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Original Article

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Robotic Versus Laparoscopic Surgery for Rectal Cancer after Preoperative Chemoradiotherapy: Case-Matched Study of Short-Term Outcomes

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Purpose

Robotic surgery is expected to have advantages over laparoscopic surgery; however, there are limited data regarding the feasibility of robotic surgery for rectal cancer after preoperative chemoradiotherapy (CRT). Therefore, we evaluated the short-term outcomes of robotic surgery for rectal cancer.

Materials and Methods

Thirty-three patients with cT3N0-2 rectal cancer after preoperative CRT who underwent robotic low anterior resection (R-LAR) between March 2010 and January 2012 were matched with 66 patients undergoing laparoscopic low anterior resection (L-LAR). Perioperative clinical outcomes and pathological data were compared between the two groups.

Results

Patient characteristics did not differ significantly different between groups. The mean operation time was 441 minutes (R-LAR) versus 277 minutes (L-LAR, $p < 0.001$). The open conversion rate was 6.1% in the R-LAR group and 0% in the L-LAR group ($p=0.11$). There were no significant differences in the time to flatus passage, length of hospital stay, and postoperative morbidity. In pathological review, the mean number of harvested lymph nodes was 22.3 in R-LAR and 21.6 in L-LAR ($p=0.82$). Involvement of circumferential resection margin was positive in 16.1% and 6.7%, respectively ($p=0.42$). Total mesorectal excision (TME) quality was complete in 97.0% in R-LAR and 91.0% in L-LAR ($p=0.41$).

Conclusion

In our study, short-term outcomes of robotic surgery for rectal cancer after CRT were similar to those of laparoscopic surgery in respect to bowel function recovery, morbidity, and TME quality. Well-designed clinical trials are needed to evaluate the functional results and long-term outcomes of robotic surgery for rectal cancer.

Key words
Rectal neoplasms, Robotic surgical procedures, Laparoscopy

Introduction

In the current era of minimally invasive surgery, laparoscopic surgery for colorectal cancer is widely accepted and performed as a standard operative technique. Several randomized trials [1-4] have shown that laparoscopic colectomy is oncologically safe and yields better short-term outcomes with less postoperative pain, superior cosmetic results, faster recovery times, and shorter hospital stays than open surgery. However, several limitations of laparoscopic surgery for rectal cancer have been suggested [2,5]. In patients with a deep and narrow pelvis, total mesorectal excision (TME) using straight laparoscopic instruments featuring a range of motion with application of a linear stapler to the distal rectum within the pelvis is technically demanding. In addition, laparoscopic surgery requires a highly trained assistant to hold the camera in a stable manner.

A robotic surgical system was recently introduced and has been suggested to have advantages over laparoscopy in surgeries within a confined space [6]. This robotic system provides increased degrees of freedom for instruments, filters physiological tremors, and offers a stable 3-dimensional camera view, which makes rectal dissection more comfortable and easier than laparoscopic surgery [7]. The short-term outcomes of robot-assisted colorectal surgery have indicated its safety and feasibility [8-13]; however, these studies included small numbers of patients who were treated heterogeneously, especially those receiving neoadjuvant chemoradiotherapy (CRT). In earlier studies the proportion of patients who received preoperative CRT was 8.9%-58% [9-11,13].

Therefore, the aim of our study was to evaluate our preliminary experience of robot-assisted surgery in patients with rectal cancer after preoperative CRT based on our significant experience with laparoscopic surgery. To increase homogeneity between the two groups, we selected a case-matched cohort of patients who underwent conventional laparoscopic surgery and compared them with those who underwent robot-assisted surgery.

Materials and Methods

1. Materials

We reviewed the prospectively collected records of patients with mid or low rectal cancer after preoperative CRT who underwent robotic surgery at the National Cancer Center between March 2010 and January 2012. The inclusion criteria were as follows: histologically proven adenocarcinoma located ≤ 9 cm from the anal verge; locally advanced rectal cancer (cT3N0-2) treated with preoperative CRT; no previous or concurrent malignancy at another site; and no evidence of distant metastasis at the time of surgery. We identified and matched 33 patients (1:2) with 66 patients who underwent laparoscopic surgery. Matching criteria included patient age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) score, tumor stage, and CRT method (long course vs. short course). Patients with a histological diagnosis other than adenocarcinoma, familial adenomatous polyposis, or hereditary nonpolyposis colorectal cancer were excluded.

Tumor location was defined as the distance between the distal margin of the tumor and the anal verge as measured using rigid sigmoidoscopy and a digital rectal examination. The tumor stage was recorded postoperatively according to the American Joint Committee on Cancer staging system. The tumor response to CRT was described according to the tumor regression grade scale proposed by Dworak et al. [14]. Use of the robot versus laparoscopy was based on the surgeon's clinical decision and patient preference. As robotic surgery has been suggested to have benefits in surgeries performed in a narrow space, surgeons considered the robotic surgery for patients with a narrow pelvis and low lying rectal cancer after CRT. The patients were given a full explanation of the costs and possible benefits of robotic surgeries and underwent robotic surgery under their consent. This study protocol was approved by Institutional Review Board of National Cancer Center (NCCNCS-12-609).

Patients were preoperatively staged by endorectal ultrasound, magnetic resonance imaging, computed tomography (CT) and positron emission tomography. Preoperative concurrent chemotherapy was administered to all patients following a 5-fluorouracil–based regimen. Long-course CRT was delivered to the entire pelvis at a dose of 45 Gy in 25 fractions, followed by 5.4 Gy in 3 fractions within 6 weeks. Short-course CRT consisted of a total dose of 25 Gy with daily fractions of 5 Gy for 5 days. The intervals between CRT completion and operation were 6 to 8 weeks in patients with long-course CRT and 4 to 8 weeks in those with short-course CRT. A prospective study investigating the efficacy of delayed surgery after short-course CRT had been conducted in our center between February 2010 and October 2011 [15], of which patients were included in this study. In consequence, surgery after short-course CRT was performed in 4 to 8 weeks.

The perioperative clinical outcomes were recorded and analyzed. The operation time was recorded from the start of the operation to the time of wound closure. Anastomotic leakage was defined as peritonitis confirmed through clinically apparent leakage (discharge from the pelvic drain containing pus or fecal material) or radiological evidence (a complicated fluid collection or an abscess on CT scan or rectal water-soluble contrast study). In the pathologic data, the circumferential resection margin (CRM) was considered positive when the distance between the tumor and the proper rectal fascia was ≤ 1 mm. TME quality was classified macroscopically as complete, nearly complete, or incomplete [16].

2. Operative techniques

Robot-assisted surgery was performed using a da Vinci S Surgical System (Intuitive Surgical Inc., Sunnyvale, CA). The patient was placed in the modified Lloyd-Davis position. We performed total robot-assisted surgery without changing the position of the robotic cart, but the robotic arms were repositioned for the pelvic TME procedure as described by Choi et al. [17]. We used a six-port system. One 12-mm port was inserted for the 30° camera approximately 2 cm right and

Table 1. Patient characteristics

Characteristic	Robot (n=33)	Laparoscopy (n=66)	p-value
Age (yr)	57.0±9.6	58.2±9.8	0.86
Sex			
Male	23 (69.7)	46 (69.7)	1.00
Female	10 (30.3)	20 (30.3)	
Body mass index (kg/m^2)	23.2±2.3	23.3±3.1	0.86
Comorbidity	15 (45.5)	29 (43.9)	0.89
Previous abdominal surgery	7 (21.2)	20 (30.3)	0.39
ASA score			
1	15 (45.5)	37 (56.1)	0.14
2	18 (54.5)	25 (37.9)	
3	0	4 (6.1)	
Tumor location	5.41±1.9	5.57±2.1	0.84
Tumor size (cm)	3.14±2.0	2.97±1.5	0.81
Stage			
0	3 (9.1)	8 (12.1)	0.89
I	8 (24.2)	12 (18.2)	
II	10 (30.3)	20 (30.3)	
III	12 (36.7)	26 (39.4)	
Tumor regression grade			
0	2 (6.1)	1 (1.5)	0.28
1	7 (21.2)	11 (16.7)	
2	17 (51.5)	42 (63.6)	
3	6 (18.2)	6 (9.1)	
4	1 (3)	6 (9.1)	
Method of preoperative CRT			
Short course	12 (36.4)	22 (33.3)	0.76
Long course	21 (63.6)	44 (66.7)	
Pre-CRT CEA (ng/mL)	7.69±12.8	6.94±9.3	0.87
Post-CRT CEA (ng/mL)	3.11±2.8	3.03±3.5	0.91
Operative procedure			
LAR	31 (93.9)	61 (92.4)	0.88
Hartmann's operation	0	1 (1.5)	
Miles' operation	2 (6.1)	4 (6.1)	

Values are presented as mean±standard deviation or number (%). ASA, American Society of Anesthesiologists; CRT, chemoradiotherapy; CEA, carcinoembriogenic antigen; LAR, low anterior resection.

lateral to the supraumbilical area. Four 8-mm ports were used for the robotic arms and placed in the following locations: the McBurney point; the right subcostal area on the midclavicular line (MCL); the left subcostal area, approximately 2-cm medial to the MCL; and the counter-McBurney point. One additional 5-mm port between the first and second 8-mm ports was used by the surgical assistant.

The surgical technique was standardized as follows. First, the inferior mesenteric vein was divided adjacent to the fourth portion of the duodenum. The inferior mesenteric artery was then ligated and the sympathetic para-aortic nerve plexus and superior hypogastric nerve were preserved. Colonic mobilization was performed using medial-to-lateral dissection similar to standard laparoscopic techniques [4]. The splenic flexure was mobilized for tension-free anastomosis as necessary. After these procedures, the second and third robotic arms were undocked and moved to the third and fourth ports, respectively. Rectal mobilization was started at the level of the sacral promontory along the avascular presacral plane. Posterior dissection was performed in this plane down to the pelvic floor and the inferior hypogastric nerve was preserved. A left lateral dissection was performed, followed by a right lateral dissection. Anterior dissection was performed under Denonvilliers' fascia using Cadiere forceps in the third arm for retracting the seminal vesicle, prostate, or vagina. After complete rectal mobilization, a digital rectal examination was performed to evaluate the distal resection margin.

The robotic surgical system was then undocked and the remaining procedures were performed laparoscopically. To transect the rectum, we replaced the first 8-mm port with an 11-mm port and used one or two endoscopic linear staplers as appropriate. The specimen was extracted via a 4- to 6-cm abdominal incision across the fourth port. A double staple colorectal or a hand-sewn coloanal anastomosis was performed. Finally, a diverting loop ileostomy was created at the specimen extraction site and a pelvic drain was placed via the third port.

3. Statistical analysis

The chi-square tests or Fisher exact test for categorical variables and Student t test or the Mann-Whitney test for continuous variables were used to assess the statistical differences between the two groups. Values of $p < 0.05$ were considered statistically significant. Statistical analyses were performed using SPSS ver. 12.0 (SPSS Inc., Chicago, IL).

Results

We first performed robot-assisted surgery for rectal cancer in March 2010 and had performed a total of 33 of these surgeries by July 2011. Table 1 summarizes the characteristics of the patients who underwent robotic low anterior resection (R-LAR, n=33) or laparoscopic low anterior resection (L-LAR, n=66). The patients' baseline demographics including age, sex, BMI, comorbidities, previous history of abdominal surgery, ASA score, and carcinoembryogenic antigen level did not differ significantly between groups. The mean distance of the tumor from the anal verge was 5.4 cm in the R-LAR group and 5.6 cm in the L-LAR group. Tumor-related factors, including location, size, stage, and regression grade, were also similar between the two groups. All patients underwent preoperative CRT, and a similar proportion of patients underwent long-course CRT (p=0.76). Low anterior resection was the predominant procedure performed in both the R-LAR and L-LAR groups (93.9% vs. 92.4%, respectively).

Comparison of perioperative clinical outcomes is shown in Table 2. The estimated blood loss did not differ significantly between groups. Two patients in the R-LAR group required conversion to open surgery compared to no patients in the L-LAR group. The mean operation time was significantly longer in the R-LAR group. The mean time from console to wound closure was 377±88 minutes in the R-LAR group. Postoperatively, the mean time to first flatus passage was 2.1 days in the R-LAR group and 1.9 days in the L-LAR group (p=0.21). The mean hospital stay was 10.9 days in the R-LAR group and 13.1 days in the L-LAR group (p=0.64).

No postoperative mortality occurred in either group. The overall perioperative complication rates were similar between groups (Table 2). Anastomosis leakage occurred in three patients (9.1%) in the R-LAR group and seven patients (10.6%) in the L-LAR group. In all, 3% of patients in both groups underwent reoperations. The one patient who underwent reoperation in the R-LAR group was a 72-year-old man who had undergone a previous Miles' operation and had several underlying diseases including liver cirrhosis, diabetes mellitus, hypertension, and hypothyroidism. The reoperation was performed for ileus on postoperative day 8. Bowel congestion was observed and segmental resection of colon with stoma creation was performed. The patient was discharged on postoperative day 33.

A similar number of lymph nodes was observed in both groups (p=0.82) (Table 3). Negative CRM involvement was achieved in 83.9% of patients in the R-LAR group and 93.3% of patients in the L-LAR group (p=0.42). TME quality was complete in 97% of patients in the R-LAR group and 91% of those in the L-LAR group (p=0.41).

Discussion

In this preliminary study, perioperative clinical outcomes and postoperative short-term outcomes of R-LAR were comparable to those of L-LAR in patients with rectal cancer. Studies of robotic surgery for rectal cancer reported on heterogeneously treated patients and included only 8.9%-58% of patients with CRT [10,11,13,18,19]. The current study included only preoperatively treated patients and demonstrated the feasibility of robotic surgery for locally advanced low-lying rectal cancer even after preoperative CRT.

Laparoscopic surgery for rectal cancer after CRT has a steep learning curve, particularly in patients with a deep and narrow pelvis [8]. Robotic surgery was adopted to overcome the limitations associated with laparoscopic surgery. Although this was our initial experience with robotic surgery, the short-term outcomes in the R-LAR group were comparable with those of the L-LAR group performed by experienced surgeons who routinely perform > 100 laparoscopic surgeries for rectal cancer every year.

The overall complication rate was similar between the two groups. In our study, the rate of anastomosis leakage in the R-LAR group was comparable with the rates of 1.8%-13.6%

Table 2. Perioperative clinical outcomes and postoperative complications

Variable	Robot (n=33)	Laparoscopy (n=66)	p-value
Estimated blood loss (mL)	232.0±180.0	205.0±163.8	0.61
Conversion to open surgery	2 (6.1)	0	0.11
Operation time (min)	441.0±90.2	277.0±83.2	< 0.001
Flatus passage (day)	2.1±1.4	1.9±1.5	0.21
Hospital stay (day)	10.9±6.2	13.1±12.8	0.64
Postoperative morbidity (%)	15 (45.6)	26 (39.4)	0.56
Reoperation (%)	1 (3.0)	2 (3.0)	> 0.99

Values are presented as mean±standard deviation or number (%).

Table 3. Pathologic outcomes

Variable	Robot (n=33)	Laparoscopy (n=66)	p-value
No. of harvested LNs	22.3±11.7	21.6±11.0	0.82
Proximal resection margin	17.4±2.7	14.2±6.0	0.15
Distal resection margin	2.2±1.5	2.2±1.7	0.95
CRM involvement (mm)			
> 1	26 (83.9)	56 (93.3)	0.42
≤ 1	5 (16.1)	4 (6.7)	
TME quality			
Complete	32 (97.0)	60 (91.0)	0.41
Nearly complete	1 (3)	6 (9)	
Incomplete	0	0	

Values are presented as mean±standard deviation or number (%). LN, lymph node; CRM, circumferential resection margin; TME, total mesorectal excision.

reported elsewhere [10,13]. All three patients who experienced anastomosis leakage in the current study were treated conservatively.

The operation time included the robot docking time, and the initial process of setting up the robot took a significant amount of time. In accordance with the results of our study, several studies reported that the operating time was significantly longer in robotic rectal surgery than in laparoscopic rectal surgery [10,19,20]. In recent studies [21,22] analyzing the learning curves of robot-assisted rectal surgery, the initial learning was achieved after 21-35 cases. In our subgroup analysis divided into 3 groups by the time period, the operative time in the second group was less than 70 minutes compared with those in the first group (415.9.5 minutes vs. 483.5 minutes, p=0.084, respectively). After sufficient cases to overcome the learning curve for robotic surgery, the operative time in the robotic surgery, except for the docking time, would be shortened and comparable with those in the laparoscopic surgery.

The reasons for conversions in the R-LAR group were attributed to the host factor rather than technical difficulties. The first patient had rectal cancer that invaded the ureter. In the other case, we completed an ultralow anterior resection, but there was poor blood supply to the proximal descending colon.

There was no significant difference in the passage of flatus and length of hospital stay between the two groups, which implies that recovery times were similar between groups. Although robot-assisted rectal surgery was associated with a shorter hospital stay in some studies [13,18], other studies [8,11,18,23] found no difference in the length of hospital stay between robot-assisted and laparoscopic rectal cancer surgeries.

From an oncological perspective, CRM involvement, TME quality, and lymph node dissection are important considerations of rectal cancer surgery. The CRM involvement rate was higher in the R-LAR group than in the L-LAR group, although the difference was not statistically significant. CRM is related to surgical quality as well as tumor location from the rectal fascia propria. Four of five patients with CRM involvement in the R-LAR group already had tumor involvement within the mesorectal fascia prior to CRT. During follow-up, the five patients with a positive CRM had no local recurrence after 10, 22, 24, 32, and 37 months. On the other hand, TME quality of resected specimens is related to surgery quality only. TME quality in the R-LAR group was rated as complete in 97% of patients and nearly complete in 3% of patients; none were rated as incomplete. In other words, the surgical qualities were not significantly different between the R-LAR and the L-LAR groups, but the clinical tumor stages before neoadjuvant therapies were more advanced in the R-LAR group than in the L-LAR group.

In the current study, the numbers of harvested lymph nodes fulfilled the oncological principles in both groups. A recent meta-analysis found no difference in the mean number of lymph nodes collected during both surgical approaches [24]. Other pathological factors, including proximal resection margin and distal resection margin, were negative in all patients after robot-assisted or laparoscopic surgery.

This study has several limitations. First, it was retrospective in nature. To overcome this limitation, we matched the cases using several clinical variables. Accordingly, the groups were well balanced and selection bias was reduced. Second, the sample size was relatively small. However, the current study describes our initial experience with performing robot-assisted surgery, thus the number of cases is still quite low. Based on our current results, we have started a phase II randomized controlled study to evaluate the oncologic outcomes of robot-assisted surgery for rectal cancer (clinical trial registration number: NCT01591798). Third, we did not compare cost-effectiveness between the two groups. The cost of robotic equipment is much higher than that of the equipment used in laparoscopic surgery. Therefore, to justify adopting this new technology, the cost-effectiveness must also be evaluated.

Conclusion

In conclusion, short-term outcomes of robot-assisted surgery for mid or low rectal cancer after CRT were similar to those of laparoscopic surgery. The postoperative clinical outcomes such as recovery of bowel function, postoperative hospital stay and morbidity were similar to those of laparoscopic surgery even though we were not adept to the robot. Moreover, in the oncologic respect, we achieved the complete TME qualities in 97% of patients and harvested a similar number of lymph nodes in robot surgery. Robotic surgery can be performed safely in patients with rectal cancer after preoperative CRT and is expected to have comparable oncologic outcomes.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

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