






## ORIGINAL ARTICLE

# Short- and long-term outcomes of robotic-assisted laparoscopic surgery for rectal cancer: A single-center retrospective cohort study

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## Abstract

**Introduction:** Whether rectal cancer surgery by robotic-assisted laparoscopic surgery provides beneficial advantages remains controversial. Although favorable outcomes in terms of the safety and technical feasibility of robotic-assisted laparoscopic surgery have been demonstrated for rectal cancer, long-term oncological outcomes for robotic-assisted laparoscopic surgery have only been examined in a few studies. This retrospective study of subjects who underwent robotic-assisted laparoscopic surgery evaluated short- and long-term outcomes of consecutive rectal cancer patients.

**Methods:** Between November 2016 and January 2020, we analyzed the records of 62 consecutive patients who underwent robotic-assisted laparoscopic surgery for rectal adenocarcinoma without distant metastasis to evaluate short- and long-term outcomes.

**Results:** Tumors were located in the lower or mid-rectum (88.7%) in most patients. The median operative time was 357 min. No patient received transfusions, and the median blood loss was 10.5 ml. Open laparotomy was not required in any patient. A Clavien–Dindo classification of all grades was observed in 12 patients (19.4%). Positive radial margin was not observed in any patient. Duration of median follow-up was 40.5 mo, while 3-y overall survival and 3-y relapse-free survival rates were 96.8% and 85.0%, respectively. The local recurrence rate was 3.4%.

**Conclusion:** Favorable short- and long-term outcomes demonstrated robotic-assisted laparoscopic surgery was safe and technically feasible for rectal cancer.

## KEYWORDS

long-term outcomes, rectal cancer, robotic-assisted surgery

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## 1 | INTRODUCTION

Of the various types of surgery for rectal cancer, minimally invasive surgery (MIS) has become increasingly popular. As compared to open surgery (OS), MIS for rectal cancer has been shown to have many advantages due to the introduction of more advanced instruments along with the evolution of surgical techniques. When conventional laparoscopic surgery (CLS) for rectal cancer was evaluated in randomized clinical trials (RCTs), the results demonstrated similar or better short-term outcomes compared with OS,<sup>1,2</sup> along with similar long-term oncological outcomes with OS.<sup>3,4</sup> However, there are several drawbacks when performing CLS for rectal cancer with regard to working in the narrow and deep pelvis. As previously reported for CLS use in rectal cancer, this observation is reflected by a conversion rate that ranges as high as 9%–16%.<sup>2,5,6</sup> Pathological outcomes were assessed in two large RCTs with respect to the completeness of the total mesorectal excision (TME) and circumferential resection margin (CRM), which are used to determine adequate surgical resection, with the results demonstrating that there were higher positive CRM rates in CLS as compared to OS for rectal surgery.<sup>5,6</sup> These results were thought to be related to technical difficulties associated with the deep pelvis.

One of the latest advancements in the MIS field is the use of robotic-assisted laparoscopic surgery (RALS) for rectal cancer. This technique has improved ergonomics, uses articulated instruments, in addition to having a stable 3D view along with enhanced dexterity with tremor filtration and motion scaling. Thus, RALS can potentially overcome the limitations associated with CLS. Although the ROLARR randomized clinical trial compared RALS with CLS and tried to evaluate the superiority of the conversion rates, the results were not definitive.<sup>7</sup> However, favorable outcomes in terms of the safety and technical feasibility of RALS for rectal cancer have been reported by several retrospective case-control studies<sup>8–14</sup> and small randomized clinical trials.<sup>15–18</sup> Even so, long-term oncological outcomes for RALS have only been closely examined in a few reports.<sup>19–21</sup> Therefore, this retrospective study attempted to examine subjects who underwent RALS in a single center and then clarify the short- and long-term outcomes of these consecutive rectal cancer patients.

## 2 | MATERIALS AND METHODS

### 2.1 | Patients

The medical records of 62 consecutive patients with rectal adenocarcinoma without distant metastasis who

underwent RALS with radical resection at Kitasato University Hospital between November 2016 and January 2020 were examined in order to determine the short- and long-term oncological outcomes of the RALS procedure. Patients were excluded from the study if upon preoperative imaging they were found to have abdominal aortic aneurysm, common iliac artery aneurysm, or definite contiguous organ involvement. The records were available for this study, as our hospital maintains a prospective database that contains information on baseline characteristics, operative results, postoperative complications, pathological findings, and oncological outcomes. Since we have previously published a report on the short-term outcomes of patients who underwent RALS for rectal cancer, the present study contains duplicate patients.<sup>22</sup>

Our Institutional Review Board approved this study (approval number B21-071). All patients were given complete details regarding the surgical procedure, after which they all provided written consent.

### 2.2 | Perioperative management and operative procedure

Based on the Union for International Cancer Control (UICC) Tumor-Node-Metastasis (TNM) Classification, 8th edition,<sup>23</sup> some of the patients who were diagnosed as having lower rectal cancer with a clinical stage of cT3-4 or were N-positive, underwent surgery after receiving neoadjuvant chemoradiotherapy (NCRT). The NCRT procedure was dependent on the discretion of surgeons, schedule, or the patient's performance status, with the procedure administered in accordance with our previously reported institutional guidelines.<sup>24,25</sup> Surgery was performed 8–10 weeks after NCRT completion.

Standardized protocols of perioperative management were used in all patients and included antibiotic prophylaxis, mechanical bowel preparation, thrombotic prophylaxis, analgesic care, and diet resumption. After the return of the bowel movement, oral intake was then allowed and over time gradually advanced to a soft diet. Oncologists recommended adjuvant chemotherapy in some patients after their recovery from surgery, unless there were contraindications related to the patient's performance status, which included TNM stage III or TNM stage II with unfavorable pathological characteristics, such as T4, positive lymphatic invasion, and positive vascular invasion. All patients were followed regularly using an oncological follow-up program. Patients were followed-up every 3 mo for the first 3 y and every 6 mo thereafter. Blood test results, including Carcinoembryonic antigen (CEA), were checked at each visit. Chest-abdominopelvic computed tomography (CT) was performed

every 6 mo for the first 3 y and annually thereafter. Colonoscopy was performed 1 y after surgery and every 2 y thereafter. If recurrence was suspected, magnetic resonance imaging (MRI) and/or positron emission tomography (PET)-CT was used to confirm the diagnosis of metastasis. Surgery was considered for patients with good performance status with resectable recurrence. The follow-up time was calculated as the time interval from surgery until death or the last follow-up date.

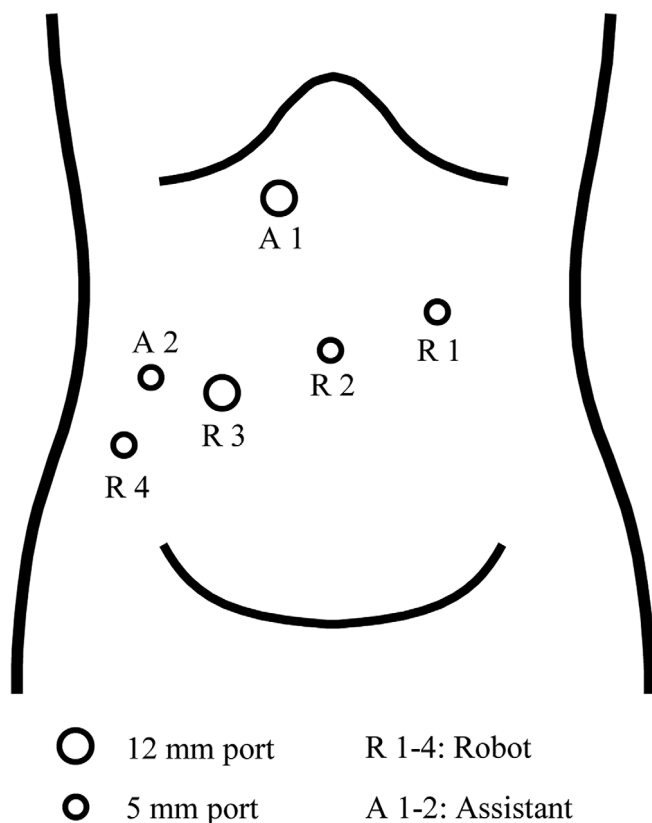
Using the Da Vinci Si or Xi Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) as a six- or five-port system, two certified surgeons performed the RALS. Five ports were generally placed in the Xi Surgical System, six ports were placed in some cases when the suction was needed for excessive fluid, such as for the patients who were administered NCRT (Figure 1). Six ports were generally placed in the Si Surgical System. After placing patients in a lithotomy position with the head down at 15–20° and the right side down at 15°, a colonic and pelvic phase was used to perform all procedures. Inferior mesenteric artery and vein ligations along with left-sigmoid mesocolon mobilization were performed in the

colonic phase, while pelvic dissection using TME or tumor-specific mesorectal excision (TSME) were performed in the pelvic phase. The distal rectum was divided more than 3 cm below the lower border of the tumor in performing TSME for tumors of the upper or mid-rectum. In contrast, the distal rectum was divided more than 2 cm below the lower border of the tumor when performing TME for tumors of the lower rectum.<sup>26</sup> The distal rectum was intracorporeally divided with a linear articulated endostapler loaded with a 45 mm or 60 mm cartridge in the patients who underwent anterior resection (AR). An intracorporeal double-stapling technique with a circular staple 25 mm in AR, or transanal hand-sewn suture in intersphincteric resection (ISR), was used when restoring the bowel continuity. En bloc regional lymphadenectomy was used in all patients who underwent curative standard resection. When the short diameter of the lateral lymph node was swollen over 7 mm on pre-NCRT CT and MRI, lateral lymph node dissection (LLND) was performed. LLND was performed around the common iliac vessel, internal iliac vessel, and obturator space, and in the fat tissue outside the pelvic plexus, while preserving all of the autonomic nerves. If necessary during the LAR and ISR, a diverting ileostomy was constructed.

### 2.3 | Study outcomes

After obtaining all of the pertinent medical records, data for patient age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, preoperative CEA level, tumor level from the anal verge, tumor location, NCRT, type of operation, LLND, diverting ileostomy, blood flow test using indocyanine green (ICG), operative time, console time, learning curve, blood loss, transfusion, conversion to open laparotomy, combined resection, days to soft diet, postoperative hospital stay, adjuvant chemotherapy, postoperative complications, reoperation, postoperative mortality, tumor size, histological grade, lymphatic invasion, vascular invasion, proximal margin (PM), distal margin (DM), positive radial margin (RM), number of lymph nodes harvested, clinical and pathological TNM stage, along with the long-term oncological outcomes for analyzing relapse-free survival rate (RFS), local recurrence rate (LRR), and overall survival rate were then collected from these documents.

For classification of the tumor location, the rectum was divided into upper, mid, and lower rectum. When the lower border of the tumor was located proximal to the peritoneal reflection, it was defined as being in the upper and mid-rectum. Moreover, when the center of the tumor was located proximal and distal to the lower



**FIGURE 1** Port placement in the Xi Surgical System. Five ports (A 1 and R1-4) were generally placed, six ports (A1-2 and R1-4) were placed in some cases when the suction was needed for excessive fluid such as for the patients who were administered NCRT

border of the 2nd sacral vertebra, it was defined as being in the upper and mid-rectum, respectively. When the lower border of the tumor was located distal to the peritoneal reflection, it was defined as being in the lower rectum. The time between the initial skin incision and the completion of the wound closure was defined as the operative time. The time it took for the TME or TSME procedures when using the Da Vinci Surgical System was defined as the console time. Learning curves were examined, the graph of raw operative times plotted, and spline curve for each of the consecutive patients who underwent RALS without LLND by surgeons A and B, respectively. An unintended extension of the laparotomy beyond the incision that was necessary for specimen retrieval was defined as conversion to open laparotomy from RALS. Events that occurred during the postoperative hospital stay or within 30 d after surgery were defined as postoperative complications, reoperation, and mortality that occurred during this time period. The Clavien–Dindo (CD) classification was used to categorize all postoperative complications.<sup>27</sup> The diagnosis of anastomotic leakage was based on clinical suspicion and CT imaging. In order to assess the quality of the surgery, the pathological parameters of the surgical specimens, including PM, DM, RM, and the number of lymph nodes harvested were recorded.

## 2.4 | Statistical analysis

Descriptive data are presented as the mean and standard deviation (SD) or median and range for continuous variables and as the number of patients and percentage for categorical variables. After using the Kaplan–Meier method to analyze the RFS rate, LRR, and overall survival rate, the results were compared using the log-rank test.  $p < 0.05$  was considered statistically significant. All statistical analyses were performed using the statistical software JMP pro version 14 (SAS Institute, Cary, NC, USA).

## 3 | RESULTS

### 3.1 | Baseline patient characteristics

The baseline characteristics of the 62 patients, with 43 male patients (69.4%) and 19 female patients (30.6%), are presented in Table 1. Tumors were primarily located in the lower or mid-rectum (88.7%) in most patients, with a median tumor level from the anal verge of 54 mm. There were 23 clinical stage I (37.1%), 16 stage II (25.8%), and 23 stage III patients (37.1%). In the clinical stage II

TABLE 1 Baseline characteristics of patients with rectal cancer ( $n = 62$ )

Characteristics	<i>n</i> (%) or mean $\pm$ SD or median [range]
Age, y	65.0 $\pm$ 10.8
Sex	
Male	43 (69.4)
Female	19 (30.6)
Body mass index, kg/m <sup>2</sup>	23.1 $\pm$ 2.9
ASA score	
1	12 (19.4)
2	45 (72.6)
3	5 (8.1)
Preoperative CEA level, ng/ml	3.5 [0.6–225]
Tumor level from anal verge, mm	54 [24–137]
Tumor location	
Upper rectum <sup>a</sup>	7 (11.3)
Mid rectum <sup>a</sup>	13 (21.0)
Lower rectum <sup>b</sup>	42 (67.7)
cT stage <sup>c</sup>	
T1	14 (22.6)
T2	12 (19.4)
T3	31 (50.0)
T4	5 (8.1)
cN stage <sup>c</sup>	
N0	39 (62.9)
N1	20 (32.3)
N2	3 (4.8)
cM stage <sup>c</sup>	
M0	62 (100.0)
M1	0 (0.0)
cStage <sup>c</sup>	
I	23 (37.1)
II	16 (25.8)
III	23 (37.1)
IV	0 (0.0)
Neoadjuvant chemoradiotherapy	8 (38.1 <sup>d</sup> )

Abbreviation: ASA, American Society of Anesthesiologists.

<sup>a</sup>Upper or mid-rectum was defined as the lower border of the tumor located proximal to the peritoneal reflection.

<sup>b</sup>Lower rectum was defined as the lower border of the tumor located distal to the peritoneal reflection.

<sup>c</sup>Clinical stage, TNM Classification of Malignant Tumors, Eighth Edition.

<sup>d</sup>Data were analyzed in clinical stage II and III patients with lower rectal cancer.

and III patients with lower rectal cancer, eight patients (8/25, 38.1%) who had provided informed consent underwent NCRT.

### 3.2 | Operative results

The operative results are shown in Table 2. Sphincter-preserving surgeries were performed in the majority of the patients (80.6%). LLNDs were only performed in 6.5% of the patients. Of the patients who underwent reconstruction surgeries, such as AR and ISR, a diverting ileostomy was constructed in 41 patients (82.0%). In 27 patients (54.0%) who underwent reconstruction, blood flow tests using ICG were performed prior to the anastomosis. The median operative and median console times were 357 and 198.5 min, respectively. Learning curves are shown in Figure 2. The number of patients who underwent RALS without LLND by surgeons A and B were 32 and 26, respectively. The first 20 patients almost

**TABLE 2** Operative results of patients with rectal cancer ( $n = 62$ )

Characteristics	<i>n</i> (%) or median [range]
Type of operation	
High anterior resection	3 (4.8)
Low anterior resection	39 (62.9)
Intersphincteric resection	8 (12.9)
Abdominoperineal resection	12 (19.4)
Lateral lymph node dissection	4 (6.5)
Diverting ileostomy	41 (82.0 <sup>a</sup> )
Blood flow test by using ICG	27 (54.0 <sup>a</sup> )
Operative time, min	357 [202–747]
Without lateral lymph node dissection	355 [202–682]
With lateral lymph node dissection	626 [480–747]
Console time	198.5 [108–340]
Blood loss, ml	10.5 [5–394]
Without lateral lymph node dissection	6 [5–394]
With lateral lymph node dissection	125 [5–270]
Transfusion	0 (0.0)
Conversion to laparotomy	0 (0.0)
Combined resection	0 (0.0)
Days to soft diet, d	1 [1–34]
Postoperative hospital stay, d	10 [6–62]
Adjuvant chemotherapy	18 (52.9 <sup>b</sup> )

Abbreviation: ICG, indocyanine green.

<sup>a</sup>Data were analyzed in patients with anterior resection and intersphincteric resection.

<sup>b</sup>Data were analyzed in pathological stage II and III patients.

formed the learning phase in the spline curves for both surgeons A and B. None of the patients received any transfusions during the surgery, and the median blood loss was 10.5 ml. Conversion to open laparotomy was not needed in any of the patients. The median days to a soft diet and median postoperative hospital stay were 1 and 10 d, respectively. Adjuvant chemotherapy was administered to 18 patients (52.9%) who were diagnosed as pathological stage II and III.

### 3.3 | Postoperative complications

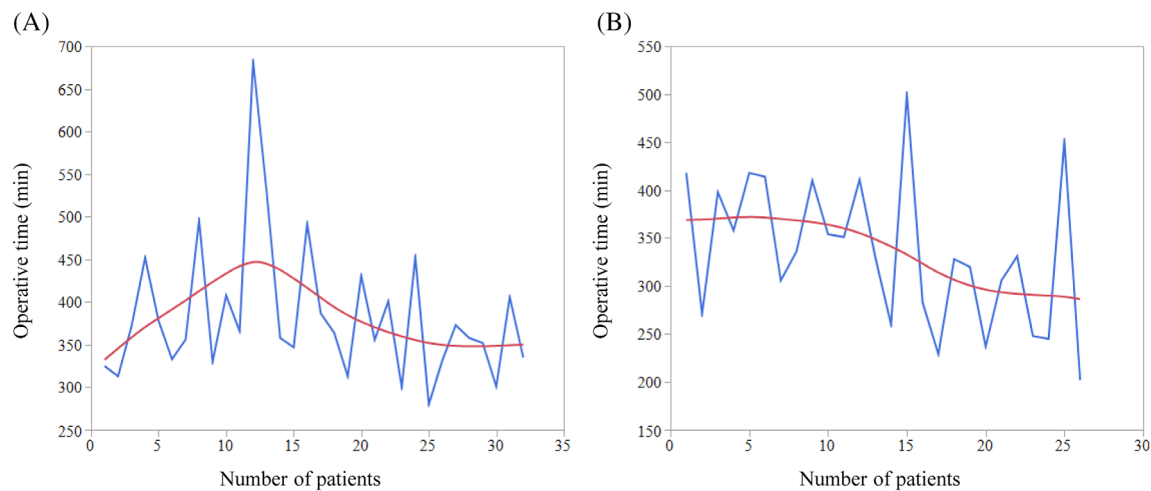
Table 3 lists the postoperative complications. A CD classification of all grades occurred in 12 patients (19.4%), while five patients (8.1%) had a CD classification of more than grade III. In six patients (12.0%) who underwent reconstruction surgeries, anastomotic leakage with a CD classification of more than grade II was observed. None were observed to have urinary retention, bleeding, or pneumonia. Only one patient (1.6%) had anastomotic leakage that required a reoperation. No operative mortality was observed in the present study.

### 3.4 | Pathological findings

Table 4 lists the pathological findings. A positive radial margin, which indicates a positive surgical dissection plane microscopically, was not observed in any of the patients. In addition, negative proximal and distal margins were observed in all patients. The mean number of harvested lymph nodes was 15.8, while 22 patients (35.5%) were found to have lymph node metastasis.

### 3.5 | Long-term outcomes

The median follow-up duration was 40.5 mo (range 16.4–66.6 mo). Lung relapse in stage II and liver relapse in stage III resulted in the death of one patient. The results for the overall cohort showed that the 3-y overall survival rate was 96.8%, the 3-y RFS rate was 85.0%, and the 3-y LRR was 3.4% (Figure 3c). The 3-y overall survival rates for stages 0/I/pCR vs II vs III were 100.0% vs 91.7% vs 95.5% ( $p = 0.3692$ ), respectively (Figure 3a). The 3-y RFS rates for stages 0/I/pCR vs II vs III were 96.4% vs 83.3% vs 71.8% ( $p = 0.0674$ ), respectively (Figure 3b). Although comparison of overall survival rates between the pathological stages found no significant difference, the low pathological stages tended to be a better prognosis in RFS rates. Observed relapse patterns included lung metastasis in three (4.8%), liver metastasis in one (1.6%), local



**FIGURE 2** Learning curve. (a) Graph of raw operative times plotted and spline curve for each of the 32 consecutive patients who underwent RALS without LLND by surgeon A. (b) Graph of raw operative times plotted and spline curve for each of the 26 consecutive patients who underwent RALS without LLND by surgeon B

**TABLE 3** Postoperative complications of patients with rectal cancer ( $n = 62$ )

Characteristics	<i>n</i> (%)
Overall, CD classification in all grades	12 (19.4)
Anastomotic leakage	6 (12.0 <sup>a</sup> )
Small bowel obstruction	1 (1.6)
Wound infection	3 (4.8)
Urinary retention	0 (0.0)
Chyle ascites	1 (1.6)
diarrhea	1 (1.6)
Bleeding	0 (0.0)
Pneumonia	0 (0.0)
CD classification $\geq$ Grade III	5 (8.1)
Reoperation	1 (1.6)
30-day postoperative mortality	0 (0.0)

Abbreviation: CD, Clavien–Dindo.

<sup>a</sup>Data were analyzed in patients with anastomosis.

recurrence in two (3.2%), distant lymph node including para-aortic lymph node metastasis in three (4.8%), and peritoneal dissemination in one patient (1.6%). Surgery was performed in one (stage III) patient who developed lung metastasis, while two (stages II and III) patients underwent systemic chemotherapy. Hepatectomy was performed in one (stage III) patient who developed liver metastasis. Surgical resection was performed in one (stage II) patient who developed local recurrence, while one (stage III) patient underwent radiation therapy. Distant lymph node including para-aortic lymph node metastasis developed in three (stage III) patients, while one (stage III) patient developed peritoneal dissemination

and subsequently underwent systemic chemotherapy for recurrent disease.

## 4 | DISCUSSION

As this long-term patient follow-up examined patients who were operated on by only two certified surgeons in a single center, this made it possible to avoid any confounding effects related to different surgical procedures and abilities associated with several surgeons. The first 20 patients almost formed a learning phase for two surgeons in the analysis of the learning curve for RALS without LLND. To clarify whether there are differences for short- and long-term outcomes among the period in this study, we subanalyzed the short- and long-term outcomes for RALS by comparing the results in the periods between the learning phase and the experienced phase. The learning phase (LP) was defined as the period during which two surgeons performed the RALS until there were 20 patients, and the experienced phase (EP) was defined as each period during which two surgeons performed the RALS after 20 patients. The number of patients in the LP and EP period were 40 and 18, respectively. There were no significant differences in baseline characteristics between the groups. The median operative time in the LP period and in the EP period were 358 and 333 min, respectively ( $p = 0.1160$ ). The median console time in the LP period and in the EP period were 210.5 and 180.5 min, respectively ( $p = 0.0669$ ). In short-term outcomes, the median blood loss in two periods were 16 and 5 ml ( $p = 0.3689$ ), the rate of conversion to open laparotomy in two periods were 0% and 0%, the rate of

**TABLE 4** Pathological findings of patients with rectal cancer ( $n = 62$ )

Characteristics	<i>n</i> (%) or mean $\pm$ SD
Tumor size, mm	36.3 $\pm$ 16.0
Histological grade	
G1-2 (pap/tub) <sup>a</sup>	61 (98.4)
G3 (muc/por/sig) <sup>b</sup>	1 (1.6)
Lymphatic invasion	
Presence	21 (33.9)
Absence	41 (66.1)
Vascular invasion	
Presence	35 (56.5)
Absence	27 (43.5)
Proximal margin, mm	164.2 $\pm$ 56.8
Distal margin, mm	28.5 $\pm$ 17.8
Positive radial margin	0 (0.0)
Number of lymph nodes harvested	15.8 $\pm$ 10.0
Without lateral lymph node dissection	14.7 $\pm$ 9.0
With lateral lymph node dissection	32.3 $\pm$ 10.4
p/yp T stage <sup>c</sup>	
T0/Tis	3 (4.8)
T1	21 (33.9)
T2	13 (21.0)
T3	20 (32.3)
T4	5 (8.1)
p/yp N stage <sup>c</sup>	
N0	40 (64.5)
N1	17 (27.4)
N2	5 (8.1)
p/yp Stage <sup>c</sup>	
0/pCR	2 (3.2)
I	26 (41.9)
II	12 (19.4)
III	22 (35.5)
IV	0 (0.0)

<sup>a</sup>Papillary adenocarcinoma / well or moderately differentiated tubular adenocarcinoma.

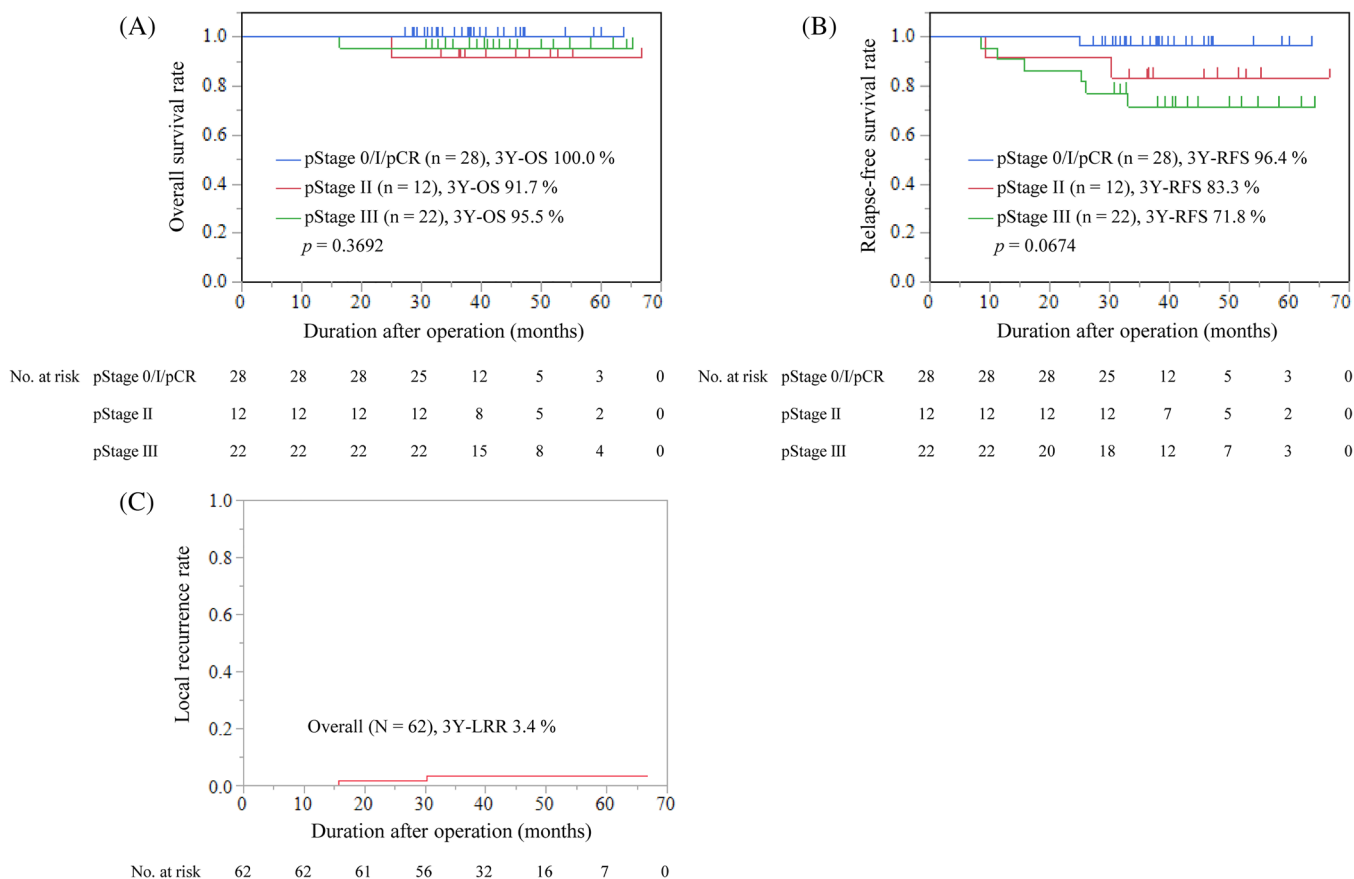
<sup>b</sup>Mucinous adenocarcinoma / poorly differentiated adenocarcinoma / signet-ring cell carcinoma.

<sup>c</sup>Pathological stage, TNM Classification of Malignant Tumors, Eighth Edition.

postoperative complications (CD classification in all grades) in two periods were respectively 22.5% and 16.7% (9/40 vs 3/18,  $p = 0.6065$ ), the rate of anastomotic leakage in two periods were respectively 12.1% and 13.3%

(4/33 vs 2/15,  $p = 0.9068$ ), the median DM in two periods were respectively 29.0 and 30.2 mm ( $p = 0.8257$ ), the rate of positive radial margin in the two periods were 0% and 0%, respectively, and the mean number of lymph nodes harvested in two periods were 14.5 and 15.1 ( $p = 0.8055$ ), respectively. In long-term outcomes, the 3-y RFS in the LP period and in the EP period were 89.4% and 83.3% ( $p = 0.4205$ ), respectively, and the 3-y LRR in two periods were 2.5% and 0.0% ( $p = 0.5023$ ), respectively. Although the operative time and console time in the LP period slightly tended to be longer compared with those in the EP period, the significant differences in the short- and long-term outcomes were not observed in the periods between the LP and the EP groups. Even though this study required initial learning curves for two surgeons, our results demonstrated that RALS for rectal cancer was possible without any conversions to open laparotomy, with only a small amount of blood loss, requiring no transfusions, having an early recovery of bowel function, a low rate of complications, no positive resection margins, and good long-term oncological outcomes.

However, this study was not a comparative study designed to determine if RALS, CLS, or OS was better. In order to determine if the present findings were appropriate, we decided to compare our RALS outcomes to previous large RCTs (the COREAN trial,<sup>1,3</sup> the COLOR II trial,<sup>2,4</sup> and the ALaCaRT trial<sup>6,28</sup>), which compared CLS with OS for rectal cancer, and to the ROLARR trial,<sup>7</sup> which compared CLS with RALS for rectal cancer. Analysis of these four RCTs found that the CLS group had a mean or median operative time of 210–261 min, while the times in the OS group were 188–197 min, and 298.5 min in the RALS group. The median operative time of the RALS patients in our study who did not undergo LLND was 355 min, while the median console time was 198.5 min. Our operative time required an additional 156.5 min compared to the console time. Several previous studies that examined operative times for CLS and OS as compared to RALS for rectal cancer determined that there was a significantly longer operative time for RALS.<sup>18,29–32</sup> Consistent with the results of these previous studies, our results showed that RALS had a longer operative time. The reason for this prolonged RALS operative time can be primarily attributed to the time required to dock the robotic system, change instruments, and undock the system if the patient's position needs to be changed. Previous studies including RCT and case-matched analysis reported that the operative times were 288–339 min in RALS for rectal cancer, and the median operative time in this study was slightly longer than that in the previous studies.<sup>7,18,29,30</sup> This might be attributed to our results for the RALS procedure that included the learning curve period, which has been previously reported to range from



**FIGURE 3** Survival rate and local recurrence rate. (a) Overall survival rate according to the pathological stage with the number at risk. (b) Relapse-free survival rate according to the pathological stage with the number at risk. (c) cumulative local recurrence rate with the number at risk. 3Y-OS, 3-y overall survival, 3Y-RFS, 3-y relapse-free survival, 3Y-LRR, 3-y local recurrence rate

20 to 75 cases.<sup>33–37</sup> Actually, the first 20 patients almost formed the learning phase in this study. Thus, our operative time could potentially be shortened, provided we have personnel with expertise experience such as working with the camera and manipulation of the robotic forceps, in conjunction with additional practice in setting up the robotic system.

The technical complexity of MIS is reflected by the conversion rate to open laparotomy. It is clinically important that a low conversion rate to open laparotomy be achieved, as patients are more likely to develop postoperative complications and local recurrence after conversion to open laparotomy.<sup>38,39</sup> In the COREAN trial,<sup>1</sup> the CLS group was reported to have a 1.2% rate of conversion to open laparotomy, while it was 16% in the COLOR II trial,<sup>2</sup> 9% in the ALaCaRT trial,<sup>6</sup> and 12.2% in the ROLARR trial.<sup>7</sup> With the exception of the COREAN trial, in which all procedures were conducted by highly skilled specialists, in the CLS groups there were relatively high rates of conversion to open laparotomy. In contrast to these previous trials, our results were remarkable in that our study had no patients in which there was a conversion

to open laparotomy from RALS. While the superiority of the conversion rate to open laparotomy in RALS versus CLS ( $p = 0.16$ ) was not demonstrated in the ROLARR trial, a lower conversion rate for RALS versus CLS has been reported by several other meta-analyses.<sup>31,32,40–42</sup>

The median blood loss reported by the three large RCTs, the COREAN trial,<sup>1</sup> the COLOR II trial,<sup>2</sup> and the ALaCaRT trial,<sup>6</sup> was 100–200 ml in the CLS group, while it was 150–400 ml in the OS group. The median or mean blood loss in the case-matched analysis that previously reported in RALS for rectal cancer were 15.0–49.6 ml.<sup>10,13,14</sup> In contrast, there was an extremely low blood loss, with a median amount of 10.5 ml without any transfusions in our study. When the RALS group was compared to the CLS and OS groups in other previous studies, the results similarly showed that there was less blood loss in the RALS group.<sup>9–11,13,14,17</sup>

The complication rates in the previous four large RCTs were 21.2%–40.0% in the CLS group, 23.5%–37.0% in the OS group, and 33.1% in the RALS group.<sup>1,2,6,7</sup> In addition, evaluation of the anastomotic leakage and urinary retention found that the rates were 1.2%–13.0% and



6.1%–10.0% in the CLS group, 0.0%–10.0% and 4.1% in the OS group, and 12.2% and 7.2% in the RALS group, respectively.<sup>1,2,6,7</sup> Postoperative complications exhibited a relatively low rate in the present study (19.4%) in addition to having a similar anastomotic leakage rate (12.0%) when compared to the outcomes of the four RCTs. Moreover, urinary retention did not occur in any of our patients. The robotic system makes it possible to accurately perform anatomical dissections within a deep and narrow pelvis, thereby helping to ensure that there would be greater preservation of pelvic autonomic functions. The potential benefits that have been reported for RALS in previous studies included a lower complication rate, shorter postoperative hospital stay, and more favorable functional results and numerous studies have discussed multiple factors associated with the robotic approach that appear to make it more advantageous as compared to the conventional laparoscopic approach for rectal cancer.<sup>8,10,12,13,29,31,41–43</sup> This was also observed in the present study, as our results showed that the number of days to a soft diet along with the postoperative hospital stay were similar or even better versus that seen for the outcomes of RCTs.<sup>1,2,6,7</sup>

The results of our analysis indicated that there were remarkable outcomes for the resection margin status, with none of the patients found to have positive RM, PM, or DM. Comparison of the outcomes with regard to the distance of the PM and DM in our study were similar to that reported in the RCTs.<sup>1,2,6</sup> The number of harvested lymph nodes reported by the four large RCTs were 13–24 in the CLS group and 14–18 in the OS group,<sup>1,2,6,7</sup> which were similar to that found in the present study (15.8). Thus, when evaluating the quality of oncological resection between our results for the RALS group and the outcomes of the RCTs reported for the CLS and OS groups, the results were comparable. Even so, other pathological parameters, such as circumferential resection margin (CRM), which is an important predictor of oncological prognosis, will need to be evaluated in further studies.

In the COREAN trial,<sup>3</sup> there was a 2.6% local recurrence rate at 3 y in the CLS group, while it was 4.9% in the OS group. In the COLOR II trial,<sup>4</sup> there was a 5% local recurrence rate at 3 y in the CLS and OS groups. The previous cohort studies in RALS for rectal cancer reported that there were 0.5%–3.5% local recurrence rate at 5 y.<sup>20,21</sup> In the present study, we found there was a 3.4% local recurrence rate at 3 y. The RFS rate and overall survival rate at 3 y in the COREAN trial<sup>3</sup> were 79.2% and 91.7% in the CLS group, and 72.5% and 90.4% in the OS group, respectively. For the COLOR II trial,<sup>4</sup> the RFS rate and overall survival rate at 3 y in the CLS group were 74.8% and 86.7%, while they were 70.8% and 83.6% in the OS group, respectively. The 3-y RFS and the 3-y overall

survival rates for the present study were 85.0% and 96.8%, respectively. Thus, there were similar outcomes for the local recurrence rates between these studies and our study, in addition to also finding slightly favorable RFS and overall survival rates as compared to the outcomes of the RCTs. The previous cohort studies in RALS for rectal cancer reported that the 5-y RFS rate according to the pathological stage I/II/III were 93.5–93.6%/75.0–100%/77.6–83.8%.<sup>20,21</sup> Although the median follow-up duration in this study was slightly shorter than those in the previous studies, our long-term outcomes were comparable (3-y RFS according to pathological stage 0/I/pCR vs II vs III: 96.4% vs 83.3% vs 71.8%). In another previous study, the propensity score matching was used to analyze the results and reported that RALS appeared to be a good prognostic factor as compared to CLS for overall survival and for cancer-specific survival, which suggests there may be potential oncological benefits.<sup>30</sup> On the other hand, a meta-analysis found comparable oncological outcomes for overall survival when the RALS and CLS groups were examined.<sup>31</sup> However, to definitively prove these results, a longer follow-up duration and further studies including large RCTs will need to be conducted in order to reveal the true long-term oncological outcomes. If the future studies demonstrate the superiority for RALS in terms of long-term outcomes compared to other approaches, RALS including remote surgery might be changed and replaced as a standard approach in surgery for rectal cancer from now on.

The good short- and long-term outcomes found in the present study demonstrated both the safety and technical feasibility of RALS for rectal cancer. However, there were some limitations. First, this retrospective study only included 62 patients and was not a comparative study. In order to confirm the effectiveness in terms of short- and long-term outcomes for RALS compared with CLS and OS, larger RCTs will need to be conducted. The second limitation of the present study was that the median follow-up duration was only 40.5 mo. As a result, it will be essential to conduct a longer follow-up in order to demonstrate conclusive evidence concerning the clinical benefits for RALS. Third, we did not assess sexual function, with only voiding function evaluated. Fourth, although we examined pathological parameters for the assessment of surgical and oncological quality by evaluating PM, DM, and RM, we did not examine the CRM. Thus, our pathological analysis could be inadequate for the purposes of assessing the completeness of TME quality. Finally, the total cost of RALS was not assessed. A definitive evaluation of this treatment modality versus CLS and OS will need to be conducted with regard to the cost-effectiveness of these methodologies.

In conclusion, this single-center retrospective cohort study demonstrated that the use of RALS for rectal cancer was both safe and technically feasible in addition to having favorable short- and long-term outcomes.

## AUTHOR CONTRIBUTIONS

Takahiro Yamanashi, Hirohisa Miura, Toshimichi Tanaka, Akiko Watanabe, Takuya Goto, Keigo Yokoi, and Ken Kojo contributed to data collection and analyses. Masahiro Niihara, Kei Hosoda, and Takashi Kaizu contributed to article preparation. Keishi Yamashita, Takeo Sato, Yusuke Kumamoto, Naoki Hiki, and Takeshi Naitoh contributed to the revision of the draft. All authors approved the final article for publication.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ETHICS STATEMENT

This study was approved by the Ethics Committee of the Kitasato University Hospital (approval number B21-071) and it conforms to the provisions of the Declaration of Helsinki.

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## REFERENCES

- Kang SB, Park JW, Jeong SY, et al. Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial. *Lancet Oncol*. 2010; 11(7):637-645.
- van der Pas MH, Haglind E, Cuesta MA, et al. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol*. 2013; 14(3):210-218.
- Jeong SY, Park JW, Nam BH, et al. Open versus laparoscopic surgery for mid-rectal or low-rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): survival outcomes of an open-label, non-inferiority, randomised controlled trial. *Lancet Oncol*. 2014;15(7):767-774.
- Bonjer HJ, Deijen CL, Abis GA, et al. A randomized trial of laparoscopic versus open surgery for rectal cancer. *N Engl J Med*. 2015;372(14):1324-1332.
- Fleshman J, Branda M, Sargent DJ, et al. Effect of laparoscopic-assisted resection vs open resection of stage II or III rectal cancer on pathologic outcomes: the ACOSOG Z6051 randomized clinical trial. *JAMA*. 2015;314(13):1346-1355.
- Stevenson AR, Solomon MJ, Lumley JW, et al. Effect of laparoscopic-assisted resection vs open resection on pathological outcomes in rectal cancer: the ALaCaRT randomized clinical trial. *JAMA*. 2015;314(13):1356-1363.
- Jayne D, Pigazzi A, Marshall H, et al. Effect of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer: the ROLARR randomized clinical trial. *JAMA*. 2017; 318(16):1569-1580.
- Kim JY, Kim NK, Lee KY, Hur H, Min BS, Kim JH. A comparative study of voiding and sexual function after total mesorectal excision with autonomic nerve preservation for rectal cancer: laparoscopic versus robotic surgery. *Ann Surg Oncol*. 2012; 19(8):2485-2493.
- Yamaguchi T, Kinugasa Y, Shiomi A, Tomioka H, Kagawa H. Robotic-assisted laparoscopic versus open lateral lymph node dissection for advanced lower rectal cancer. *Surg Endosc*. 2016; 30(2):721-728.
- Yamaguchi T, Kinugasa Y, Shiomi A, Tomioka H, Kagawa H, Yamakawa Y. Robotic-assisted vs conventional laparoscopic surgery for rectal cancer: short-term outcomes at a single center. *Surg Today*. 2016;46(8):957-962.
- Kim HJ, Choi GS, Park JS, et al. Selective lateral pelvic lymph node dissection: a comparative study of the robotic versus laparoscopic approach. *Surg Endosc*. 2018;32(5):2466-2473.
- Kim HJ, Choi GS, Park JS, Park SY, Yang CS, Lee HJ. The impact of robotic surgery on quality of life, urinary and sexual function following total mesorectal excision for rectal cancer: a propensity score-matched analysis with laparoscopic surgery. *Color Dis*. 2018;20(5):O103-O113.
- Matsuyama T, Endo H, Yamamoto H, et al. Outcomes of robot-assisted versus conventional laparoscopic low anterior resection in patients with rectal cancer: propensity-matched analysis of the National Clinical Database in Japan. *BJS Open*. 2021;5(5):zrab083. doi:10.1093/bjsopen/zrab083
- Sueda T, Tei M, Nishida K, et al. Short-term outcomes of robotic-assisted versus conventional laparoscopic-assisted surgery for rectal cancer: a propensity score-matched analysis. *J Robot Surg*. 2021;16:323-331.
- Baik SH, Ko YT, Kang CM, et al. Robotic tumor-specific mesorectal excision of rectal cancer: short-term outcome of a pilot randomized trial. *Surg Endosc*. 2008;22(7):1601-1608.
- Jiménez Rodríguez RM, Díaz Pavón JM, de La Portilla de Juan F, Prendes Sillero E, Hisnard Cadet Dussort JM, Padillo J. Prospective randomised study: robotic-assisted versus conventional laparoscopic surgery in colorectal cancer resection. *Cir Esp*. 2011;89(7):432-438.
- Debaek Y, Zaghoul A, Farag A, Mahmoud A, Elattar I. Robotic-assisted versus conventional laparoscopic approach for rectal cancer surgery, first Egyptian academic center experience, RCT. *Minim Invasive Surg*. 2018;2018:5836562.

18. Kim MJ, Park SC, Park JW, et al. Robot-assisted versus laparoscopic surgery for rectal cancer: a phase II open label prospective randomized controlled trial. *Ann Surg.* 2018;267(2):243-251.
19. Park EJ, Cho MS, Baek SJ, et al. Long-term oncologic outcomes of robotic low anterior resection for rectal cancer: a comparative study with laparoscopic surgery. *Ann Surg.* 2015;261(1):129-137.
20. Yamaguchi T, Kinugasa Y, Shiomi A, et al. Short- and long-term outcomes of robotic-assisted laparoscopic surgery for rectal cancer: results of a single high-volume center in Japan. *Int J Color Dis.* 2018;33(12):1755-1762.
21. Katsuno H, Hanai T, Masumori K, et al. Short- and long-term outcomes of robotic surgery for rectal cancer: a single-center retrospective cohort study. *Surg Today.* 2020;50(3):240-247.
22. Miura H, Sato T, Tanaka T, et al. Short-term outcomes of robot-assisted surgery for rectal cancer. *Kitasato Med J.* 2020;50:152-157.
23. Brierley JDGM, Wittekind C. *TNM Classification of Malignant Tumors.* 8th ed. Wiley Blackwell; 2017.
24. Sato T, Kokuba Y, Koizumi W, Hayakawa K, Okayasu I, Watanabe M. Phase I trial of neoadjuvant preoperative chemotherapy with S-1 and irinotecan plus radiation in patients with locally advanced rectal cancer. *Int J Radiat Oncol Biol Phys.* 2007;69(5):1442-1447.
25. Sato T, Ozawa H, Hatate K, et al. A phase II trial of neoadjuvant preoperative chemoradiotherapy with S-1 plus irinotecan and radiation in patients with locally advanced rectal cancer: clinical feasibility and response rate. *Int J Radiat Oncol Biol Phys.* 2011;79(3):677-683.
26. Watanabe T, Muro K, Ajioka Y, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2016 for the treatment of colorectal cancer. *Int J Clin Oncol.* 2018;23(1):1-34.
27. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240(2):205-213.
28. Stevenson ARL, Solomon MJ, Brown CSB, et al. Disease-free survival and local recurrence after laparoscopic-assisted resection or open resection for rectal cancer: the Australasian laparoscopic cancer of the rectum randomized clinical trial. *Ann Surg.* 2019;269(4):596-602.
29. Kang J, Yoon KJ, Min BS, et al. The impact of robotic surgery for mid and low rectal cancer: a case-matched analysis of a 3-arm comparison—open, laparoscopic, and robotic surgery. *Ann Surg.* 2013;257(1):95-101.
30. Kim J, Baek SJ, Kang DW, et al. Robotic resection is a good prognostic factor in rectal cancer compared with laparoscopic resection: long-term survival analysis using propensity score matching. *Dis Colon Rectum.* 2017;60(3):266-273.
31. Li X, Wang T, Yao L, et al. The safety and effectiveness of robot-assisted versus laparoscopic TME in patients with rectal cancer: a meta-analysis and systematic review. *Medicine (Baltimore).* 2017;96(29):e7585.
32. Prete FP, Pezzolla A, Prete F, et al. Robotic versus laparoscopic minimally invasive surgery for rectal cancer: a systematic review and meta-analysis of randomized controlled trials. *Ann Surg.* 2018;267(6):1034-1046.
33. Sng KK, Hara M, Shin JW, Yoo BE, Yang KS, Kim SH. The multiphasic learning curve for robot-assisted rectal surgery. *Surg Endosc.* 2013;27(9):3297-3307.
34. Kim HJ, Choi GS, Park JS, Park SY. Multidimensional analysis of the learning curve for robotic total mesorectal excision for rectal cancer: lessons from a single surgeon's experience. *Dis Colon Rectum.* 2014;57(9):1066-1074.
35. Park EJ, Kim CW, Cho MS, et al. Multidimensional analyses of the learning curve of robotic low anterior resection for rectal cancer: 3-phase learning process comparison. *Surg Endosc.* 2014;28(10):2821-2831.
36. Yamaguchi T, Kinugasa Y, Shiomi A, et al. Learning curve for robotic-assisted surgery for rectal cancer: use of the cumulative sum method. *Surg Endosc.* 2015;29(7):1679-1685.
37. Huang YM, Huang YJ, Wei PL. Outcomes of robotic versus laparoscopic surgery for mid and low rectal cancer after neoadjuvant chemoradiation therapy and the effect of learning curve. *Medicine (Baltimore).* 2017;96(40):e8171.
38. Chan AC, Poon JT, Fan JK, Lo SH, Law WL. Impact of conversion on the long-term outcome in laparoscopic resection of colorectal cancer. *Surg Endosc.* 2008;22(12):2625-2630.
39. Law WL, Poon JT, Fan JK, Lo SH. Comparison of outcome of open and laparoscopic resection for stage II and stage III rectal cancer. *Ann Surg Oncol.* 2009;16(6):1488-1493.
40. Memon S, Heriot AG, Murphy DG, Bressel M, Lynch AC. Robotic versus laparoscopic proctectomy for rectal cancer: a meta-analysis. *Ann Surg Oncol.* 2012;19(7):2095-2101.
41. Xiong B, Ma L, Huang W, Zhao Q, Cheng Y, Liu J. Robotic versus laparoscopic total mesorectal excision for rectal cancer: a meta-analysis of eight studies. *J Gastrointest Surg.* 2015;19(3):516-526.
42. Sun Y, Xu H, Li Z, et al. Robotic versus laparoscopic low anterior resection for rectal cancer: a meta-analysis. *World J Surg Oncol.* 2016;14:61.
43. Law WL, Foo DCC. Comparison of short-term and oncologic outcomes of robotic and laparoscopic resection for mid- and distal rectal cancer. *Surg Endosc.* 2017;31(7):2798-2807.

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