Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): 10-year follow-up of an open-label, non-inferiority, randomised controlled trial

Ji Won Park, Sung-Bum Kang, Jie Hao, Seok-Byung Lim, Hyo Seong Choi, Duck-Woo Kim, Hee Jin Chang, Dae Yong Kim, Kyung Hae Jung, Tae-You Kim, Gyeong Hoon Kang, Eui Kyu Chie, Sun Young Kim, Dae Kyung Sohn, Jae-Sung Kim, Hye Seung Lee, Jee Hyun Kim, Seung-Yong Jeong, Jae Hwan Oh**

Summary

Background Laparoscopic surgery has been widely used for rectal cancer; however, its long-term outcomes remain controversial. This study aimed to assess the long-term oncological safety of laparoscopic surgery for rectal cancer using 10-year follow-up data of the Comparison of Open versus laparoscopic surgery for mid or low REctal cancer After Neoadjuvant chemoradiotherapy (COREAN) trial.

Methods The COREAN trial is a, open-label, non-inferiority, randomised controlled trial. Eligible participants were aged 18–80 years, had cT3N0–2M0 middle or low rectal cancer with lesions located within 9 cm of the anal verge, and had been treated with preoperative chemoradiotherapy. Patients were randomly assigned (1:1) to open or laparoscopic surgery with a computer-generated random allocation sequence with a random permuted block design. Neither patients nor clinicians were masked to treatment assignment. Open or laparoscopic total mesorectal excision was done 6–8 weeks after the administration of preoperative concurrent chemoradiotherapy (fluoropyrimidines alone, doublet therapy, or triplet therapy) at a dose of 50·5 Gy over 5·5 weeks. Postoperative adjuvant chemotherapy was administered for 4 months. The primary endpoint of 3-year disease-free survival was published previously. Here, we report 10-year overall survival, disease-free survival, and local recurrence. Analyses were done in the modified intention-to-treat population of all participants who were randomly assigned and provided follow-up data. This study is registered with ClinicalTrials.gov, NCT00470951.

Findings Of the 340 patients enrolled in the COREAN trial between April 4, 2006, and Aug 26, 2009 (170 patients in each group), two patients in the laparoscopic surgery group moved abroad and were lost to follow-up, so were not included in this 10-year analysis. The median duration of follow-up was 143 months (IQR 122–156). No differences were observed in 10-year overall survival (74·1% [95% CI 66·8–80·0] in the open surgery group *vs* 76·8% [69·6–82·5] in the laparoscopic surgery group; p=0·44), 10-year disease-free survival (59·3% [51·1–66·5] *vs* 64·3% [56·0–71·5]; p=0·20), or 10-year local recurrence (8·9% [5·2–15·0] *vs* 3·4% [1·4–7·9]; p=0·050) between the open surgery and laparoscopic surgery groups at 10 years after surgery. The stratified hazard ratios, adjusted for ypT and ypN classification and tumour regression grade, for open surgery versus laparoscopic surgery were 0·94 (95% CI 0·63–1·43) for overall survival, 1·05 (0·74–1·49) for disease-free survival, and 2·22 (0·78–6·34) for local recurrence.

Interpretation The 10-year follow-up of the COREAN trial confirms the long-term oncological safety of laparoscopic surgery in patients with rectal cancer treated with preoperative chemoradiotherapy. Similar to open surgery, laparoscopic surgery does not compromise long-term survival outcomes in rectal cancer when performed by well trained surgeons.

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Introduction

Surgical resection has been the main treatment for colorectal cancer for several decades. As a minimally invasive approach for surgical resection, laparoscopic surgery was introduced. Laparoscopic surgery has the benefits of reduced postoperative pain and faster recovery from surgery than open surgery. However, the status of laparoscopic surgery has not been established yet for rectal cancer. A subset analysis of the Conventional versus Laparoscopic-Assisted Surgery In Colorectal Cancer (CLASICC) trial comparing the clinical outcomes of laparoscopic surgery to those of open surgery in colorectal cancer showed that 5-year survival outcomes were not different between laparoscopic and open surgeries in patients with rectal cancer.[1] Notably, two randomised trials (COlorectal cancer Laparoscopic or Open Resection [COLOR] II and Comparison of Open versus laparoscopic surgery for mid or low REctal cancer After Neoadjuvant

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*Contributed equally

Department of Surgery (J W Park MD, Prof S-Y Jeong MD), **Department of Internal Medicine** (Prof T-Y Kim MD), **Department of Pathology** (Prof G H Kang MD, Prof H S Lee MD), **and Department of Radiation Oncology** (Prof E K Chie MD), **Seoul National University College of Medicine, Seoul National University Hospital, Seoul, South Korea; Cancer Research Institute, Seoul National University, Seoul, South Korea** (J W Park, Prof S-Y Jeong, Prof T-Y Kim, Prof G H Kang, Prof E K Chie); **Department of Surgery** (Prof S-B Kang MD, D-W Kim MD), **Department of Radiation Oncology** (Prof J-S Kim MD), **and Department of Internal Medicine** (Prof J H Kim MD), **Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea; Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA, USA** (J Hao PhD); **Department of Colon and Rectal Surgery** (Prof S-B Lim MD) **and Department of Oncology** (Prof K H Jung MD, S Y Kim MD), **Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; and Center for Colorectal Cancer, Research Institute and Hospital, National Cancer Center, Goyang, South Korea** (H S Choi MD, H J Chang MD, Prof D Y Kim MD, Prof D K Sohn MD, Prof J H Oh MD)

Correspondence to:
Prof Seung-Yong Jeong, Department of Surgery, Seoul National University College of Medicine, Seoul National University Hospital, Seoul 03080, South Korea
syjeong@snu.ac.kr

Research in context

Evidence before this study

We searched PubMed for clinical trials published in English up to Dec 31, 2020, with the MeSH keywords "rectal neoplasms" AND "laparoscopy". Among the trials comparing outcomes between open surgery and laparoscopic surgery for rectal cancer, five multicentre randomised clinical trials reported survival outcomes. These five trials were high-quality clinical trials. The CLASICC trial showed that laparoscopic surgery has long-term outcomes similar to those of open surgery for rectal cancer. However, the design of this study did not focus on rectal cancer. The COLOR II and COREAN trials showed similar short-term pathological and 3-year survival outcomes between groups. Although the ACOSOG Z6051 and ALaCaRT trials also reported similar 2-year survival outcomes, these trials did not show non-inferiority of laparoscopic surgery in terms of composite pathological endpoints. Thus, the findings of previous randomised trials are contradictory. To elucidate the oncological safety of laparoscopic surgery for rectal cancer, long-term survival outcomes of patients in these trials have to be assessed. Radiotherapy is associated with delayed recurrence in rectal cancer. Notably, in patients with rectal cancer treated with preoperative chemoradiotherapy, the time to recurrence tends to be longer than that in patients without preoperative treatment. For a definite assessment of survival outcomes of patients with rectal cancer treated with preoperative chemoradiotherapy, a follow-up longer than 5 years is necessary.

Added value of this study

This study assessed the long-term outcomes of open versus laparoscopic surgery for patients with rectal cancer on the basis of 10-year follow-up data from the COREAN trial. To the best of our knowledge, this study is the first to report extended follow-up survival outcomes of patients in a randomised clinical trial that compared open and laparoscopic resection for locally advanced rectal cancer treated with preoperative chemoradiotherapy. No differences in overall survival, disease-free survival, or local recurrence after 10 years of follow-up were observed between patients who had open surgery compared with those who had laparoscopic surgery. The results provide evidence of the long-term oncological safety of laparoscopic surgery for patients with rectal cancer.

Implications of all the available evidence

Considering the main results of the ACOSOG Z6051 and ALaCaRT trials, laparoscopic resection for rectal cancer remains a technically challenging procedure. In carefully selected cases, including cases without invasion of adjacent tissues, a laparoscopic approach can be one of the surgical options when performed by well qualified colorectal surgeons.

chemoradiotherapy [COREAN] trial) have shown the mid-term oncological safety of laparoscopic surgery compared with that of open surgery in rectal cancer.[2,3] However, two other randomised trials (ACOSOG Z6051 and Australasian Laparoscopic Cancer of the Rectum [ALaCaRT] trial) did not show non-inferiority of laparoscopic surgery versus open surgery for rectal cancer for the primary endpoint of composite pathological outcome.[4,5] This composite pathological outcome, including the quality of total mesorectal excision, circumferential radial margin, and distal margin, can affect long-term oncological outcomes. These trials raised concerns about the oncological safety of laparoscopic surgery for rectal cancer. Although the findings of these randomised trials were contradictory, use of the laparoscopic approach has increased in clinical practice.[6]

To date, four previous randomised trials have reported mid-term survival outcomes for patients with rectal cancer; their results showed no differences in 2-year or 3-year survival outcomes between laparoscopic and open surgery.[2,3,7,8] COLOR II and COREAN trials reported similar results for 3-year locoregional recurrence (COLOR II) and disease-free survival (COREAN) as for the primary endpoints. Although laparoscopic surgery did not meet the non-inferiority criteria in the ACOSOG Z6051 and ALaCaRT trials, the 2-year disease-free survival and recurrence after laparoscopic surgery (secondary endpoints) were not significantly different from those after open surgery. However, the long-term oncological safety of laparoscopic surgery in patients with rectal cancer has not been confirmed.

The COREAN trial was an open-label, non-inferiority, randomised trial that compared the safety and efficacy of laparoscopic surgery to that of open surgery for middle or low rectal cancer treated with preoperative chemoradiotherapy. Between April 4, 2006, and Aug 26, 2009, 340 patients were randomly assigned to open surgery (n=170) or laparoscopic surgery (n=170). In the primary results of the COREAN trial, the difference in 3-year disease-free survival was –6·7% (72·5% for the open surgery group *vs* 79·2% for the laparoscopic surgery group), achieving non-inferiority.[3] Because the time to local recurrence tends to be prolonged after preoperative treatment in rectal cancer, an extended follow-up is required to assess definitive survival outcomes.[9] Thus, we extended the follow-up period by 10 years from the date when the last patient was randomly assigned. This study aimed to assess the long-term outcomes of open versus laparoscopic surgery for patients with rectal cancer on the basis of 10-year data from the COREAN trial.

Methods

Study design and participants

This open-label, non-inferiority, randomised controlled trial compared outcomes between open and laparoscopic surgery in patients with rectal cancer treated with

preoperative chemoradiotherapy. Short-term outcomes and the primary endpoint of the trial have been reported previously.[3,10] The study protocol is available online.

As described previously, the COREAN trial enrolled patients with middle or low rectal cancer who had received preoperative chemoradiotherapy at three tertiary referral hospitals in South Korea.[3,10] Patients aged 18–80 years diagnosed with cT3N0–2M0 adenocarcinoma with lesions located within 9 cm or less from the anal verge were included. Those with synchronous distant metastasis, another primary malignancy, severe medical disease, and intestinal perforation or obstruction, and pregnant patients were excluded. Clinical staging was performed based on abdominal CT, MRI, and transanal ultrasound. Clinical staging, imaging, and pathology were reviewed by experts at each institution. However, the quality of total mesorectal excision was centrally reviewed. The study protocol was approved by the institutional review board of each participating hospital. All patients provided written informed consent.

Randomisation and masking

Patients were randomly assigned (1:1) to laparoscopic or open surgery. The random allocation sequence was computer generated with a random permuted block design at the Center for Clinical Trials at the National Cancer Center, Goyang, South Korea. The investigators were masked to randomisation sequence, and random assignment was performed at the coordinating centre by telephone. The stratification factors included sex and preoperative chemotherapy regimen. Neither patients nor clinicians were masked to treatment assignment. However, the radiologists and pathologists were masked to treatment assignment.

Procedures

Open or laparoscopic total mesorectal excision was done 6–8 weeks after the administration of preoperative concurrent chemoradiotherapy at a dose of 50·5 Gy over 5·5 weeks with either fluoropyrimidines alone—fluorouracil and leucovorin or capecitabine or tegafur-uracil and leucovorin; doublet therapy—capecitabine and irinotecan; or triplet therapy—capecitabine, irinotecan, and cetuximab.[10] Open surgery was performed with lower midline incision. Inferior mesenteric vessels were highly ligated. Rectum was mobilised by dissecting along the mesorectal plane while preserving the hypogastric nerves. Laparoscopic surgery was performed with five ports. The rectum was resected in the same manner as in open surgery. Detailed procedures were published previously.[10]

Postoperative adjuvant chemotherapy was administered for 4 months using one of the following three chemotherapeutic regimens: (1) fluorouracil and leucovorin (four cycles of an intravenous bolus injection of fluorouracil [400 mg/m² per day] and leucovorin [20 mg/m² per day] day 1–5 every 4 weeks); (2) capecitabine (six cycles of capecitabine [1250 mg/m²] twice daily for 14 days, followed by 7 days rest for each cycle); or (3) FOLFOX (eight cycles of oxaliplatin [85 mg/m² per day] on day 1, fluorouracil intravenous bolus [400 mg/m² per day] on day 1, and fluorouracil continuous infusion [2400 mg/m²] for 46 h every 2 weeks).[3] All patients were followed up regularly. Physical examination, carcinoembryonic antigen tests, and chest radiography were done every 3 months for the first 2 years, every 6 months for the next 3 years, and every 6 months or 1 year thereafter. Abdominopelvic CT was done every 6 months for the first 5 years and every 6 months or annually thereafter. Colonoscopy was scheduled 1 year from the date of surgery and once every 2 years thereafter. After 5 years from surgery, the patients were followed up every 1 or 2 years. Tumour relapse was diagnosed radiologically on the basis of detection of an increase in size of the lesions over time or pathologically by biopsy or surgical resection. Patients who were lost to follow-up were removed from the study.

For the **COREAN trial protocol** see http://ncc.re.kr/common/downloadByFileURL.jsp?path=/downloadFiles/Protocol179.pdf

Outcomes

The primary endpoint was disease-free survival 3 years after surgery. Secondary endpoints were postoperative

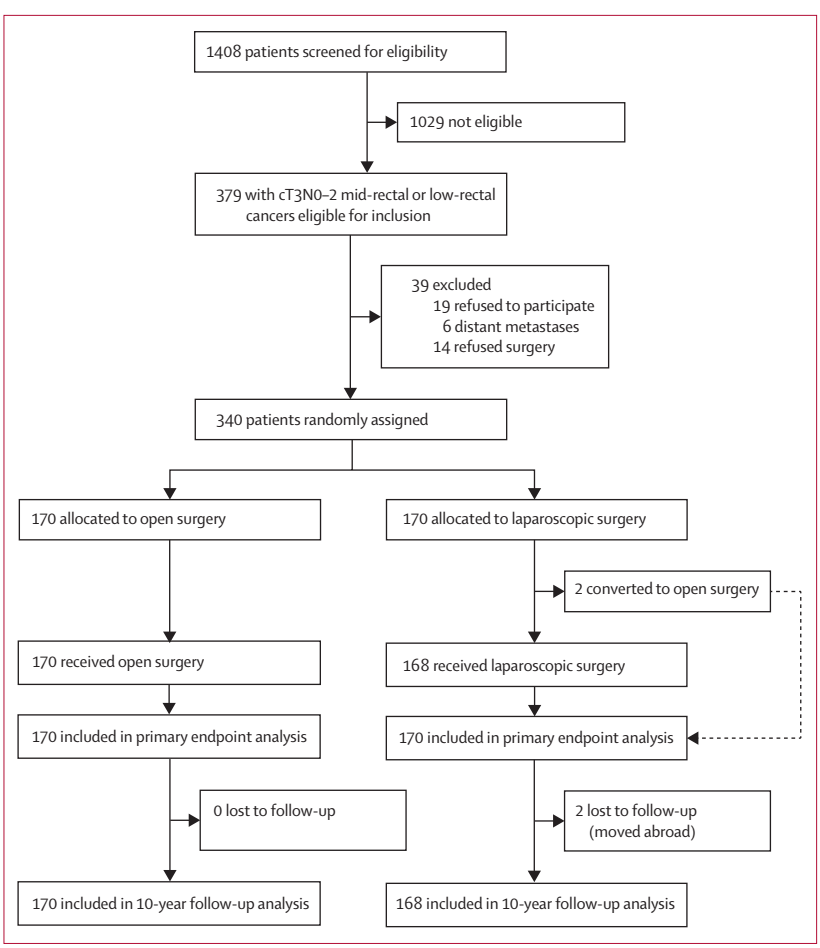

Figure 1: **Trial profile**

	Open surgery (n=170)	Laparoscopic surgery (n=168)
Age, years	59·1 (9·9)	57·8 (11·1)
Sex		
Male	110 (65%)	109 (65%)
Female	60 (35%)	59 (35%)
Body-mass index, kg/m²		
≤25	106 (62%)	106 (63%)
>25	64 (38%)	62 (37%)
American Society of Anesthesiologists grade		
1	65 (38%)	67 (40%)
2	98 (58%)	96 (57%)
3	7 (4%)	5 (3%)
Preoperative carcinoembryonic antigen serum level, ng/mL		
≤5	154 (91%)	155 (92%)
>5	16 (9%)	13 (8%)
Clinical N classification		
cN0	52 (31%)	57 (34%)
cN+	118 (69%)	111 (66%)
Tumour distance from anal verge, cm		
0–3	46 (27%)	35 (21%)
3–6	59 (35%)	65 (39%)
6–9	65 (38%)	68 (40%)
Preoperative chemotherapy		
Fluoropyrimidines alone	156 (92%)	154 (92%)
Doublet*	1 (1%)	3 (2%)
Triplet†	13 (8%)	11 (7%)
Postoperative chemotherapy		
Fluoropyrimidines alone	149 (88%)	148 (88%)
Oxaliplatin based	13 (8%)	11 (7%)
None	8 (5%)	9 (5%)

Data are mean (SD) or n (%). *Capecitabine and irinotecan. †Capecitabine, irinotecan, and cetuximab.

Table 1: **Baseline characteristics**

	Open surgery (n=170)	Laparoscopic surgery (n=168)	p value
Tumour differentiation			
Well differentiated or moderately differentiated	163 (96%)	162 (96%)	1·00†
Poorly differentiated, signet ring cell, or mucinous	6 (4%)	5 (3%)	..
Unknown	1 (1%)	1 (1%)	..
Tumour regression grade scale			
1	35 (21%)	25 (15%)	0·038*
2	89 (52%)	74 (44%)	..
3	24 (14%)	30 (18%)	..
4	22 (13%)	39 (23%)	..
ypT classification			
ypT0	24 (14%)	39 (23%)	0·065†
ypTis	1 (1%)	5 (3%)	..
ypT1	6 (4%)	9 (5%)	..
ypT2	40 (24%)	40 (24%)	..
ypT3	96 (56%)	73 (43%)	..
ypT4	3 (2%)	2 (1%)	..
ypN classification			
ypN0	113 (66%)	133 (79%)	0·0023*
ypN1	43 (25%)	18 (11%)	..
ypN2	14 (8%)	17 (10%)	..
Circumferential resection margin			
Positive (≤1 mm)	7 (4%)	5 (3%)	0·78†
Negative (>1 mm)	163 (96%)	163 (97%)	..
Macroscopic quality of total mesorectal excision specimen			
Complete or nearly complete	150 (88%)	154 (92%)	0·57*
Incomplete	11 (6%)	8 (5%)	..
Unknown	9 (5%)	6 (4%)	..

Data are n (%). yp=pathological stage classified after pretreatment. *χ^2 test. †Fisher's exact test.

Table 2: **Operative and pathological data**

short-term outcomes; long-term outcomes (overall survival, local recurrence, and port site and wound site recurrence); quality of life assessments; urinary and sexual function; and anorectal function. Overall survival was defined as the time from randomisation to death from any cause. Disease-free survival was defined as the time from randomisation to recurrence, death from any cause, or development of secondary malignancy. Local recurrence was defined as any clinically proven tumour relapse within the pelvis or perineum. Distant recurrence was defined as any clinically proven tumour relapse outside the pelvis. Any local or distant recurrence was considered an event of recurrence. In this Article, we report prespecified survival and recurrence outcomes at 10 years after the last patient was randomly assigned.

Statistical analysis

In the COREAN trial, we hypothesised that 3-year disease-free survival rates with open surgery would be 75%, and set the non-inferiority margin at 15%, based on a previous study.[11] Considering a 2·5% one-sided type I error and 10% follow-up loss, 340 patients were needed to achieve a power of 85%.

Pathological variables, including tumour differentiation, tumour regression grade, tumour and node classification after pretreatment, circumferential resection margin, and macroscopic quality of total mesorectal excision specimen, were analysed using the χ^2 or Fisher's exact tests. The Kaplan-Meier method was used to estimate overall survival, disease-free survival, and local recurrence and the log-rank test was used to compare survival distribution. Stratified Cox regression analysis with incorporation of the stratification factors was done to estimate the hazard ratios (HRs). Multivariable Cox regression analysis was done to adjust for confounding factors that were significant in the univariate analysis and non-balanced between the two groups. Subgroup analyses for overall survival were

	Open surgery (n=170)	Laparoscopic surgery (n=168)	Difference
Overall survival			
5 year	82·4% (75·7 to 87·3)	87·5% (81·5 to 91·7)	–5·1% (–13·3 to 3·1)
10 year	74·1% (66·8 to 80·0)	76·8% (69·6 to 82·5)	–2·7% (–12·4 to 7·1)
Disease-free survival			
5 year	68·1% (60·5 to 74·6)	76·1% (68·9 to 81·9)	–8·0% (–18·0 to 2·2)
10 year	59·3% (51·1 to 66·5)	64·3% (56·0 to 71·5)	–5·1% (–16·9 to 7·0)
Local recurrence			
5 year	7·0% (3·9 to 12·3)	2·5% (1·0 to 6·6)	4·5% (–1·1 to 10·3)
10 year	8·9% (5·2 to 15·0)	3·4% (1·4 to 7·9)	5·5% (–2·2 to 13·3)

Data are % (95% CI).

Table 3: **Survival rate according to surgical procedure**

done within preoperative clinical factors. A two-sided p value of less than 0·05 was considered statistically significant. Analyses were done in the modified intention-to-treat population of all randomly assigned participants excluding those lost to follow-up.

All analyses were done using R statistics (version 3.6.1) and Python (version 3.7.3). This trial was registered with ClinicalTrials.gov, number NCT00470951.

Role of the funding source

The funder of this study had no role in study design, data collection, data analysis, data interpretation, or the writing of the report.

Results

Of the 340 patients enrolled in the COREAN trial between April 4, 2006, and Aug 26, 2009, two patients from the laparoscopic group required conversion to open surgery, and were retained in the laparoscopic surgery group for analyses. During long-term follow-up, two patients in the laparoscopic surgery group moved abroad and were lost to follow-up, so were not included in this 10-year analysis (figure 1). Thus, 338 patients (170 in the open surgery group and 168 in the laparoscopic surgery group) were included in this analysis.

The baseline characteristics were well balanced between the two groups (table 1). The tumour differentiation, circumferential margin involvement, and quality of total mesorectal excision were not different between the two groups. However, pathological tumour (ypT) and node (ypN) classification and tumour regression grade were different across the two groups (table 2).

Median follow-up time was 143 months (IQR 122–156). No significant differences were observed in overall survival, disease-free survival, or local recurrence

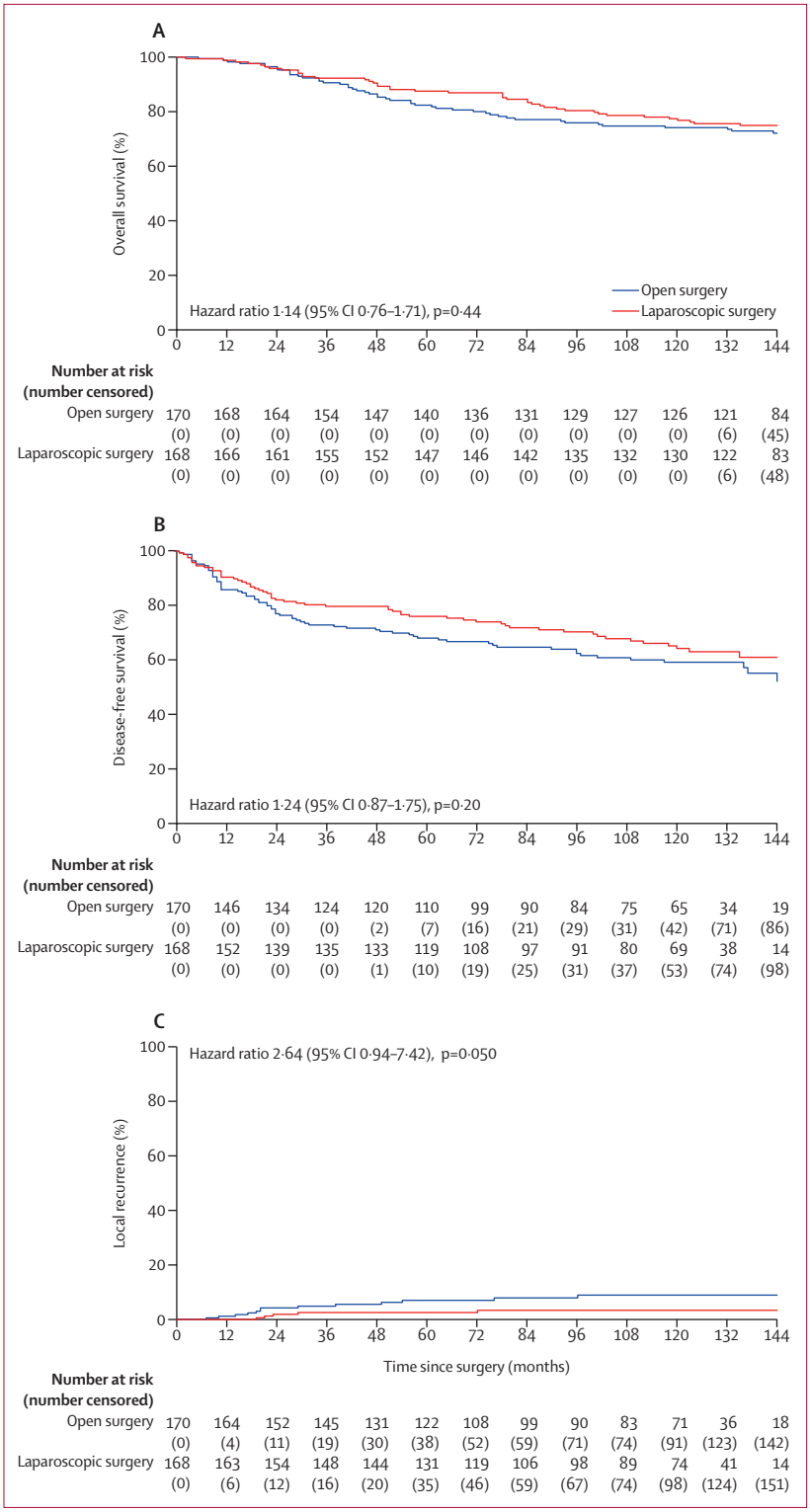

Figure 2: **Kaplan-Meier curves showing overall survival (A), disease-free survival (B), and local recurrence (C) of patients in the laparoscopic and open surgery groups**

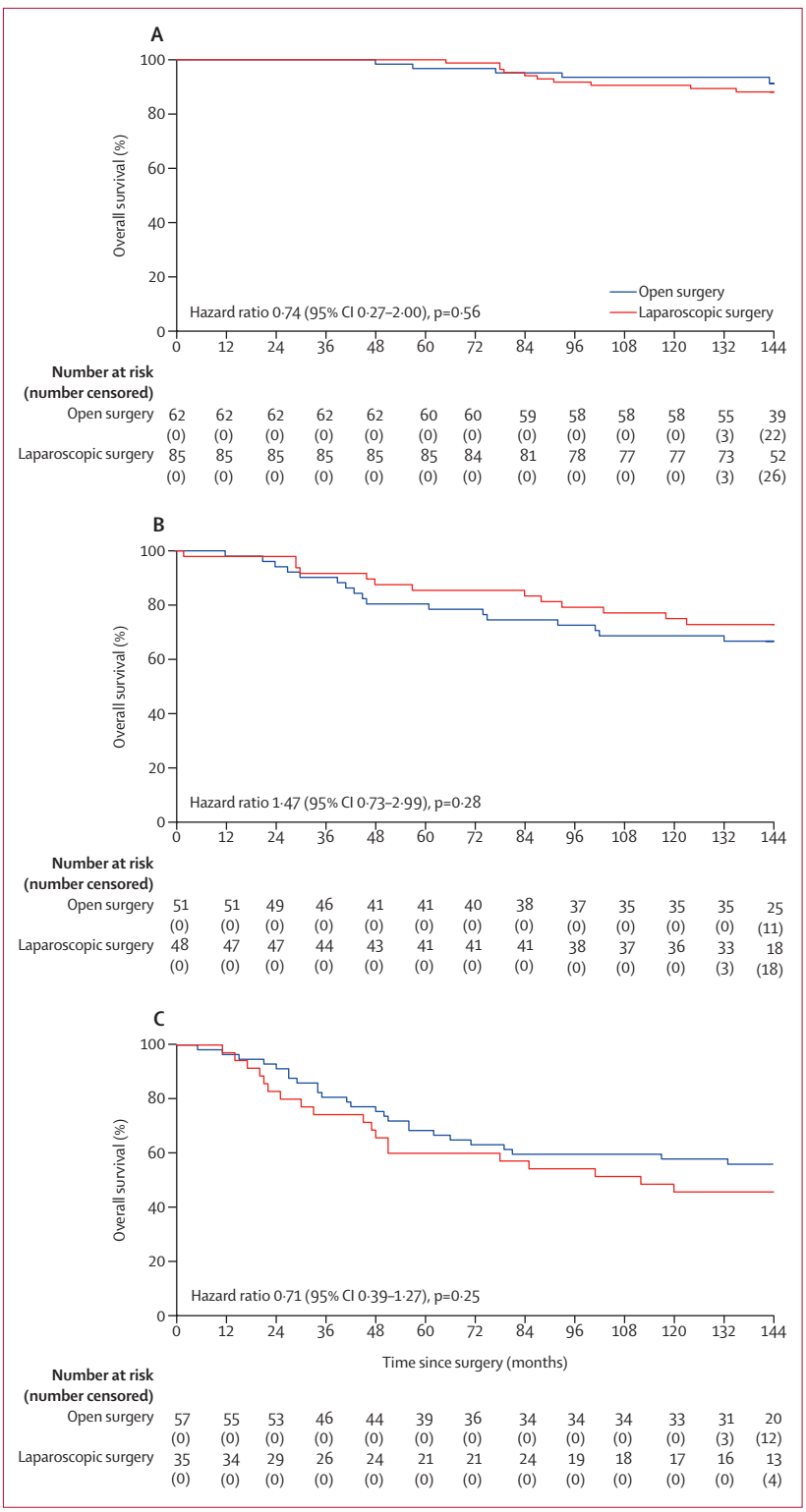

Figure 3: **Kaplan-Meier curves showing overall survival according to tumour stage**
(A) Stage 0/1. (B) Stage 2. (C) Stage 3.

between the open surgery and laparoscopic surgery groups at 5 years and 10 years after surgery (table 3, figure 2). Univariate analyses, stratified by sex and preoperative chemotherapeutic regimen, showed no difference in overall survival, disease-free survival, or local recurrence between the two groups (appendix p 6). The per-protocol analysis of 336 patients who had surgery as assigned showed no differences in overall survival, disease-free survival, and local recurrence for the open and laparoscopic groups (data not shown). Furthermore, stage-specific analysis showed no difference in overall survival, disease-free survival, and local recurrence between the two groups (figure 3; appendix pp 2, 7–10).

46 (27%) of 170 patients in the open surgery group and 33 (20%) of 168 patients in the laparoscopic surgery group (p=0·11) had a recurrence. The distribution of recurrence locations did not differ between the two groups (appendix p 3). Local recurrences occurred in 13 (8%) patients in the open surgery group and five (3%) patients in the laparoscopic surgery group (p=0·056). Distant recurrences occurred in 41 (24%) patients in the open surgery group and 31 (18%) in the open surgery group (p=0·20). The most common site of distant recurrence in both groups was the lung (28 [16%] in the open surgery group *vs* 21 [13%] in the laparoscopic surgery group; appendix p 3). The distribution of locations of local and distant recurrences did not differ between the two groups (appendix p 3). No wound or port-site recurrence occurred in either of the groups. In patients with local recurrence, multifocality of local recurrence, treatment for local recurrence, and status after treatment were not different between the two groups (appendix p 4). Although most patients with recurrence had recurrences within 3 years after surgery (68 [86%] of 79), eight (10%) had recurrences identified after 5 years (appendix p 5). Three (17%) of 18 local recurrences and six (8%) of 72 distant recurrences were detected from more than 5 years after surgery. Proportions of patients with recurrence, according to time interval after surgery, did not differ between the two groups (appendix p 5).

Subgroup analyses for overall survival were done on the basis of age, sex, body-mass index, American Society of Anesthesiologists grade, preoperative carcinoembryonic antigen level, clinical N classification, and tumour distance from the anal verge (appendix p 11). Slight numerical improvements were noted for the laparoscopic group compared with the open surgery group in the subgroups of female patients and patients with tumours located 0–3 cm from the anal verge, but differences were not significant.

The ypT and ypN classification and tumour regression grade were different between the two groups despite randomisation. However, stratified multivariable analysis with adjustment for these variables showed no significant differences in overall survival (HR 0·94 [95% CI 0·63–1·43]), disease-free survival (1·05 [0·74–1·49]), or

local recurrence (2·22 [0·78–6·34]) between the groups (appendix p 6).

Discussion

This 10-year follow-up analysis of the COREAN trial showed that long-term overall survival, disease-free survival, and local recurrence in patients who had laparoscopic surgery were similar to those in patients who had open surgery for locally advanced rectal cancer. Through a 10-year follow-up, this study assessed survival outcomes of patients with rectal cancer treated with preoperative chemoradiotherapy. Notably, this study identified that delayed recurrence (>5 years after surgery) constituted 10% of all recurrences, 17% of all local recurrences, and 8% of all distant recurrences. These results are similar to those of a previous study.[9] In addition to the similar mid-term outcomes of several randomised trials for laparoscopic surgery in patients with rectal cancer, this study showed that the similar outcomes between the laparoscopic and open surgery groups were maintained in 10-year follow-up surveillance.[2,3,7,8] In the follow-up study of the CLASICC trial (exceeding 10 years), which compared the outcomes of laparoscopic and open surgeries in patients with colorectal cancer, there were no differences in overall survival, disease-free survival, or local recurrence.[12] These results have supported the long-term oncological safety of laparoscopic surgery for rectal cancer.

However, the oncological safety of laparoscopic surgery has been called into question on the basis of the findings of some trials. The CLASICC trial showed a non-significant higher involvement of circumferential resection margin in the laparoscopic surgery group. In the ACOSOG Z6051 and ALaCaRT trials, composites of pathological factors of laparoscopic surgery were not non-inferior to those of open surgery.[4,5] However, the results did not reveal significant differences in the mid-term oncological outcomes.[7,8] Although the findings of the ALaCaRT trial favoured open surgery on the basis of the estimates of treatment effect, it is unclear whether this is due to the unfavourable effects of laparoscopic surgery or the higher proportion of patients with positive nodes in the laparoscopic surgery group.[8] A systematic review and meta-analysis of randomised trials of open versus laparoscopic surgery for rectal cancer that compared the quality of surgical resection between open and laparoscopic surgery showed that the rate of non-complete (nearly complete or incomplete) mesorectal excision was higher in patients who had laparoscopic surgery than those who had open surgery, but the positive rate of circumferential and distal resection margin was not significantly different.[13] Notably, another meta-analysis of randomised trials comparing open versus laparoscopic surgery for rectal cancer identified that the rate of nearly complete mesorectal excision was higher in those who had laparoscopic surgery, whereas the rate of incomplete mesorectal excision was similar with each approach.[14] Because long-term survival outcomes are similar for patients that have complete and nearly complete mesorectal excision, it is more reasonable that the rate of incomplete mesorectal excision be compared for assessing the quality of surgical resection.[15] A recent non-inferiority meta-analysis of randomised trials comparing open with laparoscopic surgery for rectal cancer, based on non-inferiority margins defined according to the consensus of 58 worldwide experts, showed that the surgical quality of laparoscopic resection was non-inferior to that of open resection.[16]

See Online for appendix

Beyond surgical quality, the most reliable endpoints to judge the oncological safety of laparoscopic surgery are long-term survival outcomes. In a recent network meta-analysis, overall survival, disease-free survival, and local recurrence were similar between laparoscopic and open surgery for the treatment of rectal cancer.[17] In congruence with this finding, the COREAN trial showed similar long-term outcomes between the groups. Furthermore, with long-term follow-up, the rate and pattern of recurrence in the laparoscopic surgery group were not different from those in the open surgery group. There were no port-site recurrences in the laparoscopic group. Notably, the laparoscopic approach did not promote delayed recurrences—ie, those detected longer than 5 years after surgery in patients with rectal cancer treated with preoperative chemoradiotherapy. Even in the multivariable analysis, adjusted for pathological T and N classification and tumour regression grade, overall survival, disease-free survival, and local recurrence in the laparoscopic group were not significantly different from those in the open surgery group. Along with the results of this study, long-term outcomes of the COLOR II, ACOSOG Z6051, and ALaCaRT trials will offer further clarity regarding the long-term oncological safety of laparoscopic resection for rectal cancer.

Because laparoscopic surgery for rectal cancer can be technically challenging in patients with a narrow pelvis or bulky tumour, appropriate training for laparoscopic resection is essential. To overcome the learning curve for laparoscopic rectal surgery, at least 50 laparoscopic rectal surgeries must be performed.[18] In addition to the minimum number of surgeries for experience, various training methods, including education materials, conferences, workshops, and fellowship programmes, can shorten the learning curve. In the COREAN trial, surgeons participated in the trial after conducting the required minimum number of surgeries, qualification through live demonstrations, and assessment of an unedited video by the trial steering committee.[10] A study showed that novice surgeons who were technically accredited could safely perform laparoscopic mesorectal excision.[19] Accreditation for competence in laparoscopic rectal surgery can facilitate the implementation of this procedure safely. In particular, for surgical trials, the adoption of structural objective assessment tools is

required to reduce performance bias.[20] It is recommended that rectal cancer be laparoscopically resected only by technically qualified colorectal surgeons in selected patients, because it has only been assessed in trials with experienced surgeons.

One of the important prerequisite steps of laparoscopic rectal surgery is the selection of appropriate patients. Because patients who require conversion to open surgery have a higher risk of poor long-term prognosis, patients with a high risk of suboptimal resection are inappropriate for laparoscopic rectal surgery.[21] In this trial, patients with clinically diagnosed T4 tumours were excluded because of the limitations of the laparoscopic approach in such cases, including the use of straight laparoscopic instruments and the challenge of deep pelvic exposure.

The goal of minimally invasive surgery in rectal cancer is to acquire short-term benefits while maintaining long-term prognosis. With respect to short-term benefits, laparoscopic surgery has resulted in reduced operative blood loss, faster postoperative recovery, reduced need for analgesics, and shorter hospital stay.[22] Additionally, some nationwide and population-based studies have shown that survival outcomes of laparoscopic rectal surgery were better than those of open surgery.[23,24] In laparoscopic surgery, magnified surgical view and reduced perioperative surgical stress might positively affect long-term survival. However, these results have not been reproduced in randomised trials.

A limitation of this study was that pathological responses differed between the laparoscopic surgery and open surgery groups, despite randomisation and similar clinical T and N classifications. These differences between the two groups occurred by chance. We did not observe any randomisation bias related to the surgical technique. This discrepancy between the two groups might have affected the long-term survival outcomes. Notably, the ALaCaRT trial also had similar differences in pathological N classifications. To adjust for the differences in our cohort, we did stratified multivariable analyses. After adjustment, survival outcomes were still not significantly different between the two groups. Another limitation was the distribution of the body-mass index of patients in this study. The median body-mass index was lower than 25 kg/m² (median 24·2 kg/m² [IQR 21·6–26·1]), which is lower than the median in other trials. Because a high body-mass index is related to difficulty in laparoscopic rectal surgery, outcomes of laparoscopic surgery might be different in populations with higher body-mass index.

The strength of this study was the collection and analysis of 10-year follow-up data. This period of follow-up can detect delayed events for patients with rectal cancer treated with preoperative chemoradiotherapy. To our knowledge, of the several randomised trials for laparoscopic surgery in patients with rectal cancer, this study is the first to investigate long-term survival outcomes. The findings of this study support the evidence for the long-term safety of laparoscopic surgery in rectal cancer.

In conclusion, the 10-year follow-up analysis of the COREAN trial showed that laparoscopic surgery for locally advanced rectal cancer after preoperative chemoradiotherapy can provide survival outcomes similar to those of open surgery. Laparoscopic surgery does not compromise long-term survival outcomes in rectal cancer when performed by well qualified colorectal surgeons.

Contributors

S-BL, DYK, KHJ, HSC, S-BK, and S-YJ were responsible for the conception and design of this study. JWP, S-BK, S-BL, HSC, D-WK, HJC, DYK, KHJ, T-YK, GHK, EKC, SYK, DKS, J-SK, HSL, JHK, S-YJ, and JHO collected and assembled data. JWP, S-BK, JH, S-YJ, and JHO analysed and interpreted the data. JWP, JH, S-YJ, and JHO wrote the report. S-BK, S-BL, HSC, D-WK, HJC, DYK, KHJ, T-YK, GHK, EKC, SYK, DKS, J-SK, HSL, and JHK revised the report for intellectual content. All authors had full access to all the data and accept responsibility to submit for publication. JWP, S-YJ, and JHO accessed and verified the data in the study.

Declaration of interests

We declare no competing interests.

Data sharing

Data collected for this study can be made available on request to the corresponding author.

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