

ORIGINAL ARTICLE

# 직장암에서 복강경과 개복 수술법의 장기 임상 결과의 비교: 단일 기관 후향적 연구

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## Long-term Outcomes of Laparoscopic versus Open Surgery for Rectal Cancer: A Single-center Retrospective Analysis

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**Background/Aims:** Laparoscopic surgery has been proven to be an effective alternative to open surgery in patients with colon cancer. However, data on laparoscopic surgery in patients with rectal cancer are insufficient. The aim of this study was to compare the long-term outcomes of laparoscopic and open surgery in patients with rectal cancer.

**Methods:** A total of 307 patients with rectal cancer who were treated by open and laparoscopic curative resection at Kosin University Gospel Hospital (Busan, Korea) between January 2002 and December 2011 were reviewed retrospectively.

**Results:** Regarding treatment, 176 patients underwent an open procedure and 131 patients underwent a laparoscopic procedure. The local recurrence rate after laparoscopic resection was 2.3%, compared with 5.7% after open resection ( $p=0.088$ ). Distant metastases occurred in 6.9% of the laparoscopic surgery group, compared with 24.4% in the open surgery group ( $p<0.001$ ). In univariate analysis, age ( $\geq 75$  years vs.  $\leq 60$  years), preoperative staging, surgical approach (open vs. laparoscopic), elevated initial CEA level, elevated follow-up CEA level, number of positive lymph nodes, and postoperative chemotherapy affected overall survival and disease free survival. However, in multivariate analysis, the surgical approach apparently did not affect long-term oncologic outcome.

**Conclusions:** In this study, long-term outcomes after laparoscopic surgery for rectal cancer were not inferior to those after open surgery. Therefore, laparoscopic surgery would be an alternative operative tool to open resection for rectal cancer, although further investigation is needed. (Korean J Gastroenterol 2015;65:273-282)

**Key Words:** Rectal neoplasms; Conversion to open surgery; Laparoscopy

## INTRODUCTION

Colorectal cancer is the third most commonly diagnosed cancer in males and the second in females worldwide.<sup>1</sup> In the United States, an estimated 40,000 new cases of rectal cancer will occur and an estimated 50,310 people will die from

rectal and colon cancer combined in 2014.<sup>2</sup> In Eastern Asia, rectal cancer occurs in more than 16 per 100,000 individuals per year and accounts for more than 168,000 deaths per year.<sup>3</sup> Over the last two decades, the introduction of total mesorectal excision and preoperative chemoradiation has led to improved local control and survival for patients with

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rectal cancer.<sup>4,5</sup> Several randomized controlled trials have confirmed that the long-term oncologic outcome of laparoscopic resection is equivalent to that of open resection for colon cancer.<sup>6-9</sup> The laparoscopic approach for colon cancer surgery has demonstrated earlier recovery of bowel function, less postoperative pain, and decreased hospital stay compared with open surgery.<sup>5,9-11</sup> However, data regarding laparoscopic surgery in patients with rectal cancer are insufficient. Several recent studies have reported on the short-term or long-term outcomes of laparoscopic surgery for rectal cancer; these studies showed that laparoscopic surgery is feasible, with few complications and long-term outcomes similar to those for open surgery.<sup>12-15</sup> Due to difficulties in pelvic exposure, rectal dissection, and sphincter preservation, laparoscopic surgery for rectal cancer is known to be technically more difficult than open surgery.

The aim of this study was to compare the long-term outcomes of laparoscopic surgery with those of open surgery in patients with rectal cancer, and to contribute to establishing the role of laparoscopic surgery in treatment of rectal cancer.

## SUBJECTS AND METHODS

### 1. Patients

We began performing laparoscopic surgery for rectal cancer in 2002. The analysis included 307 patients who underwent resection for rectal cancer between January 2002 and December 2011 at Kosin University Gospel Hospital (Busan, Korea). Rectal cancer was defined as a cancer that forms in the tissues of the rectum (located 15 cm or less from the anal verge on rigid sigmoidoscopy) according to the National Cancer Institute definition.<sup>16</sup> The location of the tumor was categorized as lower (less than 5 cm from anal verge), middle (6-10 cm from anal verge), or upper rectum (11-15 cm from anal verge). For preoperative staging, patients underwent a full pre-operative workup including a colonoscopy, as well as flexible sigmoidoscopy and abdominal CT with additional MRI or ano-rectal ultrasound. PET-CT was also performed after September 2004. Patients with stage IV rectal cancer were excluded. The medical records of all patients were reviewed retrospectively, including patient characteristics, surgical procedures, pathologic findings, and long-term follow-up data. This study was approved by the institutional review board of Kosin University College of Medicine (KUGH IRB No.

14-104).

### 2. Treatment

Among patients with T3N0 or greater TNM preoperative staging, neoadjuvant concurrent chemoradiotherapy (CCRT) was selected by decision of a multidisciplinary team conference. Radiotherapy consisted of 56.0 Gy total in 28 fractions (200 cGy daily, Monday-Friday), delivered with an energy of 10 MV photons via a three-field box technique to the primary tumor and to the mesorectal, presacral, and internal iliac lymph nodes. CCRT consisted of a continuous infusion of 5-fluorouracil (425 mg/m<sup>2</sup>) plus leucovorin (20 mg/m<sup>2</sup>) on days 1-5 and 29-33 of radiotherapy, and one or two rounds of chemotherapy were added after CCRT. At six to ten weeks after CCRT, patients were re-staged with CT and proceeded to surgery.

Both open and laparoscopic surgery for rectal cancer were performed by three experienced colorectal surgeons (A.B.K., B.S.U., and L.S.H.). Selection of the surgical approach was decided by the surgeon and patient with full information regarding the procedures, including the possibility of morbidity. The same oncologic guidelines were followed in performance of all procedures in both groups: adequate resection margins, 'en bloc' vascular resection and lymphadenectomy and minimal intraoperative manipulation of the tumor. Patients with upper rectal tumors underwent partial mesorectal excision with a 5-cm gross tumor margin from the inferior pole of the tumor. Patients with middle and lower rectal tumors underwent total mesorectal excision. Our first laparoscopic surgery was performed in 2002, and the frequencies of these procedures increased each year. Laparoscopic resection was performed using the 5-trocar technique with high ligation of the inferior mesenteric artery, medial to lateral mobilization of the left colon and splenic flexure, rectal transection with a laparoscopic stapler, and double-stapled anastomosis. Protective ileostomy was rarely performed. Patients who underwent surgery using an initial laparoscopic approach, which was then converted to open surgery, belonged to the open surgery group. Conversion to open surgery was performed in most of these patients, as an abdominal incision larger than that necessary for specimen retrieval was created.

After surgery, patients with pathologic T3N0 or greater TNM staging received additional chemotherapy consisting of oral folinic acid, oral capecitabine, intravenous 5-fluorouracil

plus leucovorin, or FOLFOX regimen (combination of oxaliplatin, 5-fluorouracil, and leucovorin). However, postoperative radiotherapy was rarely performed.

### 3. Follow-up

After the operation, patients were seen at 3-month intervals for the first 2 years, then at 6-month intervals for the next 3 years, and after 5 years, annually at an outpatient clinic. Follow-up examination included CEA measurement per three months, chest X-ray and abdominal CT per six months during the first 2 years, and annually thereafter. CEA is routinely detected as a tumor biomarker and an auxiliary indicator for the preoperative diagnosis of colorectal cancer, as well as an early predictor of recurrence. Elevated initial CEA level refers to higher than normal range at the time of diagnosis, and elevated follow-up CEA level refers to elevation of CEA level during the follow-up period. Colonoscopy and PET-CT were also performed annually. Recurrence was diagnosed by endoscopic biopsy, surgical resection, and/or radiological imaging study. Local recurrence was defined as any recurrence within the pelvic cavity, and distant recurrence was defined as any recurrence outside the pelvic cavity.

### 4. Statistical analysis

Student's t-test and chi-square test for continuous and categorical variables, as appropriate, were performed to de-

termine significant differences between open and laparoscopic resection. Kaplan-Meier method was used for estimation of the overall survival (OS) and disease-free survival (DFS). The OS was measured from the date of diagnosis of rectal cancer to the date of death or of the final follow-up. DFS was measured from the date of diagnosis of rectal cancer to the date of disease progression or of the final follow-up. The log-rank test was used for comparison of time-to-event distributions; the Cox proportional-hazards regression model was used for univariate and multivariate models. p-values lower than 0.05 were considered to indicate statistical significance. Statistical analysis was performed using IBM SPSS Statistics version 20.0 (IBM Co., Armonk, NY, USA).

## RESULTS

### 1. Patient characteristics

Between January 2002 and December 2011, a total of 307 patients underwent surgery for rectal cancer; 176 patients underwent open surgery (open surgery group), and 131 patients underwent laparoscopic surgery (laparoscopic surgery group). Baseline characteristics of both groups are summarized in Table 1. There were no significant differences in sex, age, or tumor stage between the two groups, but tumor locations differed significantly.

**Table 1.** Patient Characteristics

Characteristic	Open (n=176)	Laparoscopy (n=131)	p-value
Gender			0.153
Male	89 (50.6)	77 (58.8)	
Female	87 (49.4)	54 (41.2)	
Age (yr)	59 (22-85)	61 (33-88)	0.252
Location			0.002
Lower ( $\leq 5$ cm from anal verge)	45 (25.6)	26 (19.8)	
Middle (6-10 cm from anal verge)	84 (47.7)	45 (34.4)	
Upper (11-15 cm from anal verge)	47 (26.7)	60 (45.8)	
Preoperative staging			0.056
I	33 (18.8)	40 (30.5)	
II	45 (25.6)	29 (22.1)	
III	98 (55.7)	62 (47.3)	
Neoadjuvant CCRT			0.293
Yes	26 (14.8)	14 (10.7)	
No	150 (85.2)	117 (89.3)	
Adjuvant chemotherapy			0.008
Yes	130 (73.9)	78 (59.5)	
No	46 (26.1)	53 (40.5)	

Values are presented as n (%) or mean (range).  
CCRT, concurrent chemoradiotherapy.

## 2. Pathological data

Macroscopically incomplete resected specimens were recorded in 4 of 131 patients (3.1%) after laparoscopic surgery and 12 of 176 patients (6.8%) after open surgery. No significant difference in tumor histology was observed between the two groups. The proportion of patients with a positive circumferential resection margin was 4.0% in the laparoscopic surgery group and 3.1% in the open surgery group ( $p=0.951$ ). The median number of lymph nodes harvested after surgery was not significantly different in the two groups ( $p=0.946$ ); however, the mean number of positive lymph nodes after open surgery was significantly higher than that after laparoscopic surgery ( $p=0.003$ ). The median proximal resection margin was 10 cm after laparoscopic surgery and 13.5 cm after open surgery; the distal resection margin was 3.0 cm after laparoscopic surgery and 2.0 cm after open surgery (Table 2).

## 3. Postoperative recurrence rates

Open surgery was performed more often than laparoscopic surgery from 2002 to 2007, whereas between 2008

and 2011, laparoscopic surgery was performed more often than open surgery. The overall median time of follow-up period was 44 months (8-142 months), and 51 months (8-142 months) and 40 months (11-135 months) for the open surgery group and laparoscopic surgery group, respectively. The overall median time to recurrence was 18 months (5-136 months), and 11 months (5-37 months) and 21 months (5-136 months) for the open surgery group and laparoscopic surgery group, respectively (Table 3).

The recurrence rate for the open surgery group was 30.1%, and that of the laparoscopic surgery group was 9.2%. In the open surgery group, 10 patients (5.7%) had a local recurrence and 43 patients (24.4%) had distant recurrence. In the laparoscopic surgery group, 3 patients (2.3%) had a local recurrence and 9 patients (6.9%) had distant recurrence. A statistically significant difference was observed between the two groups ( $p < 0.001$ ). The sites of distant recurrence in both groups are summarized in Table 3.

## 4. Overall survival and disease free survival

The OS of the open surgery group and laparoscopic surgery

**Table 2.** Pathological Data

Variable	Open (n=176)	Laparoscopy (n=131)	p-value
Completeness of resection			0.304
Complete	163 (92.6)	126 (96.2)	
Partially complete	12 (6.8)	4 (3.1)	
Incomplete	1 (0.6)	1 (0.8)	
Histology			0.846
Well differentiated	44 (28.0)	36 (27.5)	
Moderately differentiated	118 (63.0)	88 (67.2)	
Poorly differentiated	10 (6.6)	5 (3.8)	
Mucinous	4 (2.4)	2 (1.5)	
Circumference resection margin			0.951
Positive	7 (4.0)	4 (3.1)	
Negative	122 (69.3)	67 (51.1)	
Missing data	47 (26.7)	60 (45.8)	
Number of harvested lymph nodes			0.946
Total group	13.0 (0-48.0)	12.0 (0-83.04)	
Missing data	4	5	
Number of positive lymph nodes			0.003
Total group	2.62±4.45	1.39±2.52	
Missing data	4	4	
Distance to proximal resection margin (cm)			< 0.001
Total group	13.5 (1.5-40.0)	10.0 (0.8-33.0)	
Missing data	11	5	
Distance to distal resection margin (cm)			0.181
Total group	2.0 (0-10.0)	3.0 (0-8.5)	
Missing data	11	5	

Values are presented as n (%), median (range), n only, or mean±SD.

**Table 3.** Postoperative Recurrence according to Surgical Procedure

	Total (n=307)	Open (n=176)	Laparoscopy (n=131)	p-value
Period of performance of operation				< 0.001
January 2002-December 2004	47 (15.3)	43 (24.4)	4 (3.0)	
January 2005-December 2007	99 (32.2)	85 (48.3)	14 (10.7)	
January 2008-December 2011	161 (52.5)	48 (27.3)	113 (86.3)	
Duration of follow-up (mo)	44 (8-142)	51 (8-142)	40 (11-135)	< 0.001
Time to recurrence (mo)	18 (5-136)	20 (5-136)	11 (5-37)	0.076
Recurrence after operation				< 0.001
Local recurrence	13 (4.3)	10 (5.7)	3 (2.3)	0.088
Distant recurrence	52 (16.9)	43 (24.4)	9 (6.9)	< 0.001
No recurrence	242 (78.8)	123 (69.9)	119 (90.8)	
Site of distant recurrence				0.958
Liver	13 (4.2)	10 (5.7)	3 (2.3)	
Lungs	20 (6.5)	17 (9.7)	3 (2.3)	
Bone	3 (1.0)	3 (1.7)	0 (0)	
Lymph nodes	2 (0.7)	2 (1.1)	0 (0)	
Peritoneum	4 (1.3)	3 (1.7)	1 (0.8)	
Ovary	1 (0.4)	1 (0.6)	0 (0)	
Multiple organ involvement	9 (2.9)	7 (4.0)	2 (1.5)	

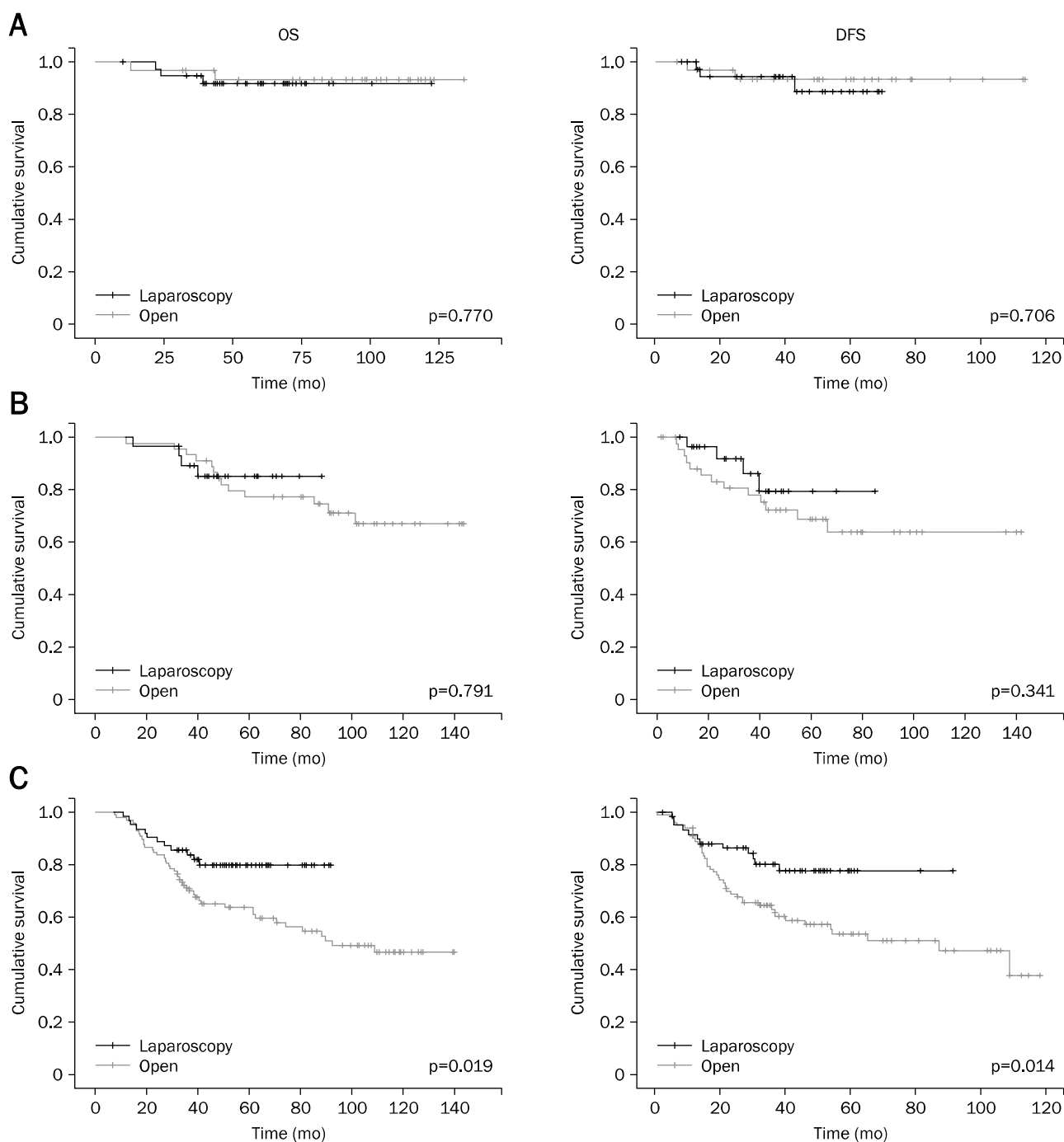
Values are presented as n (%) or median (range).

group at 5 years was 72.5% and 84.8%, respectively. Statistically significant OS and DFS according to preoperative staging between the two groups were observed only in patients with stage 3; however, statistical significance was not observed in patients with stage 1 and stage 2 (Fig. 1). In addition, excluding DFS in patients with middle rectal tumor, the OS and DFS according to tumor location between the two groups were not statistically significant (Fig. 2).

Cox regression analysis was performed for identification of prognostic factors of OS and DFS. Results of univariate analysis of factors of OS and DFS are shown in Table 4. In multivariate analysis, the prognostic factors affecting OS were age ( $\geq 75$  years vs.  $\leq 60$  years, hazard ratio [HR] 2.47, 95% CI 1.08-5.67,  $p=0.033$ ), elevated initial CEA level (HR 2.16, 95% CI 1.29-3.60,  $p=0.003$ ), elevated follow-up CEA level (HR 3.68, 95% CI 2.59-5.23,  $p < 0.001$ ), number of positive lymph nodes (HR 1.19, 95% CI 1.12-1.27,  $p < 0.001$ ), and postoperative chemotherapy (HR 0.29, 95% CI 0.13-0.67,  $p=0.004$ ). The prognostic factors affecting DFS were age ( $\geq 75$  years vs.  $\leq 60$  years, HR 3.30, 95% CI 1.43-7.63,  $p=0.005$ ), elevated initial CEA level (HR 1.76, 95% CI 1.06-2.91,  $p=0.029$ ), elevated follow-up CEA level (HR 3.72, 95% CI 2.63-5.26,  $p < 0.001$ ), number of positive lymph nodes (HR 1.14, 95% CI 1.07-1.21,  $p < 0.001$ ), and postoperative chemotherapy (HR 0.20, 95% CI 0.09-0.49,  $p < 0.001$ ) (Table 5).

## DISCUSSION

Results of this study shows that long-term outcomes after laparoscopic resection are better than those after conventional open resection for rectal cancer. The COREAN trial, which compared open and laparoscopic surgery for middle or lower rectal cancer after neoadjuvant chemotherapy, showed that laparoscopic resection for locally advanced rectal cancer after preoperative chemoradiotherapy provides similar outcomes with respect to DFS as open resection.<sup>16</sup> As reported in the COLOR II trial, in selected patients treated by skilled surgeons, laparoscopic surgery provided safety, resection margins, and completeness of resection similar to those of open surgery, and in-hospital recovery time was decreased after laparoscopic surgery.<sup>17</sup> In this study, significantly higher OS was observed for the laparoscopic surgery group compared with the open surgery group ( $p=0.012$ ), and the DFS was also significantly higher in the laparoscopic surgery group compared with the open surgery group ( $p=0.005$ ). Patients with rectal cancer who underwent laparoscopic surgery also had lower recurrence rates than those who underwent open surgery ( $p < 0.001$ ). In our hospital, laparoscopic surgery was performed mainly after January 2008 (Table 3), and the mean follow-up duration of the laparoscopic surgery group was shorter than that of the open surgery group (41 months vs. 56 months,  $p < 0.001$ ). This may be a function of

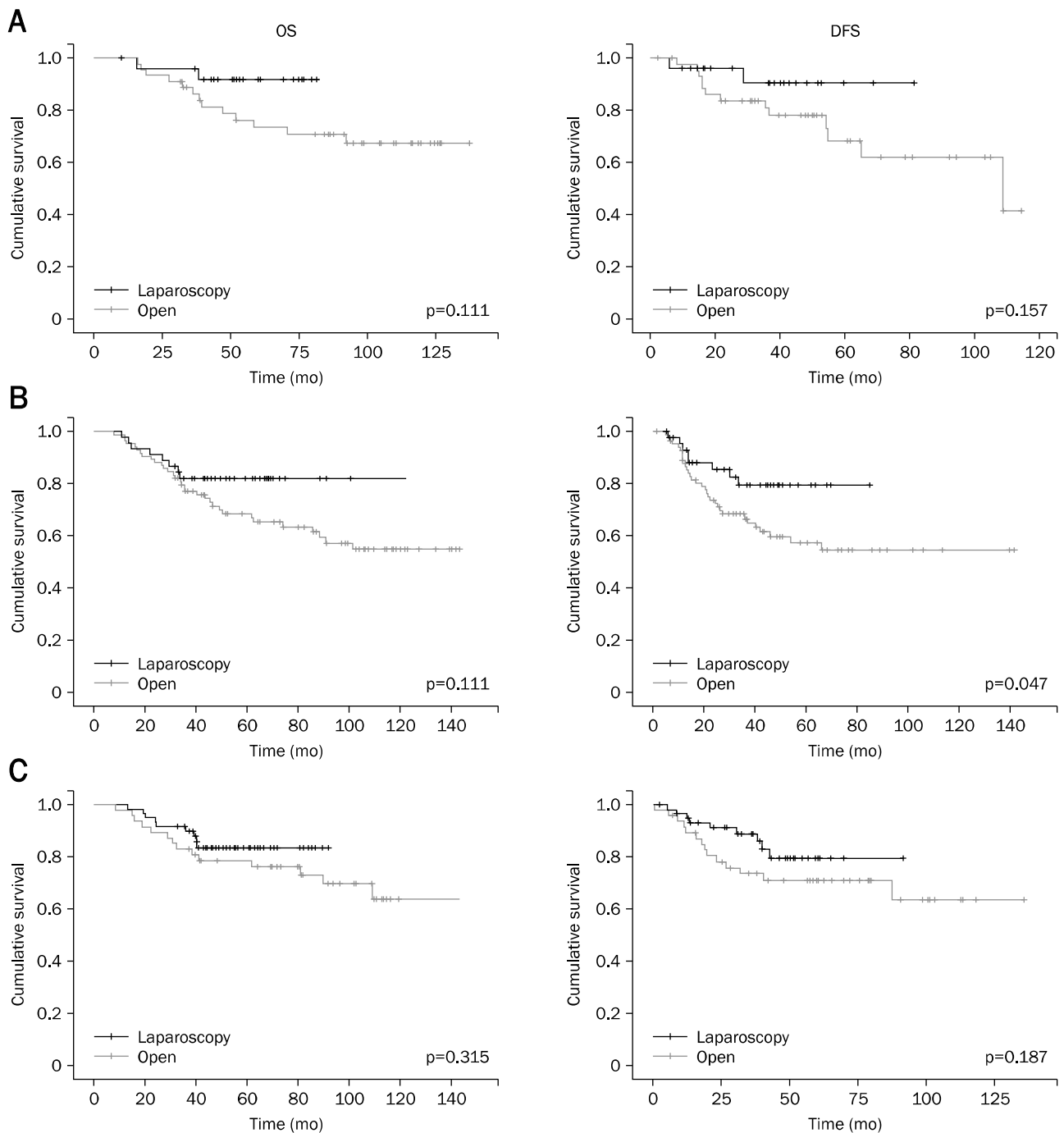


**Fig. 1.** Comparison of overall survival (OS) and disease-free survival (DFS) according to preoperative staging between open surgery group and laparoscopic surgery group. (A) Stage 1. (B) Stage 2. (C) Stage 3.

the lower recurrence rates and better OS or DFS of the laparoscopic surgery group compared with those of the open surgery group.

In this study, we evaluated long-term outcomes according to preoperative tumor stage. da Luz Moreira et al.<sup>12</sup> reported on the recurrence rates of a laparoscopic surgery group and

an open surgery group; they found that rates for stage I were 3.7% (1/27) vs. 6.3% (2/32); for stage II, 29.4% (5/17) vs. 19.0% (4/21); and for stage III, 17.9% (5/28) vs. 33.3% (6/18). Ng et al.<sup>18</sup> reported a recurrence rate of 20.0% (8/40) for a laparoscopic surgery group and 25.0% (9/36) for an open surgery group. In the current study, the OS and DFS ac-



**Fig. 2.** Comparison of overall survival (OS) and disease-free survival (DFS) according to tumor location between open surgery group and laparoscopic surgery group. (A) Upper (11-15 cm from anal verge). (B) Middle (6-10 cm from anal verge). (C) Lower ( $\leq 5$  cm from anal verge).

cording to preoperative staging between the two groups was not statistically significant in patients with stage 1 and stage 2; however, the OS and DFS of the laparoscopic surgery group were better than those of the open surgery group in patients with stage 3 (Fig. 1). These results are attributed to a larger number of positive lymph nodes in the open surgery group

compared with the laparoscopic surgery group ( $2.62 \pm 4.45$  vs.  $1.39 \pm 2.52$ ,  $p=0.003$ ; Table 2). We also evaluated recurrence rates according to tumor location in the rectum. A distal rectal tumor may easily metastasize initially to the lungs because the inferior rectal vein drains into the inferior vena cava bypassing the portal venous system.<sup>19</sup> Tarantino

**Table 4.** Univariate Analysis of Overall Survival and Disease-free Survival

Factor	Overall Survival		Disease-free Survival	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
Age (yr)				
60-74 vs. $\leq 60$	1.46 (0.88-2.44)	0.144	1.51 (0.94-2.44)	0.091
$\geq 75$ vs. $\leq 60$	2.47 (1.08-5.67)	0.033	3.79 (1.85-7.77)	< 0.001
Male vs. female	1.21 (0.78-1.89)	0.404	1.31 (0.84-2.04)	0.232
Open vs. laparoscopic surgery	1.94 (1.14-3.28)	0.014	2.09 (1.24-3.52)	0.006
Tumor location				
Middle vs. lower	1.62 (0.89-2.92)	0.114	1.60 (0.89-2.90)	0.120
Upper vs. lower	1.08 (0.57-2.08)	0.807	1.04 (0.54-1.99)	0.910
Stage 2 vs. stage 1	3.29 (1.22-8.93)	0.019	3.45 (1.27-9.36)	0.015
Stage 3 vs. stage 1	6.19 (2.48-15.45)	< 0.001	5.59 (2.24-13.97)	< 0.001
Histology (well/moderate vs. poorly/mucinous)	0.94 (0.38-2.32)	0.887	0.85 (0.34-2.11)	0.727
Completeness of resection (R1/R2 vs. R0)	2.00 (0.96-4.16)	0.063	1.98 (0.95-4.12)	0.067
Positive CRM	0.86 (0.67-1.10)	0.234	0.83 (0.64-1.06)	0.138
Number of harvested LNs	0.99 (0.97-1.02)	0.787	1.00 (0.97-1.03)	0.983
Number of positive LNs	1.17 (1.12-1.23)	< 0.001	1.15 (1.11-1.20)	< 0.001
Distance to proximal RM	0.99 (0.96-1.02)	0.558	0.99 (0.96-1.02)	0.622
Distance to distal RM	1.01 (0.89-1.14)	0.861	0.99 (0.88-1.12)	0.882
Elevated initial CEA level	3.12 (1.97-4.95)	< 0.001	2.91 (1.84-4.60)	< 0.001
Elevated follow-up CEA level	3.46 (2.59-4.61)	< 0.001	3.69 (2.76-4.93)	< 0.001
Preoperative CCRT	0.82 (0.44-1.51)	0.519	0.93 (0.50-1.72)	0.810
Postoperative chemotherapy	0.18 (0.08-0.39)	< 0.001	0.19 (0.09-0.41)	< 0.001

CRM, circumferential resection margin; LNs, lymph nodes; RM, resection margin; CCRT, concurrent chemoradiotherapy.

**Table 5.** Multivariate Analysis of Overall Survival and Disease-free Survival

Factor	Overall Survival		Disease-free Survival	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
Age (yr)				
60-74 vs. $\leq 60$	1.46 (0.88-2.44)	0.144	1.41 (0.85-2.35)	0.186
$\geq 75$ vs. $\leq 60$	2.47 (1.08-5.67)	0.033	3.30 (1.43-7.63)	0.005
Open vs. laparoscopic surgery	1.06 (0.57-1.98)	0.845	1.49 (0.78-2.85)	0.222
Stage 2 vs. stage 1	0.73 (0.12-4.48)	0.732	0.43 (0.07-2.73)	0.369
Stage 3 vs. stage 1	0.99 (0.17-6.05)	0.998	0.46 (0.07-2.92)	0.412
Number of positive LNs	1.19 (1.12-1.27)	< 0.001	1.14 (1.07-1.21)	< 0.001
Elevated initial CEA level	2.16 (1.29-3.60)	0.003	1.76 (1.06-2.91)	0.029
Elevated follow-up CEA level	3.68 (2.59-5.23)	< 0.001	3.72 (2.63-5.26)	< 0.001
Postoperative chemotherapy	0.29 (0.13-0.67)	0.004	0.20 (0.09-0.49)	< 0.001

LNs, lymph nodes.

et al.<sup>20</sup> reported that the distance of tumor from anal verge (< 5 cm) is one of the predictors for poor OS (HR 1.93, 95% CI 1.11-3.37,  $p=0.039$ ). On the other hand, Das et al.<sup>21</sup> found that a greater distance from anal verge (> 5 cm) independently predicted a lower downstaging rate in patients who received preoperative chemoradiation for rectal cancer. In this study, excluding DFS in patients with middle rectal tumor, the OS and DFS according to tumor location between two groups was not statistically significant (Fig. 2). To date, long-term outcomes according to tumor location in the rectum remain con-

troversial; therefore further studies are needed.

OS rates ranging from 62.8% to 91.0% following laparoscopic rectal resection have been reported.<sup>18,22-25</sup> In this study, the 5-year OS of the open surgery group and of the laparoscopic surgery group were 72.5% and 84.8%, respectively. The independent predictors of OS were old age ( $\geq 75$  years), elevated initial CEA level, elevated follow-up CEA level, number of positive lymph nodes, and postoperative chemotherapy. These factors were also included among independent predictors of DFS (Table 5). According to some authors, the



prognosis for colorectal cancer in the elderly is not significantly different from that of younger patients.<sup>26-29</sup> However, the relation between age and outcomes from colorectal cancer surgery is complex and may be confounded by differences in stage at presentation, tumor location, pre-existing comorbidities, and type of treatment received.<sup>28</sup> Results of univariate Cox regression analysis showed that long-term oncologic outcome was better in the laparoscopic surgery group compared with the open surgery group (Table 4); however, in multivariate Cox regression analysis, the surgical approach (laparoscopic vs. open) apparently did not affect long-term oncologic outcome (Table 5). Based on these results, patients with old age, elevated initial CEA level, elevated follow-up CEA level, larger number of positive lymph nodes, or without preoperative chemotherapy require more careful follow-up observation after surgery than other patients.

Data from this study indicate that long-term outcomes after laparoscopic surgery are not inferior to those after open surgery for rectal cancer. Although this study was a retrospective, single-center study, our results suggest that laparoscopic surgery would be a valid alternative operative tool to open surgery for rectal cancer. Further randomized trials evaluating the outcomes of laparoscopic surgery for rectal cancer will be needed to enable clinical acceptance of laparoscopic surgery for treatment of rectal cancer.

## REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. *CA Cancer J Clin* 2011;61:69-90.
2. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA Cancer J Clin* 2014;64:9-29.
3. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893-2917.
4. Kapiteijn E, Kranenbarg EK, Steup WH, et al. Total mesorectal excision (TME) with or without preoperative radiotherapy in the treatment of primary rectal cancer. Prospective randomised trial with standard operative and histopathological techniques. Dutch ColoRectal Cancer Group. *Eur J Surg* 1999;165:410-420.
5. Sauer R, Becker H, Hohenberger W, et al; German Rectal Cancer Study Group. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med* 2004;351:1731-1740.
6. Clinical Outcomes of Surgical Therapy Study Group. A comparison of laparoscopically assisted and open colectomy for colon cancer. *N Engl J Med* 2004;350:2050-2059.
7. Buunen M, Veldkamp R, Hop WC, et al; Colon Cancer Laparoscopic or Open Resection Study Group. Survival after laparoscopic surgery versus open surgery for colon cancer: long-term outcome of a randomised clinical trial. *Lancet Oncol* 2009;10:44-52.
8. Jayne DG, Guillou PJ, Thorpe H, et al; UK MRC CLASICC Trial Group. Randomized trial of laparoscopic-assisted resection of colorectal carcinoma: 3-year results of the UK MRC CLASICC Trial Group. *J Clin Oncol* 2007;25:3061-3068.
9. Lacy AM, García-Valdecasas JC, Delgado S, et al. Laparoscopy-assisted colectomy versus open colectomy for treatment of non-metastatic colon cancer: a randomised trial. *Lancet* 2002;359:2224-2229.
10. Delaney CP, Chang E, Senagore AJ, Broder M. Clinical outcomes and resource utilization associated with laparoscopic and open colectomy using a large national database. *Ann Surg* 2008;247:819-824.
11. Kemp JA, Finlayson SR. Outcomes of laparoscopic and open colectomy: a national population-based comparison. *Surg Innov* 2008;15:277-283.
12. da Luz Moreira A, Mor I, Geisler DP, Remzi FH, Kiran RP. Laparoscopic resection for rectal cancer: a case-matched study. *Surg Endosc* 2011;25:278-283.
13. Lujan J, Valero G, Biondo S, Espin E, Parrilla P, Ortiz H. Laparoscopic versus open surgery for rectal cancer: results of a prospective multicentre analysis of 4,970 patients. *Surg Endosc* 2013;27:295-302.
14. Ng SS, Lee JF, Yiu RY, et al. Laparoscopic-assisted versus open total mesorectal excision with anal sphincter preservation for mid and low rectal cancer: a prospective, randomized trial. *Surg Endosc* 2014;28:297-306.
15. Seshadri RA, Srinivasan A, Tapkire R, Swaminathan R. Laparoscopic versus open surgery for rectal cancer after neoadjuvant chemoradiation: a matched case-control study of short-term outcomes. *Surg Endosc* 2012;26:154-161.
16. 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;15:767-774.
17. van der Pas MH, Haglind E, Cuesta MA, et al; COLOrectal cancer Laparoscopic or Open Resection II (COLOR II) Study Group. Laparoscopic versus open surgery for rectal cancer (COLOR II): short-term outcomes of a randomised, phase 3 trial. *Lancet Oncol* 2013;14:210-218.
18. Ng SS, Leung KL, Lee JF, et al. Laparoscopic-assisted versus open abdominoperineal resection for low rectal cancer: a prospective randomized trial. *Ann Surg Oncol* 2008;15:2418-2425.
19. Chiang JM, Hsieh PS, Chen JS, Tang R, You JF, Yeh CY. Rectal cancer level significantly affects rates and patterns of distant metastases among rectal cancer patients post curative-intent surgery without neoadjuvant therapy. *World J Surg Oncol* 2014;12:197.
20. Tarantino I, Warschkow R, Worni M, et al. Elevated preoperative CEA is associated with worse survival in stage I-III rectal cancer patients. *Br J Cancer* 2012;107:266-274.
21. Das P, Skibber JM, Rodriguez-Bigas MA, et al. Predictors of tumor response and downstaging in patients who receive preoperative chemoradiation for rectal cancer. *Cancer* 2007;109:1750-1755.
22. Baik SH, Gincher M, Mutch MG, Birnbaum EH, Fleshman

- JW. Laparoscopic vs open resection for patients with rectal cancer: comparison of perioperative outcomes and long-term survival. *Dis Colon Rectum* 2011;54:6-14.
23. Braga M, Frasson M, Vignali A, Zuliani W, Capretti G, Di Carlo V. Laparoscopic resection in rectal cancer patients: outcome and cost-benefit analysis. *Dis Colon Rectum* 2007;50:464-471.
24. Laurent C, Leblanc F, Wütrich P, Scheffler M, Rullier E. Laparoscopic versus open surgery for rectal cancer: long-term oncologic results. *Ann Surg* 2009;250:54-61.
25. Lujan J, Valero G, Hernandez Q, Sanchez A, Frutos MD, Parrilla P. Randomized clinical trial comparing laparoscopic and open surgery in patients with rectal cancer. *Br J Surg* 2009;96:982-989.
26. Irvin TT. Prognosis of colorectal cancer in the elderly. *Br J Surg* 1988;75:419-421.
27. Mulcahy HE, Patchett SE, Daly L, O'Donoghue DP. Prognosis of elderly patients with large bowel cancer. *Br J Surg* 1994;81:736-738.
28. Colorectal Cancer Collaborative Group. Surgery for colorectal cancer in elderly patients: a systematic review. *Lancet* 2000;356:968-974.
29. Vironen JH, Sainio P, Husa AI, Kellokumpu IH. Complications and survival after surgery for rectal cancer in patients younger than and aged 75 years or older. *Dis Colon Rectum* 2004;47:1225-1231.