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Long-term oncologic outcomes of laparoscopic versus open resection following stent insertion for obstructing colon cancer: a multi-center retrospective study

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Abstract

Background This study compared oncologic outcomes between open and laparoscopic surgery following self-expanding metallic stents insertion for obstructing colon cancer.
Methods This retrospective study included 50 patients who underwent open surgery and 44 patients who underwent laparoscopic surgery for obstructing left-sided colon cancer at four tertiary referral hospitals between June 2005 and December 2013.
Results The median follow-up periods were 48 months and 47 months in the open and laparoscopic groups, respectively. The median operative time, time to soft diet, and length of stay were comparable between the groups. Four cases converted to open surgery (9.1%) in the laparoscopic group. The morbidity within 30 days after surgery was comparable between the groups (OR 0.931; 95% CI 0.357–2.426; $p=0.884$). The proximal and distal resection margins, the histologic grade of tumor, TNM stage, median tumor size, and presence of lymphovascular invasion did not differ significantly between the groups. The 5-year overall survival (OS) rates of the open and laparoscopic groups were 67.1% and 71.7% (HR 1.028, 95% CI 0.491–2.15, $p=0.942$) and the 5-year disease-free survival (DFS) rates were 55.8% and 61.5% (HR 0.982; 95% CI 0.522–1.847; $p=0.955$), respectively. The recurrence pattern did not differ between the groups. Multivariate analysis showed that sex ($p=0.027$), nodal stage ($p=0.043$), and the proportion of patients receiving postoperative adjuvant chemotherapy ($p=0.002$) were independent prognostic factors for OS. The proportion of patients receiving postoperative adjuvant chemotherapy ($p=0.017$) was an independent prognostic factor for DFS.
Conclusions Laparoscopic resection following stent insertion for obstructing colon cancer can be performed safely, with long-term oncologic outcomes comparable with those of open surgery.

Keywords Colonic neoplasm · Stent · Laparoscopy · Outcome

Approximately, 80% of colonic obstruction is due to malignant lesions [1, 2], and 15–20% of the patients with colorectal carcinoma present with acute obstruction that requires urgent decompression at initial presentation [3, 4]. The morbidity and mortality rates of emergency operation in such cases are 30% and 7%, respectively and only 60% of patients

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who undergo Hartmann's procedure (resection of the colonic segment involved with end colostomy) can achieve closure of the colostomy [1, 5].

Since the introduction of colonic stents to relieve acute colonic obstruction in 1991 by Dohmoto [6], self-expanding metallic stent (SEMS) has been increasingly used as a bridge to subsequent elective surgery. SEMS allows elective definitive surgery with time for stabilization, necessary workup for patients' medical condition, improved nutritional status of patients, time for proper preoperative staging that avoids unnecessary surgical exploration, proximal colon evaluation by colonoscopy, and increased the likelihood of a primary anastomosis.

Colonic obstruction has been considered a relative contraindication for laparoscopic surgery due to poor surgical field caused by the distended bowel and potential hazard of injury to the fragile bowel. However, SEMS provides an opportunity for bowel preparation and makes laparoscopic surgery possible. In our previous study, we reported the feasibility and safety of laparoscopic resection following stent insertion for obstructing left-sided colon cancer [7]. However, while stenting is becoming a more frequent treatment modality, studies with a sizable number of patients using stent–laparoscopic approach as a bridge to surgery remain lacking. The aim of our multi-center study was to compare oncologic outcomes between open and laparoscopic surgery following SEMS insertion for obstructing colon cancer.

Materials and methods

Patients

A total of 94 consecutive patients (50 in the open surgery group; 44 in the laparoscopic group) with curative resection following stent insertion as a bridge to surgery were included. This study was conducted in four university hospitals between June 2005 and December 2013. The indications for stent placement in patients with malignant left-sided colonic obstruction were uniform across the participating centers and included the clinical features of colonic obstruction such as obstipation and abdominal distension upon admission. The diagnosis was confirmed using plain abdominal film and/or computed tomography (CT) scan. CT of the abdomen was performed in all patients before the insertion of colonic stents. Exclusion criteria in this study were (1) patients who underwent palliative surgery, (2) patients with stage IV tumor, (3) patients with synchronous or previous malignancies, and (4) failure of "bridge to surgery" approach following SEMS insertion. Stents were inserted by gastroenterologists who had encountered more than 100 cases of colonic malignant obstruction, and the choice between open and laparoscopic approaches was based on the surgeon's preference.

The clinicopathological and oncological outcomes were collected retrospectively by reviewing the electronic medical records. We included the sources of the retrieved information. Information regarding patient demographics included data regarding age, sex, American Society of Anesthesiologists classification, body mass index, tumor location, and preoperative carcinoembryonic antigen (CEA). Perioperative details included type of operation, operative time, time to soft diet, length of hospital stay, perioperative complications, and histopathological findings.

Evaluation parameters

We defined right-sided colon cancer as cancer of the cecum and the ascending colon up to the hepatic flexure, and left-sided colon cancer as cancer of the splenic flexure and cancer in regions distal to the splenic flexure, including the rectosigmoid colon. Bridge time was defined as the stent insertion date to the operation date. Conversion to open surgery was defined as interruption of the laparoscopic approach, followed by the need for a laparotomy at any time to complete the entire surgical procedure. The seventh edition of the American Joint Committee on Cancer classification system was used to determine the pathological tumor depth, the number of metastasized lymph nodes, and cancer stage. A postoperative clinical examination, measurement of serum CEA levels, chest radiography every 3 months, and chest/abdominal CT every 6 months were performed during each follow-up examination over a period of 3 years. After 3 years, the follow-up interval was changed to 6 months. Recurrence was defined as the presence of radiologically confirmed or histologically proven tumor. Location of recurrence was defined as the first site of recurrence after complete resection. Local recurrence was defined as any tumor recurrence in the surgical field; local recurrence with synchronous systemic recurrence included systemic recurrence. Overall survival (OS) was defined as the time from the date of surgery to the date of the latest follow-up visit or the date of death due to any cause, and disease-free survival (DFS) was defined as the time from surgery to any type of recurrence.

Statistical analyses

Data were expressed as medians with interquartile range (IQR). Differences in clinicopathological features between patients who underwent open and laparoscopic surgery were analyzed using the Chi-square test or logistic regression with odds ratios (OR) and 95% confidence intervals (CI) for categorical variables and the Student's *t* test for continuous variables. Survival rates were determined using the Kaplan–Meier method, and log-rank tests were used to compare survival rates among subgroups. Log-rank tests were also used for univariate analysis, and independent prognostic factors were identified with multivariate analysis using the Cox proportional hazards model to calculate hazard ratios (HR). Age (≤ 60 or > 60 years), sex (female or male), preoperative CEA (≤ 5 or > 5), surgical approach (open or laparoscopic), sidedness (right sided or left sided), bridge time (≤ 12 days or > 12 days), tumor depth (T2, T3, or T4), nodal stage (N0 or N1 and N2), histology (well and moderately differentiated or poorly differentiated and mucinous), lymphovascular invasion (positive or negative), perinodal extension (positive or negative), and adjuvant chemotherapy (no or yes) were included as covariates. The results of the Cox model analysis were reported using HR and 95% CIs. All statistical tests were performed with IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY). A *p*-value < 0.05 was considered statistically significant.

Results

Patient characteristics

The demographic characteristics, such as age, preoperative CEA, physical status according to the American Society of Anesthesiology status, body mass index, and location of tumor, did not differ significantly between the open and laparoscopic groups (Table 1). The proportion of male patients in the laparoscopic group was higher than that in the open group (81.8% vs. 52.0%, $p = 0.002$). No significant difference was found between the open and laparoscopic groups in bridge time (12 vs. 11 days; IQR 8–15 vs. 6–17; $p = 0.253$) (Table 2).

Perioperative clinical outcomes

The operative time was marginally significantly longer in the laparoscopic group than in the open group (188 vs. 180 min; IQR 155–212 vs. 165–240; $p = 0.057$). The procedure was converted to open surgery in 4 of 44 patients (9.1%) assigned to undergo laparoscopic surgery. Bowel dilatation with poor surgical view ($n = 2$) was the most common cause of conversion among the four cases, with other cases of severe adhesion ($n = 1$) and small bowel invasion ($n = 1$). Colostomy was marginally significantly more performed in the open group than in the laparoscopic group (4 vs. 0%, $p = 0.055$). No apparent differences were found in the time to soft diet and length of hospital stay. Morbidity within 30 days after surgery was comparable between the open and laparoscopic groups (24.0% vs. 22.7%; OR 0.931, 95% CI 0.357–2.426; $p = 0.884$); two and two patients (4.0 and 4.5%) had anastomotic leakage; 0 and three patients (0 and 6.8%), ileus; four and three patients (8.0 and 6.8%), intraabdominal abscess; one and one patient (2.0 and 2.3%), pulmonary complication; one and 0 patient (2.0 and 0%), pseudomembranous colitis; two and 0 patients (4.0% and 0%), surgical site infection; one and 0 patient (2.0 and 0%), wound dehiscence; 0 and one patient (0 and 2.3%), voiding difficulty; and one and 0 patient (2.0 vs. 0%) sepsis. Two patients (4.0%) in the open group and one patient (2.3%) in the laparoscopic

Table 1 Patient and tumor characteristics

	Open surgery (*N* = 50)	Laparoscopic surgery (*N* = 44)	*P* value
Age (years), median (range)	66 (40–83)	69 (45–88)	0.185
Sex			0.002
Male	26 (52.0)	36 (81.8)	
Female	24 (48.0)	8 (18.2)	
Preoperative CEA (ng/mL), median (range)	5.1 (1.0-260.8)	3.8 (0.4–81.9)	0.218
ASA groups, *n* (%)			0.268
I	24 (48.0)	17 (38.6)	
II	23 (46.0)	20 (45.5)	
III	3 (6.0)	7 (15.9)	
BMI (kg/m^2), median (range)	21.7 (15.6–28.9)	22.9 (16.0-33.5)	0.384
Location of tumor (*n*, %)			0.873
Ascending colon	3 (6.0)	2 (4.5)	
Transverse colon	3 (6.0)	2 (4.5)	
Descending colon	13 (26.0)	8 (18.2)	
Sigmoid colon	5 (10.0)	5 (11.4)	
Bridge time (days), median (range)	12 (0–101)	11 (2–55)	0.780

CEA carcinoembryonic antigen, *ASA* American Society of Anesthesiologists, *BMI* body mass index

Table 2 Perioperative outcomes

	Open surgery (*N* = 50)	Laparoscopic surgery (*N* = 44)	*P* value
Operative time (min), median (range)	180 (110–255)	188 (120–500)	0.057
Conversion, *n* (%)		4 (9.1)	
Colostomy formation, *n* (%)	4 (8.0%)	0 (0)	0.055
Time to soft diet (day), median (range)	7 (1–26)	7 (3–26)	0.650
Length of stay (day), median (range)	11 (0–50)	10 (6–44)	0.187
Morbidity within 30 days after surgery, *n*, (%)			
Overall	12 (24.0)	10 (22.7)	0.884
Anastomotic leakage	2 (4.0)	2 (4.5)	
Ileus	0 (0)	3 (6.8)	
Intraabdominal abscess	4 (8.0)	3 (6.8)	
Pulmonary complication	1 (2.0)	1 (2.3)	
Pseudomembranous colitis	1 (2.0)	0 (0)	
Surgical site infection	2 (4.0)	0 (0)	
Wound dehiscence	1 (2.0)	0 (0)	
Voiding difficulty	0 (0)	1 (2.3)	
Sepsis	1 (2.0)	0 (0)	
Reoperation within 30 days after surgery, *n* (%)	2 (4.0)	1 (2.3)	0.635
Mortality within 30 days after surgery, *n* (%)	1 (2.0)	0 (0)	0.346
Adjuvant chemotherapy, *n* (%)	35 (70.0)	38 (86.4)	0.066

group required reoperation within 30 days after surgery ($p = 0.635$). One mortality (2.0%) occurred within 30 days after surgery in the open surgery group. The proportion of patients receiving postoperative adjuvant chemotherapy was marginally significantly higher in the laparoscopic group than in the open group (86.4 vs. 70.0%; OR 2.714; 95% CI 0.948–7.774; $p = 0.066$).

Postoperative pathologic results

The tumor and nodal stage, histologic grade of tumor, median numbers of harvested lymph nodes, median tumor size, and presence of lymphovascular invasion and perineural invasion, and proximal resection margin did not differ significantly between the open and laparoscopic groups (Table 3). The median length of the distal resection margin was significantly longer in the open group than in the laparoscopic group (6 vs. 5.6 cm; IQR 3.0–10.0 vs. 1.5–6.4; $p = 0.042$).

Oncologic outcomes

The median follow-up period was 48 months (IQR 29–67) in the open group and 47 months (IQR 34–60) in the laparoscopic group ($p = 0.784$). The 5-year OS rates of the open and laparoscopic groups were 67.1% and 71.7% (HR 1.028; 95% CI 0.491–2.15; $p = 0.942$) and the 5-year DFS rates were 55.8 and 61.5% (HR 0.982; 95% CI 0.522–1.847; $p = 0.955$), respectively (Fig. 1). In the open group, the numbers of local and distant recurrences were 4 (8.0%) and 13 (26.0%). In the laparoscopic group, these numbers were 1 (2.3%) and 12 (27.3%). These distributions of recurrence did not differ between the two groups ($p = 0.486$). The local recurrence rate was 8.0% in the open group and 2.3% in the laparoscopic group and the systemic recurrence rate was 26.6% in the open group and 27.3% in the laparoscopic group.

Univariate and multivariate survival analyses of prognostic factors

Table 4 summarizes the univariate analysis. Univariate analyses revealed that the histologic grade of tumor, the presence of perineural invasion, and the proportion of patients receiving postoperative adjuvant chemotherapy were significantly associated with OS and that the presence of perineural invasion was significantly associated with DFS. Multivariate analysis showed that sex (HR 0.241; 95% CI 0.069–0.850; $p = 0.027$), nodal stage (HR 2.692; 95% CI 1.034–7.009; $p = 0.043$), and the proportion of patients receiving postoperative adjuvant chemotherapy (HR 0.215; 95% CI 0.082–0.563; $p = 0.002$) were independent prognostic factors for OS and that the proportion of patients receiving postoperative adjuvant chemotherapy (HR 0.352; 95% CI 0.149–830; $p = 0.017$) was an independent prognostic factor for DFS (Table 5).

Table 3 Postoperative pathologic outcomes

	Open surgery (N=50)	Laparoscopic surgery (N=44)	P value
Tumor stage, *n* (%)			0.310
T2	0 (0)	1 (2.3)	
T3	40 (80.0)	38 (86.4)	
T4	10 (20.0)	5 (11.4)	
Nodal stage, *n* (%)			0.110
N0	20 (55.6)	24 (54.5)	
N1	12 (33.3)	8 (18.2)	
N2	4 (11.1)	12 (27.3)	
Histology, *n* (%)			0.355
Well differentiated	2 (4.0)	0 (0)	
Moderately differentiated	41 (82.0)	41 (93.2)	
Poorly differentiated	5 (10.0)	2 (4.5)	
Mucinous	2 (4.0)	1 (2.3)	
Retrieved LNs, median (range)	21 (2–122)	37 (13–77)	0.089
PRM (cm), median (range)	9.5 (2.5–85)	10.1 (0.4–90)	0.342
DRM (cm), median (range)	6 (1.0–30.0)	5.6 (0.4–20.0)	0.042
Tumor size (cm), median (range)	7.0 (2.3–16.5)	7.0 (1.1–13.8)	0.540
Lymphovascular invasion, *n* (%)	22 (44.0)	27 (61.4)	0.093
Perineural invasion, *n* (%)	22 (44.0)	24 (54.5)	0.307

LNs lymph nodes, *PRM* proximal resection margin, *DRM* distal resection margin

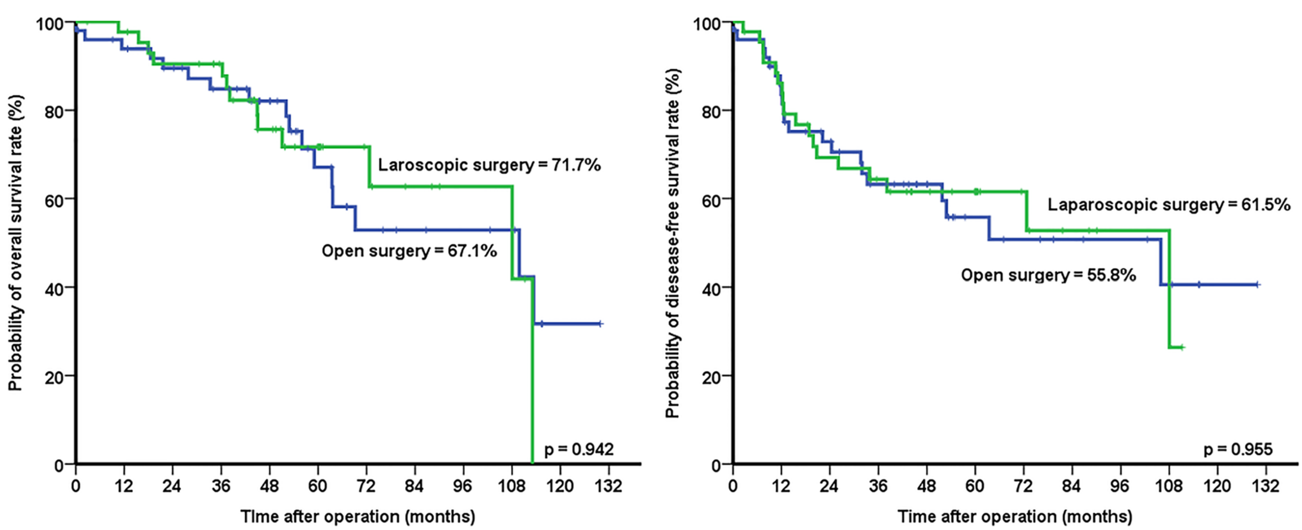

Fig. 1 Comparison of the 5-year OS and DFS rates between the laparoscopic and open groups

Discussion

In this study, two minimally invasive approaches, namely, stent insertion for “bridge to surgery” and laparoscopic surgery, were integrated into the management of patients with obstructing colon cancer. The multi-center retrospective study demonstrated the feasibility and safety of stent-laparoscopic approach. The short-term clinicopathological outcomes and long-term oncologic outcomes of this approach were comparable with those of the open surgery following stent insertion for obstructing colon cancer. To our knowledge, this study is the first multi-center cohort study comparing the oncologic outcomes of stent-laparoscopic approach with those of open surgery as a bridge to surgery for obstructing colon cancer.

Table 4 Prognostic factors of survival by univariate analysis

Prognostic factor	No. ($n=94$)	OS (%)	*P* value	DFS (%)	*P* value
Age			0.051		0.376
≤60	30	80.7		59.9	
>60	64	64.5		57.3	
Sex			0.074		0.179
Male	62	65.2		54.8	
Female	32	76.7		67.0	
Preoperative CEA (ng/ml)			0.276		0.193
≤5	54	75.7		68.9	
>5	40	57.7		40.8	
Surgical approach			0.942		0.955
Open	50	67.1		55.8	
Laparoscopic	44	71.1		61.5	
Sidedness			0.495		0.332
Right sided	10	90.0		80.0	
Left sided	84	68.4		56.9	
Bridge time (days)			0.118		0.929
≤12	45	72.7		57.4	
>12	49	67.4		60.7	
Tumor stage			0.382		0.840
T2 and T3	79	70.4		58.3	
T4	15	62.5		62.5	
Nodal stage			0.066		0.060
N0	49	77.9		68.9	
N1 and N2	45	61.0		48.7	
Histology			0.050		0.279
Well and moderately	84	74.5		61.7	
Poorly and mucinous	10	37.5		40.0	
Lymphovascular invasion			0.118		0.067
No	45	72.7		64.0	
Yes	49	67.4		54.6	
Perineural invasion			0.037		0.010
No	48	73.3		70.6	
Yes	46	65.9		46.6	
Adjuvant chemotherapy			0.016		0.120
No	21	42.3		42.8	
Yes	73	64.7		58.9	

OS overall survival, *DFS* disease-free survival, *CEA* carcinoembryonic antigen

Despite technical improvements in laparoscopic colectomy, colonic obstruction has been considered as a relative contraindication for laparoscopic surgery due to the insufficient working space caused by the distended bowel, poor surgical field, and fragility of the colon. Moreover, as tumors that cause luminal obstruction are mostly bulky and locally advanced, stent-laparoscopic approach might be associated with increased technical difficulty. In the present study, the conversion rate was 9.1% in the laparoscopic group. The operative time and morbidity within 30 days after surgery were significantly not different between the two groups. In addition, stoma formation was not required in the laparoscopic group, and four patients (8.0%) in the open group underwent colostomy with primary tumor resection. These results show the advantages of laparoscopic surgery and that the presence of a stent insertion does not compromise the laparoscopic approach.

While obstructed colon cancer can often be treated with one-stage resection with primary anastomosis, the results on the oncologic outcomes of the use of stent insertion as a bridge to surgery in the literature remain controversial. Maruthachalam et al. [8] reported a significant increase in cytokeratin 20 mRNA expression and suggested that stent insertion might result in dissemination of malignant cells

Table 5 Prognostic factors of survival in multivariate analysis

Prognostic factor	OS		DFS	
	HR (95% CI)	*P* value*	HR (95% CI)	*P* value*
Age				
> 60 vs. ≤ 60	1.872 (0.621–5.639)	0.265	0.893 (0.390–2.045)	0.789
Sex				
Female vs. male	0.241 (0.069–0.850)	0.027	0.488 (0.182–1.307)	0.154
Sidedness				
Left vs. right	0.404 (0.043–3.775)	0.426	1.128 (0.228–5.570)	0.883
Surgical approach				
Laparoscopic vs. open	0.768 (0.309–1.910)	0.571	0.805 (0.374–1.735)	0.580
Bridge time				
> 12 days vs. ≤ 12 days	1.188 (0.482–2.925)	0.708	1.193 (0.577–2.465)	0.634
CEA				
> 5 vs. ≤ 5	1.453 (0.597–3.536)	0.410	1.731 (0.837–3.580)	0.139
Tumor stage				
T2 and T3 vs. T4	1.152 (0.340–3.902)	0.288	0.809 (0.286–2.290)	0.690
Nodal stage				
Positive vs. ≤ negative	2.692 (1.034–7.009)	0.043	1.495 (0.694–3.224)	0.305
Histology				
Poorly differentiated and mucinous vs. well and moderately differentiated	2.822 (0.919–8.661)	0.070	1.197 (0.430–3.336)	0.731
Lymphovascular invasion				
Yes vs. no	1.361 (0.482–3.846)	0.561	1.784 (0.787–4.044)	0.166
Perineural invasion				
Positive vs. ≤ negative	2.218 (0.932–5.276)	0.072	1.194 (0.922–3.971)	0.081
Adjuvant chemotherapy				
Yes vs. no	0.215 (0.082–0.563)	0.002	0.352 (0.149–0.830)	0.017

HR hazard ratio, *CI* confidence interval, *CEA* carcinoembryonic antigen

into the circulation. The European Society of Gastrointestinal Endoscopy clinical guideline recommends the use of stent in young and fit patients with a potentially curable left-sided malignant colonic obstruction. This was recommended because it does not decrease the postoperative mortality in the general population and stent insertion may be associated with an increased risk of tumor recurrence [9]. A meta-analysis published in 2015 demonstrated that the 5-year OS rates in the bridge to surgery and emergency surgery groups were 57.2 and 67.1%, respectively. Moreover, the 5-year DFS rates in the bridge to surgery and emergency surgery groups of the five studies were 48.4 and 59.0%, respectively, with no significant difference between the two groups. These results suggest that surgery following stent insertion could be a promising alternative strategy for obstructed colon cancer [10]. In this study, the 5-year OS and DFS rates were 71.5 and 58.8%, respectively, and these results reflected the oncologic safety of the surgery following stent approach.

In this study, the proportion of patients receiving postoperative adjuvant chemotherapy was marginally significantly higher in the laparoscopic group than in the open group (86.4 vs. 70.0%, $p = 0.066$). The proportion of patients receiving postoperative adjuvant chemotherapy was an important prognostic factor in univariate and multivariate analyses. Kim et al. [11] reported that the laparoscopic group receives adjuvant chemotherapy at a somewhat greater rate than the open group (66.2% vs. 59.4%, $p < 0.01$). They also reported that a 2-year OS rate is better for laparoscopic surgery than open surgery (81.9% vs. 73.2%, $p < 0.01$) in the treatment of colon cancer. Although the long-term oncologic outcomes did not differ significantly between the two groups, stent-laparoscopy approach seemed to be associated with greater rates of compliance for adjuvant chemotherapy in this study.

For patients who have undergone potentially curative resection of colon cancer, the benefits of adjuvant treatment have been most clearly demonstrated in stage III (node-positive) disease [12, 13]. In the current study, the local recurrence and systemic recurrence rate were 5.3% and 26.6%, respectively, in all patients who underwent "bridge to surgery" approach, and the proportion of patients receiving postoperative adjuvant chemotherapy was an independent prognostic factor for OS and DFS. These results suggest that adjuvant chemotherapy plays a significant role in the setting of stent insertion following curative resection for obstructed colon cancer.

The current study has several limitations. These include the retrospective design of the study, potential selection bias due to a physician- or institution-based bias in the selection of stent insertion in patients with obstructed colon cancer, the lack of standard SEMS protocol, and the differences in practices across the participating centers. Nevertheless, our data collection limited the amount of missing data and multicentric recruitment provided a major advantage over single-centric studies by producing a far larger sample size in this rare clinical setting.

Conclusion

Laparoscopic resection following stent insertion for obstructing colon cancer can be performed safely, with long-term oncologic outcomes comparable with those of open surgery.

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Compliance with ethical standards

Disclosures Drs. Sung Uk Bae, Chun-Seok Yang, Sohyun Kim, Dae Ro Lim, Woon Kyung Jeong, Dae Dong Kim, Jae Hwang Kim, Eung Jin Shin, Yoo Jin Lee, Ju Yup Lee, Nam Kyu Kim, Seong Kyu Baek have no conflicts of interest or financial ties to disclose.

Ethical approval IRB approval for this study across the multiple centers performed in accordance with the principles of the Declaration of Helsinki. The formal informed consent was waived.

Informed consent The formal informed consent was waived.

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