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Surgical Outcomes of Laparoscopic and Open D3 Dissection for Clinical Stage II/III Descending Colon Cancer

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Abstract. *Aim: To compare the surgical outcomes of laparoscopic colectomy (LAC) with Japanese D3 dissection for descending colon cancer (DCC) with those of open colectomy (OC). Patients and Methods: Seventy-two patients who underwent OC or LAC with D3 dissection for clinical stage II/III DCC between September 2002 and June 2019 were evaluated in terms of short-term outcomes. The long-term outcomes of the 59 patients who underwent surgery between September 2002 and June 2016 were evaluated. Results: Twenty-six patients underwent OC and 46 patients underwent LAC. The blood loss was significantly less in the LAC group. The complication rate was similar in both groups. The rates of 5-year overall survival (95.8% in the OC group vs. 89.9% in the LAC group) and relapse-free survival (79.2% in the OC group vs. 82.1% in the LAC group) were similar in both groups. Conclusion: LAC is an acceptable treatment option for stage II/III DCC.*

Recently, the safety and oncological validity of laparoscopic surgery for colon cancer have been reported in large randomized controlled trials (1-5). In Japan, the Japan Clinical Oncology Group (JCOG) similarly conducted a randomized trial (JCOG0404) and demonstrated that laparoscopic colectomy (LAC) with Japanese D3 dissection could be an acceptable treatment option for patients with stage II or III colon cancer (6, 7). However, transverse colon cancer (TCC) and descending colon cancer (DCC) were excluded from that clinical trial. Large-scale European and American randomized controlled trials also have excluded TCC and included a relatively small number of DCCs (1-5); this is most likely due to the technical demand of LAC for these types of cancers (8). In addition, the incidence of DCC is as low as 6-10% of all colon cancers (9-11). Although several investigators have reported the feasibility and safety of LAC for transverse and splenic flexure colon cancers (12-14), a limited number of studies have reported the applicability of LAC for DCC only (15). A large part of the procedure for DCC is different from that for TCC; therefore, the feasibility of LAC for DCC remains unclear.

D3 dissection is the standard surgical procedure for clinical stage II/III colon cancer patients in Japan (16), whereas complete mesocolic excision (CME) with central vascular ligation (CVL) is widely used to treat colon cancer in Western countries. This study aimed to evaluate the feasibility of LAC with D3 dissection for clinical stage II/III DCC, by comparing the short- and long-term outcomes with those of open colectomy (OC).

Patients and Methods

Patients and ethical considerations. This study was a retrospective cohort study initiated based on a prospectively collected institutional database at the Shizuoka Cancer Center Hospital. Between September 2002 and June 2019, a total of 85 patients, who had been preoperatively diagnosed with adenocarcinoma of the descending colon and clinical stage II/III DCC, underwent colectomy with D3 dissection at the Shizuoka Cancer Center Hospital. The exclusion criteria were simultaneous surgery, synchronous or metachronous colorectal cancer, other combined malignancies (except for carcinoma *in situ*), previous colectomy (except for appendectomy), and intestinal perforation. Eleven patients who underwent simultaneous surgery and two patients who underwent a previous colectomy before the surgery for DCC were excluded. Thus, 72 patients with DCC (26 patients treated with OC and 46 patients treated with LAC) were enrolled in this study (Figure 1). Eventually, these patients were examined to determine the short-term outcomes. The long-term outcomes were analyzed for 59 patients who underwent surgery for DCC between September 2002 and June 2016. Patients diagnosed with Stage IV DCC were excluded (Figure 1).

In this study, DCC was defined as carcinoma that developed from the distal site of the splenic flexure to the sigmoid colon-descending colon junction (SDJ). Tumor location was diagnosed based on contrast enema and/or computed tomography (CT). Preoperative clinical staging was performed based on the results of colonoscopy,

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Key Words: Laparoscopic colectomy, descending colon cancer, D3 dissection, long-term outcomes, short-term outcomes.

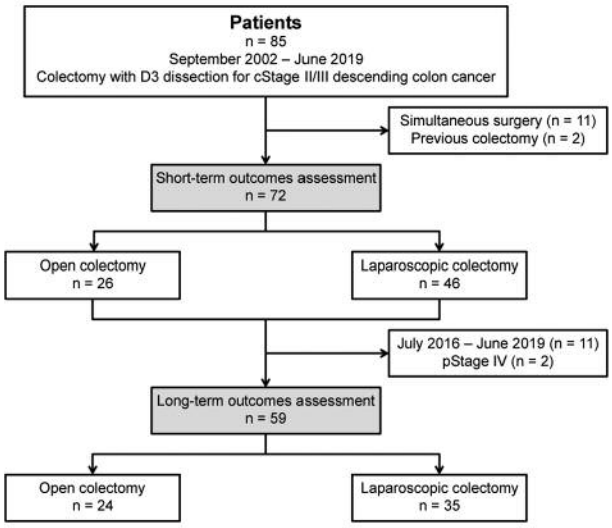

Figure 1. *Flowchart of patient selection.*

contrast enema, and CT, using the 8th edition of the tumor node metastasis (TNM) classification (17).

Surgical procedures. Resection of the colon with D3 dissection was performed according to the Japanese Classification of Colorectal Carcinoma (18). In D3 dissection for DCC, lymph nodes were dissected with ligation of the root of the inferior mesenteric artery (IMA) or with ligation of the root of the left colic artery (LCA), in order to preserve the IMA. If the left branch of the middle colic artery (MCAlt) entered within 10 cm of the tumor, the MCAlt was also ligated at its root, and lymphadenectomy was performed around the MCA. When the accessory middle colic artery (19, 20) was present within 10 cm of the tumor, it was ligated at the inferior border of the pancreas. Mobilization of the splenic flexure was performed in all patients. The anastomosis was performed using a functional end-to-end anastomosis (FEEA), a hand-sewn technique, or a double stapling technique (DST). In LAC for DCC, the five-port technique was employed. Ligation of vessels, D3 dissection, and mobilization of the colon were performed using medial-to-lateral approaches. The incision was extended within 8 cm and covered with wound protectors. The specimen was extracted before the anastomosis was performed. Previously, we did not routinely close mesenteric defects caused by colectomy for DCC. More recently, we routinely did this whenever possible to prevent internal hernia. Conversion to open surgery was defined as an unplanned additional skin incision for the control of intraoperative complications or due to severe adhesion or unexpected tumor extension.

Adjuvant therapy and follow-up. Postoperative pathological staging was conducted using the 8th edition of the TNM classification (17). Patients with pathological stage III were recommended to undergo adjuvant chemotherapy (16). Basically, the patients were followed-up every 3 months during the first 3 years and every 6 months thereafter. Blood tests were conducted during each follow-up visit and were assessed for tumor markers. Chest-abdomen-pelvic CT was performed every 6 months. Total colonoscopy was performed in the first, third, and fifth years after surgery.

Table I. *Short-term patient characteristics.*

Variables	Open colectomy (n=26)	Laparoscopic colectomy (n=46)	*p*-Value
Gender			0.799
Male	18 (69.2)	30 (65.2)	
Female	8 (30.8)	16 (34.8)	
Age (years)	66 (50-82)	64 (45-77)	0.408
BMI (kg/m^2)	23.0 (17.0-37.0)	23.0 (16.3-31.0)	0.707
Clinical stage			0.209
II	7 (26.9)	20 (43.5)	
III	19 (73.1)	26 (56.5)	
Tumor size (mm)	50 (30-90)	41 (15-75)	0.076
Tumor location			0.406
Proximal third of the DC	8 (30.8)	17 (37.0)	
Middle third of the DC	9 (34.6)	9 (19.6)	
Distal third of the DC	9 (34.6)	20 (43.5)	
Previous operation	7 (26.9)	15 (32.6)	0.791
ASA-PS			0.310
1	6 (23.1)	13 (28.3)	
2	17 (65.4)	32 (69.3)	
3	3 (11.5)	1 (2.2)	

Values are expressed as number (percentage) or median value (range). BMI, Body mass index; ASA-PS, American Society of Anesthesiologists-Physical Status; DC, descending colon.

Outcome variables. Data regarding patient characteristics were collected and analyzed. The short-term outcomes, including perioperative outcomes, postoperative complications, and pathological results, were compared between both the LAC and OC groups. Postoperative complications within 30 days were stratified according to the Clavien–Dindo classification system (21). The long-term outcomes, including the 5-year overall survival (OS) and relapse-free survival (RFS) rates, were compared between both the LAC and OC groups.

Statistical analyses. Parametric variables were expressed as median values. To compare the OC group to the LAC group, Fisher's exact test, the chi-squared test, and the Mann-Whitney *U*-test were used, as appropriate. OS and RFS rates were calculated using the Kaplan-Meier method and compared using the log-rank test. A *p*-value of <0.05 was considered statistically significant. All statistical analyses were performed using R software version 3.4.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Compliance with ethical standards. This study was approved by the institutional review board of Shizuoka Cancer Center Hospital (Institutional code: J2019-51-2019-1-3).

Results

Short-term outcomes. Short-term outcomes and patient characteristics are summarized in Table I. In total, 72 patients were analyzed for short-term outcomes. Twenty-six (36.1%) patients underwent OC, while 46 (63.9%) patients underwent LAC. There were no significant differences in patient

Table II. *Perioperative outcomes*.

	Open colectomy (n=26)	Laparoscopic colectomy (n=46)	*p*-Value
Operative time (minutes)	202 (111-287)	210 (141-299)	0.086
Blood loss (ml)	125 (0-698)	20 (0-570)	<0.01
Anastomosis			0.206
FEEA	24 (92.3)	40 (87.0)	
Hand-sewn	1 (3.8)	0 (0)	
DST	1 (3.8)	6 (13.0)	
Preservation of IMA	15 (57.7)	28 (60.9)	0.808
Conversion		2 (4.3)	
Closure of mesenteric defects	1 (4.5)	15 (32.6)	0.018
Length of postoperative hospital stay (days)	8 (6-49)	7 (6-34)	<0.01

Values are expressed as number (percentage) or median (range). FEEA, Functional end-to-end anastomosis; DST, double stapling technique; IMA, inferior mesenteric artery.

Table III. *Postoperative complications*.

	Open colectomy (n=26)	Laparoscopic colectomy (n=46)	*p*-Value
≥Grade II (Clavien-Dindo)	4 (15.4)	7 (15.2)	1.000
Pneumonia	0 (0)	3 (6.5)	
Urinary tract infection	1 (3.8)	2 (4.3)	
Enteritis	0 (0)	1 (2.2)	
Internal hernia	0 (0)	1 (2.2)	
Wound infection	0 (0)	1 (2.2)	
Bowel obstruction of duodenum	0 (0)	1 (2.2)	
Bowel obstruction of small intestine	1 (3.8)	0 (0)	
Chylous ascites	1 (3.8)	0 (0)	
Lymphocyst	1 (3.8)	0 (0)	
Paralytic ileus	1 (3.8)	0 (0)	
Re-operation	1 (3.8)	1 (2.2)	1.000
Mortality	0 (0)	0 (0)	

Values are expressed as number (percentage).

characteristics between the two groups. Perioperative outcomes are summarized in Table II. All patients underwent D3 dissection. Operative times were similar between the two groups. The blood loss was significantly less in the LAC group than in the OC group (125 ml in the OC group *vs*. 20 ml in the LAC group, $p<0.01$). Anastomosis types were not significantly different between the two groups. In the LAC group, conversion to open surgery was required in two (4.3%) patients because of severe adhesion and tumor invasion. The closure of mesenteric defects was performed and was significantly more in the LAC group than in the OC group (4.5% in the OC group *vs*. 32.6% in the LAC group, $p=0.018$). The length of postoperative hospital stay was significantly shorter in the LAC group than in the OC group (8 days in the OC group *vs*. 7 days in the LAC group, $p<0.01$).

Postoperative complications are summarized in Table III. The frequencies of postoperative complications (≥grade II Clavien-Dindo) were similar between the two groups. Two patients underwent re-operation. One patient in the OC group underwent re-operation for bowel obstruction of the small intestine, while the other patient was in the LAC group and underwent re-operation for an internal hernia. Postoperative mortality did not occur in either group.

Pathological results are summarized in Table IV. The median value of proximal resection margins in the LAC group was 100 mm, which was comparable to the OC group. Distal resection margins in the LAC group were significantly longer than in the OC group (115 mm in the OC group *vs*. 134 mm in the LAC group, $p=0.046$). Patients in both groups underwent complete resection of the primary tumor with negative resection margins. Lymph nodes were harvested in both groups and the number of harvested lymph nodes was significantly higher in the LAC group than in the OC group (27 in the OC group *vs*. 33 in the LAC group, $p=0.041$).

Long-term outcomes. Long-term outcomes were analyzed in a total of 59 patients, including 24 patients in the OC group and 35 patients in the LAC group (Figure 1). Patient characteristics and oncological outcomes are summarized in Table V. There were no significant differences in patient characteristics between the two groups. The median length of the follow-up period was 60 months. There was no statistical difference in the rate of 5-year OS rate (95.8% in the OC group *vs*. 89.9% in the LAC group, $p=0.723$) (Figure 2a) and 5-year RFS rate (79.2% in the OC group *vs*. 82.1% in the LAC group, $p=0.726$) (Figure 2b) between the two groups. The long-term outcomes were similar between the two groups.

Discussion

We evaluated the short- and long-term outcomes of LAC with D3 dissection for DCC, by comparing them with those of OC. Although a previous study reported short-term outcomes of LAC for DCC only (15), the sample size was small, and researchers did not investigate the long-term outcomes. In Japan, Yamaguchi *et al*. conducted a multicenter retrospective study for TCC and DCC collected from the databases of 45 hospitals (12). However, the targets of the analysis included TCC, and the percentage of cases with DCC was 31.3%. Moreover, in these two previous studies (12, 15), the proportion of patients with tumors of pathological stage 0/I was high, and D3 dissection was

Table IV. *Pathological results.*

	Open colectomy (n=26)	Laparoscopic colectomy (n=46)	*p*-Value
Proximal resection margin (mm)	90 (50-211)	100 (48-455)	0.738
Distal resection margin (mm)	115 (60-220)	134 (55-375)	0.046
Resection margin			1.000
R0	25 (96.2)	45 (97.8)	
R1	0 (0)	0 (0)	
R2	1 (3.8)	1 (2.2)	
Only local	0	0	
Only distant	1	1	
Both	0	0	
Number of lymph nodes harvested	27 (12-51)	33 (11-79)	0.041
Pathological stage			0.611
I	0 (0)	2 (4.3)	
II	13 (50.0)	18 (39.1)	
III	12 (46.2)	25 (54.3)	
IV	1 (3.8)	1 (2.2)	
Tumor differentiation			0.180
Well or moderately differentiated	22 (84.6)	44 (95.7)	
Poorly differentiated or mucinous	4 (15.4)	2 (4.3)	

Values are expressed as number (percentage) or median value (range).

Table V. *Oncological outcomes and patient characteristics.*

	Open colectomy (n=24)	Laparoscopic colectomy (n=35)	*p*-Value
Gender			0.423
Male	17 (70.8)	21 (60.0)	
Female	7 (29.2)	14 (40.0)	
Age (years)	66 (50-82)	64 (45-77)	0.594
BMI (kg/m^2)	23.1 (17.0-37.0)	22.9 (16.3-31.0)	0.835
Tumor location			0.592
Proximal third of the DC	7 (29.2)	10 (28.6)	
Middle third of the DC	8 (33.3)	8 (22.9)	
Distal third of the DC	9 (37.5)	17 (48.6)	
Pathological stage			0.507
I	0 (0)	2 (5.7)	
II	12 (50.0)	14 (40.0)	
III	12 (50.0)	19 (54.3)	
Adjuvant chemotherapy	6 (25)	17 (48.6)	0.103

Values are given as number (percentage) or median value (range). BMI, Body mass index; DC, descending colon; CEA, carcinoembryonic antigen; CA 19-9, carbohydrate antigen 19-9.

performed in 40.6% patients (12). Therefore, further investigation is required to evaluate the feasibility of LAC with D3 dissection for DCC. The present study was restricted to patients with clinical stages II/III DCC and patients who underwent D3 dissection, which is the standard surgical procedure for clinical stage II/III colorectal cancer in Japan (16). In Western countries, CME with CVL is the standard surgical procedure. Although there were differences in the extent of longitudinal resection and the lymph node yields between CME with CVL and D3 dissection (22), both techniques were based on similar principles and provided good oncological specimens (22, 23). To our knowledge, our study is the first to report the feasibility of LAC with D3 dissection for DCC only.

In previous reports (1-5, 7, 12), the operation times in LAC were longer than those in OC. However, the operation times in both arms were almost equivalent in this study. In this study, there was significantly less bleeding in the LAC group. The length of postoperative hospital stay in the LAC group was significantly shorter than that in the OC group. The rate of conversion in this study was 4.3% and equivalent to or better than that in other studies (2, 3, 5, 7).

The postoperative complication rate was similar between the OC and LAC groups and comparable to that of the randomized studies, which investigated tumors at other colon sites (1-5, 7). Previously, it was reported that leaving the mesenteric defects caused by colectomy may increase the incidence of internal hernia and subsequent small bowel obstruction, especially in left-sided laparoscopic colectomy (24-26). In this study, we did not close mesenteric defects in 31 (67.4%) patients in the LAC group; consequently, one patient (3.2%) developed internal hernia and underwent re-operation. No patients who underwent closure of mesenteric defects develop an internal hernia. Although we close mesenteric defects whenever possible, there is no consensus regarding the closure of such defects during LAC (24-26). Further investigations are warranted to assess the feasibility of closing mesenteric defects during LAC.

As for the pathological results, all patients in this study underwent complete resection of the primary tumor with negative resection margins. Several studies have suggested that an increase in the lymph node yield is associated with a better long-term survival rate for patients with colon cancer (9, 27, 28). A multicenter retrospective study reported that a minimum 12-lymph node threshold was supported as a measure to improve a discriminatory capacity in prognosis and as a quality-control parameter of hospital performance in colorectal cancer surgery (29). In this study, the median number of harvested lymph nodes in both groups was greater than 12, with significantly more lymph nodes being harvested in the LAC group. In D3 dissection, the resection margin of the bowel was determined so that the pericolic lymph node could be dissected (16). Metastasis of the pericolic lymph node at a distance of 10 cm or more from the tumor edge is rare (30); therefore, the resection margin of the bowel and mesentery should be determined to include a range

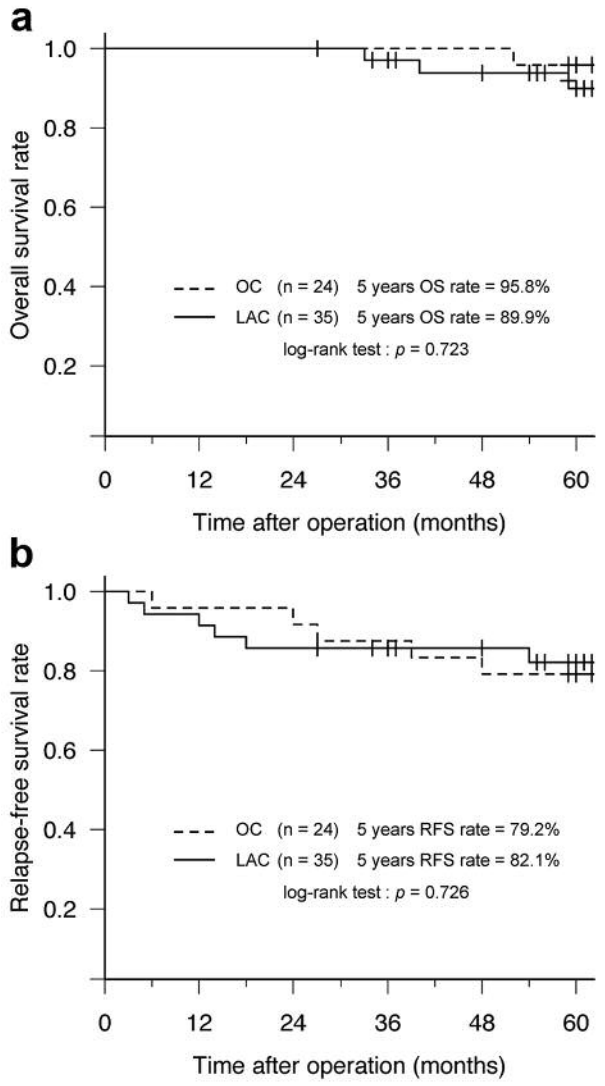

Figure 2. *Oncological outcomes. (a) Kaplan–Meier curve for comparison of 5-year survival; (b) Kaplan–Meier curve for comparison of relapse-free survival. OC, Open colectomy; LAC, laparoscopic colectomy.*

of 10 cm from the tumor edge (16). In the present study, the median length of the proximal and distal resection margins in the LAC group was more than 100 mm. Under this condition, enough mobilization of the splenic flexure can ensure a sufficient resection margin. Collectively, the present findings suggest that short-term outcomes of LAC with D3 dissection for clinical stage II/III DCC are better than those of OC.

The long-term outcomes of LAC for only DCC have not been investigated in a larger scale study. In the JCOG0404 trial (7), which was a randomized control trial to evaluate laparoscopic D3 dissection, the 5-year OS rate was 90.4% in OC and 91.8% in LAC, while the 5-year RFS rate was 80% in OC and 79% in LAC. However, the patients with TCC or DCC were excluded from JCOG0404, because they require high-level laparoscopic techniques (7). In the present study, the 5-year OS and RFS rates of the LAC group were 89.9% and 82.1%, respectively, which were comparable to the OC group. These results were similar to the JCOG0404 trial (12). These findings suggest that LAC with D3 dissection for DCC of clinical stage II/III is an acceptable treatment option, in terms of long-term prognosis.

This study had several limitations. First, this was a single institutional retrospective study, and the sample size was small. To overcome this problem, additional randomized controlled trials are required to validate our results. Second, the present study had a bias regarding the date of operation. At our institution, the indication for laparoscopic surgery for descending colon cancer has gradually expanded. Therefore, OC tended to be performed earlier than LAC, and it was possible that regimens of adjuvant chemotherapy or systemic chemotherapy for postoperative recurrence were different between the groups. In addition, the frequency of patients who underwent adjuvant chemotherapy tended to be lower in the OC group than in the LAC group. This may have influenced oncological outcomes. Third, surgeons who had varied surgical experience were involved in this study; thus, the outcomes were possibly influenced by the operator's expertise. However, it would be difficult to plan large randomized trials because the incidence of DCC is low among colon carcinomas. Despite these limitations, our retrospective study is currently presumed to be a practical approach for evaluating the clinical benefits of this procedure.

Conclusion

Short-term outcomes of LAC with D3 dissection for DCC were better than those of OC. Regarding long-term outcomes, LAC with D3 dissection for DCC was comparable to OC. LAC with D3 dissection is an acceptable treatment option for clinical stage II/III DCC.

Conflicts of Interest

The Authors declare no conflicts of interest or financial ties.

Authors' Contributions

Tadahiro Kojima and Hitoshi Hino drafted the paper. Hitoshi Hino designed this study. Akio Shiomi, Hiroyasu Kagawa, Yusuke Yamaoka, Shoichi Manabe, Marie Hanaoka, Shunichiro Kato obtained and analyzed data.

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