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ORIGINAL ARTICLE

Surgical outcomes of robotic, laparoscopic, and open low anterior resection after preoperative chemoradiotherapy for patients with advanced lower rectal cancer

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Abstract

Purpose We investigated the surgical outcomes of robotic low anterior resection (LAR) for lower rectal cancer after preoperative chemoradiotherapy (pCRT).

Methods A total of 175 patients with lower rectal cancer who underwent LAR after pCRT between 2005 and 2020 were stratified into open (OS, $n=65$), laparoscopic (LS, $n=64$), and robotic surgery (RS, $n=46$) groups. We compared the clinical, surgical, and pathological results among the three groups.

Results The RS and LS groups had less blood loss than the OS group ($p<0.0001$). The operating time in the RS group was longer than in the LS and OS groups ($p<0.0001$). The RS group had a significantly longer mean distal margin than the LS and OS groups (25.4 mm vs. 20.7 mm and 20.3 mm, respectively; $p=0.026$). There was no significant difference in the postoperative complication rate among the groups. The local recurrence rate in the RS group was comparable to those in the LS and OS groups.

Conclusion Robotic LAR after pCRT was performed safely for patients with advanced lower rectal cancer. It provided a longer distal margin and equivalent local control rates.

Keywords Laparoscopic surgery · Open surgery · Robotic surgery · Rectal cancer · Chemoradiotherapy

Introduction

The incidence of colorectal cancer is increasing. It is now the third most common cancer and the second leading cause of cancer-related deaths worldwide [1]. Improving treatment outcomes is an urgent concern, particularly for rectal cancer, because of its high potential for local recurrence and distant metastasis after surgery.

Total mesorectal excision (TME) is the gold standard of surgical treatment for rectal cancer [2, 3]. Laparoscopic TME is widely accepted as a minimally invasive procedure with excellent short-term results and long-term oncologic safety [4, 5], as well as less postoperative pain, faster recovery, better conformity, and shorter postoperative hospitalization times than open surgery [6, 7]. However, laparoscopic TME is technically difficult, because laparoscopic instruments have limited flexibility in the deep and narrow pelvic space. Recently introduced robotic surgery (RS) systems address the limitations of laparoscopic surgery, by increasing instrumental freedom, allowing tremor control, and providing a stable three-dimensional camera view for deep pelvic manipulation. Several studies have demonstrated that RS achieves safe and effective short-term results in patients with rectal cancer [8–11].

Preoperative chemoradiotherapy (pCRT) helps to reduce local recurrence and improve tumor resectability through tumor downstaging of advanced lower rectal cancer. Tumor downstaging also reduces the likelihood of positive radial margins (RMs) and the need for a permanent stoma [12–14]. In fact, pCRT is now a standard treatment for advanced lower rectal cancer in Europe and the United States [15, 16].

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Our facility began prescribing pCRT for advanced lower rectal cancer in 2003 [17, 18], and introduced the da Vinci robotic surgery system in 2012. Since 2012, we have managed advanced lower rectal cancer with pCRT and robotic TME; however, the surgical outcomes of RS versus those of laparoscopic and open surgery have not been fully elucidated. We conducted this study to evaluate the safety and oncologic feasibility of RS after pCRT in patients with advanced lower rectal cancer. We also compared the clinical results of robotic, laparoscopic, and open surgery in patients with rectal cancer who underwent low anterior resection (LAR) after pCRT.

Methods

Patients

In this retrospective study, we reviewed 175 patients with advanced lower rectal cancer, who underwent LAR after pCRT at the University of Tokyo Hospital between 2005 and 2020. Patients were stratified into an open surgery (OS) group ($n=65$), a laparoscopic surgery (LS) group ($n=64$), and a robotic surgery (RS) group ($n=46$). Patients with multiple cancers, simultaneous distant metastasis, and colitis-related cancers were excluded from the analysis.

All patients underwent preoperative colonoscopy, chest and abdominopelvic computed tomography, and pelvic magnetic resonance imaging to evaluate the status of local disease infiltration and identify distant metastasis. pCRT was administered for clinical ≥ T3 lower rectal cancer below the peritoneal reflection. The pCRT regimen consisted of 5-fluorouracil (5FU)-based chemotherapy and long-term radiation therapy of 50.4 Gy administered in 28 fractions. Curative resection was scheduled 6–8 weeks after pCRT completion, and all patients underwent LAR with TME. The choice of surgical approach transitioned over time (Fig. 1). From 2005 to 2012, most procedures were done via OS, following which there was a shift to LS in line with its increasing popularity and widespread use. From 2018, when national health insurance in Japan started covering RS for rectal cancer, the number of robotic procedures started to increase. Colorectal anastomosis was performed with the double-stapling technique in all patients. Patients with lateral pelvic lymph nodes larger than 8 mm and suspected metastases underwent lateral pelvic lymph node dissection (LPND), regardless of their response to pCRT [19–21]. A preventive diverting stoma was created when indicated.

A detailed database with clinical, surgical, and pathological information was provided for statistical analysis. We defined the distal margin as the distance between the lower verge of the primary tumor [or scar tissue in patients with pathological complete response (pCR)] and the distal verge of the bowel specimen. RM was defined as the closest distance between the tumor tissue and the lateral resection margin. It was considered positive for RM if the tumor was exposed on the lateral resection margin. Data on local recurrence were obtained from clinical charts. Postoperative surgical complications with a Clavien–Dindo score of 2 or more were recorded. The local ethics committees of the University of Tokyo Hospital approved this study (3252-[12]), and informed consent was obtained in the form of an opt-out option available online (http://all-1su.umin.jp/custom8.html).

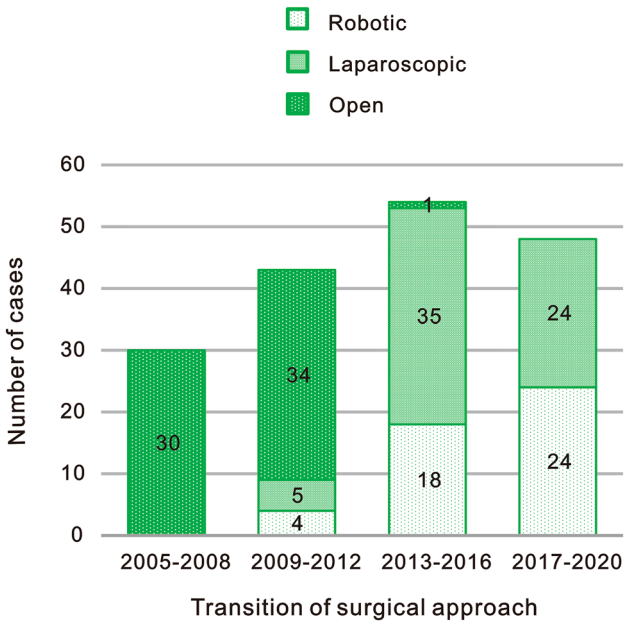

Fig. 1 Transition of surgical approaches: 2005–2020. From 2005 to 2012, open surgery accounted for 88% of surgical procedures. There was then a shift to laparoscopic surgery following its increasing popularity and widespread use. From 2018, the rate of robotic surgery started to increase after its approval for cover by national insurance in Japan

Statistical analysis

All statistical data were analyzed using the JMP Pro 16 software package (SAS Institute Inc., Cary, NC, USA). Continuous variables are presented as medians (interquartile ranges) or means (standard deviation) and analyzed using the Kruskal–Wallis test. Categorical variables are presented as numbers (%) and assessed using the Pearson's chi-squared test or Fisher's exact test, as appropriate. A p value <0.05 was considered significant.

Results

Clinical demographics

Table 1 summarizes the clinical demographics of the RS, LS, and OS group. Male patients accounted for more than half of all three groups. There were no significant differences in sex, age, body mass index, laparotomy history, or tumor height from the anal verge among the three groups, but the RS group included significantly more patients with advanced clinical N stage disease. The 5-FU/Leucovorin (LV) regimen was the most common CRT regimen used in all the groups, although 5-FU/LV/CPT-11 was significantly more frequent in the RS group.

Operative demographics

Table 1 summarizes the operative data of the RS, LS, and OS group. The RS and LS groups had significantly less blood loss (median, 55 ml and 40 ml, respectively) than the OS group (median, 500 ml), while operating times were significantly longer in the RS group (median, 390 min) than in the LS and OS groups (median, 315 min and 243 min, respectively). Even when limiting the analysis to patients who did not undergo LPND, the RS group had the longest operative time (median, 353 min). LPND was performed most frequently in the RS group (26%). The RS and LS groups had significantly higher rates of diverting stoma creation (74% and 66%, respectively) than the OS group (18%).

Pathological outcomes

Table 2 shows the pathological outcomes of the RS, LS, and OS groups. The pCR rates of the RS, LS, and OS groups were 11%, 6%, and 15%, respectively, with an overall pCR rate of 11% (19/175). There were no significant differences in the pathological T and N stages, tumor size, lymphatic invasion, tumor differentiation, or number of dissected lymph nodes among the three groups, although venous invasion was significantly higher in the RS and OS groups than in the LS group. None of the patients in the three groups demonstrated positive RMs. Although there was no significant difference in tumor height from the anal verge among

Table 1 Clinical and operative demographics of rectal cancer patients who underwent low anterior resection with double-stapling technique anastomosis after chemoradiation therapy

Factors	Robotic ($n=46$)	Laparoscopic ($n=64$)	Open ($n=65$)	p value
Sex, *n* (%)				0.859
Male	29 (63%)	43 (67%)	41 (63%)	
Age (years)	61 (SD 11.4)	63 (SD 10.4)	61 (SD 9.3)	0.577
BMI (kg/m^2)	22.6 (SD 3.0)	22.4 (SD 3.3)	23.3 (SD 3.1)	0.121
History of laparotomy, *n* (%)	10 (22%)	20 (31%)	20 (31%)	0.488
Height from AV (mm)	55.4 (SD 14.0)	59.8 (SD 16.1)	57.5 (SD 20.8)	0.428
Clinical T stage, *n* (%)				0.597
T3	42 (91%)	61 (95%)	62 (95%)	
T4	4 (9%)	3 (5%)	3 (5%)	
Clinical N stage, *n* (%)				0.041
N0	18 (39%)	36 (56%)	41 (63%)	
N1-3	28 (61%)	28 (44%)	24 (37%)	
CRT regimen, *n* (%)				0.0002
5-FU/LV	26 (57%)	58 (91%)	52 (80%)	
5-FU/LV/CPT-11	19 (41%)	5 (8%)	10 (15%)	
Others	1 (2%)	1 (1%)	3 (5%)	
Duration from end of CRT to surgery (weeks)	8.7 (7.6–9.8)	8.1 (7.4–9.3)	6.6 (5.3–7.5)	< 0.0001
Blood loss (ml)	55 (18–156)	40 (10–157)	500 (297–787)	< 0.0001
Blood loss without LPND (ml)	50 (10–112)	20 (10–100)	495 (290–783)	< 0.0001
Operative time (min)	390 (325–508)	315 (262–393)	243 (197–320)	< 0.0001
Operative time without LPND (min)	353 (295–435)	306 (257–356)	241 (192–303)	< 0.0001
LPND, *n* (%)	12 (26%)	9 (14%)	3 (5%)	0.0052
Diverting stoma, *n* (%)	34 (74%)	42 (66%)	12 (18%)	< 0.0001

CRT, chemoradiation therapy; LAR, low anterior resection; DST, double-stapling technique; SD, standard deviation; BMI, body mass index; AV, anal verge; 5-FU, 5-fluorouracil; LV, leucovorin calcium; LPND, lateral lymph node dissection

Table 2 Pathological outcomes

Factors	Robotic ($n=46$)	Laparoscopic ($n=64$)	Open ($n=65$)	p value
Pathological T stage, *n* (%)				0.250
CR	5 (11%)	4 (6%)	10 (15%)	
T1-2	14 (30%)	30 (47%)	23 (36%)	
T3-4	27 (59%)	30 (47%)	32 (49%)	
Pathological N stage, *n* (%)				0.142
N0	30 (65%)	46 (72%)	53 (82%)	
N1-3	16 (35%)	18 (28%)	12 (18%)	
Pathological stage, *n* (%)				0.172
CR	6 (13%)	4 (6%)	10 (15%)	
1–2	24 (52%)	42 (66%)	43 (66%)	
3	16 (35%)	18 (28%)	12 (19%)	
CRT grade, *n* (%)				0.0077
1	13 (28%)	26 (41%)	35 (54%)	
2	28 (61%)	34 (53%)	19 (30%)	
3	5 (11%)	4 (6%)	10 (15%)	
Unknown	0	0	1 (1%)	
Tumor size (mm)	27.3 (SD 15.3)	24.4 (SD 13.3)	25.2 (SD 15.8)	0.394
Tumor differentiation, *n* (%)				0.690
WD	32 (70%)	42 (66%)	40 (62%)	
MD/PD	13 (28%)	21 (33%)	21 (32%)	
Lymphatic invasion, *n* (%)	4 (9%)	2 (3%)	3 (5%)	0.387
Venous invasion, *n* (%)	22 (48%)	16 (25%)	35 (54%)	0.002
RM involvement, *n* (%)	0	0	0	
Number of dissected lymph nodes	12 (SD 5.6)	13 (SD 7.2)	10 (SD 5.1)	0.193
Lateral lymph node metastasis rate, *n* (%)	4 (9%)	3 (5%)	0	0.043
Distance to distal margin (mm)	25.4 (SD 11.0)	20.7 (SD 8.9)	20.3 (SD 10.2)	0.026

CR, complete response; CRT, chemoradiation therapy; WD, well differentiated; MD, moderately differentiated; PD, poorly differentiated; RM, radial margin

the three groups, the RS group had a significantly longer mean distance to the distal margin than the LS and OS groups (25.4 mm vs. 20.7 mm and 20.3 mm, respectively; $p=0.026$).

Postoperative outcomes

As shown in Table 3, there was no significant difference in the rate of postoperative complications of Clavien–Dindo

Table 3 Postoperative outcomes

Factors	Robotic ($n=46$)	Laparoscopic ($n=64$)	Open ($n=65$)	p value
Postoperative complications, *n* (%)				
Overall complications	7 (15%)	10 (16%)	16 (25%)	0.325
Anastomotic leakage	0 (0.0%)	1 (2.0%)	2 (3.0%)	0.337
Postoperative ileus	4 (9.0%)	5 (8.0%)	4 (6.0%)	0.876
Urinary dysfunction	2 (4.0%)	1 (2.0%)	1 (2.0%)	0.678
Surgical site infection	0 (0.0%)	2 (3.0%)	4 (6.0%)	0.240
Adjuvant treatment, *n* (%)	20 (43%)	24 (38%)	10 (15%)	0.0024
Postoperative follow-up period (months)	41 (25–68)	60 (48–70)	116 (78–142)	<0.0001
Local recurrence, *n* (%)	2 (4.0%)	1 (2.0%)	4 (6.0%)	0.488

score ≥ 2 among the three groups. Notably, the RS group had no surgical site infections, including anastomotic leakage.

During the median follow-up period of 64.9 months, the RS group had two (4%) cases of local recurrence, which was comparable to the LS and OS groups (2% and 6%, respectively).

Discussion

The present study investigated the surgical outcomes of robotic, laparoscopic, and open LAR approaches after pCRT in patients with advanced lower rectal cancer. In accordance with the findings of previous studies [22–25], our results demonstrated that robotic LAR required longer operating times than laparoscopic and open LAR. Similar results were observed in the group of patients who did not undergo LPND. The longer operating times may be attributed to the additional time required to setup and dock the robotic system. In contrast, the amount of blood loss in the RS group was equivalent to that in the LS group and significantly less than that in the OS group. Blood loss is an independent risk factor for postoperative adverse events, cancer recurrence, and poor overall survival [26–28]. Hence, less blood loss is one of the advantages of the endoscopic approach, which includes RS [23, 24].

The diverting stoma rate of the OS group was remarkably different from that of the RS and LS groups. This was attributed to the transition of surgical approaches over time within our hospital, because most of the OS procedures in this study were performed between 2005 and 2012. We shifted our focus to safer surgical options, because anastomotic leakage is a fatal postoperative complication. Thus, we created diverting stomas for patients with a high probability of anastomotic leakage based on comorbidities and a positive intraoperative air leak test, and for patients whose anastomosis sites were close to the anus [29, 30].

Although there was no significant difference in the tumor height from the anal verge among the three groups, it should be noted that the RS group had a significantly longer distal margin than the LS and OS groups. The longer distal margin in the RS group was compatible with a recent network meta-analysis that compared robotic, open, laparoscopic, and transanal surgical approaches for rectal cancer [31]. An adequate distal resection margin contributes to better oncologic outcomes for lower rectal cancer, with 1–2 cm recommended [32, 33]. The superiority of RS to secure a longer distal margin is probably due to the excellent maneuverability of the robotic arms in the limited pelvic space.

The rates of overall complications did not differ significantly among the groups, although the RS group had the lowest complication rate and none of these patients experienced anastomotic leakage. The rate of diverting stoma was highest in the RS group, which might have accounted for the absence of anastomotic leakage [29]; however, we believe that RS provided a technical advantage because 2% of the LS group patients with comparable stoma creation rates suffered anastomotic leakage.

Prognostic analysis revealed that the RS group had a local recurrence rate comparable to those of the LS and OS groups. Although the RS group included more patients with clinical lymph node involvement, a good local recurrence rate of 93% was observed in this group. As anastomotic leakage is associated with increased local recurrence, the low anastomotic leakage rate in this study may have contributed to the favorable outcomes. The results of this study suggest that robotic LAR after pCRT is a safe and feasible treatment option for advanced lower rectal cancer, from an oncological perspective [34].

Our study has some limitations. First, it was a retrospective, single-center study of a relatively small number of cases. A prospective study with a larger number of patients is required. Second, it compared patients from a single institution over a 16-year period, during which time the surgical approaches, CRT regimen, duration from end of CRT to surgery, and adjuvant chemotherapy for rectal cancer changed. The CRT grade also differed among the three groups, and the proportion of patients who underwent adjuvant chemotherapy was higher in RS and LS groups than in the OS group. These factors might have affected the local recurrence rate. Third, while preserving sexual function is claimed to be an advantage of RS for lower rectal cancer, this study did not examine sexual function, which remains a topic for future studies [35, 36]. Finally, since the follow-up periods of the three groups differed, the overall survival rate and relapse-free survival rate need to be evaluated in future prospective studies involving a larger number of patients.

In conclusion, robotic LAR was found to be as safe as LS or OS for patients with advanced lower rectal cancer, following pCRT. Robotic LAR provided longer distal margins and equivalent oncologic outcomes.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Consent to participate Written informed consent was obtained from all participants in the study.

Consent for publication The participants consented to the journal submission.

Ethics approval This study was approved by the Ethics Committees of the University of Tokyo (No. 3252-(12)).

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