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Laparoscopic-assisted versus open total mesorectal excision with anal sphincter preservation for mid and low rectal cancer: a prospective, randomized trial

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Abstract
Background This single-center, prospective, randomized trial was designed to compare the short-term clinical outcome between laparoscopic-assisted versus open total mesorectal excision (TME) with anal sphincter preservation (ASP) in patients with mid and low rectal cancer. Long-term morbidity and survival data also were recorded and compared between the two groups.
Methods Between August 2001 and August 2007, 80 patients with mid and low rectal cancer were randomized to receive either laparoscopic-assisted (40 patients) or open (40 patients) TME with ASP. The median follow-up time for all patients was 75.7 (range 16.9–115.7) months for the laparoscopic-assisted group and 76.1 (range 4.7–126.6) months for the open group. The primary endpoint of the study was short-term clinical outcome. Secondary endpoints included long-term morbidity rate and survival. Data were analyzed by intention-to-treat principle.
Results The demographic data of the two groups were comparable. Postoperative recovery was better after laparoscopic surgery, with less analgesic requirement ($P < 0.001$), earlier mobilization ($P = 0.001$), lower short-term morbidity rate ($P = 0.043$), and a trend towards shorter hospital stay ($P = 0.071$). The cumulative long-term morbidity rate also was lower in the laparoscopic-assisted group ($P = 0.019$). The oncologic clearance in terms of macroscopic quality of the TME specimen, circumferential resection margin involvement, and number of lymph nodes removed was similar between both groups. After curative resection, the probabilities of survival at 5 years of the laparoscopic-assisted and open groups were 85.9 and 91.3 %, respectively ($P = 0.912$). The respective probabilities of being disease-free were 83.3 and 74.5 % ($P = 0.114$).
Conclusions Laparoscopic-assisted TME with ASP improves postoperative recovery, reduces short-term and long-term morbidity rates, and seemingly does not jeopardize survival compared with open surgery for mid and low rectal cancer (http://ClinicalTrials.gov Identifier: NCT00485316).

Keywords Total mesorectal excision · Laparoscopic surgery · Anal sphincter preservation · Rectal cancer · Randomized trial

Laparoscopic surgery for colorectal cancer has been shown by several large-scale, multicenter, randomized trials to have faster postoperative recovery and similar oncologic outcomes compared with open surgery [1–10]. However, only three of these published multicenter trials have recruited patients with rectal cancer, which include the United Kingdom Medical Research Council trial of Conventional versus Laparoscopic-Assisted Surgery In Colorectal Cancer (CLASICC), the Comparison of Open versus laparoscopic surgery for mid and low REctal cancer After Neoadjuvant chemoradiotherapy (COREAN) trial, and the COlorectal cancer Laparoscopic or Open Resection (COLOR) II trial [6–10]. The CLASICC trial reported a trend towards higher circumferential resection margin (CRM) positivity among patients undergoing laparoscopic anterior resection when compared with open surgery, which

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raised serious concerns regarding the oncologic safety of laparoscopic surgery for rectal cancer [6]. At present, the COREAN trial and the COLOR II trial have reported short-term outcomes only, and long-term oncologic data are eagerly awaited [9, 10]. Because of lack of good-quality evidence on long-term outcome and survival, both the American Society of Colon and Rectal Surgeons and the Society of American Gastrointestinal and Endoscopic Surgeons have considered it too premature to endorse laparoscopic surgery for curable rectal cancer [11–13].

We have recently reported the 5 and 10-year results of a randomized trial comparing laparoscopic-assisted and open resection for upper rectal cancer [14, 15]. Our study confirmed that laparoscopic-assisted anterior resection for upper rectal cancer is associated with fewer long-term complications and similar 10-year oncologic outcomes compared with open surgery. In another randomized trial, we have shown that laparoscopic-assisted abdominoperineal resection improves postoperative recovery and seemingly does not jeopardize 5-year survival compared with open surgery for low rectal cancer located within 5 cm from the anal verge [16].

Laparoscopic-assisted total mesorectal excision (TME) with anal sphincter preservation (ASP) for mid and low rectal cancer often has been regarded as one of the most complex operations in the field of colorectal surgery [17]. Besides oncologic clearance, morbidity associated with the coloanal anastomosis and functional impairment secondary to pelvic autonomic nerve injury are major concerns of laparoscopic-assisted TME with ASP [18]. Patients with mid rectal cancer were therefore excluded from the early randomized trials at our institution [14–16]. However, with advancement in laparoscopic technology and accumulation of laparoscopic experience, we decided to embark on a new randomized trial in 2001 that was designed to compare the short-term clinical outcome (including postoperative recovery and short-term morbidity) between laparoscopic-assisted versus open TME with ASP in patients with mid and low rectal cancer. Long-term morbidity and survival data also were recorded and compared between the two groups.

Methods

Patient selection and randomization

Between August 2001 and August 2007, patients diagnosed with mid and low rectal cancer, of which the lowest margin of the tumor was located between 5 and 12 cm from the anal verge as determined by rigid sigmoidoscopy [19], were recruited to the study and randomized to receive either laparoscopic-assisted (Lap) or conventional open (Open) TME with ASP. All patients provided written, informed consent. We excluded the following patients: patients with tumor larger than 6 cm or with tumor infiltration to the adjacent organs on computed tomography, patients who presented with recurrent disease, patients with synchronous colorectal tumors, patients with intestinal obstruction or perforation, patients who required neoadjuvant therapy (see "preoperative management"), and patients who did not consent to randomization. Randomization was performed on the day before surgery according to a computer-generated random sequence kept concealed by an independent operating theater coordinator. It was not possible to blind either the investigators or patients to the treatment method. The study was approved by local ethics committee, and registered with http://ClinicalTrials.gov (NCT00485316).

Preoperative management

The details regarding preoperative workup and preparation were described previously [16].

Between 2001 and 2006, the standard treatment for locally advanced rectal cancer (pathologic stage T3, T4, and/or node-positive disease) at our institution was surgery followed by adjuvant 5-fluorouracil-based chemoradiotherapy. Neoadjuvant therapy was not offered during this period because its effectiveness was not yet fully established, and there were concerns about higher risk of postoperative morbidity [20]. Since September 2006, with accumulation of new supporting evidence [21, 22], we began to offer long-course neoadjuvant chemoradiotherapy to selected patients with radiologic T3, T4, and/or node-positive disease at our institution. However, as neoadjuvant therapy might have an impact on the short-term clinical outcome after TME, we decided to exclude those patients who required neoadjuvant therapy from the study to avoid "contamination" of the earlier cohort of patients (recruited between 2001 and 2006) who did not receive such treatment.

Operative techniques

All operations were performed by surgeons experienced in both laparoscopic and colorectal surgery. Each participating surgeon had undertaken at least 60 laparoscopic rectal resections (including 20 TMEs or abdominoperineal resections) before joining the trial. Our laparoscopic techniques for anterior resection and abdominoperineal resection were described previously [16, 23]. For TME with ASP, after lateral-to-medial mobilization of the sigmoid colon and division of the lymphovascular pedicle, the rectum together with the whole mesorectum was mobilized along the "Holy plane" down to the pelvic floor with electrocautery. The ureters, the hypogastric nerves, and the

pelvic parasympathetic plexus were safeguarded. The lower rectum was transected with laparoscopic linear staplers introduced through the right lower quadrant port. The splenic flexure was mobilized if extra bowel length was needed to facilitate the construction of a tension-free anastomosis. The specimen was then extracted with plastic bag protection through the left lower quadrant port, which was extended to approximately 4 cm, and the anastomosis (straight coloanal) was completed intracorporeally by the double stapling technique. Creation of protective loop ileostomy was left to discretion of operating surgeons depending on his/her technical evaluation of the quality of the anastomosis.

Postoperative management and data collection

The details regarding postoperative management were described previously [16, 23]. Patients with pathologic stage T3, T4, and/or node-positive disease received adjuvant 5-fluorouracil-based chemoradiotherapy.

The follow-up protocol was described previously [15, 16]. Data regarding perioperative outcome, long-term morbidity, recurrence, and survival were prospectively recorded. Bowel function after ileostomy closure, bladder function, and sexual function also were recorded prospectively with a standard proforma during clinic visits. The last follow-up was in February 2012. The survival status was cross-checked with the networked computer database of the local hospital authority.

Study endpoints and definitions

The primary endpoint of the study was short-term clinical outcome, including postoperative recovery and short-term morbidity. Long-term morbidity and survival were recorded as secondary endpoints.

Short-term morbidity was defined as any complication that occurred during hospital stay or within 30 days after the primary surgery. Long-term morbidity was defined as any surgery-related complication requiring readmission and/or treatment that occurred after hospital discharge or more than 30 days after the primary surgery. The definitions of adhesion-related bowel obstruction and incisional hernia were described previously [15].

The definitions of curative resection, CRM involvement, locoregional recurrence, and port site recurrence also were described previously [15].

Sample size estimation and statistical analysis

According to the prospectively collected colorectal cancer database at our institution, the overall short-term morbidity rates among patients with mid and low rectal cancer who underwent Lap and Open TME with ASP between 1997 and 2001 were approximately 35 and 55 %, respectively. With accumulation of laparoscopic experience over time, we expected a further reduction in short-term morbidity rate in the Lap group. With the assumption that the Lap approach could reduce short-term morbidity rate by at least 50 %, a sample size of 48 patients in each group was needed to yield a power of 80 % with a significance level of 0.05.

Data were analyzed by intention-to-treat principle. The χ^2 test (or Fisher's exact test when appropriate), Student's t test, and Mann–Whitney U test were used to compare categorical, parametric, and nonparametric data, respectively. Cumulative event rates (including time to first notice of a long-term morbidity, recurrence, disease-free interval, and survival) were calculated by the Kaplan–Meier method, and differences between the groups were compared with log-rank test. For the calculation of disease-free interval, patients who died without having disease recurrence were censored at the time of death. $P < 0.05$ was taken as significant.

Results

Between August 2001 and August 2007, 128 consecutive patients diagnosed with mid and low rectal cancer (located between 5 and 12 cm from the anal verge) were assessed for eligibility; of these 48 did not meet the inclusion criteria: 7 with tumor infiltration to the adjacent organs, 1 with recurrent disease, 5 with synchronous colorectal tumors, 4 with intestinal obstruction or perforation, 9 requiring neoadjuvant therapy, and 22 refused to participate. Recruitment to the study was extremely difficult since 2006. In particular, many patients expressed a preference for Lap TME and refused to participate in the study because of increasing publicity and demand for minimally invasive surgery in our locality. Furthermore, neoadjuvant therapy, which was an exclusion criterion of the study, was offered more liberally to our patients with locally advanced rectal cancer since September 2006. Because of these reasons, we decided to stop recruitment in August 2007 before reaching the calculated sample size. A total of 80 patients were finally recruited to the study and randomized to either Lap ($n = 40$) or Open ($n = 40$) TME with ASP (Fig. 1). The two groups of patients had comparable demographic data (Table 1). In the Lap group, three patients (7.5 %) required conversion to open surgery because of unexpected local tumor invasion ($n = 1$), dense adhesions ($n = 1$), and staple line failure with rectal stump dehiscence ($n = 1$). No patient was lost to follow-up and all patients were available for analysis of the primary and secondary endpoints. The median follow-up time for all patients was 75.7 (range

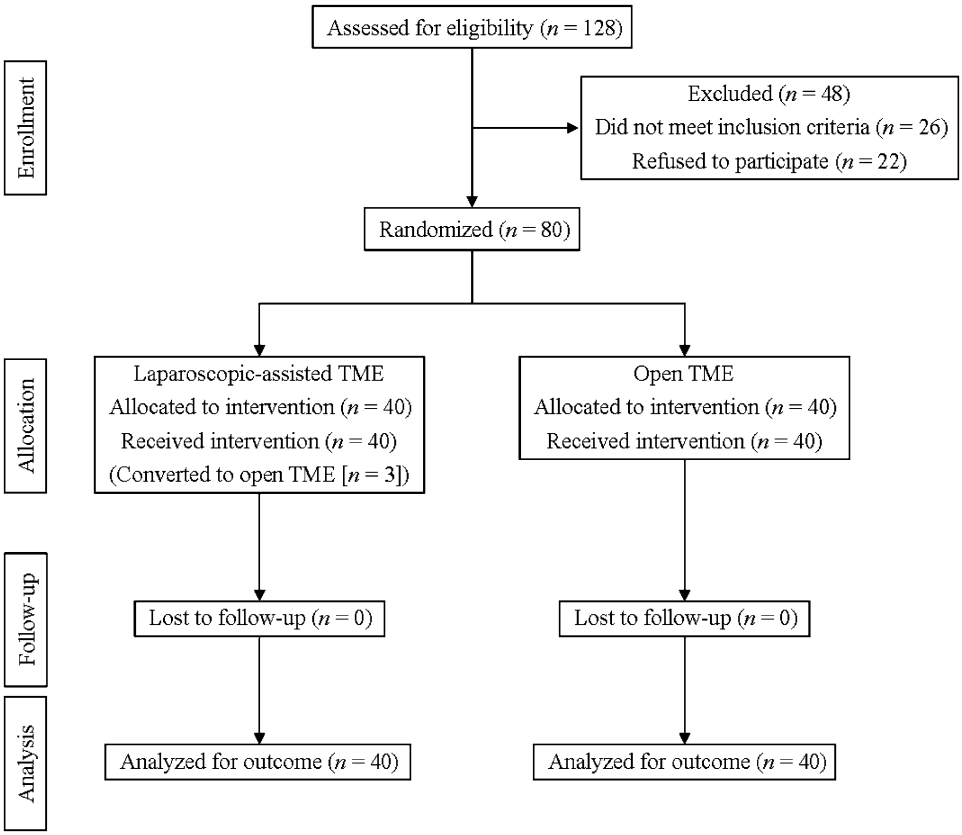


Fig. 1 Trial profile. *TME* total mesorectal excision

Table 1 Demographic data

	Lap group	Open group	*P* value
Number of patients	40	40	–
Sex (male/female)	24/16	22/18	0.651[a]
Age (years, mean ± SD)	60.2 ± 11.3	62.1 ± 12.6	0.475[b]
Body mass index (kg/m^2, mean ± SD)	23.1 ± 3.4	22.4 ± 3.2	0.316[b]
Preoperative hemoglobin (g/dL, mean ± SD)	12.9 ± 1.9	12.8 ± 1.7	0.738[b]
Preoperative CEA (μg/L, median and range)	5.9 (0.2–251)	6.8 (1–165)	0.375[c]
Number of patients with comorbidities (%)	22 (55 %)	24 (60 %)	0.651[a]
Tumor location from anal verge (cm, mean ± SD)	6.9 ± 1.7	7.1 ± 2	0.656[b]
Number of patients with tumor located ≤7 cm from anal verge	26 (65 %)	22 (55 %)	0.361[a]
Tumor length (cm, mean ± SD)	4.3 ± 1.8	4.3 ± 1.3	0.989[b]
AJCC staging (I/II/III/IV)	5/15/16/4	6/11/19/4	0.81[a]
Adjuvant chemotherapy			0.151[a]
AJCC stage II	12	3	
AJCC stage III	12	15	
Adjuvant radiotherapy			0.635[a]
AJCC stage II	10	5	
AJCC stage III	7	10	
Follow-up time of all patients (months, median and range)	75.7 (16.9–115.7)	76.1 (4.7–126.6)	0.187[c]
Follow-up time of living patients (months, median and range)	84.6 (52.2–115.7)	92.7 (55.8–126.6)	0.159[c]

SD standard deviation, *CEA* carcinoembryonic antigen, *AJCC* American Joint Committee on Cancer

[a] χ^2 test or Fisher's exact test

[b] Student's *t* test

[c] Mann–Whitney *U* test

Table 2 Perioperative outcome and pathologic data

	Lap group	Open group	*P* value
Conversion (%)	3 (7.5 %)	–	–
Number of patients with protective loop ileostomy (%)	20 (50 %)	26 (65 %)	0.175[a]
Height of anastomosis from anal verge (cm, mean ± SD)	3.9 ± 0.8	4.1 ± 1.1	0.426[b]
Operative time (minutes, mean ± SD)	211.6 ± 53.0	153 ± 41.1	<0.001[b]
Blood loss (mL, mean and range)	141.8 (0–2,000)	361.1 (5–2,500)	<0.001[c]
Blood transfusion (units, mean and range)	0.13 (0–4)	0.42 (0–5)	0.078[c]
Postoperative analgesic requirement (number of injections, mean and range)	4.8 (0–18)	16.8 (0.8–52)	<0.001[c]
Duration of parenteral analgesia (days, mean and range)	2.8 (0–8)	4.5 (2–11)	<0.001[c]
Time of first bowel motion (days, mean and range)	3.1 (1–9)	3.1 (1–10)	0.644[c]
Time to resume fluid diet (days, mean and range)	2.7 (1–7)	3.6 (2–11)	0.005[c]
Time to resume normal diet (days, mean and range)	5.8 (4–11)	6.7 (4–18)	0.06[c]
Time to walk independently (days, mean and range)	4.7 (2–12)	6.2 (3–16)	0.001[c]
Hospital stay (days, mean and range)	10.5 (5–35)	15 (6–167)	0.071[c]
Lymph nodes removed (mean ± SD)	17.7 ± 8.4	14.8 ± 5.6	0.075[b]
Distal resection margin (cm, mean ± SD)	2.6 ± 1.5	2.9 ± 1.4	0.301[b]
CRM involvement (%)	3 (7.5 %)	2 (5 %)	1.000[a]
Complete and intact mesorectum (%)	36 (90 %)	37 (92.5 %)	1.000[a]

SD standard deviation

[a] χ^2 test or Fisher's exact test

[b] Student's *t* test

[c] Mann–Whitney *U* test

16.9–115.7) months for the Lap group and 76.1 (range 4.7–126.6) months for the Open group.

Perioperative outcome

Table 2 shows the perioperative outcome of the two groups of patients. The operative time was significantly longer in the Lap group than that in the Open group, but the operative blood loss in the Lap group was significantly less. Measures of postoperative recovery including analgesic requirement, return of bowel function, and mobilization were all significantly better in the Lap group. There also was a trend towards shorter hospital stay in the Lap group.

The overall short-term morbidity rate was significantly lower in the Lap group than that in the Open group (Table 3). There were no operative deaths. Urinary retention was the most common short-term morbidity in both groups. Septic morbidity including chest infection, wound infection, and urinary tract infection occurred more frequently in the Open group.

Long-term morbidity and functional outcome

In the Lap group, 18 of 20 patients received closure of ileostomy at a median time of 10.8 (range 4.9–27.2) months after TME, while 23 of 26 patients in the Open group received closure of ileostomy at a median time of 10.8 (range 1.4–64.6) months after TME. Five patients did not have ileostomy closure because of progression of malignancy ($n = 2$), locoregional recurrence ($n = 2$), and patient refusal ($n = 1$).

Table 3 summarizes the crude incidence of long-term morbidity. More patients in the Open group developed long-term morbidity requiring hospitalization and reoperation. The cumulative probabilities of long-term morbidity rates at 5 years were 18.3 % for the Lap group and 43 % for the Open group ($P = 0.019$, log-rank test). Approximately 50 % of the long-term morbidity was either related to the creation or closure of the protective loop ileostomy.

Bowel function was evaluated in 68 patients (33 in the Lap group) who had a follow-up of at least 24 months after restoration of bowel continuity. The mean number of bowel motions at 24 months was similar in both groups: 3.4 ± 1.8 times per day in the Lap group and 3.4 ± 2.1 times per day in the Open group ($P = 0.99$, Student's *t* test). Three patients in the Lap group and two patients in the Open group had minor incontinence to liquid stool ($P = 0.668$, Fisher's exact test).

At the conclusion of follow-up, two patients each in both groups developed incomplete urinary bladder denervation as confirmed by urodynamics and were managed conservatively with medications. Erectile dysfunction that precluded sexual intercourse was observed in 5 of 18 (27.8 %) sexually active men in the Lap group and 5 of 11 (45.5 %) sexually active men in the Open group ($P = 0.432$, Fisher's exact test). All female patients were sexually inactive before and after surgery.

Oncologic clearance and survival

The oncologic clearance in terms of macroscopic quality of the TME specimen, distal resection margin, and CRM

Table 3 Short-term and long-term morbidity

	Lap group	Open group	*P* value
Short-term morbidity			
Anastomotic leak	1 (1)	–	
Subclinical anastomotic leak	–	2	
Intraabdominal abscess	1	1	
Chest infection	–	3	
Wound infection	1	7	
Urinary tract infection	3	8	
Urinary retention	8	9	
Prolonged ileus	3	5	
Acute confusion	–	1	
Gouty attack	1	1	
Phlebitis	1	–	
Others	–	2	
Operative death	–	–	
Total number of patients with short-term morbidity (%)	13 (32.5 %)	22 (55 %)	0.043[a]
Long-term morbidity			
Adhesion-related bowel obstruction	4 (4)	7 (4)	
Anastomotic leak after closure of ileostomy	–	1 (1)	
Incisional hernia at the ileostomy site	2 (2)	1 (1)	
Incisional hernia at the specimen extraction site	1 (1)	–	
Parastomal hernia	1	3 (2)	
Prolapsed ileostomy	–	2 (2)	
Enterocutaneous fistula	–	1	
Rectovaginal fistula	–	1 (1)	
Chronic discharging sinus from rectal anastomosis	–	1 (1)	
Total number of patients with long-term morbidity (%)	8 (20 %)	17 (42.5 %)	0.03[a]
Total number of patients requiring operation for long-term morbidity (%)	7 (17.5 %)	12 (30 %)	0.189[a]

Data in parentheses are number of patients requiring reoperation unless otherwise indicated

[a] χ^2 test

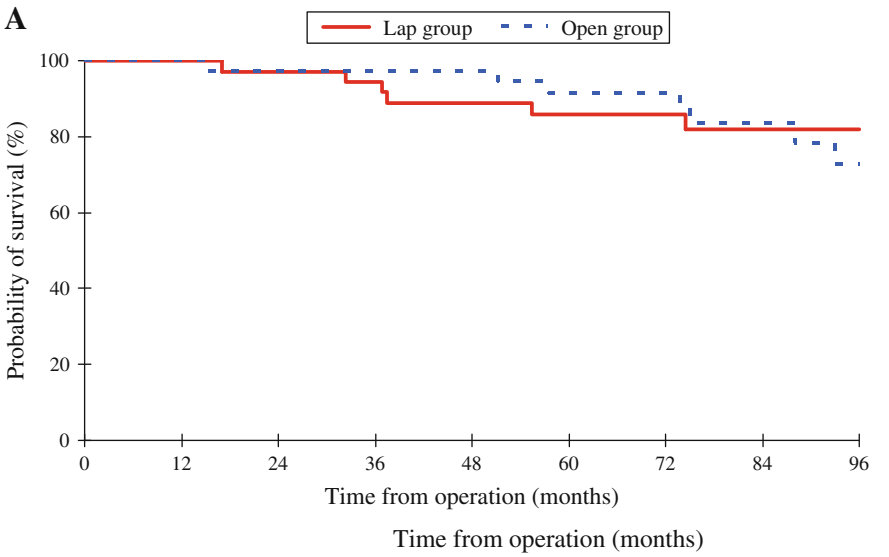
involvement was similar between both groups (Table 2). There was a trend towards greater mean number of lymph nodes removed in the Lap group than in the Open group. Notably, 7 patients in the Lap group and 10 patients in the Open group had fewer than 12 lymph nodes removed in the specimen ($P = 0.412$, χ^2 test).

After curative resection, the probabilities of overall survival at 5 and 8 years were 85.9 and 82 %, respectively for the Lap group, and 91.3 and 72.7 %, respectively for the Open group ($P = 0.912$, log-rank test; Fig. 2A). There was also no significant difference in the probabilities of being disease-free at 5 years (83.3 vs. 74.5 %) and 8 years (79.5 vs. 58.2 %) between the Lap and Open groups ($P = 0.114$, log-rank test; Fig. 2B). The pattern of recurrence is shown in Table 4. The overall locoregional recurrence rates at 5 years were not different between the two groups (Lap, 2.8 vs. Open, 8.9 %; $P = 0.187$, log-rank test). There was no port site recurrence in this study.

Discussion

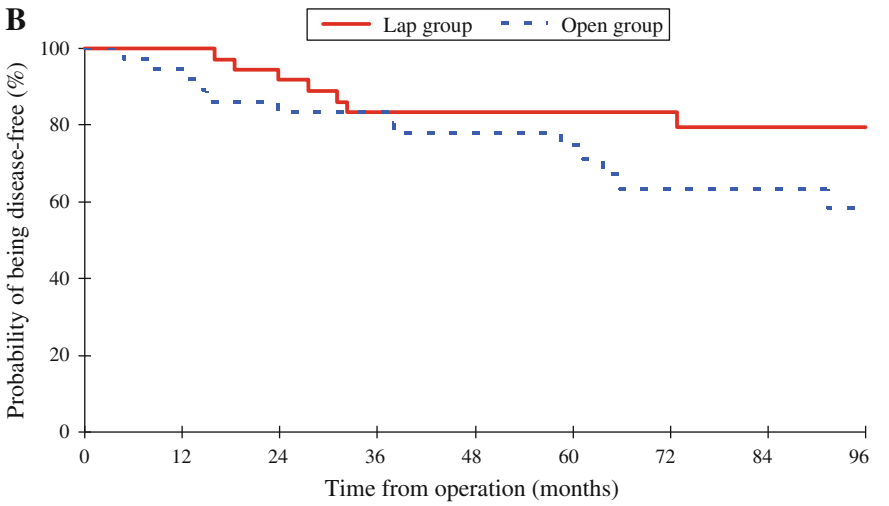
This study was designed to compare the short-term and long-term outcomes between laparoscopic-assisted versus open TME with ASP in patients with mid and low rectal cancer. Our results showed that the laparoscopic approach was associated with earlier postoperative recovery, lower short-term and long-term morbidity rates, comparable functional outcomes, and similar oncologic clearance and long-term survival compared with the open counterpart.

To date, there has been only one randomized trial that was specifically designed to compare laparoscopic versus open TME with ASP for rectal cancer [24]. However, this study did not provide any details on method of randomization or sample size estimation, and no long-term survival data were reported. Therefore, to the best of our knowledge, our study is the first randomized trial comparing laparoscopic and open TME with ASP that provides data on long-term outcomes and survival.



Time from operation (months)

Number at risk	0	12	24	36	48	60	72	84	96
Lap group	36	36	35	34	32	27	22	16	7
Open group	36	36	35	35	34	27	24	17	13



Time from operation (months)

Number at risk	0	12	24	36	48	60	72	84	96
Lap group	36	36	33	30	30	27	22	16	7
Open group	36	34	30	30	28	22	16	14	11

Fig. 2 Survival curves of laparoscopic-assisted versus open TME for rectal cancer generated by the Kaplan–Meier method. **A** Overall survival after curative resection ($P = 0.912$, log-rank test). **B** Probability of being disease-free after curative resection ($P = 0.114$, log-rank test)

The overall short-term morbidity rate in the laparoscopic arm of our study was 32.5 %, which is higher than the rate reported in the COREAN trial (21.2 %) [9], but lower than that in the CLASICC trial for rectum (40 %) [6] and the COLOR II trial (40 %) [10]. The characteristics of the recruited patients including age, body mass index, American Society of Anesethesiologists grading, and tumor staging were similar between the four rectal cancer trials. We therefore believe that the great variation in morbidity rates among these trials may be partly explained the different rates of conversion (1.2 % in the COREAN trial, 7.5 % in our study, 17 % in the COLOR II trial, and 34 % in the CLASICC trial), which in turn are closely related to the different levels of experience of the participating surgeons. In the CLASICC trial, the trial design required that every surgeon had undertaken at least 20 laparoscopic resections, and most of the surgeons were probably still on their learning curve [6, 25]. Surgical "teams" that wished to participate in the COLOR II trial were requested to submit unedited recordings of five consecutive

Table 4 Survival and recurrence (AJCC stage I–III diseases)

	Lap group ($n = 36$)	Open group ($n = 36$)	P value
Probability of survival at 5 years	85.9 % (SE 5.8 %)	91.3 % (SE 4.8 %)	0.912[a]
Probability of survival at 8 years	82 % (SE 6.8 %)	72.7 % (SE 9.3 %)	
Crude recurrence rate	7 (19.4 %)	13 (36.1 %)	0.114[b]
Locoregional alone	0	2 (5.6 %)	
Distant alone	6 (16.7 %)	9 (25 %)	
Both locoregional and distant	1 (2.8 %)	2 (5.6 %)	
Port-site/wound	0	0	
Probability of being disease-free at 5 years	83.3 % (SE 6.2 %)	74.5 % (SE 7.4 %)	0.114[a]
Probability of being disease-free at 8 years	79.5 % (SE 7.0 %)	58.2 % (SE 9.3 %)	
Overall locoregional recurrence rate at 5 years	2.8 % (SE 2.7 %)	8.9 % (SE 4.9 %)	0.187[a]
Overall locoregional recurrence rate at 8 years	2.8 % (SE 2.7 %)	15.9 % (SE 8.1 %)	
Overall distant recurrence rate at 5 years	16.7 % (SE 6.2 %)	21 % (SE 7.1 %)	0.236[a]
Overall distant recurrence rate at 8 years	20.5 % (SE 7.0 %)	38.3 % (SE 9.5 %)	

AJCC American Joint Committee on Cancer, *SE* standard error

[a] Log-rank test

[b] χ^2 test

laparoscopic TMEs for assessment of competency, but the experience of individual surgeon was uncertain [10]. On the other hand, the participants in the COREAN trial were experienced surgeons in Korea who came from high-volume centers [9]. We also had overcome our learning curve for laparoscopic TME when we began our trial [26], and therefore our laparoscopic results were better than that of the CLASICC trial and the COLOR II trial.

In addition to short-term benefits, our study also showed significant long-term benefit of the laparoscopic approach in terms of lower overall late morbidity rate at 5 years compared with the open approach. This finding concurs with our previous study on laparoscopic-assisted anterior resection and confirms the long-term safety of laparoscopic surgery for rectal cancer [15]. However, unlike the previous study, we were unable to show a lower incidence of adhesion-related bowel obstruction in the laparoscopic TME group despite a lower conversion rate in the present study. Laparoscopic TME entails more extensive rectal dissection/peritoneal incision and creation of ileostomy and hence may cause more adhesion formation than laparoscopic anterior resection [27, 28].

Regarding the long-term functional outcomes (bowel and urosexual) after TME, no significant differences were found between the laparoscopic and open groups. Although acute urinary retention was the most common short-term morbidity in our study, almost all patients recovered completely, with the exception of two patients each in both groups who developed long-term micturition problem that required medical treatment.

The quality of TME surgery and oncologic clearance in terms of resection margins were similar between the laparoscopic and the open groups in our study. There was even a trend towards greater number of lymph nodes removed in the laparoscopic group. These findings are in accordance with those reported by Lujan et al. [29]. The magnified vision and better exposure provided by the laparoscopic approach may allow more accurate rectal dissection to be performed in narrow pelvises and therefore may explain the greater number of lymph nodes harvested within the specimens.

There is no controversy that a detailed analysis of long-term oncologic outcomes is mandatory to establish the role of laparoscopic surgery for treating rectal cancer. To date, only few randomized trials have reported 5-year survival data. Lujan et al. [29] reported similar 5-year overall survival rates between laparoscopic (72.1 %) and open (75.3 %) surgery for rectal cancer. For the rectal cancer patients in the CLASICC trial, the 5-year overall survival rates also were not different statistically between the laparoscopic (60.3 %) and open (52.9 %) groups [8]. However, both studies were not specifically designed and powered to address long-term oncologic endpoints. In our study, with a median follow-up of more than 7 years among living patients, the probabilities of overall survival at 5 years were 85.9 % for the laparoscopic group and 91.3 % for the open group. At 8 years, the overall survival rates also were not different between the laparoscopic (82 %) and open (72.7 %) groups. The slightly more favorable long-term oncologic outcomes in our study may be partly explained by the fact that all our surgical procedures were TME with ASP, whereas the other two trials had included abdominoperineal resection in their analysis. Furthermore, learning curve issues may also account for the discrepancies between our results and those reported by the CLASICC trial.

Our study had several limitations. First, mainly because of patient refusal, we were unable to reach our intended sample size and hence the study may not have adequate power to show significant differences in all the parameters measured. Indeed, patient's preference for one form of surgery has been identified to be the most common reason

for nonentry of eligible patients into surgical randomized trials [5, 30]. Second, our study also was not powered to address long-term oncologic outcomes; the relatively small sample size may not allow very firm conclusion regarding long-term survival to be drawn. However, our study may contribute important survival data to meta-analyses in the future. Third, neoadjuvant therapy, which is regarded as the standard treatment for advanced rectal tumors nowadays, was not offered to our patients, as its effectiveness was not yet fully established during the early period of the study. Nevertheless, our study design may allow for evaluation of the genuine impact of TME alone (without neoadjuvant therapy) on the short-term outcomes after surgery. Furthermore, a recent study has confirmed that neoadjuvant chemoradiotherapy did not confer any long-term survival benefit over adjuvant chemoradiotherapy for locally advanced rectal cancer [31]. Fourth, we did not use a fast-track perioperative program because it was not the standard care in our institution [16, 23]. This may account for the slightly longer length of hospital stay for both groups in this study. Another reason for delayed hospital discharge despite good recovery after surgery is due to stoma education and management [32]. Fifth, health-related quality of life issues (e.g., physical, psychologic, and social functioning, and general well-being) were not evaluated in our study. Further randomized trials should incorporate this important outcome measure in the assessment to better define the role of laparoscopic surgery for rectal cancer.

In conclusion, this single-center, prospective, randomized trial, albeit small in sample size, demonstrates that laparoscopic-assisted TME with ASP improves postoperative recovery, reduces short-term and long-term morbidity rates, and seemingly does not jeopardize long-term survival compared with open surgery for mid and low rectal cancer. Forthcoming phase III, multicenter, randomized trials, including the American College of Surgeons Oncology Group Z6051 trial [11], and the long-term reports of the COREAN trial and the COLOR II trial [9, 10], will more definitely evaluate whether laparoscopic surgery will emerge as the standard of care for patients with rectal cancer in the future.

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