64.3)	32 (76.2)	
Yes	70 (33.3)	60 (35.7)	10 (23.8)	
Adjuvant chemotherapy				0.006
Yes	163 (77.6)	137 (81.5)	26 (61.9)	
No	47 (22.4)	31 (18.5)	16 (38.1)	
Recurrence				0.755
No	154 (73.3)	124 (73.9)	30 (71.4)	
Yes	56 (26.7)	44 (26.2)	12 (28.6)	

Data are expressed as number (%).

SEMS, self-expanding metallic stent; LN, lymph node; Muc, mucinous adenocarcinoma; Sig, signet-ring cell carcinoma.

<sup>a</sup>No T1, T2 stage were presented. <sup>b</sup>No stage I was presented.

Patients' data were collected from each hospital's colon cancer patient registry including the demographic and clinicopathological characteristics, surgical outcomes, recurrence, and survival records. Patients were divided into two groups based on the initial treatment modality for the comparison analysis; SEMS insertion and emergent surgery.

The HANARO stent (M.I. Tech Corp., Ltd., Seoul, Korea) or the Niti-S stent (Taewoong Medical, Corp., Ltd., Gimpo, Korea) were used in all cases of SEMS insertion. Whether to perform SEMS insertion or emergent surgery was decided by each surgeon in consultation with an endoscopist. Complications such as perforation, stent expansion, and resolution of the bowel distension were checked serial plain abdominal films after the SEMS was inserted. Mechanical bowel preparation before surgery was performed if SEMS insertion was successful.

Oncological long-term outcomes were compared between two groups. The primary outcomes were 5-year overall survival (OS) and 5-year disease-free survival (DFS). The OS was defined as the time interval from the date of operation to the date of expire or last visit to the clinic. The DFS was defined as the time interval from the date of operation to the date of confirmation of can-

cer recurrence or last visit to the clinic. Subsequently, subgroup analysis in stages II and III colon cancer, respectively.

## Definitions

We defined symptomatic obstructive colon cancer as pathological confirmation of adenocarcinoma with clinical symptom of obstruction (abdominal distention, pain, tenderness, and no stool passage) and radiological finding of obstruction in CT scan or endoscopic finding of obstruction with failure of passing through tumor lesion. The right colon was defined as the cecum, ascending colon, hepatic flexure colon, and transverse colon, while the left colon was defined as the splenic flexure colon, descending colon, sigmoid colon, and rectosigmoid colon above the peritoneal reflection. The clinical success of SEMS insertion was defined as performing mechanical bowel preparation following the resolution of bowel distension. On the other hand, clinical failure was defined as the inability to perform bowel preparation due to unresolved obstruction and bowel perforation that occurred during or immediately after stent insertion.

## Statistical analysis

The comparison for categorical variables was analyzed with the chi-square or Fisher exact test. The univariate prognostic significance of variables was determined using the Cox proportional hazard model. Variables resulted as significantly related to the survival rate in univariate analysis were consequently explored in multivariate analysis employing the Cox multiple regression model. Survival analyses were calculated using the Kaplan-Meier method and comparisons of survival curves were performed using the log-rank test. Significant value was defined as a *p* value less than 0.05. All statistical analyses were performed using IBM SPSS for Windows (version 24.0; IBM Corp., Armonk, NY, USA).

## RESULTS

A total of 210 patients were included in this study. The median follow-up duration was 44 months with interquartile range of 17 to 61 months. The clinicopathological characteristics and surgical outcomes were compared in two groups and summarized in Table 1. The mean age of the patients was  $65.8 \pm 12.4$  years and male-to-female ratio was 1.1:1. Among 210 patients, 168 patients (80.0%) were initially treated with SEMs insertion followed by elective surgery and 42 patients (20.0%) were treated with emergent surgery. Clinical success rate of SEMs insertion was 92.3%, and the failure of SEMs insertion were observed in 13 patients (7.8%). The bowel decompression after SEMs insertion was done in all cases. Older age (51.8% vs. 73.8%,  $p = 0.001$ ) was associated with emergent surgery group. The rate of left-sided colon cancer (83.9% vs. 54.8%,  $p < 0.001$ ), laparoscopic approach (55.4% vs. 23.8%,  $p < 0.001$ ), and adequate lymph node (LN) harvest number more than 12 (93.5% vs. 69.0%,  $p < 0.001$ ) were significantly higher in SEMs insertion group than emergent surgery group. In pathological finding, N stage (N1, 31.5% vs. 23.8%; N2, 26.8% vs. 16.7%;  $p = 0.046$ ) and TNM stage (stage III, 58.3% vs. 40.5%;  $p = 0.038$ ) were significantly higher in SEMs insertion group, whereas T stage, histologic type, vascular invasion, lymphatic invasion, and perineural invasion showed no significant difference. The rate of adjuvant chemotherapy (81.5% vs. 61.9%,  $p = 0.006$ ) was significantly higher in SEMs insertion group, but the recurrence rate was similar in both groups.

The outcomes of the univariate and multivariate analyses that were conducted to identify significant prognostic factors for OS and DFS in symptomatic obstructive colon cancer were demonstrated in Table 2 and 3, respectively. In terms of OS, emergent surgery (hazard ratio [HR], 2.176; 95% confidence interval [CI], 1.088–4.354;  $p = 0.028$ ), vascular invasion (HR, 3.944; 95% CI, 1.901–8.182;  $p < 0.001$ ), and omitting adjuvant chemotherapy (HR, 2.462; 95% CI, 1.208–5.020;  $p = 0.013$ ) were poor prognostic factors in univariate analysis. In multivariate analysis, emergent surgery

(HR, 2.153; 95% CI, 1.031–4.495;  $p = 0.041$ ), vascular invasion (HR, 6.257; 95% CI, 2.784–14.061;  $p < 0.001$ ), and omitting adjuvant chemotherapy (HR, 3.107; 95% CI, 1.394–6.925;  $p = 0.006$ ) were correlated to be poor prognostic factors. In terms of DFS, N stage (N1: HR, 3.112; 95% CI, 1.490–6.498;  $p = 0.003$ ; N2: HR, 4.862; 95% CI, 2.389–9.896;  $p < 0.001$ ), vascular invasion (HR, 3.102; 95% CI, 1.602–6.005;  $p = 0.001$ ), lymphatic invasion (HR, 2.397; 95% CI, 1.342–4.282;  $p = 0.003$ ), and perineural invasion (HR, 1.811; 95% CI, 1.069–3.071;  $p = 0.027$ ) were poor prognostic factors in univariate analysis. In multivariate analysis, N stage (N1: HR, 3.095; 95% CI, 1.316–7.284;  $p = 0.010$ ; N2: HR, 4.156; 95% CI, 1.671–10.333;  $p = 0.002$ ) was the only poor prognostic factor.

Subgroup univariate analysis of OS and DFS in stage II and stage III were represented in Supplementary Table 1 and 2, respectively, and multivariate analyses of subgroups were summarized in Table 4. In stage II colon cancer, omitting adjuvant chemotherapy was the independent poor prognostic factor (HR, 3.133; 95% CI, 1.013–9.689;  $p = 0.047$ ) for OS. In stage III colon cancer, LN harvest less than 12 (HR, 5.166; 95% CI, 1.471–18.141;  $p = 0.010$ ) and vascular invasion (HR, 4.790; 95% CI, 2.064–11.135;  $p < 0.001$ ) were found as poor prognostic factors for OS, and vascular invasion (HR, 4.790; 95% CI, 1.092–4.268;  $p = 0.027$ ) was found to be the poor prognostic factor for DFS.

Survival analyses using the Kaplan-Meier curve are shown in (Fig. 2). The survival rate was analyzed using the prognostic factors defined in multivariate analysis as the dependent variable; emergent surgery, N stage, vascular invasion, and omitting adjuvant chemotherapy. The 5-year OS rates were 85.7% and 71.4% in SEMs insertion and emergent surgery, respectively ( $p = 0.024$ ). In N stage, the 5-year DFS rates were 88.4%, 68.3%, and 53.8% in N0, N1, and N2, respectively ( $p < 0.001$ ). The 5-year OS rates in noninvasion and vascular invasion were 86.4% and 47.4%, respectively ( $p < 0.001$ ). The 5-year OS rates in performing and omitting adjuvant chemotherapy were 84.7% and 76.6%, respectively ( $p = 0.010$ ).

## DISCUSSION

In this study, we have identified the prognostic factors for symptomatic obstructive colon cancer. Emergent surgery rather than SEMs insertion, presence of vascular invasion, and omission of adjuvant chemotherapy were the prognostic factors to lower the survival rates, where higher N stage appeared to be the significant prognostic factor for recurrence. Regarding SEMs insertion compared to emergent surgery, laparoscopic approach was more available and adequate LN dissection was more performed.

When emergent surgery is performed for obstructive colon cancer, laparotomy is more considered for the reason that severe bowel dilatation is present [11]. Our study also showed that emergent surgery had a higher rate of laparotomy approach than

**Table 2.** Univariate and multivariate analysis of overall survival in symptomatic obstructive colon cancer

Variable	Total <sup>a)</sup> (n = 210)	Univariate		Multivariate	
		HR (95% CI)	p value	HR (95% CI)	p value
Age (yr)					
≤65	92 (43.8)	Reference			
>65	118 (56.2)	1.465 (0.746–2.876)	0.265		
Sex					
Male	111 (52.9)	Reference			
Female	99 (47.1)	0.670 (0.343–1.311)	0.242		
Initial treatment					
SEMS insertion	168 (80.0)	Reference		Reference	
Emergent	42 (20.0)	2.176 (1.088–4.354)	0.028	2.153 (1.031–4.495)	0.041
Tumor location					
Right sided	46 (21.9)	Reference			
Left sided	164 (78.1)	0.806 (0.367–1.771)	0.591		
Surgical approach					
Laparoscopic	103 (49.0)	Reference			
Conventional	107 (51.0)	1.366 (0.835–3.193)	0.152		
T stage					
3	175 (83.3)	Reference			
4	20 (9.5)	1.442 (0.657–3.165)	0.361		
N stage					
0	95 (45.2)	Reference			
1	63 (30.0)	1.356 (0.607–3.028)	0.458		
2	52 (24.8)	1.756 (0.801–3.851)	0.160		
LN harvest					
≥12	186 (88.6)	Reference			
<12	24 (11.4)	2.118 (0.880–5.101)	0.094		
Histologic type					
Well/moderate	176 (83.8)	Reference			
Poor/Muc/Sig	34 (16.2)	1.299 (0.540–3.124)	0.559		
Vascular invasion					
No	191 (91.0)	Reference		Reference	
Yes	19 (9.0)	3.944 (1.901–8.182)	<0.001	6.257 (2.784–14.061)	<0.001
Lymphatic invasion					
No	96 (45.7)	Reference			
Yes	114 (54.3)	1.831 (0.915–3.663)	0.088		
Perineural invasion					
No	140 (66.7)	Reference			
Yes	70 (33.3)	1.394 (0.712–2.726)	0.332		
Adjuvant chemotherapy					
Yes	163 (77.6)	Reference		Reference	
No	47 (22.4)	2.462 (1.208–5.020)	0.013	3.107 (1.394–6.925)	0.006

HR, hazard ratio; CI, confidence interval; SEMS, self-expanding metallic stent; LN, lymph node; Muc, mucinous adenocarcinoma; Sig, signet-ring cell carcinoma.

<sup>a)</sup>Number (%).

**Table 3.** Univariate and multivariate analysis of disease-free survival in symptomatic obstructive colon cancer

Variable	Total <sup>a)</sup> (n = 210)	Univariate		Multivariate	
		HR (95% CI)	p value	HR (95% CI)	p value
Age (yr)					
≤65	92 (43.8)	Reference			
>65	118 (56.2)	1.250 (0.736–2.214)	0.409		
Sex					
Male	111 (52.9)	Reference			
Female	99 (47.1)	0.873 (0.515–1.479)	0.613		
Initial treatment					
SEMS insertion	168 (80.0)	Reference			
Emergent	42 (20.0)	1.248 (0.659–2.365)	0.497		
Tumor location					
Right sided	46 (21.9)	Reference			
Left sided	164 (78.1)	0.787 (0.423–1.465)	0.450		
Surgical approach					
Laparoscopic	103 (49.0)	Reference			
Conventional	107 (51.0)	1.486 (0.872–2.532)	0.146		
T stage					
3	175 (83.3)	Reference			
4	20 (9.5)	1.617 (0.883–2.962)	0.119		
N stage					
0	95 (45.2)	Reference		Reference	
1	63 (30.0)	3.112 (1.490–6.498)	0.003	3.095 (1.316–7.284)	0.010
2	52 (24.8)	4.862 (2.389–9.896)	<0.001	4.156 (1.671–10.333)	0.002
LN harvest					
≥12	186 (88.6)	Reference			
<12	24 (11.4)	0.751 (0.272–2.078)	0.581		
Histologic type					
Well/moderate	176 (83.8)	Reference			
Poor/Muc/Sig	34 (16.2)	1.199 (0.587–2.446)	0.619		
Vascular invasion					
No	191 (91.0)	Reference		Reference	
Yes	19 (9.0)	3.102 (1.602–6.005)	0.001	1.750 (0.810–3.777)	0.154
Lymphatic invasion					
No	96 (45.7)	Reference		Reference	
Yes	114 (54.3)	2.397 (1.342–4.282)	0.003	0.934 (0.442–1.975)	0.859
Perineural invasion					
No	140 (66.7)	Reference		Reference	
Yes	70 (33.3)	1.811 (1.069–3.071)	0.027	1.176 (0.652–2.124)	0.590
Adjuvant chemotherapy					
Yes	163 (77.6)	Reference			
No	47 (22.4)	1.319 (0.665–2.617)	0.429		

HR, hazard ratio; CI, confidence interval; SEMS, self-expanding metallic stent; LN, lymph node; Muc, mucinous adenocarcinoma; Sig, signet-ring cell carcinoma.

<sup>a)</sup>Number (%).

**Table 4.** Multivariate analysis of OS and DFS in symptomatic obstructive colon cancer stage II and stage III

Variable	Total (n = 95)	Stage II				Total (n = 115)	Stage III			
		OS		DFS			OS		DFS	
		HR (95% CI)	p value	HR (95% CI)	p value		HR (95% CI)	p value	HR (95% CI)	p value
Initial treatment										
SEMS insertion	70 (73.7)	Reference		Reference						
Emergent	25 (26.3)	2.092 (0.684–6.400)	0.196	2.702 (0.808–9.040)	0.107					
Surgical approach										
Laparoscopic	41 (43.2)			Reference						
Conventional	54 (56.8)			6.309 (0.782–50.923)	0.084					
LN harvest										
≥12						108 (93.9)	Reference			
<12						7 (6.1)	5.166 (1.471–18.141)	0.010		
Vascular invasion										
No						97 (84.3)	Reference		Reference	
Yes						18 (15.7)	4.790 (2.061–11.135)	<0.001	2.159 (1.092–4.268)	0.027
Adjuvant chemotherapy										
Yes	67 (70.5)	Reference								
No	28 (29.5)	3.133 (1.013–9.689)	0.047							

OS, overall survival; DFS, disease-free survival; HR, hazard ratio; CI, confidence interval; SEMS, self-expanding metallic stent; LN, lymph node.

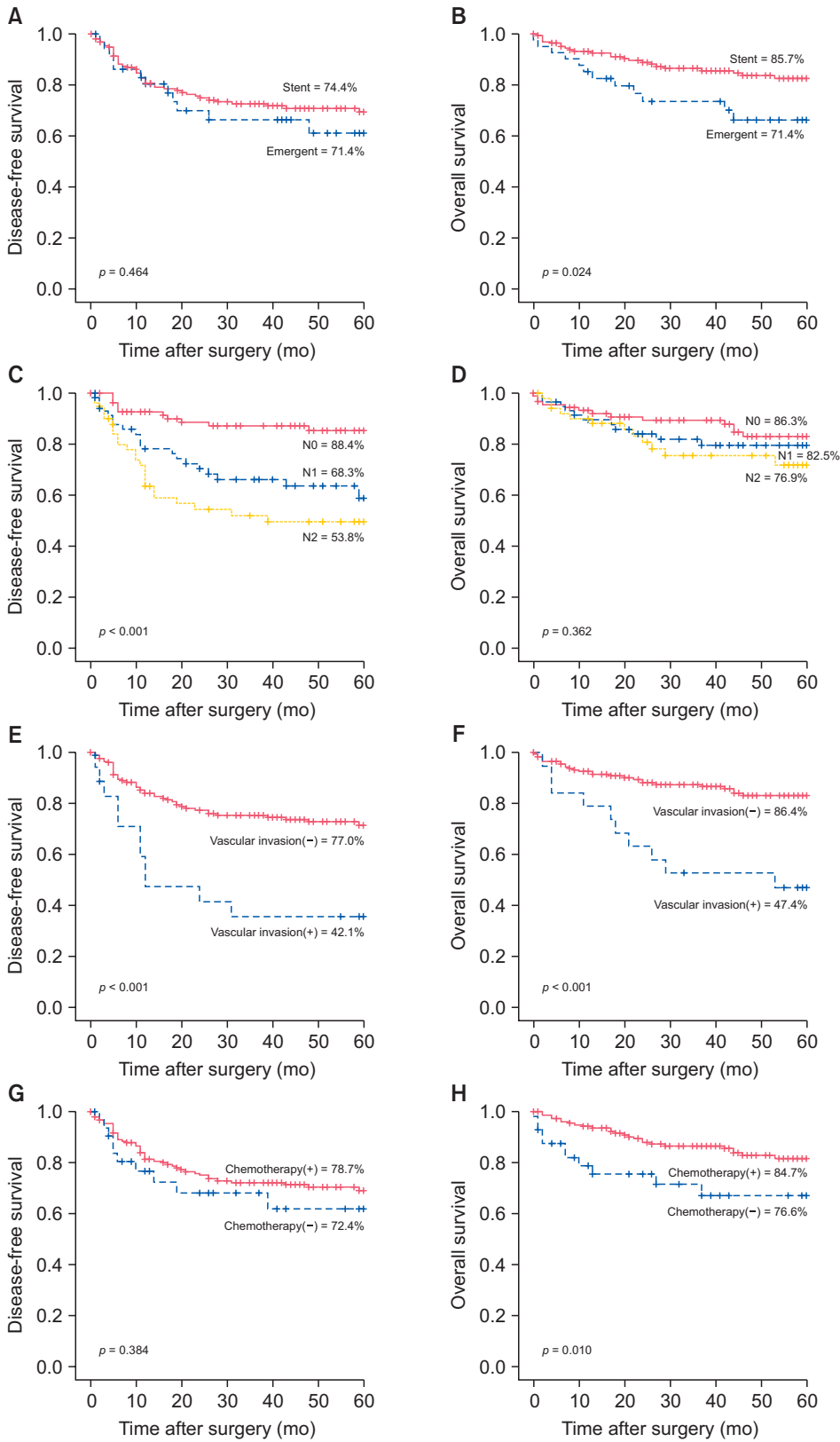
SEMS insertion (76.2% vs. 44.6%,  $p < 0.001$ ). From previous studies, laparoscopic approach is known to have advantages in postoperative complications and morbidities when compared to open surgery [13–15]. In the aspect of the oncologic outcome, one meta-analysis has analyzed that adequate LN dissection was more performed in laparoscopy [15]. With the higher rate of laparoscopy, SEMS insertion also showed a higher rate of adequate LN harvest in our results (93.5% vs. 69.0%,  $p < 0.001$ ). Furthermore, the time interval between SEMS insertion and followed surgery allows for recovery of nutritional status and resolution of bowel dilatation, which improves the postoperative outcome [16]. For these reasons, it is interpreted that emergent surgery rather than SEMS insertion appeared to be the risk factor for symptomatic obstructive colon cancer.

SEMS insertion has been reported to have superior short-term outcomes such as primary anastomosis rate and postoperative complications, as well as comparable long-term oncological outcomes compared to conventional emergent surgery [2,8–12]. Our

study result showed a correlative outcome in 5-year OS rate (58.7% vs. 71.4%,  $p = 0.024$ ). On the contrary, some studies reported that high local recurrence rates in SEMS insertion [17–21]. Sloothaak et al. [17] demonstrated a randomized controlled trial which resulted in the tendency of a higher rate of recurrence in emergent surgery group (4-year DFS rates, 49% vs. 30%;  $p = 0.149$ ). Silent perforation, which is reported to occur up to 20% in SEMS insertion, or mechanical pressure induced by the metallic stent may be the reasons for tumor dissemination to increase local recurrence [22–24]. According to our study results, SEMS insertion showed similar rate of 5-year DFS and recurrence compared to those of emergent surgery (5-year DFS rate: 74.4% vs. 71.4%,  $p = 0.464$ ; recurrence: 26.2% vs. 28.6%,  $p = 0.755$ ). If survival is more favorable without the risk of recurrence, we can consider SEMS insertion as the choice of the treatment in symptomatic obstructive colon cancer more safely.

One of the prognostic factors for symptomatic obstructive colon cancer found in our results was the presence of vascular





**Fig. 2.** Survival curves of disease-free survival and overall survival in symptomatic obstructive colon cancer for prognostic factor of initial treatment (A, B), N stage (C, D), vascular invasion (E, F), and adjuvant chemotherapy (G, H).

invasion. In recent, the significance of vascular invasion in colon cancer has been emphasized that its impact on prognosis is comparable to LN status (N stage). Qwaider et al. [25] stated that stage II colon cancer with extramural vascular invasion had worse OS than stage III colon cancer without vascular invasion (mean survival time,  $94 \pm 8$  months vs.  $127 \pm 4$  months;  $p < 0.001$ ), and Leijssen et al. [26] showed a similar result in 5-year disease-specific survival rate (77.0% vs. 85.5%,  $p = 0.021$ ). In our data, stage II group had only one patient with vascular invasion without recurrence or death in 5 years. Vascular invasion in stage III group was found to be the risk factor in multivariate analysis and showed lower rate of 5-year OS (64.9% vs. 38.9%,  $p = 0.022$ ) and 5-year DFS (86.6% vs. 44.4%,  $p < 0.001$ ). Although it cannot be regarded as a more significant prognostic factor than N stage, if vascular invasion is identified in symptomatic obstructive colon cancer, more aggressive treatment including adjuvant chemotherapy should be considered for a better oncological outcome.

One recent meta-analysis study reported that omitting adjuvant chemotherapy resulted in a higher recurrence rate in obstructive colon cancer [27]. Although adjuvant chemotherapy is highlighted in treatment guidelines of obstructive colon cancer, surgeons hesitate to recommend chemotherapy when patient is in old age and has poor performance status [7]. Not only found as the risk factor in entire group, omission of adjuvant chemotherapy appeared to be the risk factor for OS in stage II group and presented lower rate of 5-year OS (89.6% vs. 78.6%,  $p = 0.014$ ). Considering that obstruction in colon cancer is diagnosed higher than stage II, it can be recommended that adjuvant chemotherapy should be performed regardless of stage in symptomatic obstructive colon cancer.

Our study had some limitations. Since the study was analyzed in retrospective approach, there are possibilities of unintended selection bias. A bias was induced by the fact that each surgeon decided whether to perform SEMS insertion or emergent surgery as the initial treatment and the time interval between SEMS insertion and followed surgery. There was also a bias that the surgeon decided whether to perform adjuvant chemotherapy in consideration of patient's age and performance status. In addition, perioperative factors such as postoperative complications including leakage and infection, presence of stoma formation, and period of hospitalization were not analyzed in our study. Moreover, the lack of statistical analysis with nonobstructive colon cancer appeared to be another limitation and further research is required. However, our study has strong points that subgroup analysis dividing into stages II and III was conducted to reduce the bias, and multicenter analysis has been done to evaluate numerous, different patients.

In conclusion, this study demonstrated that N stage, emergent surgery, vascular invasion, and omitting adjuvant chemotherapy were associated with poor prognosis in symptomatic obstructive

colon cancer. Therefore, we suggest SEMS insertion as the first treatment modality for symptomatic obstructive colon cancer and adjuvant chemotherapy should be performed after surgery, especially when LN metastasis or vascular invasion is identified.

## NOTES

### Ethical statements

The study was performed in accordance with the ethical guidelines of the World Medical Association Declaration of Helsinki 2013. The study protocol was approved and monitored by the Institutional Review Board of the Ethics Committee of the College of Medicine, The Catholic University of Korea (No. XC14RIMI0056) and informed consent was waived.

### Authors' contributions

Conceptualization: JHB, YSL  
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 Statistical analysis, Visualization: CHK, JHB  
 Investigation: JHB, CSL, SRH, IKL, DSL, WKK, JHK, BHK, HMC, STO, SCL, YSL  
 Methodology: CHK, JHB, YSL  
 Project administration, Supervision: YSL  
 Writing—original draft: CHK  
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### Conflict of interest

All authors have no conflicts of interest to declare.

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## Supplementary materials

Supplementary materials can be found via <https://doi.org/10.7602/jmis.2021.24.3.128>.

## REFERENCES

- Kato H, Yamashita K, Wang G, Sato T, Nakamura T, Watanabe M. Prognostic significance of preoperative bowel obstruction in stage III colorectal cancer. *Ann Surg Oncol* 2011;18:2432-2441.
- Zhang Y, Shi J, Shi B, Song CY, Xie WF, Chen YX. Self-expanding metallic stent as a bridge to surgery versus emergency surgery for obstructive colorectal cancer: a meta-analysis. *Surg Endosc* 2012;26:110-119.
- Dohmoto M, Hünerbein M, Schlag PM. Palliative endoscopic therapy of rectal carcinoma. *Eur J Cancer* 1996;32A:25-29.
- Webster PJ, Aldoori J, Burke DA. Optimal management of malignant left-sided large bowel obstruction: do international guidelines agree? *World J Emerg Surg* 2019;14:23.
- Pisano M, Zorcolo L, Merli C, et al. 2017 WSES guidelines on colon and rectal cancer emergencies: obstruction and perforation. *World J Emerg Surg* 2018;13:36.
- van Hooft JE, van Halsema EE, Vanbiervliet G, et al. Self-expandable metal stents for obstructing colonic and extracolonic cancer: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. *Endoscopy* 2014;46:990-1053.
- Benson AB, Venook AP, Al-Hawary MM, et al. NCCN guidelines insights: colon cancer, version 2.2018. *J Natl Compr Canc Netw* 2018;16:359-369.
- Matsuda A, Miyashita M, Matsumoto S, et al. Comparison of long-term outcomes of colonic stent as "bridge to surgery" and emergency surgery for malignant large-bowel obstruction: a meta-analysis. *Ann Surg Oncol* 2015;22:497-504.
- Choi JM, Lee C, Han YM, et al. Long-term oncologic outcomes of endoscopic stenting as a bridge to surgery for malignant colonic obstruction: comparison with emergency surgery. *Surg Endosc* 2014;28:2649-2655.
- Kang SI, Oh HK, Yoo JS, et al. Oncologic outcomes of preoperative stent insertion first versus immediate surgery for obstructing left-sided colorectal cancer. *Surg Oncol* 2018;27:216-224.
- Kye BH, Lee YS, Cho HM, et al. Comparison of long-term outcomes between emergency surgery and bridge to surgery for malignant obstruction in right-sided colon cancer: a multicenter retrospective study. *Ann Surg Oncol* 2016;23:1867-1874.
- Kim MK, Kye BH, Lee IK, et al. Outcome of bridge to surgery stenting for obstructive left colon cancer. *ANZ J Surg* 2017;87:E245-E250.
- Yamamoto S, Inomata M, Katayama H, et al. Short-term surgical outcomes from a randomized controlled trial to evaluate laparoscopic and open D3 dissection for stage II/III colon cancer: Japan Clinical Oncology Group Study JCOG 0404. *Ann Surg* 2014;260:23-30.
- Papageorge CM, Zhao Q, Foley EF, et al. Short-term outcomes of minimally invasive versus open colectomy for colon cancer. *J Surg Res* 2016;204:83-93.
- Liu ZH, Wang N, Wang FQ, Dong Q, Ding J. Oncological outcomes of laparoscopic versus open surgery in pT4 colon cancers: a systematic review and meta-analysis. *Int J Surg* 2018;56:221-233.
- Kye BH, Kim JH, Kim HJ, et al. The optimal time interval between the placement of self-expandable metallic stent and elective surgery in patients with obstructive colon cancer. *Sci Rep* 2020;10:9502.
- Sloothaak DA, van den Berg MW, Dijkgraaf MG, et al. Oncological outcome of malignant colonic obstruction in the Dutch Stent-In 2 trial. *Br J Surg* 2014;101:1751-1757.
- Erichsen R, Horváth-Puhó E, Jacobsen JB, Nilsson T, Baron JA, Sørensen HT. Long-term mortality and recurrence after colorectal cancer surgery with preoperative stenting: a Danish nationwide cohort study. *Endoscopy* 2015;47:517-524.
- Gorissen KJ, Tuynman JB, Fryer E, et al. Local recurrence after stenting for obstructing left-sided colonic cancer. *Br J Surg* 2013;100:1805-1809.
- Sabbagh C, Browet F, Diouf M, et al. Is stenting as "a bridge to surgery" an oncologically safe strategy for the management of acute, left-sided, malignant, colonic obstruction? A comparative study with a propensity score analysis. *Ann Surg* 2013;258:107-115.
- Arezzo A, Passera R, Lo Secco G, et al. Stent as bridge to surgery for left-sided malignant colonic obstruction reduces adverse events and stoma rate compared with emergency surgery: results of a systematic review and meta-analysis of randomized controlled trials. *Gastrointest Endosc* 2017;86:416-426.
- Kim SJ, Kim HW, Park SB, et al. Colonic perforation either during or after stent insertion as a bridge to surgery for malignant colorectal obstruction increases the risk of peritoneal seeding. *Surg Endosc* 2015;29:3499-3506.
- Malgras B, Brullé L, Lo Dico R, et al. Insertion of a stent in obstructive colon cancer can induce a metastatic process in an experimental murine model. *Ann Surg Oncol* 2015;22 Suppl 3:S1475-S1480.
- van Hooft JE, Bemelman WA, Oldenburg B, et al. Colonic stenting versus emergency surgery for acute left-sided malignant colonic obstruction: a multicentre randomised trial. *Lancet Oncol* 2011;12:344-352.
- Qwaider YZ, Sell NM, Stafford CE, et al. Adjuvant chemotherapy benefits on patients with extramural vascular invasion in stages II and III colon cancer. *J Gastrointest Surg* 2021;25:2019-2025.
- Leijssen LG, Dinaux AM, Amri R, et al. Impact of intramural and extramural vascular invasion on stage II-III colon cancer outcomes. *J Surg Oncol* 2019;119:749-757.
- Manceau G, Voron T, Mege D, et al. Prognostic factors and patterns of recurrence after emergency management for obstructing colon cancer: multivariate analysis from a series of 2120 patients. *Langenbecks Arch Surg* 2019;404:717-729.