#### ORIGINAL ARTICLE



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# Short-term and long-term outcomes of laparoscopic colectomy with multivisceral resection for surgical T4b colon cancer: Comparison with open colectomy

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#### Abstract

**Aim:** In response to the rising use of laparoscopic surgery, recent studies have shown that laparoscopic multivisceral resections for locally advanced colon cancer are safe, feasible, and provide acceptable oncological outcomes. However, the usefulness of laparoscopic multivisceral resection remains controversial. Here, we aimed to compare short-term and long-term outcomes between laparoscopic and open multivisceral resection approaches for treating locally advanced colon cancer.

**Methods:** We retrospectively collected data on 1315 consecutive patients admitted to the National Hospital Organization, Osaka National Hospital, for surgical treatment of colorectal cancer between 2010 and 2017. We assessed invasiveness in terms of operating times, blood loss, and complications. Oncological outcomes included 5-year survival rates and recurrences.

**Results:** We included 85 patients that underwent a colectomy with a multivisceral resection for locally advanced colon cancer; of these, 38 were treated with a laparoscopic approach and 47 were treated with an open approach. Compared to the open surgery group, the laparoscopic group had significantly less blood loss (median volume: 25 vs 140 mL, P < 0.001), a lower complication rate (10.5% vs 29.8%, P = 0.036), and shorter hospital stays (12 vs 15 days, P = 0.028). After excluding patients with stage IV colon cancer, the groups showed similar pathologic outcomes and no significant differences in 5-year disease-free survival (73.9% vs 67.4%; P = 0.664) or 5-year overall survival (75.8% vs 67.7%; P = 0.695).

**Conclusion:** A laparoscopic approach for locally advanced colon cancer could be less invasive than an open approach without affecting oncological outcomes in selected patients.

#### KEYWORDS

laparoscopic surgery, locally advanced colon cancer, long-term outcomes, multivisceral resection, short-term outcomes

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## 1 | INTRODUCTION

Due to advances in surgical techniques, instrumentation, and knowledge of anatomy in the field of colorectal cancer, surgical invasiveness has been reduced by performing a laparoscopic colectomy. The laparoscopic colectomy can be applied to a wide range of conditions—from early to advanced cancer and from colon cancer to rectal cancer. Large-scale randomized controlled trials and meta-analyses have indicated that laparoscopic surgery for colon cancer is equivalent or better than open surgery with regard to safety, feasibility, blood loss, postoperative pain, cosmesis, length of hospital stay, and oncological outcomes.<sup>1-10</sup>

Locally advanced colorectal cancers sometimes invade or adhere to adjacent organs. In those cases, it is often difficult to determine whether adhesions between the tumor and the adjacent organs are due to a malignant invasion or a benign inflammatory change: consequently, radical removal requires an en bloc multivisceral resection with a safe margin.<sup>11,12</sup> In those cases, several guidelines recommend open surgery, including the European Association of Endoscopic Surgery, the Society of American Gastrointestinal and Endoscopic Surgeons, and the French Society of Digestive Surgery, because serious complications are associated with extended en bloc multivisceral resections. Moreover, little evidence has been published on oncological outcomes with laparoscopic surgery.<sup>13-15</sup> The Japanese Society for Cancer of the Colon and Rectum (JSCCR) also stated that the indications for performing laparoscopic surgery to treat locally advanced colorectal cancers should be carefully considered, based on findings from the open-label, multi-institutional, randomized, phase III trial, JCOG0404.<sup>16</sup>

In response to the rising use of laparoscopic surgery, recent studies have demonstrated that laparoscopic multivisceral resections are safe, feasible, and provide acceptable oncological outcomes.<sup>17,18</sup> However, the usefulness of laparoscopic multivisceral resections for treating locally advanced colorectal cancers remains controversial, and no reports have discussed long-term outcomes for laparoscopic multivisceral resections with a sufficient median follow-up period (i.e., >5 years). Currently, data are available for long-term outcomes, including survival and recurrence, from a sufficiently long follow-up. Therefore, the present study investigated patients with locally advanced colon cancer that underwent laparoscopic or open multivisceral resections and were followed for a median of >5 years. We compared the short- and long-term outcomes between the laparoscopic and open surgical approaches.

# 2 | MATERIALS AND METHODS

## 2.1 | Patients

We retrospectively collected data on 1315 consecutive patients that were admitted to the National Hospital Organization, Osaka National Hospital, for surgical treatment of colorectal cancer AGSurg Annals of Gastroenterological Surgery -WILFY

between 2010 and 2017. We identified all patients that underwent a colectomy with a multivisceral resection for a locally advanced colon cancer that had invaded or adhered to adjacent organs. Of these, we included all patients that underwent emergency surgery or a primary tumor resection with distant metastases and patients with bowel obstructions that were palliated with a colonic stent, ileus tube, and stoma before surgery. We excluded patients with rectal cancer or a recurrence of colorectal cancer.

We reviewed medical and pathology reports to collect data on clinicopathological parameters, including: sex, age, body mass index (BMI), physical status according to American Society of Anesthesiologists classifications (ASA-PS), the diameter and location of the tumor, preoperative complications and treatment, the operation type, depth of tumor invasion, lymph node metastasis, lymphatic invasion, venous invasion, the pathologic stage, proximal and distal resection margins, the histological type, and the recurrence site. We also collected information on perioperative outcomes, including operating time, blood loss volume, removal of adjacent structures, conversion to open surgery, postoperative complications, length of postoperative hospital stay, and mortality. Complications were defined as those classified as grade II or higher in the Clavien-Dindo classification system. The follow-up included physical examinations and blood tests, performed every 3 months for 3 years after the operation, and every 6 months thereafter. Computed tomography (CT) was performed every 6 months. Overall survival (OS) was defined as the time from surgery to the date of death from any cause. Diseasefree survival (DFS) was defined as the time from surgery to the date of recurrence or death from any cause. Previous abdominal surgery was categorized into major surgery (all resections of the gastrointestinal tract, with the exception of cholecystectomy, any kind of perforation, bleeding or peritonitis) or minor surgery (isolated abdominal wall procedures, cholecystectomy, appendectomy, and other limited intra-abdominal procedures), as described in the previous report by Neeff et al.<sup>19</sup>

Written informed consent was provided by all patients that participated in this study. This study was approved by the Institutional Review Board for Studies in Humans (approval number 19-77).

## 2.2 | Surgical techniques

Radical resections were performed with either open or laparoscopic surgery. In both cases, a central vascular ligation was performed, and the entire mesocolon and all lymph nodes around the vessels supplying the tumor were removed. Standard laparoscopic surgery for colon cancer at our institution was described previously.<sup>20</sup> Briefly, laparoscopic surgery was performed with five ports, including the first 12-mm trocar in the umbilicus as a camera port, another 12-mm trocar, and three 5-mm trocars. Basically, a right hemicolectomy was achieved via a retroperitoneal approach, and a left hemicolectomy, sigmoidectomy, and anterior resection were performed with a medial-to-lateral approach. However, the approach was changed, according to tumor status. The final VILEY- AGSurg Annals of Gastroenterological Surgery

incision was extended as little as possible to pull the specimen out through the umbilical incision. Which procedure would be performed depended on surgeon's techniques and the demands of the patient. As our technical skills have matured, the range of application of laparoscopic surgery has been expanded, and cases with laparoscopic multivisceral resection have increased over time. In fact, until 2012, open multivisceral resections were more common than laparoscopic multivisceral resections in our hospital (percentage of laparoscopy: 34.5%). However, since 2013, the proportion of laparoscopies has increased (62.9%); indeed, the most recent multivisceral resections were performed with laparoscopic surgery, except for difficult cases, such as cases requiring a pancreatoduodenectomy or cases with tumors >10 cm or advanced peritoneal dissemination.

In cases with bowel obstruction, a colonic stent or ileus tube was used as a bridge to surgery because postoperative complications and mortality rates are lower with elective surgery than with emergency surgery.<sup>21</sup> According to JSCCR guidelines, the decision to perform a radical resection of the primary tumor with distant metastasis was based on a comprehensive assessment of clinical conditions for each patient. These assessments included the symptoms related to the primary tumor, the metastatic status, the general condition of the patient, the prognosis, the risk of surgical complications, and the effect of resection.<sup>22</sup>

## 2.3 | Statistical analysis

Statistical analyses were performed with JMP Pro 14 software (SAS Institute, Cary, NC). Significant differences between groups were evaluated with the Mann-Whitney test,  $\chi^2$  test, or Fisher's exact test, as appropriate. OS and DFS were analyzed with the Kaplan-Meier method, and differences between the two groups were assessed with the log-rank test. Probabilities < 0.05 were considered statistically significant. Propensity scores were calculated for each patient with bivariate logistic regression on the basis of the following covariates: preoperative abscess/perforation, depth of tumor invasion, and pathologic stage. These propensity

Characteristic	Lap (N = 38)	Open (N = 47)	P <sup>†</sup>
Sex, male/female	19/19	24/23	1.000 <sup>‡</sup>
Age, years	70 (45-90)	70 (39-94)	0.863
BMI, kg/m <sup>2</sup>	22.7 (16.1-30.2)	21.9 (16.2-31.2)	0.155
ASA-PS			0.505 <sup>‡</sup>
≤2	25 (65.8%)	27 (57.5%)	
>2	13 (34.2%)	20 (42.5%)	
Previous major abdominal surgery	4 (10.5%)	3 (6.4%)	0.695 <sup>‡</sup>
Previous minor abdominal surgery	10 (26.3%)	10 (21.3%)	0.616 <sup>‡</sup>
Maximum diameter of tumor, mm	61.5 (25-150)	71.5 (25-140)	0.395
Tumor location			1.000 <sup>‡</sup>
Right side	16 (42.1%)	19 (40.4%)	
Left side	22 (57.9%)	28 (59.6%)	
Preoperative complication	5 (13.2%)	11 (23.4%)	0.274 <sup>‡</sup>
Bowel obstruction	4 (10.5%)	5 (10.6%)	
Abscess/perforation	1 (2.6%)	6 (12.8%)	
Preoperative treatment	4 (10.5%)	5 (10.6%)	1.000 <sup>‡</sup>
Stent/ileus tube	3 (8.1%)	4 (8.5%)	
Stoma creation	1 (2.7%)	1 (2.1%)	
Preoperative therapy	0	2 (4.3%)	0.500
Chemotherapy	0	1 (2.1%)	
Chemoradiotherapy	0	1 (2.1%)	

 TABLE 1
 Characteristics of patients

 with colon cancer treated with a
 laparoscopic (Lap) or open (Open)

 multivisceral resection
 Patient Color

Note: Data are expressed as the median (range) or n (%), as indicated.

Abbreviations: ASA-PS, American society of Anaesthesiologists - Physical Status; BMI, body mass index.

 $^{\dagger}\text{P-values}$  were determined with the Mann–Whitney test or

<sup>‡</sup>Fisher's exact test.

**TABLE 2** Perioperative outcomes of patients with colon cancertreated with a laparoscopic (Lap) or open (Open) multivisceralresection

Outcome	Lap (N = 38)	Open (N = 47)	P <sup>†</sup>
Operating time, min	208 (108-995)	180 (94-561)	0.155
Blood loss volume, mL	25 (0-3170)	140 (0-2780)	<0.001
Conversion to open surgery	2 (5.3%)		
Complications	4 (10.5%)	14 (29.8%)	0.036 <sup>‡</sup>
Pneumonia	1 (2.6%)	4 (8.5%)	
Wound infection	0	4 (8.5%)	
Urinary tract infection	0	3 (6.4%)	
lleus	1 (2.6%)	1 (2.1%)	
Anastomotic leakage	2 (5.3%)	0	
Bleeding	0	1 (2.1%)	
Other	0	1 (2.1%)	
Mortality	0	0	
Length of postoperative hospital stay, days	12 (6-47)	15 (6-64)	0.028

Note: Data are expressed as the median (range) or n (%), as indicated. <sup>†</sup>*P*-values were determined with the Mann-Whitney test or <sup>‡</sup>Fisher's exact test.

scores (caliper = 0.2) were used to match patients in the laparoscopic surgery group 1:1 with those in the open surgery group.

# 3 | RESULTS

## 3.1 | Patient characteristics

This study included a total of 85 patients that underwent a colectomy with a multivisceral resection for locally advanced colon cancer. Of these patients, 38 underwent laparoscopy and 47 underwent open surgery. The patient characteristics between the laparoscopy and open surgery groups were not significantly different with regard to sex, age, BMI, ASA-PS, or rates of previous abdominal surgery (Table 1). The two groups were similar, in terms of the distributions of tumor diameters and tumor locations and the proportions of preoperative complications, preoperative treatments, and preoperative therapies. The patients in the open surgery group tended to be in poorer condition compared with those in the laparoscopic surgery group, because the proportion of patients with ASA-PS of > 2 and with abscess/perforation was high in the open surgery group. **TABLE 3** Adjacent structures removed in patients withcolon cancer treated with a laparoscopic (Lap) or open (Open)multivisceral resection

Structure	Lap (N = 38)	Open (N = 47)
Abdominal wall	17	18
Retroperitoneum	6	14
Small intestine	6	14
Bladder	6	6
Omentum	4	4
Other parts of colorectum	3	5
Ovary	3	3
Gonadal vessels	1	4
Seminal vesicle	1	2
Prostate	1	2
Pancreas	0	3
Ureter	0	2
Spleen	0	2
Uterus	2	0
lliac vessels	0	1
lliopsoas	0	1
Duodenum	0	1
Stomach	0	1
Kidney	0	1
Liver	1	0

*Note*: Values are the number of structures removed. In some patients, more than one structure was removed.

## 3.2 | Perioperative outcomes

The two groups had similar median operating times, but the laparoscopy group experienced significantly less blood loss (Table 2). Similar results were obtained only in patients who required removal of solid organs (Table S1). Two cases (5.3%) required conversion to open surgery due to uncontrolled bleeding and tumor invasion into the trigone of the bladder that made it difficult to determine whether partial cystectomy or total cystectomy should be performed. Compared to the open surgery group, the laparoscopy group showed a lower rate of complication and shorter hospital stays. There were no deaths within 30 days of surgery in either group. The most common adjacent structures removed in the laparoscopy and open surgery groups, respectively, were the abdominal wall (17 vs 18), the retroperitoneum (6 vs 14), the small intestine (6 vs 14), and the bladder (6 vs 6) (Table 3). The number of patients who required removal of solid organs was 18 (47.4%) in the laparoscopic surgery group and 28 (59.6%) in the open surgery group. Two or more structures were removed in nine patients (23.7%) in the laparoscopic surgery group and 24 patients (51.1%) in the open surgery group. These data suggested that more advanced cases were included in the open surgery group.

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**TABLE 4** Pathologic outcomes (Stage IV excluded) of patientswith colon cancer treated with a laparoscopic (Lap) or open (Open)multivisceral resection

Outcome	Lap (N = 32)	Open (N = 32)	P <sup>†</sup>
Depth of tumor invasion			0.313 <sup>§</sup>
Т3	16 (50.0%)	11 (34.4%)	
T4a	5 (15.6%)	4 (12.5%)	
T4b	11 (34.4%)	17 (53.1%)	
Lymph node metastasis			1.000
Positive	10 (31.3%)	11 (34.4%)	
Negative	22 (68.7%)	21 (65.6%)	
Pathologic stage			1.000
II	22 (68.8%)	21 (65.6%)	
III	10 (31.2%)	11 (34.4%)	
Lymphatic invasion			0.203
Positive	22 (68.8%)	16 (50.0%)	
Negative	10 (31.2%)	16 (50.0%)	
Venous invasion			1.000
Positive	19 (59.4%)	19 (59.4%)	
Negative	13 (40.6%)	13 (40.6%)	
Proximal margin			0
Negative	32 (100%)	32 (100%)	
Positive	0	0	
Distal margin			0
Negative	32 (100%)	32 (100%)	
Positive	0	0	
Resection margin			0.536
Negative	27 (84.4%)	24 (75.0%)	
Positive	5 (15.6%)	8 (25.0%)	
R0 resection rate	27 (84.4%)	24 (75.0%)	0.536
Histological type			1.000
tub1, tub2, pap	29 (90.6%)	29 (90.6%)	
por, muc	3 (9.4%)	3 (9.4%)	

Note: Data are expressed as n (%).

Abbreviations: muc, mucinous carcinoma; pap, papillary adenocarcinoma; por, poorly differentiated adenocarcinoma; tub1, well-differentiated adenocarcinoma; tub2, moderately differentiated adenocarcinoma.

 $^{\dagger}\text{P-values}$  were determined with Fisher's exact test or  $^{\$}\!\chi^2$  test.

## 3.3 | Pathologic and oncological outcomes

Each group included 32 patients, after excluding stage IV cases (Table 4). We did not observe any significant differences in pathologic parameters between the two groups, in terms of the depth of tumor invasion, lymph node metastasis, venous invasion, pathologic stage, lymphatic invasion, venous invasion, proximal margin, distal

**TABLE 5** Oncological outcomes in patients with colon cancer(Stage IV excluded) treated with a laparoscopic (Lap) or open (Open)multivisceral resection

Lap (N = 32)	Open (N = 32)	P <sup>†</sup>
		0.799
18 (56.2%)	20 (62.5%)	
14 (43.8%)	12 (37.5%)	
8 (25.0%)	3 (9.4%)	
5 (15.6%)	4 (12.5%)	
1 (3.1%)	2 (6.3%)	
0	2 (6.3%)	
0	1 (3.1%)	
8 (25.0%)	9 (28.1%)	1.000
6 (18.8%)	2 (6.3%)	
0	2 (6.3%)	
1 (3.1%)	0	
0	1 (3.1%)	
0	1 (3.1%)	
0	1 (3.1%)	
0	1 (3.1%)	
1 (3.1%)	1 (3.1%)	
	(N = 32) 18 (56.2%) 14 (43.8%) 8 (25.0%) 5 (15.6%) 1 (3.1%) 0 0 8 (25.0%) 6 (18.8%) 0 1 (3.1%) 0 0 0 0 0 0 0 0 0	(N = 32) $(N = 32)$ 18 (56.2%)20 (62.5%)14 (43.8%)12 (37.5%)8 (25.0%)3 (9.4%)5 (15.6%)4 (12.5%)1 (3.1%)2 (6.3%)02 (6.3%)01 (3.1%)8 (25.0%)9 (28.1%)6 (18.8%)2 (6.3%)02 (6.3%)02 (6.3%)1 (3.1%)001 (3.1%)01 (3.1%)01 (3.1%)01 (3.1%)01 (3.1%)01 (3.1%)

Note: Data are expressed as the number (%) of patients.

Abbreviations: FOLFOX, 5-fluorouracil with leucovorin and oxaliplatin; UFT/UZEL, tegafur-uracil and leucovorin; XELOX, xeloda with oxaliplatin.

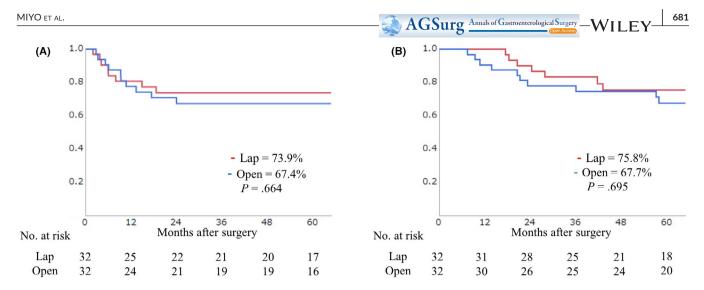
<sup>†</sup>P-values were determined with Fisher's exact test.

margin, resection margin, or histological type. The two groups included similar proportions of patients that received adjuvant chemotherapy (Table 5). Recurrence rates were similar between the two groups (25.0% vs 28.1%; P = 1.000), and the most common recurrence site was the liver in both groups.

The median follow-up periods were similar between the laparoscopy group (61.5 months, range: 3.0-111.1 months) and the open surgery group (65.2 months, range: 7.5-119.4 months; P = 0.347). The laparoscopic and open surgery groups did not differ significantly in the 5-year DFS (73.9% vs 67.4%; P = 0.664) or OS (75.8% vs 67.7%; P = 0.695; Figure 1A,B). No difference between the two groups was observed even in patients who required removal of solid organs in the 5-year DFS (64.6% vs 62.1%; P = 0.915) or OS (70.1% vs 63.6%; P = 0.969; Figure S1A,B). We applied propensity score matching considering the effect of several biases that might result from the retrospective nature of this study. After propensity score matching, there was no significant difference of oncologic outcomes between the two groups (Figure S2 and Table S2).

## 4 | DISCUSSION

Only a few previous reports have assessed the long-term outcomes for laparoscopic multivisceral resections of locally advanced



**FIGURE 1** Kaplan-Meier curves show survival after a laparoscopic multivisceral resection (Lap) or open multivisceral resection (Open). Five-year courses are shown for (A) disease-free survival and (B) overall survival; differences between the laparoscopic and open approaches were assessed with the log-rank test. Ordinate: survival rate; abscissa: months after surgery

colorectal cancers. Nishikawa et al reported that a laparoscopic approach was non-inferior to an open approach in terms of DFS (median 3-year DFS: 56.7% vs 62.7%; P = 0.578).<sup>18</sup> In another study, Takahashi et al reported that OS and DFS were comparable between the laparoscopic and open surgery groups (median 3-year OS: 92.8% vs 79.8%).<sup>23</sup> To our knowledge, no reports on laparoscopic multivisceral resections have discussed long-term outcomes with a sufficient follow-up period (>5 years). The present study was the first to present detailed oncologic outcomes with a sufficient median follow-up period of 61.5 months.

The 5-year DFS rates for the laparoscopic and open surgery groups in our study were 73.9% and 67.4%, respectively, comparable to those previously reported for open surgery (i.e., 56.9%-66.8%).<sup>18,24,25</sup> However, it is difficult to compare our results to results from previous studies that performed multivisceral resections, due to differences between studies, including the depth of tumor invasion, the presence of lymph node metastasis, and the pathologic stage. The rates of pT4b were reported to be 28.2%-70.0%, among patients undergoing multivisceral resections for colorectal cancer. Our pT4b rates were similar, with 34.4% in the laparoscopy group and 53.1% in the open surgery group.<sup>12,18,23</sup> Similar to previous studies, we found that laparoscopic surgery was associated with a lower pT4b rate than open surgery. However, this finding might have been affected by a selection bias, because more advanced cases were included in the open surgery group; this was one limitation in our retrospective study. Alternatively, the lower pT4b rate might have been due to the magnifying effect of laparoscopic surgery. Indeed, small inflammatory changes between the tumor and the adjacent organs were more likely to be detected during laparoscopic surgery compared to open surgery; thus, surgeons were more likely to resect these areas with the laparoscopic approach, compared to the open approach.

The R0 resection is the most important factor in curing colorectal cancer with a multivisceral resection.<sup>26</sup> Previous studies on multivisceral resections reported R0 resection rates of 68.4%-100% with laparoscopy and 68.8%-98.5% with open surgery. Thus, our R0 resection rates were within the published range, but on the low end.<sup>18</sup> Our results might have been affected by the pathological diagnosis, because suspicious cases, for example, cases where cauterized cancer cells near the excised edge, were included in the positive resection margin group. Kim et al reported that the local recurrence rates of multivisceral resections in the laparoscopic and open surgery groups were 7.7% and 27.3%, respectively.<sup>27</sup> In our study, local recurrences occurred in one patient in the laparoscopy group (3.1%) and in five patients in the open surgery group (15.6%), which suggested that our oncological clearance rate was acceptable. Liver recurrence rates in the laparoscopic surgery group seemed to be higher than that in the open surgery group (18.8% vs 6.3%; P = 0.257). This might result from some bias induced by the small number of cases, considering the report by Hasegawa et al showing that laparoscopic and open colectomy demonstrated comparable overall colon cancer recurrence rates and recurrence sites.<sup>28</sup> Our data supported the notion that our laparoscopic approach provided long-term outcomes similar to those provided with the open approach, but with less invasiveness.

Our study had several limitations. First, we studied a small number of cases and all patients were treated in a single institution. Some bias might be induced by the difference of characteristics in patients, including rates of previous major and minor abdominal surgery that were not significantly different between the laparoscopic and open surgery groups. How to deal with patients who underwent previous abdominal surgery in the prognosis analysis was debatable, because the extent of intraperitoneal adhesion might affect surgical difficulty. Second, the determination of the operation type, open or laparoscopic surgery, was inconsistent, because it was determined by the attending physician. The maturation of our technical skills has expanded the application of laparoscopic surgery to locally recurrent colorectal cancers that require a total pelvic exenteration or a sacral resection. We believe that laparoscopic surgery provides advantages over open WILEY- AGSurg

surgery, such as reduced blood loss, due to the pneumoperitoneum pressure applied, particularly in highly difficult surgeries, including multivisceral resections.<sup>29</sup> Additional evidence is necessary to confirm the utility of laparoscopic surgery in this subset of patients with colon cancer that require a multivisceral resection.

## DISCLOSURE

Conflict of Interest: Masaaki Miyo and other co-authors declare no conflict of interest.

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### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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