

Original Research Article

## Bridge to Surgery for Obstructing Colonic Cancer: A Comparison between Right- and Left-sided Lesions

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### Abstract

**Objectives:** Few studies have compared management and outcomes of bridge to surgery (BTS) for obstructive colonic cancer according to the location of the tumor. Additional information is needed about this procedure's characteristics and short-term and long-term outcomes. We aimed to compare patient and tumor characteristics, and outcomes of BTS for obstructive right-sided versus left-sided colonic cancers.

**Methods:** This was a retrospective, single center, cohort study. The study cohort comprised 149 patients, including 48 with right-sided and 101 with left-sided obstructive colonic cancers, who were treated with BTS between January 2007 and December 2017. Data on medical history, investigations, treatments, and prognosis were collected from an electronic database of a single hospital. The primary end points were overall (OS) and disease-free (DFS) survival and short-term surgical outcomes.

**Results:** Significantly more patients with right-sided cancers had postoperative complications (29.2% vs. 14.9%,  $p = 0.039$ ). Additionally, postoperative chemotherapy was administered to a marginally significantly greater proportion of patients with left-sided cancers (29.2% vs 45.5%,  $p = 0.057$ ). The long-term outcomes were comparable between the two groups (the 5-year OS rates were 67.6% and 80.9% [ $p = 0.117$ ] and the 5-year DFS rates were 62.2% and 58.6% [ $p = 0.671$ ]). Multivariate analyses using all studied variables showed that lymphovascular invasion, advanced T stage, and adjuvant chemotherapy were independent poor prognostic factors.

**Conclusions:** The long-term outcome was not different between the right- and left-sided groups. In a BTS setting, postoperative complications may reduce the compliance of adjuvant chemotherapy in right-sided cancers and affect long-term outcomes.

### Keywords

colon cancer, obstruction, right-sided, left-sided

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### Introduction

The incidence of obstruction in patients with colonic cancer reportedly ranges from 7% to 47%; obstruction accounts for approximately 85% of colonic emergencies[1,2]. Emergency surgery for obstructive colon cancer (OCC) is associated with high mortality and morbidity rates, and creation of

stomas[3]. The morbidity and mortality rates following these emergency surgeries can be avoided by decompression with a self-expanding metallic stent (SEMS), ileus tube, or stoma, thus gaining time for recovery and improvement in the patient's general condition. In the curative setting, serious consideration must be given to oncologic outcomes, as well as to minimizing morbidity. However, management of obstructive

tive colonic cancer is highly dependent on the site of the primary tumor and the outcomes vary according to the characteristics of patients and tumors. Nevertheless, in the setting of BTS, few studies have compared the management and outcomes of OCC according to the site of the primary tumor. The aim of this study was to compare characteristics of patients and tumors and operative outcomes of patients who had undergone BTS for right and left acute complete obstruction caused by primary colonic cancer.

## Methods

Data of all patients who had undergone resection of a primary OCC from January 2007 to December 2017 were collected from the electronic database of our hospital. The inclusion criteria were as follows: (1) symptomatic colonic obstruction requiring continuous decompressive procedure from the cecum to the rectosigmoid junction; (2) having undergone curative resection after initial decompression; and (3) obstruction caused by histologically proven colon adenocarcinoma. The exclusion criteria were as follows: (1) presentation with perforation and fecal peritonitis; (2) multiple cancers; and (3) colitis-associated cancer. Eligible patients were further subdivided into two groups depending on the site of the primary lesion. Right-sided lesions were defined as those proximal to the splenic flexure and left-sided lesions as those distal to the splenic flexure. When initial decompression using stent placement or ileus tube failed, the patient underwent emergency resection and was categorized in accordance with the initial treatment. Decision-making regarding treatment approaches was based on the patient's overall condition and on the attending physician's evaluation. Informed consent was obtained from all individual participants included in the study. The study was conducted with the approval of the Ethics Committee of our hospital (approval number 2019-30).

### Study endpoints

The primary endpoints were overall survival (OS) and disease-free survival (DFS) in both groups of patients. Short-term postoperative outcomes, including complications associated with bowel decompression, number of retrieved lymph nodes, time to resection after decompression, overall postoperative morbidity rate, overall postoperative mortality, and recovery course after surgery, were analyzed. Mortality was defined as death within 30 days or during hospital stay after resection. Overall complications were defined as surgical and nonsurgical complications occurring within 30 days or in-hospital.

### Statistical analysis

Data were analyzed using STATA software. Analysis of variance or Wilcoxon statistical methods were used to deter-

mine statistical significance. The survival rate was estimated by the Kaplan-Meier method. Univariate and multivariate analysis of the survival time was performed with Cox's proportional hazards model. A  $p < 0.05$  was considered to denote statistical significance.

## Results

### Patient's characteristics

Overall, 149 patients with OCC were included in this study, 48 (32.2%) and 101 (67.8%) in the right- and left-sided groups, respectively. Patient's characteristics and clinicopathological findings were similar between the two groups (Table 1).

### Surgical characteristics

Table 2 shows the operative findings and short-term surgical outcomes in the two groups. No differences were found in the time to resection after initial colonic decompression, operative time, complications associated with bowel decompression, or postoperative mortality. Significantly more patients had postoperative complications in the right-sided than in the left-sided group (29.2% vs. 14.9%,  $p = 0.039$ ). Additionally, postoperative chemotherapy was administered marginally more frequently in the left-sided group (29.2% vs. 45.5%,  $p = 0.057$ ).

### Oncological outcome

The 5-year OS rates of the right- and left-sided groups were 67.6% and 80.9%, respectively ( $p = 0.117$ ) and the 5-year DFS rates were 62.2 and 58.6%, respectively ( $p = 0.671$ ) (Figure 1). Multivariate analyses using all variables showed that patients with lymphovascular invasion and advanced T stage had worse OS and DFS (Table 3). Furthermore, adjuvant chemotherapy was an independent poor prognostic factor for OS in all included patients (Table 3). Although marginally significant, sidedness was not an independent prognostic factor for OS and DFS.

## Discussion

To the best of our knowledge, the present series is the first to compare the long- and short-term outcomes of patients with right- and left-sided OCC after undergoing BTS. Patients with right-sided OCC had significantly more numerous postoperative complications and received adjuvant chemotherapy marginally less frequently. The prognosis did not differ significantly between patients with right- versus left-sided OCC who had undergone BTS. Additionally, lymphovascular invasion, advanced T stage, and administration of adjuvant chemotherapy were independent prognostic factors for patients undergoing BTS for OCC.

**Table 1.** Baseline Characteristics.

		Total N = 149	Right group N = 48	Left group N = 101	p
Sex	Male	78	25	53	0.964
	Female	71	23	48	
Age	(median, IQR)	70 (62-78)	69.5 (62-78)	73 (62-78)	0.724
TNM stage	II	80	24	56	0.533
	III	69	24	45	
pT	3	95	28	67	0.352
	4a	42	14	28	
	4b	12	6	6	
pN	0	80	24	56	0.660
	1	60	20	40	
	2	9	4	5	
Lymph invasion	-	18	3	15	0.132
	+	131	45	86	
Vascular invasion	-	16	6	10	0.632
	+	133	42	91	

IQR: Interquartile range

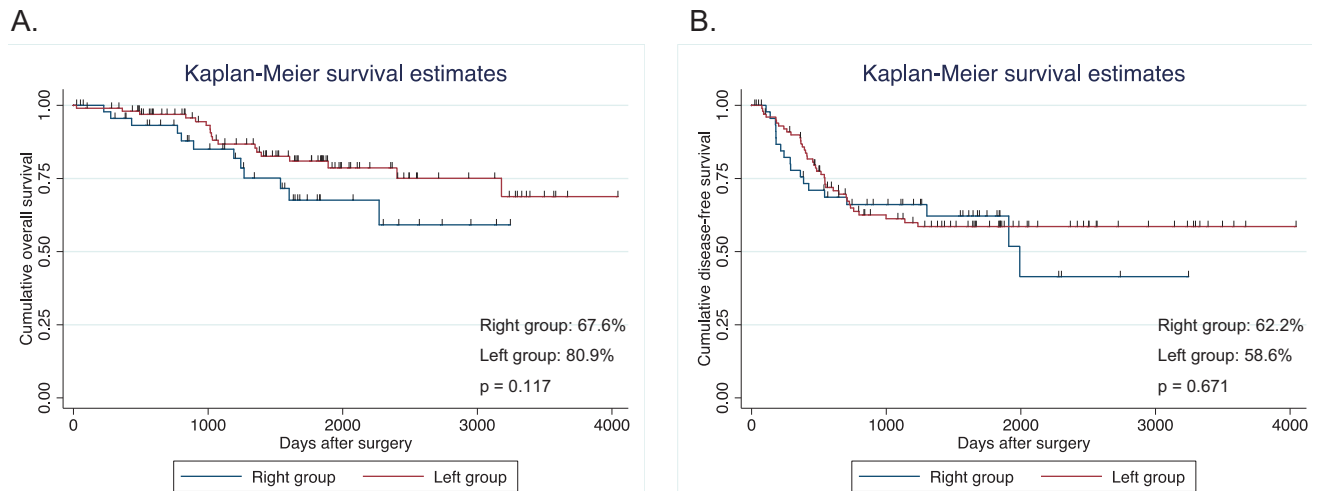
**Table 2.** Surgical Characteristics.

		Total N = 149	Right group N = 48	Left group N = 101	p
Type of intervention	Stoma	7	5	2	0.055
	Ileus tube	72	24	48	
	SEMS	70	19	51	
Operation method	Open	48	14	34	0.583
	Laparoscopy	101	34	67	
Operation time (min)	(median, IQR)	121.5 (95-161)	130 (95-148)	120 (93-167)	0.906
Number of harvested LNs	(median, IQR)	19 (11-29)	18 (11-30)	19 (12-29)	0.906
Time to resection (days)	(median, IQR)	14 (7-21)	13.5 (7.5-20.5)	14 (7-22)	0.790
Complication associated with bowel decompression	No	122	43	79	0.092
	Yes	27	5	22	
Overall postoperative mortality	No	148	48	100	0.489
	Yes	1	0	1	
Overall postoperative morbidity	No	120	34	86	0.039*
	Yes	29	14	15	
	Anastomotic leakage	3	0	3	
	Ileus	7	3	4	
	SSI	12	8	4	
Adjuvant chemotherapy	Others	7	3	4	0.057
	No	89	34	55	
	Yes	60	14	46	

SEMS: Self-expanding metallic stent; LNs: Lymph nodes; SSI: Surgical site infection

In this study, OCC occurred more frequently in patients with left-sided lesions than in those with right-sided lesions (67.8% vs. 32.2%), which is consistent with previous reports[3-6]. In addition, no significant differences were observed in patient's characteristics and pathological findings between the groups, which is also in accordance with previ-

ous reports[7]. However, there was a tendency toward more frequent lymphatic invasion in the right-sided group, as has previously been reported[8-10]. These differences may be attributable to the fact that it takes a more advanced tumor to cause proximal malignant obstruction because the feces are more fluid in the right than in the left colon.



**Figure 1.** Comparison of the 5-year overall (A) and disease-free (B) survivals between the right- and left-sided group.

**Table 3.** Factors Associated with Long-term Oncologic Outcomes.

		Overall survival multivariate analysis HR	p	Disease-free survival multivariate analysis HR	p
Age	<65	ref		ref	
	≥65	4.868 (1.528-15.509)	0.007	0.855 (0.474-1.543)	0.603
Gender	Male	ref		ref	
	Female	0.831 (0.357-1.933)	0.667	0.941 (0.537-1.651)	0.833
Sideness	Right sided	ref		ref	
	Left sided	0.492 (0.217-1.117)	0.09	1.071 (0.580-1.976)	0.827
Surgical approach	Open	ref		ref	
	lap	0.852 (0.359-2.021)	0.717	0.801 (0.435-1.472)	0.474
Lymphatic invasion	-	ref		ref	
	+	3.521 (1.844-6.723)	<0.001*	2.313 (1.418-3.774)	0.001
Vascular invasion	-	ref		ref	
	+	4.104 (2.353-7.157)	<0.001*	2.297 (1.489-3.541)	<0.001*
Differentiation	Well/moderately	ref		ref	
	Poor/undifferentiated	0.254 (0.038-1.343)	0.107	0.637 (0.242-1.678)	0.362
T stage	T3	ref		ref	
	T4	2.512 (1.123-5.616)	0.025*	1.926 (1.087-3.413)	0.025*
N stage	N0	ref		ref	
	N1-2	1.328 (0.480-3.673)	0.585	1.32 (0.639-2.728)	0.454
Adjuvant chemotherapy	No	ref		ref	
	Yes	0.320 (0.113-0.904)	0.032*	0.663 (0.315-1.394)	0.279

In emergency settings, obstruction-related dilatation of the small bowel and colon can prevent an adequate view of the operative field and manipulation of the instruments that are necessary for laparoscopic surgery. One advantage of BTS over emergency surgery is the ability to perform the procedure via a laparoscopic approach and in a single stage. In this study, no significant difference was observed in the frequency of laparoscopic surgery between the right- and left-sided groups (70.8% vs. 66.3%). Given that laparoscopic surgery has some advantages, including small incisions and

less wound pain, we believe that BTS is preferable for both right- and left-sided lesions.

Reported global morbidity rates range from 32% to 64% [11-14]. In our study, the overall morbidity rate was 19.5%, which is favorable compared with the above-cited percentages. It is noteworthy that postoperative complications occurred significantly more frequently in the right-sided group (29.1% vs. 14.9%). We could argue that this difference is attributable to more severe obstruction and inadequate decompression in right-sided compared with left-

sided OCC. It is possible that the high morbidity rate in the right-sided group is responsible for the low rate of use of adjuvant chemotherapy in this study. The proportion of patients receiving postoperative adjuvant chemotherapy was an independent prognostic factor for OS. These findings suggest that in the setting of BTS for OCC, proximal obstruction requires more careful management and compliance with adjuvant chemotherapy plays a significant role in determining long-term outcomes.

Few studies have compared long-term outcomes in patients with OCC between the right- and left-side[5,12,15]. Faucheron et al. and Frago et al. reported that long-term outcomes did not differ significantly between right- and left-sided OCC[5,12]. In contrast, Mege et al. performed a large cohort study and found that prognosis was poorer in patients with right-sided than left-sided OCC[15]. However, in their series, one-third of the patients did not receive adjuvant chemotherapy as recommended by the relevant guidelines. In the current study, OS and DFS were similar between the right- and left-sided groups and the rate of adjuvant chemotherapy in patients with stage III OCC was 71.0%. Worthy of emphasis, in our study OCC patients were treated with BTS, enabling elective definitive surgery after stabilization, the necessary workup, and improvement in the patients' nutritional status. Our protocol achieved a low rate of postoperative mortality and morbidity, and adjuvant chemotherapy was administered more frequently than in previously reported studies that focused mainly on emergency strategies, especially for right-sided OCC. We speculate that the prognosis of patients with right-sided OCC was improved by implementing BTS. Additionally, no differences were observed in long-term outcomes between the right- and left-sided groups.

In this study, the left-sided group showed a low 5-year DFS (58.6%) disproportionate to the 5-year OS (80.9%). One possible reason is that, although statistically not significant, the high frequency of pre-operative decompression by SEMS in the left-sided group impaired long-term oncologic outcome. The oncologic influence of SEMS is still controversial. However, it was previously reported that the potential for dilation resulting from SEMS may cause dissemination of localized tumors and make long-term survival in patients with curable disease worse[16]. Due to its oncological risk, SEMS as a BTS is not currently recommended as a standard treatment for left-sided malignant colonic obstruction[17]. Because of its retrospective nature, our study design is inadequate to evaluate the oncologic influence of SEMS and other decompression methods. Further study is needed to elucidate the discrepancy between the 5-year OS and DFS rates in the left-sided OCC in this study.

Our study design had some shortcomings. First, as commonly occurs in retrospective studies, there may have been a selection bias in choosing which patients to manage by a

BTS approach. Second, this was a relatively small study because of the low incidence of OCC. Third, the reported results refer to a single hospital experience and there was no reference group for comparison. Our results may require external validation.

In conclusion, the current study identified a high rate of complications and low frequency of use of adjuvant chemotherapy in patients with right-sided OCC. However, the complication rate was lower than in previous reports and the long-term outcomes did not differ between the right- and left-sided groups. Our findings suggest that, in a BTS setting, elective surgery following colonic decompression may decrease postoperative complications, achieve better compliance with adjuvant chemotherapy, and improve long-term outcomes in both groups. Further larger prospective studies are needed to evaluate the therapeutic efficacy of BTS in right- and left-sided OCC.

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#### Conflicts of Interest

There are no conflicts of interest.

#### Author Contributions

Kiyooki Sugiura analyzed and interpreted the patient data and was a major contributor to writing the manuscript.

Yuki Seo reviewed and edited the manuscript.

Takayuki Takahashi, Hideyuki Tokura, Yasuhiro Ito, Motomu Tanaka, Norihiro Kishida, Yusuke Nishi, Yoshihiko Onishi and Hikaru Aoki contributed to the acquisition of the clinical datasets.

#### Approval by Institutional Review Board (IRB)

This study was approved by the Ethics Committee of Ashikaga Red Cross Hospital (approval code 2019-30)

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